

U.S. Department of Health and Human Services

# Adequacy of the National Blood Supply

## Report to Congress

### 2020



# Table of Contents

<b>Executive Summary</b> .....	<b>1</b>
Blood Transfusions Save Lives.....	1
Outline and Purpose of the Report .....	2
Key Themes of the Responses and Recommendations .....	3
<b>Chapter 1 Background</b> .....	<b>11</b>
Congressional Action.....	12
Subcommittee Composition.....	13
Report Structure.....	13
<b>Chapter 2 Methods</b> .....	<b>14</b>
Federal Activities .....	15
Public Input .....	15
<b>Chapter 3 Continuous Recruitment of Blood Donors</b> .....	<b>16</b>
Current State Associated with the Continuous Recruitment of Blood Donors.....	16
Key Issues .....	16
Recommendations to Ensure Continuous Recruitment of Blood Donors .....	28
<b>Chapter 4 Adequacy of the Blood Supply During Public Health Emergencies</b> .....	<b>34</b>
Current Status of the U.S. Blood Supply.....	34
Key Issues .....	34
Recommendations to Ensure Adequacy of the Blood Supply During Public Health Emergencies .....	41
<b>Chapter 5 Implementation of the Transfusion-Transmissible Infections Monitoring System (TTIMS)</b> .....	<b>48</b>
Background .....	48
Current State of TTIMS.....	48
Key Issues Regarding Expansion of TTIMS to Address Additional Unmet Needs .....	50
Recommendations to Ensure a Safe Blood Supply .....	52
<b>Chapter 6 Safety and Innovation</b> .....	<b>58</b>
Current State of Safety and Innovation .....	58
Key Issues Regarding Safety And Innovation .....	58
Recommendations for Safety and Innovation .....	59
<b>Conclusion</b> .....	<b>69</b>
<b>Appendices</b> .....	<b>71</b>
Appendix A. Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019: Sec. 209. Report on Adequate National Blood Supply.....	71

Appendix B. Committee and Working Group Membership..... 72

Appendix C. Potential Future Studies for the Transfusion-Transmissible Infections Monitoring System (TTIMS) ..... 80

Appendix D. Transfusion Transmissible Risk..... 85

Appendix E. Selected ACBTSA Recommendations..... 86

Appendix F. Acronyms and Abbreviations..... 90

Appendix G. References..... 91



# Executive Summary

## Blood Transfusions Save Lives

More than 17.9 million blood transfusions occur in the U.S. every year (Jones et al., 2020). In fact, greater than 5% of patients receive transfusion, making it one of the most frequently performed procedures in U.S. hospitals (Kling, 2018). Transfusion therapy enables interventions for patients suffering traumatic injuries, undergoing surgery, or receiving treatment for cancer. Transfusions save the lives of new mothers threatened with massive obstetric hemorrhage and sustain the lives of premature babies. Transfusions ameliorate highly morbid complications experienced by patients with blood disorders.

However, little attention is given to the requirement for a readily available supply of blood. Perhaps the value of blood is best demonstrated by the consequences and costs incurred if needed blood is not available in a timely manner. Examples of such scenarios include but are not limited to the following:

- A life lost;
- A surgery canceled or delayed;
- A premature baby with anemia;
- A patient with sickle cell disease not able to receive red blood cell transfusions required to prevent strokes and life-threatening anemia; and
- A cancer program unable to support its patients before, during, and after chemotherapy or surgery

A robust, readily accessible blood supply is essential to support the U.S. healthcare system and provide assurance that enough blood is available to meet daily patient needs. Currently, our nation's blood supply is almost entirely dependent on volunteer donors and a loose network of 66 federally regulated non-profit blood centers, in addition to numerous hospital-based collection centers. In addition, the U.S. Department of Defense (DoD) manages the Armed Services Blood Program that meets the needs of our military wherever they are stationed. This loose network of blood centers has served our country well in the past, ensuring the safety and availability of blood needed every day for more than 6,000 hospitals throughout our country. However, the continued availability of a robust blood supply faces significant threats and challenges in the current environment.

The blood system is struggling to meet the daily demand for blood and ensure the necessary investments for the future of blood safety and availability. The blood donor base is rapidly aging, and innovative approaches to recruiting blood donors are compromised because of lack of funding and insufficient data about evolving donor motivations and changing social norms. Regional variations affect the blood supply across the country. While donations may exceed demand in some regions of the country at a given time, blood collections in another region may not be enough to meet the need. There can be drastic fluctuation between supply and demand, which has been exacerbated during the COVID-19 pandemic.

The legacy blood system faces considerable financial challenges caused by multiple factors, including safety advancements and the inability to raise prices for services to hospitals. The system will be challenged to sustain the balance between blood collection and blood utilization. The COVID-19 pandemic has highlighted the magnitude of these shortcomings, as well as the critical need for remediation to sustain this vital component of our nation's healthcare system.

## Outline and Purpose of the Report

This report provides a detailed account of the mounting challenges that stand in the way of an adequate blood supply for current and future patients in the United States. It contains the following seven chapters: 1) Background; 2) Methods; 3) Continuous Recruitment of Blood Donors; 4) Adequacy of the Blood Supply; 5) Implementation of the transfusion transmission monitoring system; 6) Safety and Innovation; and 7) Conclusion. The Background and Methods provide the context for the report and explain how it was developed. The other chapters offer a response to *Section 209 Report on Adequate Blood Supply (Appendix A)* of the *Pandemic and All-Hazards Preparedness and Advancing Innovation Act (PAHPAIA)* of 2019 that charged the Secretary of the Department of Health and Human Services (HHS) to submit to Congress a report containing recommendations on the following topics related to maintaining an adequate national blood supply:

1. Challenges associated with the continuous recruitment of blood donors (including those newly eligible to donate).
2. Ensuring the adequacy of the blood supply in the case of public health emergencies.
3. Implementation of the transfusion transmission monitoring system;
4. Other measures to promote safety and innovation, such as the development, use, or implementation of new technologies, processes, and procedures to improve the safety and reliability of the blood supply.



## Key Themes of the Responses and Recommendations

The chapters present the major challenges and key issues associated with the four topics outlined in Section 209 of the PAHPAIA and provide recommendations for addressing them. The major themes encompassed in the responses and recommendations include the following:

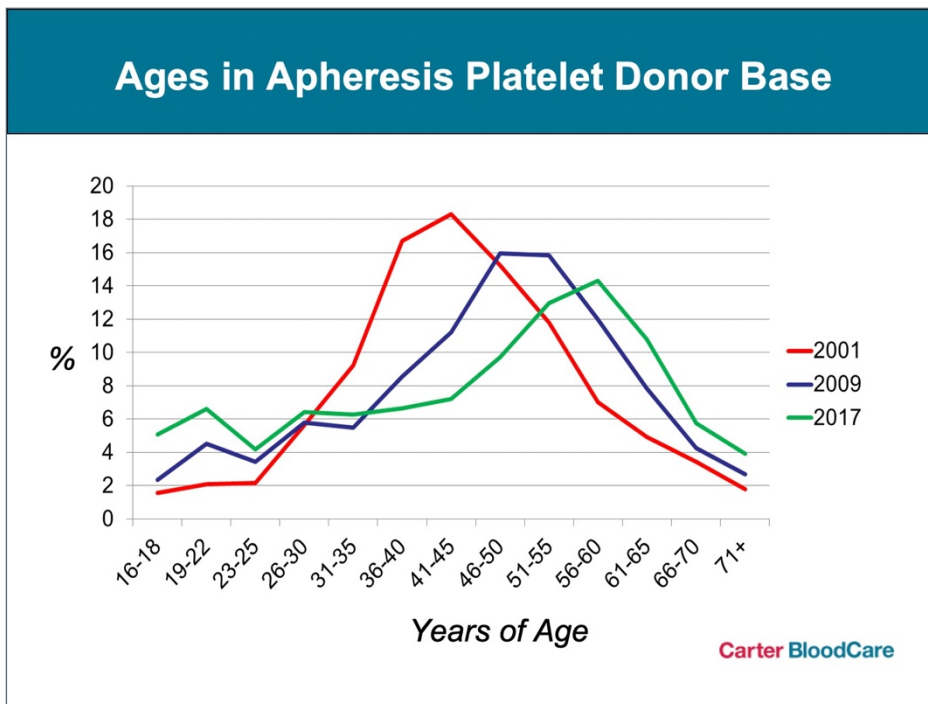
### **Collecting real-time data to meet everyday needs, respond to public health emergencies, monitor the safety of transfusion therapy, and establish research agendas to improve patient outcomes**

Blood transfusions are critical to the American public during both emergency and non-emergency periods. The public expects to receive the safest blood possible defined by the best science, immediately available when needed, whether they live in rural America or in an urban community. To meet this need, we must invest in a data infrastructure that allows us to make the best decisions across the entire blood supply chain, from blood donation to patient care.

### **Expanding the blood donor base by creating a culture of blood donation and engagement—particularly among young people and people of color—by understanding donor motivation and improving access to donation**

Blood for transfusion is donated by altruistic, non-remunerated donors built on a culture of blood donation begun during World War II. Today the blood donor population, in part motivated by the post-World War II culture, is aging (Figure 1). There is a need to determine new ways to engage younger generations of blood donors. Increased donor deferrals further affect the size of the eligible donor base, requiring new approaches to reaching potential donors. In addition, the diversity of the blood donor population must be improved to meet current and future patient needs. For example, increased donations from African Americans to African Americans results in a lower potential for alloimmunization, thereby improving outcomes for individuals with sickle cell disease. We need a national call to action and engagement.

**Figure 1: Aging of the Platelet Donor Population**



**Source:** Sayers, M., Carter BloodCare. Presentation to the Advisory Committee on Blood and Tissue Safety and Availability, August 26, 2020

**Modernizing the current business model for blood collection, innovation, and adoption of new technology.**

A critical example of rapid modernization and innovation was the speed at which the FDA, BARDA, other HHS leaders and blood centers collaborated to produce COVID-10 convalescent plasma (CCP). The COVID-19 pandemic shifted blood collection activities from blood drives at locations within communities (for example, businesses, schools, and churches) to fixed-site locations. This major change required innovative blood donor recruitment strategies and investment in new construction. These innovation and technology responses require novel regulatory approaches that maintain safety and foster expansion of the blood donor base and the blood supply while reducing costs so that investments can be made in new and better blood components.

**Addressing the erosion of blood center balance sheets and net revenue secondary to treating blood as a commodity rather than a public good**

Appropriate changes in medical practice that reduced blood utilization and the increased bargaining power of national and regional hospital systems led to dramatic loss of revenues, operating margins, and capital required to maintain and replace the current infrastructure

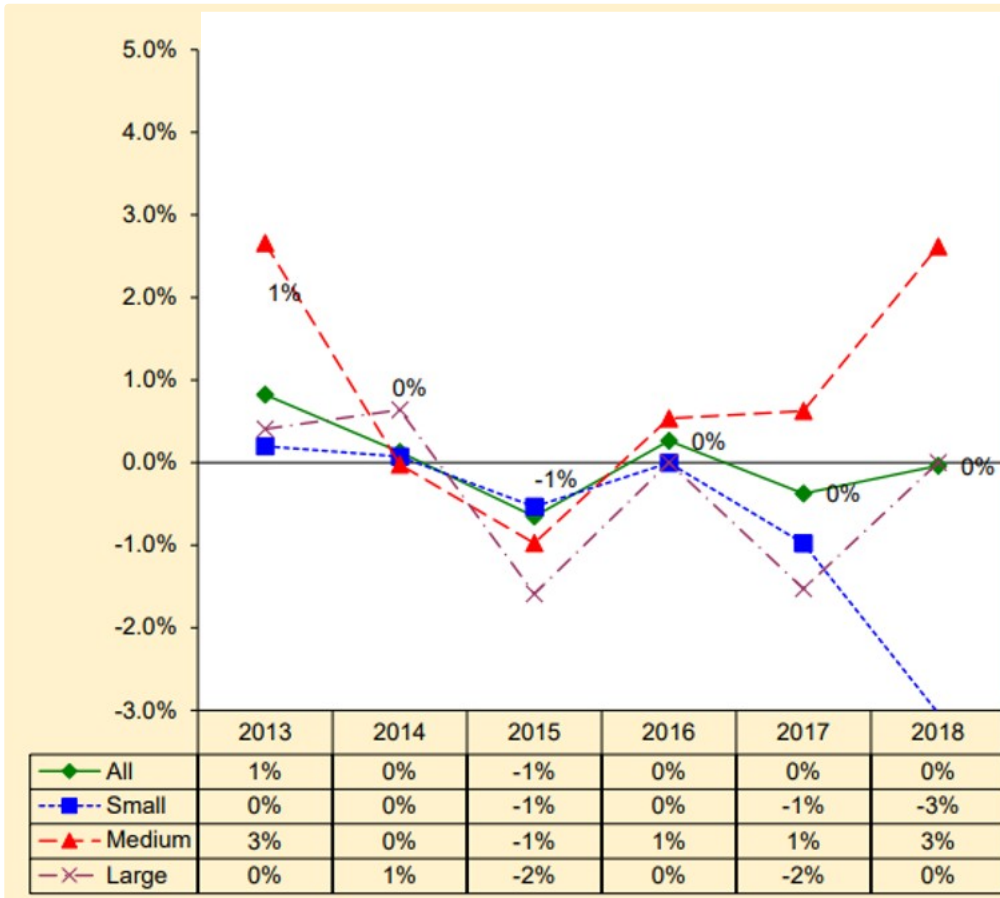
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and to invest in technology and innovation (Figures 2 and 3).

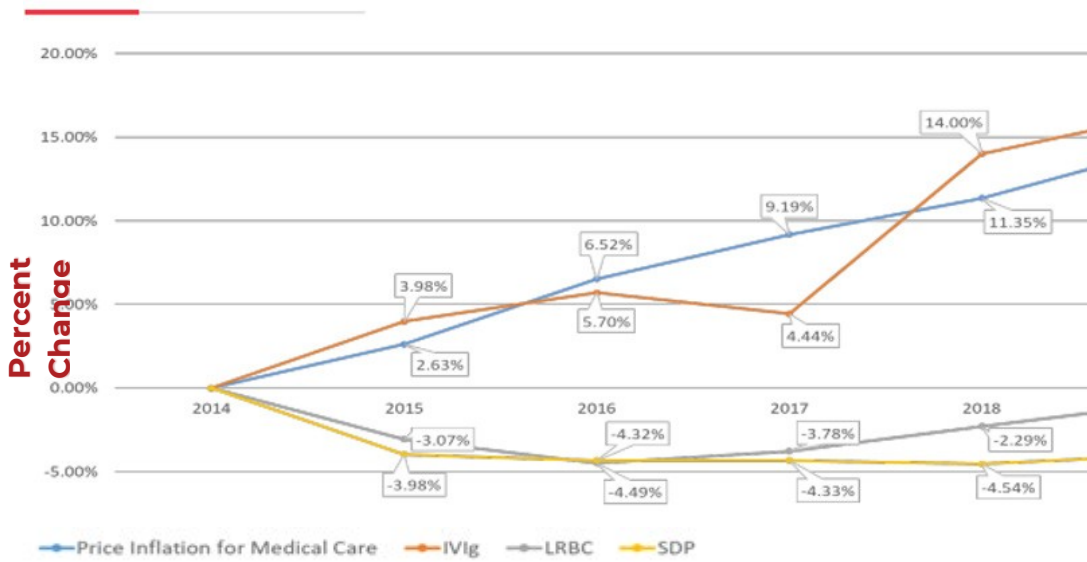
This occurred as a consequence of the bargaining power realignment that permitted hospital purchasing agents to view blood as a commodity. Prices declined despite product safety enhancements (Figure 4).

**Figure 2: Median Operating Margin (Operating Income Percent) by Year**



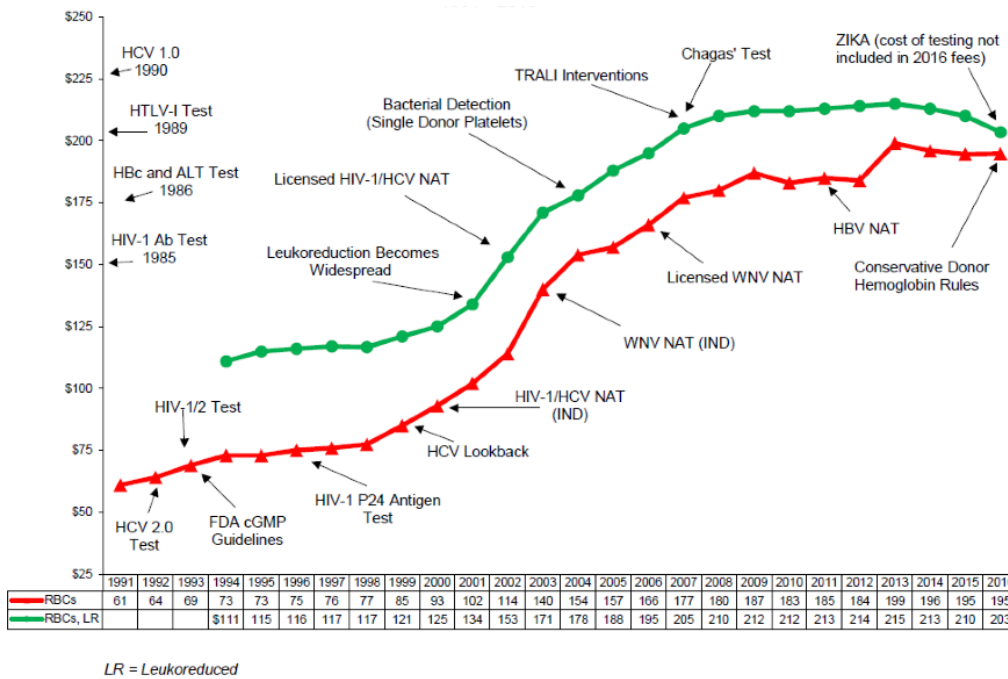
Source: Fry, K., America’s Blood Centers, 2020

**Figure 3: Percent Change per Product vs. Inflation**



Source: Block, B., Blood Centers of America, 2020

**Figure 4: Investment in Safety Advancements vs. Declining Price of Blood to Pay for Those Safety Mandates**



Source: America's Blood Centers

The legacy reimbursement system requires modernization to sustain the blood supply, provide reasonable reimbursement to supply chain vendors, and stimulate innovation to improve outcomes for patients relying on transfusion therapy.

In summary, this report and its recommendations provide the framework for ensuring the safety and the availability of the nation's blood supply into the future. The recommendations are interdependent. Together they form the foundation of the modern blood system needed to meet critical patient needs and support the advancement of medical care in our country. By executing these recommendations within the next five years—through the engagement of health care experts, Federal agencies, healthcare and blood industry leaders, and patient advocates—we will have achieved the goal of maintaining an adequate national blood supply.

The specific recommendations in response to the questions posed by Congress are the following.

### **Recommendations to Ensure Continuous Recruitment of Blood Donors (Chapter 3)**

**Recommendation 3.1: Fund studies by organizations such as the National Academy of Medicine (NAM) and/or the Agency for Healthcare Research and Quality (AHRQ) to ensure that transfusion-dependent patient needs are met, through engaging critical stakeholders to focus on the current state assessment, set a vision for the ideal future state, and outline foundational requirements to reach that goal.**

**Recommendation 3.2: Fund studies to understand the predictive social and psychological factors in blood donor motivation and develop recommendations for designing programs to attract and retain blood donors, emphasizing comparative efficacy of psychographic target marketing— versus currently used broad-sector marketing.**

- **Fund a national blood donation campaign designed to build a broad-based commitment to regular blood donation that achieves a diverse and robust donor base to meet patient needs. The publicly funded campaign should feature influencers reflective of the targeted groups below, as well as national leaders, and should run for five years to achieve sustained improvement in these areas:**
  - Increasing the percentage of younger donors (ages 20-40).
  - Increasing the diversity (both ethnic and racial) of the national donor base.
  - Reaching potential donors in both urban and rural areas.

- Educating the public on the different blood components and blood types needed to support key patient groups (e.g., O- red cells for trauma, AB plasma).

**Recommendation 3.3:** Fund a research study to determine definitively the impact of operating paid and volunteer donor programs in the United States simultaneously, and to evaluate the challenges posed by changes in demand between the two donation sectors. Lead and fund a research initiative to answer the question of impact of paid blood collection on local volunteer donation.

**Recommendation 3.4:** Fund research to target, recruit, and engage blood donors for personalized/precision medicine solutions, including molecular testing (i.e., genomic typing to meet emerging patient needs, such as sickle cell disease).

### **Recommendations to Ensure Adequacy of the Blood Supply During Public Health Emergencies (Chapter 4)**

**Recommendation 4.1:** Create, implement, and fund a comprehensive, sustainable, minimally burdensome system that monitors and makes available real-time data on the blood supply and utilization by hospitals to ensure patients have access to vital and life-saving blood components during both emergency and non-emergency periods.

**Recommendation 4.2:** Create and fund a task force that includes government and critical industry stakeholders that will map, model, and identify potential elements of the supply chain and infrastructure that will affect our ability to actively respond and ensure a sufficient blood supply during emergency and non-emergency conditions.

- Task force to develop and maintain industry-wide business continuity plan that incorporates all necessary supplies for blood collection and storage.
- Fund implementation of business continuity plans and other recommendations from the task force.

### Recommendations to Ensure a Safe Blood Supply (Chapter 5)

**Recommendation 5.1: Fund the current Transfusion-Transmissible Infections Monitoring System (TTIMS) program to ensure the safety of blood donations in the U.S. by monitoring transfusion-transmitted infections, such as human immunodeficiency virus (HIV).**

**Recommendation 5.2: Fund the expansion of the current TTIMS to 1) monitor other transfusion-transmitted infections for which blood donors are tested, 2) increase participation among all blood centers, and 3) coordinate non-transfusion transmissible infection studies of blood donors and donations (for example, donor hemovigilance).**

**Recommendation 5.3: Create a task force to include National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and private stakeholders to study, review, and evaluate the current systems to strengthen hemovigilance (and biovigilance) programs and to improve patient outcomes.**

### Recommendations for Safety and Innovation (Chapter 6)

**Recommendation 6.1: Charter and fund a public-private partnership that promotes innovation in transfusion medicine, to 1) enhance characteristics of available products (such as for increasing product shelf life through storage in lyophilized or frozen state), 2) develop new products and processes, 3) develop pathogen inactivation for all blood components, and 4) create blood alternatives or universal blood components.**

The benefits of a public-private partnership include,

- Provide additional/increased funding for basic, applied, and clinical research programs that are identified through this mechanism, with the goal of improving our understanding of transfusion medicine and the appropriate use of blood components to ensure improved patient outcomes.
- Use this public-private partnership, in coordination with FDA, to engage in dialogue on how the current regulatory standards impact innovation in transfusion medicine for the purpose of ensuring increased safety, access, and enhanced patient outcomes.

**Recommendation 6.2: Create and fund a blue-ribbon panel to address funding and reimbursement models to ensure a sustainable and innovative blood system responsive to current unmet medical needs as well as public health emergencies and other threats to the safety and availability of the blood supply and successful patient outcomes.**

We thank Congress for requesting this information and respectfully request approval and funding to ensure continued and improved blood transfusion therapy for the American public.



## Chapter 1 Background

Blood and blood components are irreplaceable therapeutics and unique health care resources. Blood transfusions are routine, medically necessary treatments for patients with certain chronic health conditions, including hemoglobinopathies such as sickle cell anemia. They are frequently required for patients who lose blood during surgery, for patients receiving treatment for cancer or blood diseases, and for premature infants. Additionally, blood transfusions are often needed for victims of trauma. More than five percent and as much as fifteen percent of all hospitalizations require blood transfusion (Goel et al., 2018; Klein, Hrouda, & Epstein, 2017). The approximated thirty percent decline in transfusions observed during the early phase of the COVID-19 pandemic when elective surgical procedures were postponed or canceled suggests elective surgeries also require a sustained blood supply (Fry, 2020). Any one of us may need a life-saving blood transfusion in our lifetime. Maintaining a safe, available blood supply for daily routine use and for public health emergencies is a public health priority.

The U.S. blood supply chain is threatened by many existing and emerging challenges, including threats to the traditional blood donor recruitment model; financial and operating stress faced by non-profit blood centers; a lack of an integrated data system to monitor blood collection and utilizations as well as donor and patient safety; emerging infectious diseases; challenges associated with the supply chain; and inadequate investment in research and innovation.

Blood and blood components traditionally originate from altruistic, voluntary, non-remunerated blood donors. The traditional donor recruitment model is centered around blood centers reaching out to eligible donors across communities. However, several factors threaten the existence of that model and negatively affect the blood supply for clinical use. These include the changing demographics of eligible donors (from those tempered by patriotic causes to those challenged by economic uncertainty); possible competition from plasma centers providing remuneration that is especially appealing during economic downturns; increasing medical deferrals; and rising costs of reaching out to eligible donors.

The U.S. blood system is composed of a complex web of private and public stakeholders including blood centers, hospitals, device manufacturers, testing laboratories, accreditation organizations, and government agencies. To monitor and ensure the safety of blood donors and patients, an integrated data system and advanced data analytics are needed to collect and analyze real-time data

across the blood supply chain. Comprehensive surveillance and safety data collected and processed using such an integrated system will enable the entire blood community to engage in thorough risk assessment, make informed decisions, and better protect patient and donor safety. Unfortunately, such an integrated data collection system that all stakeholders in the blood sector can use does not yet exist in the U.S., and data needed for informed decision-making and policymaking are lacking.

Natural hazards and emerging infectious diseases continue to pose threats to the availability and safety of the nation's blood supply. Consider the COVID-19 pandemic as an example. Available data from the Blood Centers of America (BCA) clearly show that the pandemic has already disrupted the nation's blood supply as thousands of blood drives and blood donations have been canceled. Heatmaps of the vulnerability of device manufacturers demonstrate that the COVID-19 crisis has disrupted medical devices and other critical supplies, including the manufacture of blood components. Nonetheless, the transfusion community responded vigorously and promptly by informing the public about the importance of COVID-19 CCP, collecting this potentially vital therapeutic, and distributing it to hospitals treating COVID-19 patients.

To ensure the nation has safe and available blood supply for daily clinical use for all patients, investment is needed to promote the development, evaluation, and implementation of new and existing safety processes, technologies, and products. Public health emergencies add additional pressure to the already strained supply chain. When emergencies strike, it is the blood components on the shelves of blood centers and hospitals that save lives. To ensure the U.S. has an adequate blood supply in the case of public health emergencies, Congressional funding and support is needed.

## Congressional Action

On June 24, 2019, Congress passed and the President signed the *Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019 (PAHPAIA)*, designed to advance national health security and improve the nation's preparedness and response to public health emergencies. Section 209 ([Appendix A](#)) of the legislation pertains to adequacy of the nation's blood supply. The Act requires that not later than one year after the date of its enactment, the Secretary of Health and Human Services shall submit to Congress a report containing recommendations related to maintaining an adequate national blood supply, including:

1. Challenges associated with the continuous recruitment of blood donors (including those newly eligible to donate);
2. Ensuring the adequacy of the blood supply in the case of public health emergencies;
3. Implementation of the transfusion transmission monitoring system; and
4. Other measures to promote safety and innovation, such as the development, use, or implementation of new technologies, processes, and procedures to improve the safety and reliability of the blood supply.

In response, the Office of the Assistant Secretary for Health (OASH), upon the request of the Office of the Assistant Secretary for Preparedness and Response (ASPR), formed a subcommittee (hereafter referred to as “the Subcommittee”) to help address the four inquiries and develop recommendations.

## Subcommittee Composition

The Subcommittee consisted of four working groups, comprising diverse stakeholders and various perspectives. Members of each working group included clinicians; transfusion medicine professionals; infectious disease specialists; representatives of blood centers; patient advocates; and Federal members representing the FDA, the CDC, the NIH, OASH, ASPR, and DoD ([Appendix B](#)).

## Report Structure

This report describes the current state of the nation’s blood supply, identifies key issues threatening the blood supply chain as well as gaps in research and innovation, and proposes a path forward for addressing the issues in order to ensure the adequacy of the nation’s blood supply, particularly in the case of public health emergencies. The report is focused on the four areas specified in the PAHPAIA Section 209, and it includes the following chapters:

- **Chapter 3. Continuous Recruitment of Blood Donors;**
- **Chapter 4. Adequacy of the Blood Supply During Public Health Emergencies;**
- **Chapter 5. Implementation of the transfusion transmission monitoring system;**
- **Chapter 6. Safety and Innovation; and**
- **Chapter 7. Conclusion.**

Each chapter describes the current state of its topic area, identifies key issues or threats, highlights stories from patients about their experiences, and suggests a pathway to reach a better state in five years. Each chapter also presents recommendations to the U.S. Congress for addressing the issues.

## Chapter 2 Methods

This chapter reviews the structure of the Steering Committee and mechanisms the Committee used to conduct its work, and the public comments received. This report is based on the knowledge and expertise of the Working Group members, presentations of subject matter experts, latest available scientific data, information from public comments, and patient testimonies.

### Steering Committee

The steering committee was composed of the Committee Co-Chairs, Working Group Chairs; HHS's Senior Advisor for Blood and Tissue Policy; and senior leaders of AABB, America's Blood Centers (ABC), and American Red Cross (ARC), which wrote a joint letter in 2018 urging Congress to include blood centers in reauthorizing the PAHPAIA. The steering committee oversaw progress of all four working groups, facilitated communication and coordination between the working groups, addressed overlaps and issues raised by the working groups, and reviewed this report to Congress.

### Working Groups Structure

To leverage member expertise, balance a range of perspectives, and thoroughly examine the four topic areas highlighted in Section 209 ([Appendix A](#)) of the PAHPAIA, the Subcommittee formed four working groups. Each of the four working groups was tasked to critically review their topic and make recommendations related to the group's focus area.

The working group membership encompassed a broad range of perspectives, with at least one practicing physician and one patient advocate in each group. Working group size ranged from 9 to 12 individuals.

Each working group was led by two co-chairs. Over a seven-month period, including a 60-day pause due to the COVID-19 pandemic, bimonthly working group meetings offered opportunities for open discussion among working group members and presentations from invited subject matter experts. Each working group developed a framework, identified key issues to address, broke into writing groups, developed a chapter, and made recommendations. In drafting their chapters, the working groups compiled information from expert presentations, utilized the collective knowledge of the working group members, analyzed data shared by federal agency representatives and private organizations within the blood community, and reviewed literature. In finalizing their chapters, steering committee members voted unanimously in favor of the recommendations.

## Federal Activities

The Steering Committee did not have the time nor funding needed to develop a formal federal project inventory survey. To gather information on Federal activities related to the nation's blood supply, the Subcommittee asked the federal members of the Subcommittee to provide information related to their agencies' activities.

## Public Input

The Committee solicited public comments on issues related to the Committee's work through a request for information (RFI) in the Federal Register (RFI Document [85 FR 16372](#)). Responses were received from two members of the public as well as the organizations below.

AABB

America's Blood Centers (ABC)

American Red Cross (ARC)

American Plasma Users Coalition

American Society of Hematology

Cerus Corporation

Cooley's Anemia Foundation

CSL

Behring

Grifols

HBO2 Therapeutics

Institute for Policy Integrity

New York University School of Law

Office of the Attorney General, State of California

Plasma Protein Therapeutics Association

The Joint Commission

# Chapter 3 Continuous Recruitment of Blood Donors

## Current State Associated with the Continuous Recruitment of Blood Donors

The continuous recruitment of eligible donors is likely the most significant problem facing blood centers today and in the future. Relatively short product shelf life, manufacturing and regulatory requirements, logistics, and product-specific needs require constant and agile recruitment to ensure the nation's blood supply. This chapter outlines the many challenges associated with the continuous recruitment of donors and offers recommendations to ensure patients receive the products they need, when they need them.

### Key Issues

#### Size of the U.S. Eligible Volunteer Donor Base

In a survey of the potential donor pool, which applied donor eligibility criteria to an estimated U.S. population of 327 million, 62.6 percent of Americans were regarded as eligible to donate blood, yet less than 5 percent donated in 2018 (To et al., 2019). The eligibility calculation was based on exclusion criteria, including permanent, long-term, and short-term health risks; however, relative donor unavailability was not considered. This included older donors, individuals with independent-living, ambulatory, and cognitive disability (Kraus, Lauer, Coleman, and Houtenville, 2018), the rural population living beyond the reach of blood programs' mobile operations, individuals with multiple jobs, and single parent households. These categories reduce eligibility by an estimated 50 to 75 million individuals (To et al., 2019).

Additionally, necessary FDA guidelines for blood donor eligibility, which are designed to ensure donor health and a safe blood supply, have reduced the percent of the U.S. population that are eligible to donate.



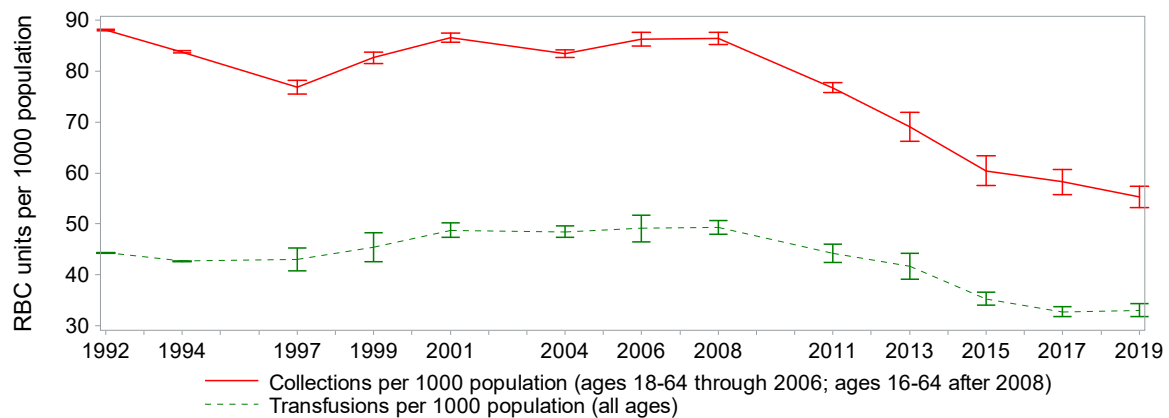
## Shifting Trends in Donor Populations and Demand Profiles

Shifting population and motivational trends are evident among volunteer blood donors. Understanding these trends will be critical to adjusting donor engagement strategies and technologies to maintain adequate blood supplies into the future.

### Shrinking Donor Base

The 2017 National Blood Collection and Utilization Survey (NBCUS) illustrates a declining donor base. From 2015 to 2017, there was a 7.2 percent decline in the total number of donors presenting to give a volunteer blood donation. The survey also shows an aging volunteer donor population, recording that 22.4 percent are under the age of 25 (Jones et al., 2020). As elderly blood donors drop off due to health and/or age, younger blood donors are not being added to the donor population at a rate high enough to sustain a stable blood supply. Figure 5 illustrates the closing gap between collections and transfusions in the United States, which can lead to periodic or sustained product shortages. The 2017 NBCUS also reported a decrease in first-time blood donors of 6.6 percent, illustrating the continued trend (Jones et al., 2020).

**Figure 5: Collections Versus Transfusions in the U.S. Between 1992 and 2019**

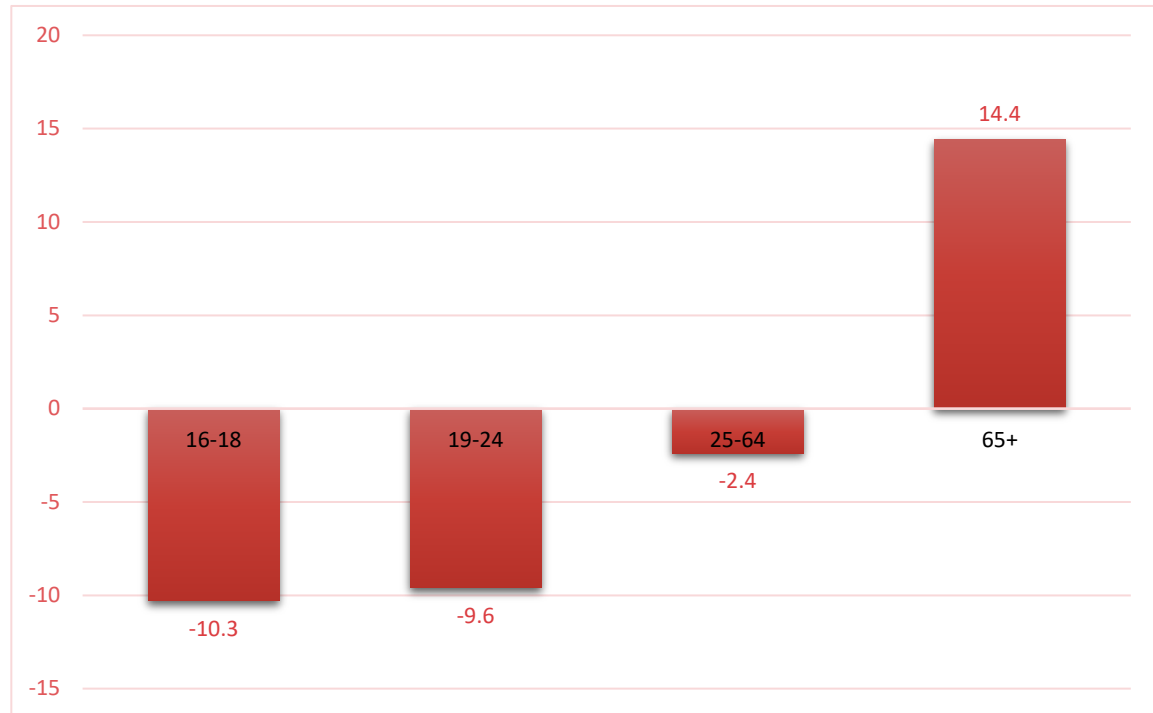


Source: Jones et al., 2020

The blood donor population is aging in nearly all developed countries (Goldman et al., 2017). Figure 6 shows the percent change among donors per age group. The y-axis represents the percent of the total donor base of active blood donations at a given time against different age categories shown on the x-axis. The decline in younger donors aged 16-24 and increase in donors aged 65 and older suggests an increasing reliance upon an aging donor base. Among younger donors, high school blood donations represent at least 17 percent and as much as 20 percent of the national blood supply (ABC, 2014; Mississippi Valley Blood Center, 2020).

Yet if those donors cannot be retained over time, there will be a disparity between demand and the available donor pool. Compounding the issue, COVID-19 has significantly disrupted scheduled blood drives, including high school collections. According to ABC, these collections saw a 30 percent reduction from March 2020-October 2020 compared to the same time period in 2019.

**Figure 6: Percent Change among Donations Stratified by Age, 2015-2017**



**Source:** Sapiano, et. al., 2020

### **Changing Demand Profile**

Diversity among donors is essential to meeting the changing demographics of the U.S. population. Donors of racial and ethnic minority populations are more likely to be a match for people with sickle cell disease and other blood disorders. Many of these patients are dependent upon transfusions over the course of their lifetimes and require precisely matched blood components. Less than optimal matching can cause patients to develop antibodies to common blood types (a process known as alloimmunization). Once this occurs, finding compatible units can be difficult, time-consuming, and expensive, and may lead to delays in patient care.

The need for blood products suitable for sickle cell patients is constant. However, donors with extended matching phenotypes represent a small proportion of the donor base. Appeals like that of the U.S. Surgeon General on World Sickle Cell Day (U.S. Department of Health and Human Services, 2020) often result in a brief

surge of donations. However, blood centers lack adequate financial resources to complete the data analysis and research to better understand donation behavior by ethnicity. Funding for studies designed to increase blood donation engagement in this area would go a long way to improve patient care.

Changing transfusion recipient demand demographics offer opportunities but also add complexities to donor recruitment. While the highest percentage of group O exists in Hispanic and Black non-Hispanic populations, their representation in the current donor population is less than other ethnic groups. Changing this will require new outreach, education, and recruitment efforts to increase the understanding of the need for blood, particularly that which is personalized to meet specific patient populations' needs.



## Patient Stories

### Grace

Grace Ndayizeye of Washington State battles sickle cell disease and currently relies on eight units of blood transfused every four weeks. These transfusions allow her to regularly attend school—something she was previously unable to do because of immense pain from the disease.

As of July 2020, Grace received more than 60 transfusions or nearly 500 units of blood. She will continue to require these transfusions until she is able to find a bone marrow donor and receive a successful transplant.

## Threats to the Volunteer Blood Donor Recruitment Model

The current environment of the volunteer blood donor recruitment model poses significant challenges for blood centers and the nation's blood supply.

### *Decreasing Donor Retention*

Many centers struggle to retain donors year over year. Maintaining a donor base requires constant replacement of donors by recruiting new donors and engaging lapsed donors who have not given in the past two years. Attracting first-time and lapsed donors often requires more advertising expenses to reach populations that centers are unable to reach via contact management systems. Research focused on understanding blood donor motivation would lead to targeted messaging and re-engagement campaigns improving retention rates and blood donation frequency.

### *Increased Reliance on Incentives Without a Complete Understanding of Motivation*

To sustain and grow collections, blood centers are increasingly reliant on non-monetary donor incentives. While some blood centers suggest that these expenditures have enhanced donations, the increased costs associated with them are not often passed along to hospitals, further straining the financial viability of blood centers. Research has found that incentives may have a positive impact on donation behavior, timing, frequency, and attracting first-time donors (France, et. al., 2020).

Various studies demonstrate a complex array of donor motivations. While altruism is prominent among older donors, first-time and younger donors may have more self-interest at heart (France et al., 2014; Warfel, France, and France, 2012). Academic motivational studies are limited but suggest targeted marketing is the best approach to address the changing motivations over time.

### *Confusion and Competition for Healthy Donors: Paid Versus Unpaid Collection Centers*

Typically, blood components needed for transfusion are supplied by volunteer, unpaid donors as an altruistic act. While incentives are often provided as a thank you for donating, it is not a cash payment. However, there are collection organizations that provide monetary compensation for individuals selling blood components, primarily Source Plasma for further manufacture. The potential competition for finding healthy individuals to engage

(either voluntary or paid) might impact recruitment for the volunteer blood donor programs. However, research is lacking. As the monetary payments increase, so might the threat to the volunteer, unpaid program. Traditionally, altruistically motivated donors tend to be safer than paid donors. One reason that volunteer donors are utilized in the current system is that paid donors were found to have a greater rate of transmissible infectious diseases.

Historically, volunteer collectors and collection operations that pay for blood collections have targeted different population segments. However, recently Source Plasma collection operations offering payment have opened new facilities in areas targeting colleges and universities and individuals with less economic resources. These audiences now must choose between the altruistic act or the financial incentive. This competition may inhibit the ability of the volunteer sector to grow its younger donor base. A lack of available national research and data regarding this subject will continue to threaten the stability of the nation's blood supply for transfusion as the current volunteer blood donor base ages.

### ***Decreasing Onsite Mobile Operations***

Organizations, such as workplaces that previously hosted onsite blood collections (mobile operations) are increasingly reluctant to hold them due to staffing levels, liability concerns, and limitations on the amount of time an employee can be away from work. The growing trend of employees working remotely has further exacerbated this issue. Educational institutions have historically been a major source of onsite donations. Yet the COVID-19 pandemic is having a major impact on the ability to conduct school-based blood drives. This may have a profoundly negative effect on long-term donor engagement as school-based drives are traditionally the first experience for many blood donors.

Additionally, the current recruitment model utilizes volunteer/civic sponsor groups to organize blood drives. These organizations are shrinking in number and experiencing an aging membership, which directly impacts how and if blood drives are conducted.

### ***Increasing Donor Deferrals Leading to a Reduction in Donor Eligibility***

There is value in studying the effect of revised donor eligibility recommendation on the donor base. Indeed, recent COVID-19–related revisions demonstrated evidence-based regulation relaxation without sacrificing safety and increased the eligible blood donors base. The 2017 NBCUS showed a 34.9 percent increase in donor deferrals from 2015 to 2017 (Sapiano et al., 2020). Donors who are deferred typically do not become committed, repeat blood donors.

***Outdated and Increasingly Non–Cost-effective Recruitment Engagement Methods***

The primary recruitment method for direct volunteer blood donor engagement is based on a tele-recruiting concept. This approach has become increasingly outdated and ineffective as many donors exclusively use texting and social media to communicate and often consider unsolicited telephone calls spam (Pongsananurak, C., 2020).

***Poorly Coordinated Donor Outreach Efforts by Competing Blood Centers***

Based on local community patient needs, the blood supply will fluctuate within appropriate inventory levels regionally. However, confusion exists between community-based blood centers providing a regional supply, multiple-community blood centers serving hospitals in a community, and a national collection system. Typically, community blood centers are the primary supplier of blood components to hospitals in their geographic footprint, and they rely on unpaid, community volunteers to give blood to support the patient needs in that region. Increasingly, as hospital systems grow regionally and nationally, there are multiple blood centers serving a region. While the national system and a few others may not be the supplier of blood to a specific region, the organization may recruit blood donors in that area to support its blood needs in other areas of the country. The lack of a national recruitment and education program forces competition for blood donors across the country between community-based blood centers and the national organization. Increased competition between blood centers for access to donors often results in confusing and inconsistent messaging.

**Cost Pressures**

There are many factors that contribute to higher cost challenges faced by all blood centers. There is a cost for recruitment, collection, processing, and distribution of the donated blood, with the costs of donor engagement increasing at an accelerated pace. Marketing methods and education of potential donors have evolved as blood centers may be competing for an individual's time and with companies who pay for Source Plasma (France, C., 2020). Keeping the pace requires the rapid adoption of advertising through social media, e-mail, text, calls, commercials, and daily static displays. Blood centers must invest in omni-channel marketing and the IT infrastructure necessary to support the outreach activities, increasing the cost of donor engagement. From 2016 to 2019, donor marketing expense per unit increased by 30 percent (ABC, 2020).



### ***Mobile Blood Drives Versus Fixed Donor Centers***

Historically, blood collection operations were focused on mobile collections. Prior to the COVID-19 pandemic (February 2020), 62 percent of collections at 34 BCA member centers took place in the mobile environment. Just five months later (July 2020), during the pandemic, 43 percent of collections took place in the mobile environment and 57 percent were conducted in a fixed blood collection facility (BCA, 2020). This is in part due to the large number of mobile blood collection operations that were canceled during the pandemic.

Donors expect easy access to blood donation opportunities given the understandable mindset that they are donating their time and resources for an activity that can take up to an hour to complete. The direct costs to maintain and operate mobile operations are greater than fixed sites due primarily to time spent driving to and from collection locations as well as the time needed to set up and tear down the mobile sites. There are also additional personnel costs in the recruitment departments to maintain relationships with sponsors, coordinate mobile schedules, and develop and print marketing materials. As blood centers respond to the ongoing impact of COVID-19, reassessment of donor engagement strategies must be undertaken. The transition to more fixed-site locations incurs costs for expansion, renovation, and new construction, as well as marketing, digital, and tele-recruitment costs for informing and scheduling blood donations.

### ***Geographical Considerations: Urban Versus Rural***

Another cost consideration is the cost difference between accessing donors in a rural versus urban setting. In larger urban areas, there is a higher likelihood of having a fixed donor center where interested donors can donate blood. In more rural areas, where the population concentration is inadequate to justify the cost of a permanent blood donation center, blood centers must conduct more costly mobile blood drives to offer donors the opportunity to donate blood in order to meet patient need.

### ***Specialty Blood Type Needs***

Another significant cost to blood centers results from the need to ensure a sustained supply of blood components to satisfy specialty type needs, which are increasing in demand relative to non-specialty types. For example, O negative blood components are important in trauma situations because they can be transfused to patients with any blood type. It is also the only type that O negative patients can safely receive. Approximately 6.6 percent of the U.S. population has O negative blood, but nearly two-times this amount (more than 12 percent) is needed to satisfy current patient treatment requirements for O negative and trauma patients.

### *Educating and Fostering Awareness*

First-time donor engagement requires a larger investment than recruiting returning blood donors. This has direct implications for blood centers. As older donors tend to become users of blood due to medical conditions, they contribute fewer donations. Blood centers incur proportionately higher prospective donor education and awareness costs simply to maintain the same overall number of donations. These “awareness-building” costs are exacerbated by typically higher donor deferral and testing loss rates from new blood donors (first-time donors tend to present with higher rates of ineligibility or relatively higher positive test rates than returning donors), wasting costly collection staff time and blood donation schedule capacity. Additionally, first-time donors tend to have higher donor reaction rates requiring increased staffing levels to respond to and treat donor reactions. Investing in studies to understand certain key education, awareness, or donor characteristics is crucial to achieving the commitment by a first-time donor to make their first donation attempt.

### *Digital Marketing*

Traditional marketing methods employed to recruit blood donors, such as calling or direct mail, are becoming more expensive and less effective. Marketing has shifted to the digital world in most industries and blood banking is no different. Some of these channels, including search engines and social media ads and filters, are costly or difficult to manage or maneuver.

The era of mass communications is closing and a new approach to granular targeted communications is prevailing. Text messaging is much more effective than direct calling, offering an 80 percent or greater open rate (Flowroute Nationwide Survey, n.d.) and 11-20 percent appointment rate (Mississippi Valley Regional Blood Center, 2020). However, text message campaigns are costly, and carriers implement charges and barriers for organizations wanting to use this as a communication method.

### ***Geo-demographic and Psychographic Analysis by Individual Blood Centers***

Many blood centers rely on costly geo-demographic and psychographic software, such as that provided by BCA and Esri GIS Tapestry, to improve effectiveness in marketing, recruitment, and collection site opening or relocating efforts. These efforts to build donor awareness and commitment, as well as associated costs, are prone to being wasted when active blood donors move outside the service area of a blood center that initially invested in donor development. Without a mechanism to connect donors to the blood programs serving the new community, the donor connection is lost unless relocated donors seek out donation opportunities in their new location.

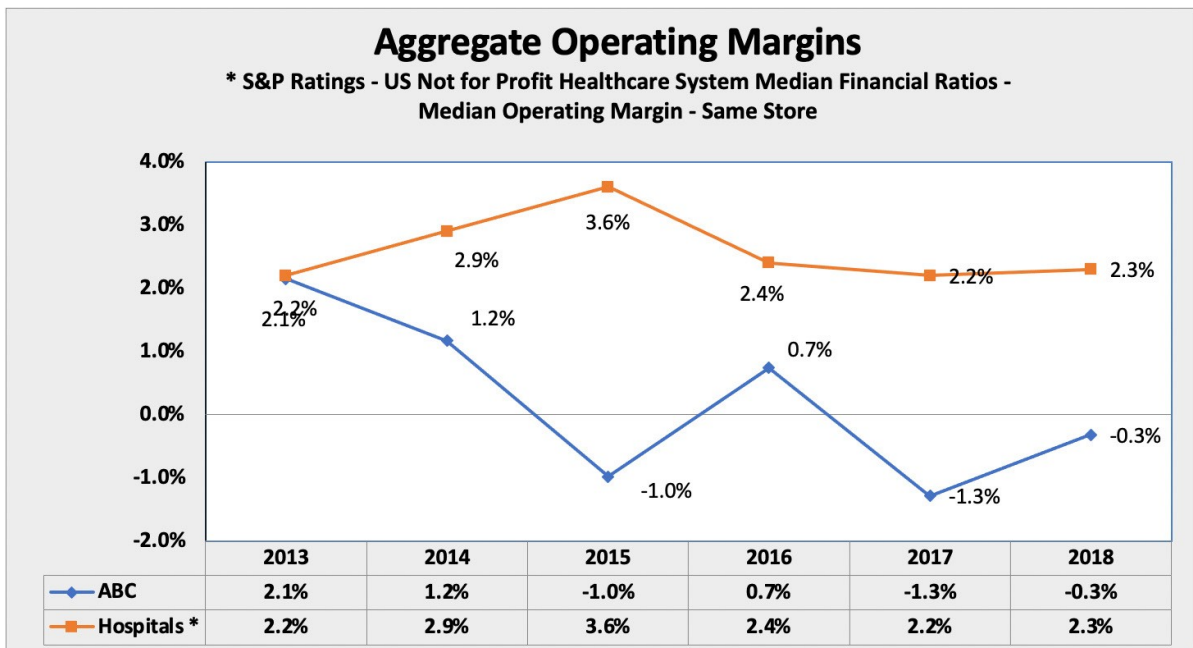
### ***Industry Response to Reduced Demand and the Risk It Creates for Future Blood Supply Resiliency***

One of the most significant cost pressures faced by blood centers is the constant need to respond and adjust to usage fluctuations. The decreased demand for red blood cells that began around 2008 and continues today has led to blood centers shedding excess operational capacity. Additionally, given declining revenues, blood centers have decreased investment in new technologies and replacement of aging infrastructure to drive down per-unit costs. Every aspect of blood centers' operations has been impacted, including reduced spending on education, recruitment, and retention of blood donors. Initially, blood centers were able to rely heavily upon the existing donor base instead of attracting new donors; however, cumulative annual donor attrition has taken a toll on the active donor base, which may jeopardize the ability to support future patient needs. During the decade from 2009 until 2019, the ARC saw a decrease of 32.5 percent of its active donor base from 3.7 million donors giving 1.73 units per year to 2.5 million donors giving 1.83 units per year (ARC, 2020). Additional data is needed to determine if the blood supply is and will continue to be sufficient.

The national blood usage rate of decline tapered significantly in the past two years, yet the reduced donor base trend continued its ten-year rate of about 3 percent loss annually, resulting in blood shortages, particularly in summer months when donor availability typically wanes. This heightened pressure has required blood centers to invest heavily in donor recruitment costs to stabilize a fragile donor base. The most recent America's Blood Centers (ABC) Financial Ratio Survey results revealed a significant increase in 2018 median donor marketing expense per unit over 2017 and 2016 (ABC, 2018).

Although the current competitive model is forcing blood centers to more efficiently use financial resources and blood donations (for example, discards due to outdated blood components have been reduced significantly over the past five years), this same competition and resulting lower pricing is also reducing resources available to invest in providing a safe and adequate blood supply. Figure 7 shows that ABC center-aggregate operating margins, which matched hospital operating margins in 2013, declined significantly through 2018 while hospital margins remained consistently positive. This disparity in financial trends highlights blood centers' need for assistance in stabilizing the national donor base.

**Figure 7: America's Blood Centers Financial Ratio Survey, 2013-2018**

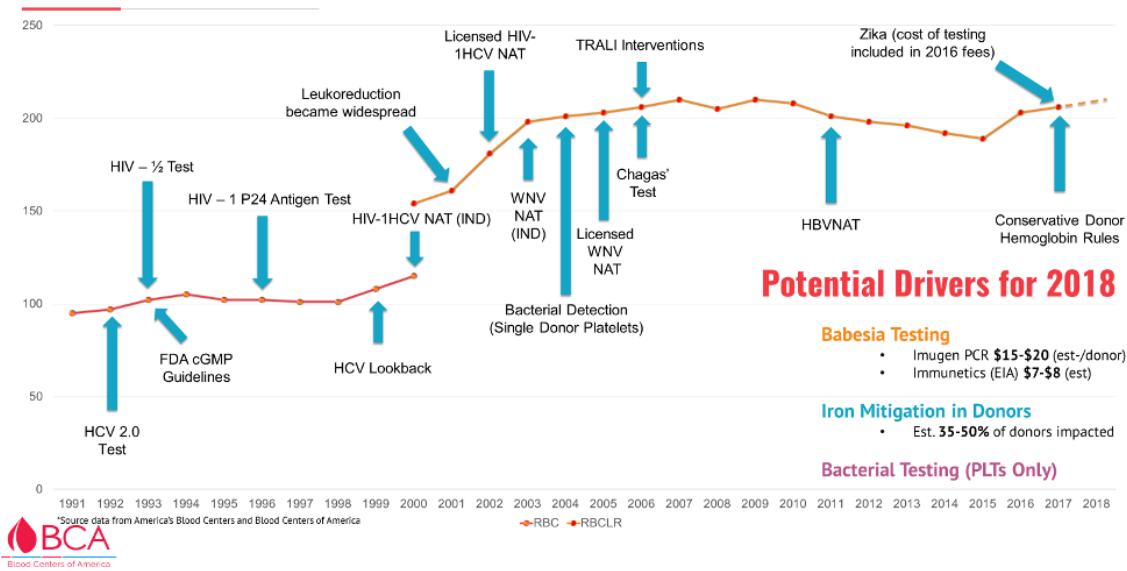


Source: America's Blood Centers, 2020

### Testing Costs

An additional strain on blood center margins is the cost of infectious disease testing and responding to emerging infectious agents. As an example, in August 2016, the blood industry began to test all blood and platelet donations for the Zika virus, resulting in a total cost of \$135 million (Ellingson et al., 2017). BCA evaluated the impact of adding testing costs to blood donation from 1991 to 2018 (Figure 8), which revealed a doubling of the cost to produce a red blood cell unit.

Figure 8: Safety Measures Driving Up the Cost of Red Blood Cells Over Time



Source: America’s Blood Centers and Blood Centers of America

Despite significant increases in the cost to test and process blood donations, blood centers have not realized any significant increases in pricing of blood components to offset increased costs (Figure 9)

Figure 9: Leukoreduced Red Blood Cell Prices: Actual vs . Inflation



\* US Department of Labor, Bureau of Labor Statistics

Any absorbed testing costs (Zika, Babesiosis, etc.) captured in this data CPI-M\* from 2013 to 2019 is 16.18%

**Source:** Blood Centers of America, 90-Day Pricing Report Data. This data is reported to BCA by all members each quarter. Weighted average. CPI-Medical (CPI-M) index. Any absorbed testing costs (Zika, Babesiosis, etc.) captured in this data CPI-M\* from 2013 to 2019 is 16.18 percent.

\* US Department of Labor, Bureau of Labor Statistics

## Recommendations to Ensure Continuous Recruitment of Blood Donors

The current environment of the volunteer blood donor recruitment model poses significant challenges for blood centers and the state of the U.S. blood supply. Having a sustainable donor base and blood supply will require investment in research, strategy development, legislative action, and funding.

**Recommendation 3.1:** Fund studies by organizations such as the National Academy of Medicine (NAM) and/or the Agency for Healthcare Research and Quality (AHRQ) to ensure that transfusion-dependent patient needs are met, through engaging critical stakeholders to focus on the current state assessment, set a vision for the ideal future state, and outline foundational requirements to reach that goal.



Priority of stakeholder work group efforts should include delivering the following outcomes:

1. Define blood supply adequacy from a clinician point of view.
2. Using the agreed upon definition of blood supply adequacy, describe the frequency and duration of inadequate blood component availability, characterize resulting negative patient outcomes, and outline operational and financial organizational impact.
3. Identify special patient need segments, such as sickle cell anemia patients, that may be underserved when the majority of patient care needs are met.

Critical stakeholders would include representatives from AABB, ABC, ARC, BCA, and the FDA, as well as patients and patient advocates, clinicians, and individuals without national organization affiliation who have published contributions to the topics and demonstrated experience in using blood components. These participants would provide critical perspectives on feasibility of suggestions, help ensure an informed approach in deliberations, and guide implementation of final recommendations.

Support should be provided to conduct a thorough current state analysis, set a vision for the ideal future state, and set the foundation for execution of the final recommendations.

**Recommendation 3.2: Fund studies to understand the predictive social and psychological factors in blood donor motivation and develop recommendations for designing programs to attract and retain blood donors, emphasizing comparative efficacy of psychographic target marketing—versus currently used broad-sector marketing.**

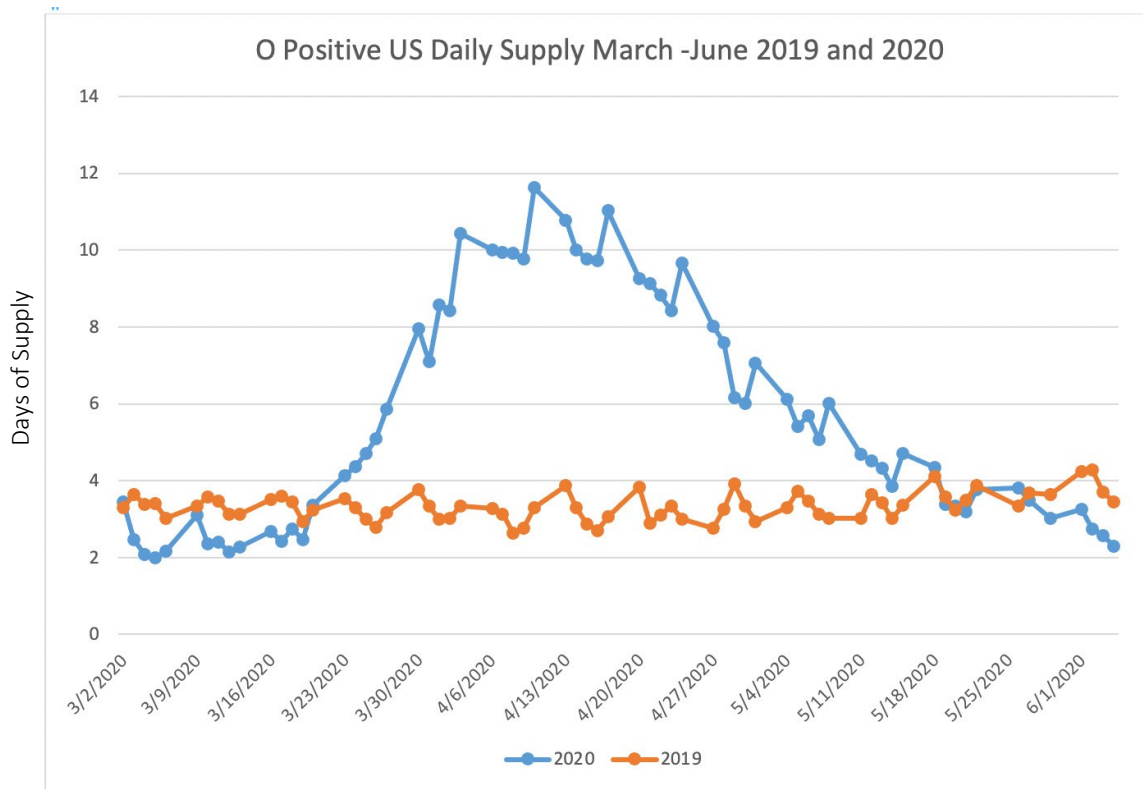
- **Fund a national blood donation campaign designed to build a broad-based commitment to regular blood donation that achieves a diverse and robust donor base to meet patient needs. The publicly funded campaign should feature influencers reflective of the targeted groups below, as well as national leaders, and should run for five years to achieve sustained improvement in these areas:**
  - Increasing the percentage of younger donors (ages 20-40).
  - Increasing the diversity (both ethnic and racial) of the national donor base.
  - Reaching potential donors in both urban and rural areas.
  - Educating the public on the different blood components and blood types needed to support key patient groups (e.g., O- red cells for trauma, AB plasma).

Funding comprehensive motivational and psychographic research studies would help identify barriers and obstacles to current volunteer blood donor recruitment programs. Research would provide valuable insights for blood centers on how to overcome the threats to the unpaid donor recruitment program, leading to a sustainable, stable blood supply.

What previously produced regular blood donation behavior may not be effective moving forward. Younger cohorts respond to incentives and paid opportunities differently than older cohorts and likely give blood for different reasons (Masser, White, Hyde, & Terry, 2008; Sadler, Shi, Bethge, and Mühlbacher, 2018). Understanding the motives, values, and the psychographic characteristics that drive individuals to either volunteer to give blood or expect payment for their blood is key to overcoming this threat to the blood donor recruitment model for non-profit blood centers.

Once donor motivations are understood, the greatest opportunity for institutional support rests in establishing and sustaining an active role as champions for the general public to seek out opportunities to donate blood and to encourage organizations to support blood drives. During the early stages of national efforts and in concert with Section 3226 of the Coronavirus Aid, Relief, and Economic Security (CARES) Act of 2020, government officials took an active and effective role in advocating for blood donations in responding to the emerging COVID-19 crisis in March 2020. Figure 10 compares the O positive blood inventory levels for BCA reporting centers from March through June in years 2019 and 2020. The significant improvement in blood inventory levels seen in 2020 over 2019 was due primarily to an effective and sustained call by public officials to donate blood, with those efforts peaking in mid-April. However, as the public call for blood donations subsided in later April 2020, the corresponding decline in O positive blood inventory was dramatic, including dipping below 2019 levels by June 1, 2020.

**Figure 10: O Positive U.S. Daily Supply March through June, 2019 and 2020**



**Source:** Blood Centers of America, 2020

A continuous commitment to blood donation by national leadership clearly makes a difference in the strength of the nation’s blood supply. It is important to note that the heavy donor support during this period was managed by the same staffing capacity as before the public call to action. This means significantly more donations were handled without adding fixed costs, which resulted in a substantially lower cost per donation. Consequently, by becoming public advocates for blood donation, national leadership can simultaneously help create a more robust blood supply and reduce the cost per unit for blood centers. This power to influence the public could also be leveraged to connect with donors of specific blood types, further strengthening the national blood supply.

Funding social and psychological research optimizes donor awareness and re-engagement opportunities, leading to increased public participation and, thus, a more robust blood supply and decreased costs for blood centers.

**Recommendation 3.3: Fund a research study to determine definitively the impact of operating paid and volunteer donor programs in the United States simultaneously, and to evaluate the challenges posed by changes in demand between the two donation sectors. Lead and fund a research initiative to answer the question of impact of paid blood collection on local volunteer donation.**

To ensure the long-term stability of the nation's blood supply, research and data are needed to understand the impact of the growing paid Source Plasma collection market compared to the declining of the nation's blood collection centers. The Source Plasma industry has experienced a sustained ten-year growth rate to meet increasing global needs for plasma products, while the blood transfusion sector has experienced a contrasting 30 percent decline in usage.

Fund studies to understand individual motivational factors leading to focused engagement efforts that reduce cost for both non-profit blood centers and for-profit blood plasma collection facilities and increase critical blood and plasma-derived products for patient care.

**Recommendation 3.4: Fund research to target, recruit, and engage blood donors for personalized/precision medicine solutions, including molecular testing (i.e., genomic typing to meet emerging patient needs, such as sickle cell disease care).**

While red blood cell (RBC) transfusion is one of the most routine therapeutic interventions used in medical practice today, RBC alloimmunization (formation of antibodies to RBC antigens other than ABO) represents a commonly recognized, yet incompletely understood adverse outcome from transfusion. Once a patient develops an RBC alloantibody, they are more likely to develop additional antibodies (Rosse et al., 1990). This phenomenon may make it difficult to find compatible RBCs for future transfusion, prolonging anemia and increasing mortality. Among at-risk patients, those with sickle cell disease display increased rates of RBC alloimmunization with up to 50 percent of transfused adult patients having at least one RBC antibody (Fasano et al., 2019). The presence of RBC antibodies in this patient population drastically complicates their transfusion management (Nickel et al., 2016), which is an integral component of their medical care.

The most effective way to minimize RBC alloimmunization is by transfusion of extended antigen-matched blood from ethnically similar donors (Hendrickson, Tormey, and Shaz, 2014). In the U.S., minorities are underrepresented in the blood donor base. As such, recruiting and retaining minority donors (specifically, African Americans), as well as systematically characterizing and integrating donors' RBC antigen profile information with existing donor data and demographics, is a critical need for supporting many patient populations, including patients with sickle cell disease.

Advances in molecular technology have provided the ability for improved stringency of RBC antigen typing for both blood donors and patients. This level of stringency is a prerequisite for those patient populations (for example, sickle cell disease) for which antigen matching is indicated but remains costly using traditional serologic methods. Utilizing FDA-approved RBC molecular typing assays for both donor and patient testing can significantly enhance matched blood availability (Denomme and Anani, 2019), and therefore patient care, especially during national and international crises. When linked to a regional and/or (preferably) national donor database, the utilization of comprehensive donor RBC antigen profiles determined by RBC molecular typing can result in long-term cost savings to the healthcare system. However, its employment requires up-front investment by regional and national blood suppliers to create large donor databases of extended typed and/or rare blood donors, as well as ongoing collaboration between hospitals and blood centers. An example of existing regional extended type and/or rare blood donor database is the New York Blood Center's PreciseMatch® program.

Fund recruitment strategies, molecular technology, and data systems to link donors and patients to deliver the precision medicine solutions necessary for patients requiring extended antigen-matched blood.

# Chapter 4 Adequacy of the Blood Supply During Public Health Emergencies

## Current Status of the U.S. Blood Supply

The U.S. blood supply is reaching a point of instability (Klein, Hrouda, and Epstein, 2017). The free-market approach to blood collection, which has worked well in the past, has become strained due to a number of factors. Blood use has declined thanks to useful changes in medical practice; however, this reduction has caused the loss of the major source of revenue for blood centers. Additionally, the costs of collecting, testing, and processing blood have continued to rise due to the increased number of mandated infectious disease tests, the need for more complex and integrated information systems, and other associated costs.

While the blood supply is the safest it has ever been, the safety measures drive up costs for blood centers. On the hospital side, the consolidation of medical systems has created a smaller number of larger hospital enterprises that have greater bargaining power. These large hospital networks take advantage of the competition between blood centers to drive down the price of blood. As the cost to collect and process blood rises, and the price hospitals pay for blood continues to fall, the commoditization of blood components has resulted in financial uncertainty and economic instability. In fact, approximately 50 percent of U.S. blood centers are now reporting dangerously narrow or negative margins, which threaten their ability to continue operations (Klein, Hrouda, and Epstein, 2017). This fragility threatens the blood supply and inhibits innovation.

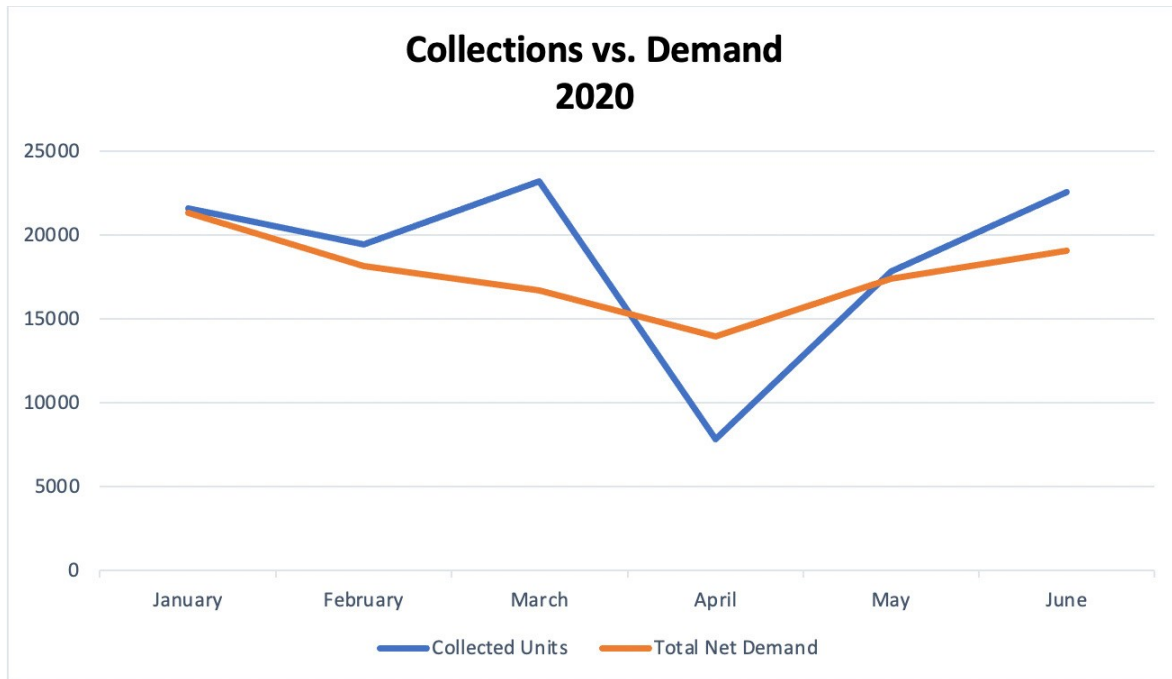
The COVID-19 pandemic has exacerbated these problems and also highlighted some key vulnerabilities within the blood industry: 1) no centralized source of real-time data to track the blood supply, and; 2) dangerous weaknesses in the supply chain for blood collection and manufacturing.

## Key Issues

### Disparate Data Collection

There is no single source of information with real-time data on blood supply and demand. The blood community currently monitors changes in supply through a manual, decentralized, imprecise process that gathers data from different reporting organizations. These disparate public and private systems provide no real-time data with which blood centers can calibrate their collections to match the blood needed by patients. As a result, shortages and wastage are both commonplace (Figure 11).

Figure 11: Collections Versus Demand, January – June 2020



Source: Gannon, B., Gulf Coast Regional Blood Center

The availability of the blood supply and blood utilization are both dynamic and must continuously be harmonized to ensure that blood is available to meet patients’ needs. While individual institutions and hospital systems have data on their blood use, general changes in utilization are not monitored or reported in real-time. The absence of comprehensive national data accounting for supply and utilization impedes the ability of blood centers, hospitals, and policymakers to take data-driven actions to ensure that the blood supply is continuously available to meet patients’ needs. The lack of aggregated real-time data on fluctuations in supply and utilization is particularly challenging for the blood system because certain blood components have a short shelf life of between days and weeks, depending on the specific blood component.

The ability to unfailingly supply the right blood to the right patient in a timely manner, regardless of location, is a measure of the “resilience” of the blood supply. The adequacy and resiliency of the blood supply and the production capacity of the blood centers are crucial to meet the nation’s day-to-day needs and to maintain adequate resources for surge capacity in the event of disasters. The adequacy and resilience are increasingly challenged by the lack of a robust nationwide database on blood product collection and utilization.

## Current Data Collection Activities to Monitor the U.S. Blood Supply

The blood supply is loosely monitored by a set of disparate public agencies and public-private partnerships. The following is a list of current activities related to monitoring the blood supply.

### *AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism*

The AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism is charged with assessing the nation's blood availability to meet the nation's demand for blood. The Task Force is a valuable, active forum that brings together the private sector blood community (BCA, ABC, ARC) and the government to support the nation and ensure the availability of the blood supply. Unfortunately, competition between blood centers and poor communication with hospital partners limits the available shared information and reduces the ability of the Task Force to guarantee blood availability.

### *Public Sector Data Collection*

Currently, the United States government administers two programs that capture data on blood collections and/or utilization. These are 1) the National Blood Collection and Utilization Survey (NBCUS), and 2) the National Healthcare Safety Network (NHSN) Hemovigilance Module.

### **National Blood Collection and Utilization Survey (NBCUS)**

Conducted by the OASH and the CDC, the NBCUS is a biennial cross-sectional survey of all U.S. blood centers and more than 2,800 hospitals that transfuse blood and blood components. The goal of this survey is to provide a statistically reliable estimate of the annual collection and utilization of blood components in the United States. Given the retrospective nature of the survey, data are not available in real time during a public health emergency.



**National Healthcare Safety Network (NHSN) Hemovigilance Module**

The NHSN is a web-based surveillance system that is used by more than 12,000 U.S. hospitals and healthcare facilities to report healthcare-associated infections and other patient safety data. The Hemovigilance Module is a component of NHSN that hospitals can use to report data on blood transfusion-related adverse events. As part of the participation protocol, hospitals also report the total number of blood and blood components transfused each month and the number of blood components that are discarded. Each year, over 130 participating facilities report data that represent approximately 7 percent of all U.S. transfusions on an annual basis (Edens et al., 2019). This infrastructure could be expanded to accept daily data reports on the blood inventory and transfusion records from all hospitals in the country. However, the manual input nature of data reporting is time-consuming and limits the number of hospitals willing to participate.

***Private Sector Data Collection***

The U.S. healthcare data systems have been developed to serve multiple segments of the medical industry and have never been integrated to create an overall picture of how patient care and medical procedures contribute to optimal patient outcomes. Any attempt to merge data from these disparate systems has required substantial manual manipulation of records and data systems. To better understand what specific patient interventions (or lack of intervention) lead to best outcomes, these data linkages must be developed. To date, several companies have addressed this issue, but data privacy, funding, and ownership have hampered progress. By encouraging the interoperability of existing blood collection databases through incentives for health IT vendors, valuable and actionable insights may be gained in support of blood supply management.

**Risks to Optimal Patient Care**

There are patients who do not have access to needed blood components. This occurs either because of their remote location or the inability of the hospitals to access needed blood components in a timely manner. This disparity in the availability of blood components also must be addressed to lessen the loss of life due to the scarcity of necessary blood transfusions. Studies have shown that when appropriate blood components are given early, not only are deaths due to hemorrhage decreased, but care is cost-effective (Callcut et al., 2020; Chang et al., 2019). Unfortunately, hospitals that do not have a full complement of blood components immediately available cannot provide optimal care.

In fact, of the 2,045 hospitals to which the ARC supplied blood components in 2019, 33 percent do not routinely store platelets ready to transfuse to bleeding patients (ARC, 2020); a separate report showed that more than 78 percent of these hospitals are located in a rural setting (Young, Ehrhart, and Mair, 2020). In another example, a recent study funded by the DoD showed that plasma, given within minutes of injury, significantly improved patient outcomes (Sperry et al., 2018).

It is imperative that Congress and the entire healthcare community work together to address the availability of all blood components. Resourcing these initiatives could lead to payment systems based on patient outcomes, and not just resource consumption.

# Patient Stories

## Nathan

In public health emergencies, there are critical needs for both those affected by the emergency and those patients who rely on the blood supply every day for their life-saving treatments. Both critical needs must be met.

On January 7, 2015, April took her four-month-old son, Nathan, to what she thought was a routine doctor's appointment. She told his pediatrician that Nathan's belly felt odd and he had been feeling sleepy for a few days. He also had pale skin, and the whites of his eyes looked "yellowish." The doctor took some blood and ordered a scan for Nathan at a nearby hospital.

At about 11 p.m. that night, his pediatrician called and told April that Nathan needed immediate medical attention because his hemoglobin was extremely low. April and her husband took him to the children's hospital, where he stayed for eight days undergoing many tests, including a bone marrow test and several different scans. During that time, Nathan received three blood transfusions. For infants, the IV line is commonly inserted in the baby's scalp. April feared she was going to lose her little boy and was horrified about what he was going through. Though he was discharged on the eighth day, there was no clear diagnosis.

Nathan suffers from an enlarged spleen and has had to return to the hospital every four to five weeks to receive blood transfusions. He's already had more than 50 units of blood! He is dependent on transfusions to live and most likely will be for the rest of his life. Doctors believe Nathan has a Gardos channel mutation, a very rare blood disorder that causes red blood cells to rapidly break apart. Rather than lasting 120 days, Nathan's red cells last only one week.

At three years old, Nathan continues to need transfusions every month or so, depending on how quickly his hemoglobin drops, and takes medication to manage his iron overload. His IV lines are now inserted into his arms. And as he's gotten older, he's become much stronger, so he must be physically held down for the transfusions. It's something that April describes as "very emotional and heart-breaking." Still, she remains grateful for the medical technology and especially to blood donors. ***"To all the donors out there, I just would like to say that you have gone above and beyond to save my son's life and the lives of others. Without blood transfusions, I would have lost my little boy. From the bottom of my heart, I thank God for donors for saving my baby and for continuing to save him every month!"***



**58+ RED CELLS**  
Gardos Channel  
Mutation

## Recommendations to Ensure Adequacy of the Blood Supply During Public Health Emergencies

Analysis of the effectiveness of the national response to the COVID-19 pandemic provides a unique opportunity to identify and correct gaps in existing systems intended to coordinate, lead, and direct needed resources for maintenance of an adequate national blood supply in the face of a large-scale disaster. The following recommendations leverage that opportunity in an effort to better meet the needs of the American public.

**Recommendation 4.1: Create, implement, and fund a comprehensive, sustainable, minimally burdensome system that monitors and makes available real-time data on the blood supply and utilization by hospitals to ensure patients have access to vital and life-saving blood components during both emergency and non-emergency periods.**

At this time, there is no comprehensive source of data collection for the national blood supply. Such a system is needed to enable monitoring of trends, evaluation of population health, and utilization of risk-based decision-making for new rules and regulations. A national data system that monitors the blood supply chain from vein to vein—or from donor to patient—is critical to our nation’s preparedness infrastructure and is essential to ensuring the adequacy of the blood supply in the case of public health emergencies.

The current state of data collection on the U.S. blood supply proved woefully inadequate during the COVID-19 pandemic. In looking for opportunities to strengthen blood supply disaster responsiveness, the importance of accurate and timely data on blood supply inventories and usage has been singled out as the top priority by the public and the blood community. The COVID-19 pandemic has made it obvious that the time has come to cease relying on current approaches to voluntary data collection from the private sector. Voluntary reporting of critical blood inventory and utilization data have resulted in reports that are too incomplete and time-lagged to allow adequate real-time disaster planning and mitigation strategies to ensure continuous adequacy of the national blood supply. Lives depend on blood availability and time is of the essence in responding to the need for this life-saving product.

To fill this critical data gap, public and private stakeholders must collaborate to design a comprehensive data infrastructure that ensures that the data supports the needs of blood centers, hospitals, supply chain manufacturers, accreditors, regulators, payers, and other organizations throughout the blood community in times of public health emergencies. The system must be designed in a manner that accounts for the confidential and proprietary nature of the data. The system must include implementation of a model for oversight by a public-private partnership, rooted in legislation, which in the event of a disaster with



significant impact to the blood supply, provides blood centers and hospitals with disaster-related governance, coordination and communication, resources, and financial support to ensure blood transfusion needs are met for the American people.

### **Relevant Public-Private Cell and Organ Transplant Models to Consider**

The U.S. government has used legislation to develop successful public-private partnerships. These past examples can serve as models for how to move forward with necessary changes in the blood industry.

The blood banking community can look to models in the related areas of stem cell and organ transplantation that have successfully developed powerful networks, databases, and distribution systems that function effectively regardless of circumstances. These programs owe their success in large part to a public-private model that anchors the vital data collection and oversight function in legislation coupled with federal support.

#### ***The National Marrow Donor Program (NMDP)***

NMDP is a non-profit organization founded in 1986 and based in Minneapolis, Minnesota. The NMDP operates the sole federally-funded and Congressionally-authorized stem cell registry in the United States, including volunteer hematopoietic cell donors and umbilical cord blood units. As of September 2016, the NMDP had facilitated more than 80,000 transplants worldwide (BeTheMatch.org, 2020).

The C.W. Bill Young Cell Transplantation Program was authorized by Congress in December 2005, when the Stem Cell Therapeutic and Research Act of 2005 was enacted. It was subsequently amended by the Stem Cell Therapeutic and Research Reauthorization Act of 2010 and 2015. Federal support for the C.W. Bill Young Cell Transplantation Program is essential to increasing patient access to transplant. The U.S. Congress continues to require access to bone marrow transplants for all patients in need.

The NMDP receives annually about \$30 million in FY20 from the U.S. government through the Health Resources and Services Administration (hrsa.gov.). The U.S. Navy also provides some funding.

### ***The United Network for Organ Sharing (UNOS)***

The United Network for Organ Sharing (UNOS) is a private, non-profit organization that, since 1986, has managed the nation's Organ Procurement and Transplant Network (OPTN) under contract with the Federal government. As of 2020, UNOS has been involved with the 819,933 U.S. transplants listed on the U.S. Department of Health and Human Services national database (National Data—OPTN, n.d.; What is UNOS? / About the Network for Organ Sharing, n.d.). It has served as a model for national transplant systems around the world, including the United Kingdom, Germany, Spain, Japan, South America, Mexico, and Canada.

The system was developed in 1984, when the government decided that the U.S. needed a national system run by a private (non-government) organization to coordinate sharing organs. This became the Organ Procurement and Transplantation Network (OPTN). In addition, the U.S. needed a system to collect and store data on transplants. This became the Scientific Registry of Transplant Recipients. In 1984, when Congress passed the National Organ Transplantation Act (NOTA) it made all of the above possible. Since the initial network contract was finalized in 1986, UNOS has served as the OPTN under contract with the U.S. Department of Health and Human Services. About 10 percent of UNOS' funding is derived directly from its Federal contract. The rest of its operating budget comes from computer registration fees paid by members, project grants from foundations and corporations, and tax-deductible charitable contributions (UNOS Facts Figures, n.d.).

## **Governance**

There must be a clearly identified authority for governance and coordination to provide a “big tent” for the various stakeholders that must be involved, to include: associations; industry partners; health departments; blood centers; hospitals; and federal, state and local authorities charged with disaster response.

### Privacy and Security

The information needed to create a national data infrastructure might include protected health information (PHI) or other sensitive material. Data security and privacy are critical and must be an integral part of this effort. Within a national data infrastructure, data security and privacy checks are necessary to ensure that patient privacy requirements, as mandated by the Health Insurance Portability and Accountability Act (HIPAA) of 1996, are satisfied and that business and corporation proprietary concerns are addressed.

### High-level Data

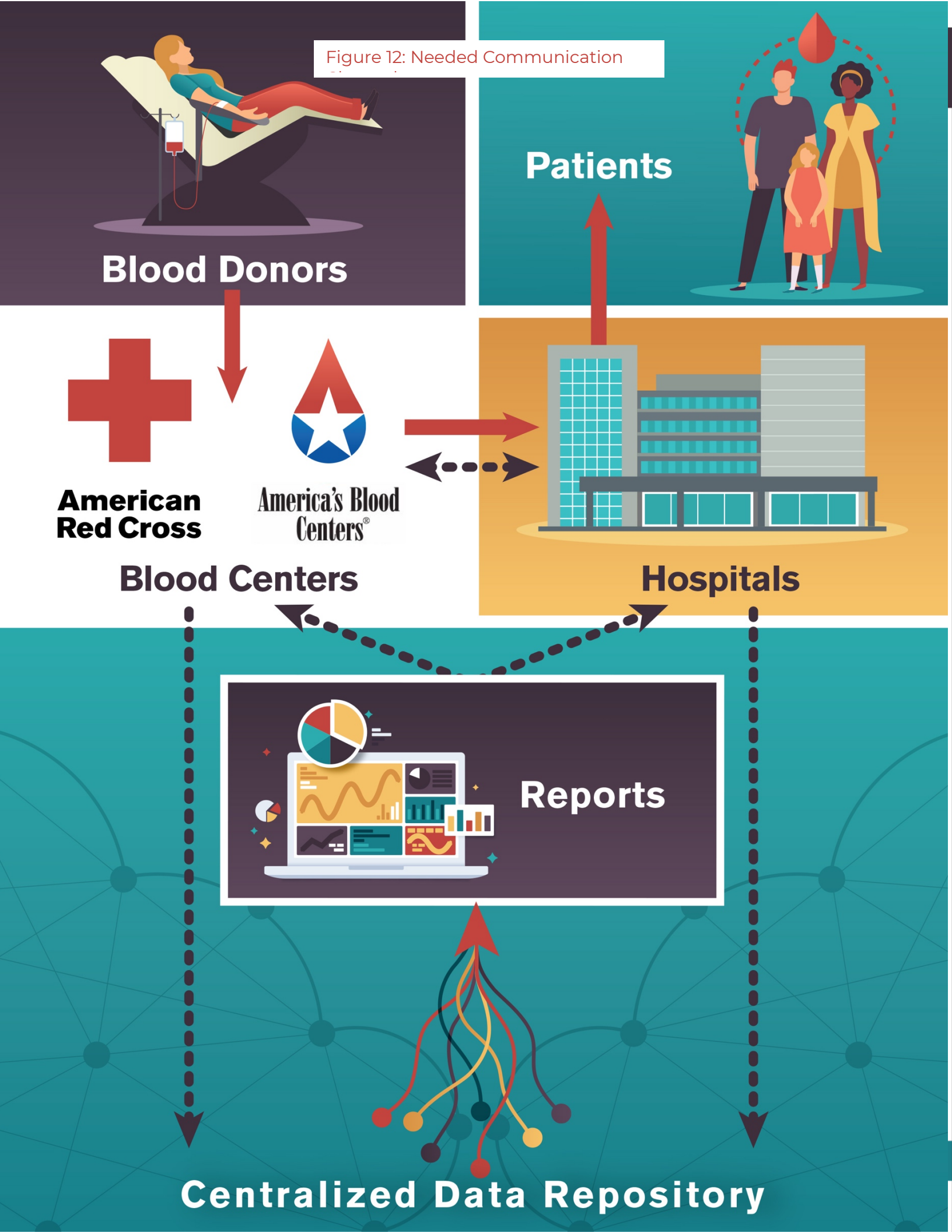
Maintenance of a safe and available blood supply is a critical component to patient care and further magnified during a public health emergency. Clinical data from patients may be needed to provide this continued support. A tool must be developed that allows for the ability to cross-level select information using the appropriate application to facilitate the recruitment of donors by blood centers and requests for products by treatment facilities. The use of this tool must not be limited to a public health emergency but have broad application to support other disaster and emergency situations that require immediate and/or continued blood support or specific blood components. The tool should offer the appropriate modules to generate reports to the industry.

### Communication Channels

The pandemic and the need for CCP has illustrated the necessity for highly specific patient information that can be used by blood centers to target collections. These links and channels of communication (illustrated in Figure 12) are currently lacking but will prove to be invaluable during short- and long-term crises when there is a dire need for specific blood components. This tool should ensure that data is coded and processed through a third party with the required privacy and security settings in place to prevent unauthorized access to restricted information for both patients and donors. A neutral third party, such as a government agency or the AABB Interorganizational Task Force, should be resourced to manage the program or tool to oversee the exchange and use of data to both support the nation's blood supply and prevent the potential for corporation bias and inflated prices. The requirement for incentives or a mandate to participate must be explored when developing this tool.



Figure 12: Needed Communication



**Recommendation 4.2: Create and fund a task force that includes government and critical industry stakeholders that will map, model, and identify potential elements of the supply chain and infrastructure that will affect our ability to actively respond and ensure a sufficient blood supply during emergency and non-emergency conditions.**

- **Task force to develop and maintain industry-wide business continuity plan that incorporates all necessary supplies for blood collection and storage.**
- **Fund implementation of business continuity plans and other recommendations from the task force.**

### **Blood Supply Vulnerabilities**

Natural disasters and the COVID-19 pandemic have highlighted critical vulnerabilities in the blood supply chain. These weaknesses must be identified and strengthened. The possible scope of the impact of a disaster on the national blood supply is vast, encompassing areas as large as the entire nation and its territories, or localizing to a single region. The abrupt change in the landscape that can occur in a disaster requires leadership skills and nimble operations in order to quickly evaluate the new situation and shift risk assessments and priorities accordingly. The ability to anticipate, prepare, assess, and respond rapidly and effectively to disasters that affect the nation's blood supply is vital to protecting our nation, citizens, and economy. Coordination and governance play prevailing roles in all facets of disaster response.

### **Supply Chain Infrastructure Vulnerabilities**

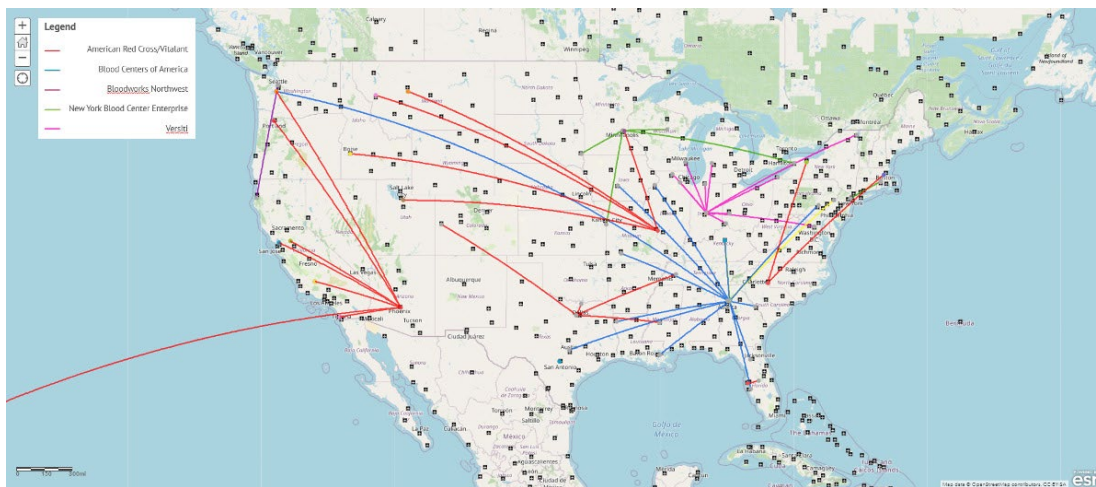
Blood components are labile and, therefore, more vulnerable to weaknesses within the supply chain. When Hurricane Maria devastated Puerto Rico in 2017, it made roads impassable and left employees without housing, electricity, or communication. These forces caused a major disruption to the industry's supply of critical blood bags, highlighting the vulnerability of the supply chain.

Over the past decade, many independent blood centers have merged; today, the largest six companies provide greater than 95 percent of the blood collected for patients. The consolidation and concentration of blood centers has increased the vulnerability of the U.S. blood supply in the event of a pandemic or natural disaster. The result of multiple mergers and acquisitions among suppliers, compounded by barriers to enter the industry due to regulatory requirements, has led to fewer manufacturers and their associated production plants serving the blood industry. In addition, there are only four primary medical plastic suppliers for U.S. blood centers. Blood is collected using highly specialized plastic kits and stored in blood-component-specific plastic bags. These medical plastic suppliers have manufacturing footprints in 10 different countries that produce 23 industry-critical products.

There are 10 primary reagent suppliers for U.S. blood centers. They have manufacturing footprints in six different countries that produce 64 industry-critical products. There are 13 ancillary suppliers for U.S. blood centers. They have manufacturing footprints in five different countries that produce 14 industry critical products (BCA, 2020).

Consolidation and concentration of testing laboratories has also increased the vulnerability of the U.S. blood supply during a pandemic or natural disaster. There are currently only six testing organizations and 22 laboratories. Figure 13 shows the six organizations and their dependence on aerial and road infrastructure to collect and test blood.

**Figure 13: Major Blood System Fixed Sites in the United States**



**Source:** Blood Centers of America, Digital Map, 2020

In summary, the creation of a national data collection center is essential for a robust, resilient, and efficient blood supply. The data collected will allow us to monitor the blood supply and respond appropriately to changes in demand so that patients are served, and waste is minimized. The data will be essential in a crisis, when we need to quickly respond to an unmet need or alter practice to maintain a safe and regular supply of blood. The creation of a comprehensive supply chain business continuity plan that is developed in close coordination with the FDA will strengthen the availability of the critical supplies we need, and enable the establishment of critical inventory levels of supplies to ensure continued operations.

# Chapter 5 Implementation of the Transfusion-Transmissible Infections Monitoring System (TTIMS)

## Background

As part of Section 209 of the PAHPAIA, HHS is required to submit a report to Congress containing recommendations for maintaining an adequate national blood supply. Public comments submitted to HHS by major blood organizations and other stakeholders call for a coordinated national response to maintain a safe blood supply in the face of future threats such as national disasters and pandemics. These letters emphasize the need for robust national data systems to 1) strengthen the nation's capacity to track factors that impact blood supply and blood utilization, and 2) monitor the outcomes of blood collection and transfusion through better surveillance (hemovigilance). Existing data collection platforms that are in active use for research or similar purposes, such as the TTIMS program, were cited as models for potential future data expansion.

Here we describe the current infrastructure of TTIMS and the opportunity to expand TTIMS into a more comprehensive, Federally-funded program that not only maintains its current responsibilities and structure, but also moves toward addressing the need for non-transfusion transmissible infection (TTI) data collection in routine operations and during public health emergencies.

## Current State of TTIMS

### Scope

Initiated in September 2015, TTIMS is a program designed to monitor transfusion-transmissible infectious diseases and to ensure the safety of the U.S. blood supply (Custer, Stramer, Glynn, Williams, & Anderson, 2016). The program is sponsored by the FDA Center for Biologics Evaluation and Research (CBER); the NIH National Heart, Lung, and Blood Institute (NHLBI); and OASH. As its core function, TTIMS collects prevalence and incidence data<sup>1</sup> derived from the screening of blood donors for HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) infection, as well as demographic data, behavioral risk factors, and biorepository samples from donors found to be seropositive for markers of these infections.

## Funding and Governance

TTIMS is funded primarily by CBER with supplemental funding from NHLBI and OASH. TTIMS is operated as a public-private partnership and governed by an executive committee as the decision-making body, a steering committee with broad representation from HHS stakeholders, and individual analysis working groups. A firewall prevents FDA from receiving individual donor or site-identified data.

Under TTIMS's current design, all TTIMS-participating blood centers participate and collect parallel sets of data for any of the TTIMS study-wide initiatives. Similarly, TTIMS-funded participants are expected to contribute scientific input—specifically, proposals for review as possible TTIMS initiatives—directly to the TTIMS Executive Committee rather than simultaneously conduct individual research. This model has worked well to date, but it is unknown if it is sustainable with an expanded program.

## Operational Structure

For efficient management and governance, TTIMS operates under a coordinating center structure, with a single federally funded entity serving as the coordinating center that is responsible for the recruitment, oversight, and funding of participant institutions. The lead scientists at the coordinating center are responsible for the design and implementation of TTIMS studies, which must be reviewed and approved by the TTIMS Executive Committee.

Currently, TTIMS is operated through two coordinating centers, the Donor Database Coordinating Center operated by the ARC, and the Laboratory and Risk Factor Coordinating Center operated by the Vitalant Research Institute (previously known as Blood Systems Research Institute). These coordinating centers work closely with the participating blood centers (ARC, Vitalant, New York Blood Center, and OneBlood) and a central testing laboratory (Creative Testing Solutions). These partners generate extensive data representing approximately 60 percent of the U.S. blood supply.

The Donor Database Coordinating Center centralizes, processes, and analyzes epidemiologic data from blood donors and donations. It establishes and manages consensus test result definitions, and rigorously validates the data-exchange processes within the study. It produces quarterly prevalence reports for transfusion transmissible infection markers for donors and donations stratified by demographic variables. Additionally, the Donor Database Coordinating Center estimates incidence for HIV, HBV, and HCV among first-time, repeat, and all blood donors.



In addition to designing and implementing detailed risk interviews for seropositive donors and controls, the Laboratory and Risk Factor Coordinating Center has initiated advanced laboratory measures to assess biological factors that may influence and/or predict blood safety. These include assessment of the TTIMS HIV-positive donor repository using HIV-1 Limiting Antigen (LAG)-Avidity testing to determine the recent HIV infection among seropositive donors and to support calculation of HIV incidence in first-time blood donors; and molecular surveillance of HIV, HCV, and HBV viral genomes to assess variants that may reflect important differences in phylogenetics or drug resistance, and changes in virus phylogenetic distributions over time. Recently the Laboratory and Risk Factor Coordinating Center, in collaboration with the CDC, completed blinded testing of targeted blood donor samples for evidence of recent anti-retroviral drug therapy or pre-exposure HIV prophylaxis medication.

### Productivity and Successes

TTIMS has been designed for broad monitoring of more than 60 percent of the U.S. blood supply. Data collected through TTIMS have supported policy changes to donor deferrals and helped demonstrate the safety of the U.S. blood supply. The current TTIMS is capable of monitoring the impact of natural and policy-driven shifts in the donor base, in particular in response to the December 2015 change in donor eligibility requirements for men who have sex with men (MSM) from a permanent deferral to a 12 month deferral for sexual contact with another man, and subsequently the April 2020 change to a three month deferral for sexual contact with another man (Steele et al., 2020.; Quiner, C., 2020).

Progress in TTIMS data collection and analysis has been strong over the past five years. As part of TTIMS function as a public-private partnership, scientists affiliated with the TTIMS Program regularly present program findings publicly at advisory committee meetings and at industry conferences (for example, AABB) and have completed six manuscripts, with another submitted for publication (Anderson et al., 2016; Custer, Stramer, Glynn, Williams, and Anderson, 2016; Custer et al., 2020; Grebe et al., 2020; Quiner et al., 2020; Steele et al., 2020.; Steele et al., Submitted for publication).

### Key Issues Regarding Expansion of TTIMS to Address Additional Unmet Needs

Expansion of TTIMS capabilities and working relationships beyond the current program could include changes to 1) monitor prevalence and incidence of all donor infections for which the U.S. blood supply is screened, 2) increase the number of blood centers participating, and 3) modify the overall work scope to address blood resource and donor safety research (for example, donor hemovigilance).

This expansion could be operationalized through the addition of a third TTIMS coordinating center for investigator-initiated monitoring and research related to donor health, safety, and blood resource dynamics. This expansion could include additional blood centers and plasma centers that collect plasma for further manufacture into therapeutic products such as clotting factors and immunoglobulins.

### **Expanded TTIMS Participant Expectation and Performance**

As noted previously, two independent blood centers, ARC and Vitalant, currently operate the Donor Database Coordinating Center and the Laboratory and Risk Factor Coordinating Center, respectively, with resulting data representing four large blood centers covering approximately 60 percent of the U.S. donated blood supply. Although competitive in many aspects of their current business models, the two coordinating centers and participating blood centers freely share data and research initiatives in regular TTIMS discussions and have successfully collaborated since the program's initiation. Sophisticated protocols for data management and quality control provide a high standard for data quality and protections for inadvertent public release of donor or blood center--specific data. The remaining blood centers in the U.S. are not under common ownership or management but, excluding a small proportion of hospital-based blood centers, are members of ABC, a proactive trade association that assists individual blood centers with generalizable functions, such as industry communications and scientific guidance.

Several stakeholders who submitted public comments regarding the Section 209 report recommended a complete national data system for blood-related data. However, this is not feasible when participation in a long-term data collection program is voluntary, even with external funding. While any U.S. blood centers not currently participating in TTIMS would be eligible for participation in a proposed and newly formed TTIMS coordinating center, participants will be expected to comply with all coordinating center-specific study protocols, manuals of procedures, and data quality control standards. TTIMS sites will need access to local, responsive institutional review boards to ensure timely required review and approval of human subjects use.

There will always be variations in individual blood center capabilities and interest regarding participation in a sophisticated data collection program. For the success and timeliness of the larger program, blood centers that cannot successfully comply with accepted study operating protocols, would be unable to participate in TTIMS. For this reason, although there may be high initial interest, it is estimated that approximately 10 to 15 blood centers may be added as permanent TTIMS participants under a new coordinating center. As described previously, blood centers are competitive in many aspects of their current business models.

Because ARC and Vitalant lead the two current TTIMS Coordinating Centers, a consortium of non-TTIMS centers may wish to organize and partner with FDA to form the new TTIMS coordinating center. The addition of 10 to 15 capable blood centers would boost TTIMS to 75 percent or more of the U.S. blood supply and should remain manageable.

## Recommendations to Ensure a Safe Blood Supply

Three recommendations have been identified for Federal government investment to ensure a safe blood supply in routine operations as well as during natural disasters and public health emergencies.

**Recommendation 5.1: Fund the current TTIMS program to ensure the safety of blood donations in the U.S. by monitoring transfusion-transmitted infections, such as HIV.**

**Recommendation 5.2: Fund the expansion of the current TTIMS to 1) monitor other transfusion-transmitted infections for which blood donors are tested, 2) increase participation among all blood centers, and 3) coordinate non-transfusion transmissible infection studies of blood donors and donations (for example, donor hemovigilance).**

## Rationale

National blood safety surveillance has been proposed and discussed by Federal advisory committees since the advent of HIV in the 1980s (Institute of Medicine [U.S.] Committee to Study HIV Transmission Through Blood and Blood Products, 1995). These historic recommendations were operationalized in 2015 with TTIMS. Since its inception, TTIMS has established a comprehensive and sophisticated monitoring capability for the safety of the U.S. blood supply (Figure 14). The data collected through TTIMS and the analyses conducted through the program have supported policy changes and documented the safety of the blood supply in the U.S. Additionally, TTIMS has been responsive to the need for additional studies, including data related to the use of pre-exposure prophylaxis and anti-retroviral therapies by individuals who wish to donate blood. Pre-exposure prophylaxis for high-risk exposures and anti-retroviral therapies for HIV infection are highly effective medications. However, dosing compliance failures may lead to incomplete protection and potential transmissible HIV infection in blood that may not be detected by current blood screening.



Figure 14: TTIMS: Current



# TTIMS: Transfusion Transmissible Infectious Monitoring System

Current Status



## American Red Cross

Donation Database  
Coordinating Center  
(ARC)

The logo for Vitalant, featuring the word "vitalant" in a lowercase sans-serif font and a stylized white "V" symbol to the right.

vitalant<sup>SM</sup>

Laboratory and Risk Factor  
Coordinating Center  
(Vitalant)

Participating Blood Collection Establishments:



American Red Cross

The logo for Vitalant, featuring the word "vitalant" in a lowercase sans-serif font and a stylized white "V" symbol to the right.

vitalant<sup>SM</sup>



New York  
Blood Center



oneblood

The United States is the only modern healthcare system that lacks a true nationalized blood supply comprising national protocols, national data warehouses, and national organizational management. While the privately owned and operated network of blood centers in the U.S. has been extremely effective at providing a safe and stable blood supply, as well as providing internationally recognized programs of research excellence, some aspects of available data have fallen short because of the macro-fragmentation of the U.S. blood system and an inability to collect high-quality and timely data related to the U.S. blood supply and its utilization.

Competition, data collection burden, lack of harmonized definitions, and lack of centralized mandates have impeded the collection of data on a voluntary basis. Well-recognized shortfalls in the U.S. blood system include the absence of a robust hemovigilance system for either blood donors or recipients; reliable predictive models for seasonal and disaster-related disruptions to blood collection; investigations into donor health (for example, toxicology); and interventional research to reduce/prevent donor adverse outcomes related to blood donation that not only cause potential harm to donors, but may also impact future donor willingness to donate (Public Health Service Biovigilance Task Group, 2009). A review of the public comments to Section 209 of the *Pandemic and All-Hazards Preparedness and Advancing Innovation Act* reflects a united appeal from the large U.S. blood collection organizations to collect better data and conduct further research in the U.S. to overcome these hurdles and support provision of a safe, ample, and sustained U.S. blood supply.

TTIMS is currently funded through five-year contracts by FDA's CBER, NIH's National Heart, Lung, and Blood Institute (NHLBI), and OASH. Agency funding is subject to agency priorities, which may change from year to year. Line item sustainable funding (for example, 30-year) would enable a dependable future for this critical blood safety monitoring, regardless of emerging priorities. Targeted funding for TTIMS from Congress would ensure the continuity of TTIMS's efforts in monitoring the safety and availability of the U.S. blood supply into the future.

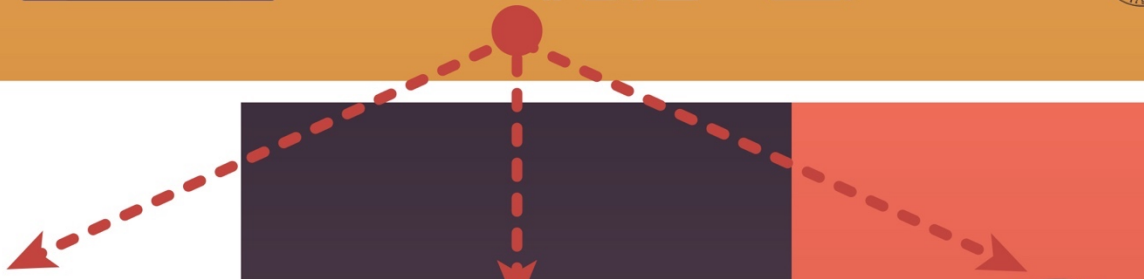
A new TTIMS coordinating center (Figure 15) with a focus on donor and donation studies unrelated to TTI will add expertise and breadth to the TTIMS work scope. As with the current TTIMS program, participating blood centers would be expected to participate in all current TTIMS protocols approved by the executive committee for that coordinating center, as well as to propose new research initiatives in the specific subject areas. These topics could include all aspects of donor hemovigilance and blood component manufacturing. The new TTIMS coordinating center could also develop and maintain broad-scale survey capability with expansion to include determination of representative donor factors needed for operational decision-making, both through large-scale surveys and (in response to emerging infectious diseases or related threats) through rapid survey capability (for example, RapidDOS, Whitaker et al, 2020). See [Appendix C](#) list of potential future studies.

Figure 15: TTIMS: Proposed



# TTIMS: Transfusion Transmissible Infectious Monitoring System

Proposed Structure



**American Red Cross**

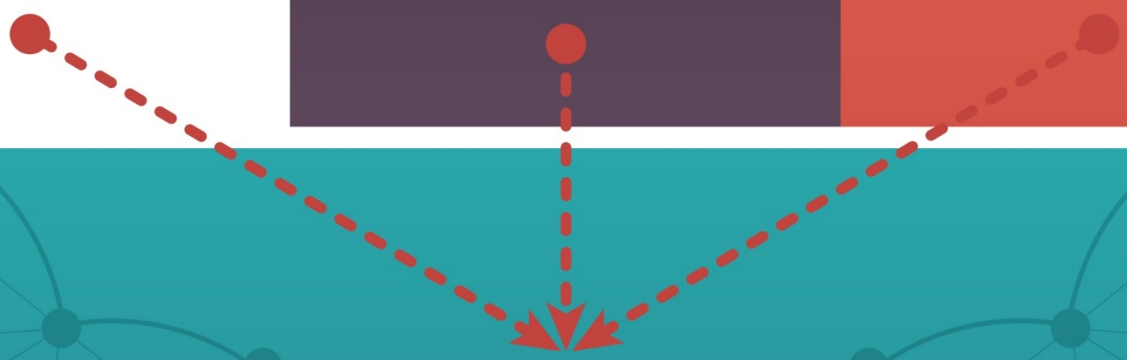
**Donation Database Coordinating Center (ARC)**



**Laboratory and Risk Factor Coordinating Center (Vitalant)**



**Future Coordinating Center (CC)**



## \*Participating Blood Collection Establishments\*



**American Red Cross**



**New York Blood Center**



**oneblood**

\*Additional Blood Collection Establishments to be added.

**Recommendation 5.3: Create a task force to include NIH, CDC, FDA, and private stakeholders to study, review, and evaluate the current systems to strengthen hemovigilance (and biovigilance) programs and to improve patient outcomes.**

The task force should

- 1. Consider existing programs (including TTIMS, CDC’s NHSN Hemovigilance Module, HHS’s NBCUS, and FDA’s Biologics Effectiveness and Safety Initiative), their integration, enhancement, and modernization to ensure interoperability and improved data management (for example, semi-automated to fully-automated data submission);**
- 2. Suggest strategies for improving participation and reducing burden, enhancing data reporting, data sharing, and engagement from stakeholders, including blood collectors, hospitals, clinicians and patients; and**
- 3. Consider a public-private partnership structure to ensure transparency and promote additional buy-in from these stakeholders.**

While donor hemovigilance and donor infection monitoring is vital, recipient hemovigilance is also essential to monitor blood transfusion safety. Public comments submitted to Congress and/or HHS by major blood organizations and other stakeholders call for a coordinated national response to maintain a safe blood supply in the face of threats such as national disasters and pandemics.

These letters emphasize the need for robust national data systems to strengthen the nation’s capacity to track factors that impact blood supply and blood utilization and that monitor the transfusion recipient outcomes through better surveillance or “hemovigilance.” Many of these comments describe a national patient hemovigilance network with the goal of increasing patient safety through data analyses that address causal factors for adverse events.

Hemovigilance/biovigilance networks have been designed and launched in the U.S. several times in the past 20 years. In 2003, the FDA-proposed rule was one of the first initiatives to address hemovigilance reporting (U.S. Food and Drug Administration, 2003). The AABB Interorganizational Task Force on Biovigilance, including the U.S. Public Health Service (PHS) and the private sector, conducted extensive assessments of blood safety gaps in both donor and recipient hemovigilance from 2006 to 2008. Assessment findings led to a recommendation from the Assistant Secretary for Health to the Advisory Committee for Blood Safety and Availability to establish a national biovigilance network to address gaps in blood and biologics safety (Public Health Service Biovigilance Task Group, 2009). It must be recognized that U.S. blood collection and transfusion activities are much larger than those covered by any other national or international hemovigilance system.

And without a national health system, implementing programs to monitor adverse events, donor health and safety, blood availability, and blood utilization has been challenging.

Some of the gaps identified by the Assistant Secretary for Health in the 2009 PHS Biovigilance Task Group report were addressed through the establishment of common definitions for adverse events in transfused patients and the development of the CDC NHSN Hemovigilance Module. The Hemovigilance Module, a component of the NHSN, is a largely voluntary web-based surveillance system used by U.S. hospitals and healthcare facilities to report data on 12 blood transfusion-related adverse reactions (i.e., when a patient develops an infection, an allergic reaction, or another adverse event as a result of a blood transfusion) and associated process errors which may result in a reaction (CDC, 2018). The Hemovigilance Module could be used by every hospital or a sample of hospitals in the U.S. as a nationwide surveillance system but additional incentives are likely needed. A comprehensive recipient hemovigilance network with national participation remains elusive.

In response to this challenge, a task force with broad public-private participation, including patient voices, is needed to identify the remaining challenges for national participation in hemovigilance systems and to recommend minimally burdensome and maximally productive strategies and funding mechanisms to mitigate such challenges.

Implementation of these three recommendations will build upon existing platforms and sustain a safe and scientifically robust blood supply for the nation's future.



# Chapter 6 Safety and Innovation

## Current State of Safety and Innovation

A sustainable blood supply is critical to a robust health care system and ensuring the well-being of our country. Because the current U.S. blood system is only partially coordinated, improvements in safety and availability in the blood supply and blood transfusion are hindered. In addition, the ability to meet the needs for both national and local surge capacity to address potential threats, including newly emerging pathogens (for example, COVID-19 and Zika virus) and natural and manmade disasters, is limited.

## Key Issues Regarding Safety And Innovation

There is an urgent need for innovations to address several issues related to

- Product availability;
- Proper use of blood components;
- New procedures and products to enhance efficacy and safety of blood components;
- Research into alternatives to current products, including cell-based and synthetic products; and
- Basic research into the pathophysiology of diseases requiring transfusion, such as sickle cell disease and trauma care, and transfusion adverse effects, such as making antibodies that destroy transfused blood components.

Overarching all of these matters is the need to encourage international cooperation and harmonization to permit introduction of innovative therapies developed in other countries; improve coordination of efforts to identify and prioritize high-impact research efforts, including expanding clinical trial sites and training opportunities; enhance educational outreach to optimize blood transfusion practices generally; and change the current reimbursement methods for blood and blood components to provide needed investments in innovation.

Importantly, the current financial underpinning of the U.S. blood system is fragile and at risk of not being able to provide current and future medically needed resources. The current reimbursement methods require revision and modification to sustain the system and to provide needed investments for innovation.

## Recommendations for Safety and Innovation

**Recommendation 6.1: Charter and fund a public-private partnership that promotes innovation in transfusion medicine, to 1) enhance characteristics of available products (such as for increasing product shelf life through storage in lyophilized or frozen state), 2) develop new products and processes, 3) develop pathogen inactivation for all blood components, and 4) create blood alternatives or universal blood components.**

As a result, from the public-private partnership recommendations,

- Provide additional/increased funding for basic and applied, and clinical research programs that are identified through this mechanism, with the goal of improving our understanding of transfusion medicine and the appropriate use of blood components to ensure improved patient outcomes.
- Use this public-private partnership, in coordination with FDA, to engage in dialogue on how the current regulatory standards impact innovation in transfusion medicine for the purpose of ensuring increased safety, access, and enhanced patient outcomes.

Countries with national blood systems have reorganized their research and development activities to align with strategic goals identified by various stakeholders, such as government, industry, trade associations, patient advocacy groups, and military, leading to improved innovation productivity. The best practices include effective hemovigilance programs, improved regulatory environment for medical devices, and more coordinated government support for research and development (R&D) as contributing to improved outcomes in those countries. U.S. policymakers could further encourage investments in research and development by sustaining or expanding government investments in blood-related programs and more closely coordinating the investments to address critical needs, including pathogen inactivation and its implementation, red cell transfusion in patients with sickle cell disease, and better understanding of appropriate blood use.

Suggestions for coordinating efforts include the development of consortia, including various stakeholders, or a public-private partnership, possibly housed within HHS, to prioritize and fund research efforts that are aligned with identified priorities and strategic goals in the field of transfusion medicine. An important aspect of coordination is the development of an acceptable governance structure that is aligned with identified public needs for the blood supply and nimble enough to ensure prompt action when needed. A unique aspect of transfusion medicine is the need to include clinical partners with the goal of improving patient outcomes and adding value to patient care. This would include infectious disease specialists, trauma surgeons, anesthesiologists, and hematologists. Figure 16 is an example of its structure.

Figure 16: Sample Structure of a Center of Excellence



Source: Nursing Strategic Plan, The Ohio State University, Wexner Medical Center, <https://wexnermedical.osu.edu/about-us/nursing/about-us/strategic-plan>

## Applied and Clinical Research Needs

### *Better Use of Existing Blood Components*

The demand for blood has decreased over the past several years due to a number of factors including improved patient blood management programs, less invasive surgeries, availability of pharmacologic agents such as erythropoietin or tranexamic acid, and revised transfusion guidelines from professional societies. Near-term basic and applied research for existing transfusion products is needed to improve understanding of the appropriate use of current products to develop and promote best practices and enhance the benefit/risk ratio. Increased clinical research and more robust clinical trial processes through



a multidisciplinary effort across multiple clinical sites is a key factor in the success of this effort.

Clinical trials on current blood components have been conducted in several populations, and successes have been made, including transfusion in the setting of trauma and red cell transfusion for preventing stroke in patients with sickle cell disease. However, many gaps in knowledge remain. Examples include:

- Red cell and platelet alloimmunization - when patients make antibodies to the transfused blood that cause adverse reactions or destroy future transfusions);
- Red blood cell autoantibody development - resulting in self-destruction of red cells leading to anemia;
- Red blood cell and platelet neonatal/pediatric transfusion - when to transfuse and how much to transfuse; and
- Trauma-induced coagulopathy - this correlates with worse outcomes from trauma; why this occurs and how best to treat it is unclear.

### ***Development of New Transfusion Products***

Several products are currently being developed to address various blood and blood-component issues, including emerging pathogens, pathogen load, stability during storage, and logistics of using platelets, plasma, red blood cells, and whole blood. A few examples of products in later stage development are described below (not all-inclusive). These products highlight the need for additional support to develop enhancements to transfusion components that would improve both efficacy and safety.

### **Oxygen Carriers**

Hemoglobin-based oxygen carriers (sometimes referred to as artificial blood) have been studied for many years. Better understanding of the role of nitric oxide and enhanced cell engineering knowledge makes their continued pursuit an important goal.

### **Dried Plasma**

For the treatment of trauma, the DoD has identified a critical need for dried plasma products that are easily deployed, easily reconstituted using solutions carried by medics, or readily available in ambulances.

**Cold-stored and Lyophilized Platelets**

There is a chronic shortage of platelets in the United States due to its short shelf life. The available supply of platelets could be improved through changes in the processing and storage of the components. These products would improve access to platelets in rural communities and in public health emergencies.

**Pathogen Reduction**

The availability of improved technologies prepares for emerging transfusion-transmitted diseases and disruptions to the testing reagent supply chain.

**Alloantibody Registry for Patients with Red Cell Antibodies**

There is no national alloantibody registry, which means one hospital is not aware of antibodies detected at other hospitals. This presents a problem for patients receiving care at more than one hospital since the evanescent nature of these antibodies places patients at risk for adverse transfusion events, which can be fatal. There is a need for a national red blood cell alloantibody registry optimally based on a collaboration between laboratory information systems and a large accreditation/regulatory body, which could facilitate appropriately matched blood for these patients (Hauser, Hendrickson, and Tormey, 2019; Williams, Lorenz, Tahir, Pham, & Marques, 2016).



# Patient Stories

## Blood Saves Lives When You Need It

by Steven M. Frank MD

In 1988, I was a third-year resident in anesthesiology on a weekend bike ride with my fiancé and two friends. I remember leaving the house and the next thing I knew, I was waking up after emergency surgery for removal of a ruptured spleen. What happened was a head-on collision with a car that had crossed over the center line,

causing me to bounce off the windshield, over the roof, and land in the grass unconscious. Two things saved my life that day. The first was my helmet, which was shattered and had obviously protected my head. The second was the six units of blood transfused during surgery, which were no doubt also life-saving. I was in hemorrhagic shock when I arrived by helicopter at the Maryland Shock Trauma Institute, and by my calculation over the course of that day, I lost 10 units of blood—equivalent to the total amount of blood in the average adult human body. If it weren't for donated blood, collected and tested for safety by blood centers like the Red Cross, as well as the hospital blood banks and transfusion medicine specialists, I wouldn't be here today.

Now, 32 years later, I run the patient blood management program for the Johns Hopkins Health System. At Johns Hopkins Hospital alone, we give about 70,000 units of blood components each year. I like to say that "blood saves lives when you need it, but only increases risks and costs when you don't." Determining who needs blood and how much to give is both an art and a science, and our goal is to reduce unnecessary transfusions, so we have enough left for patients like me who really need them. I was lucky because three years prior to my accident, the HIV test had been implemented to screen donor blood, but the hepatitis C test didn't launch until 1990. Now the blood industry has added new tests, such as those for Zika virus and babesiosis, to keep our blood supply safe from new and emerging pathogens. As an anesthesiologist who runs the blood management program at a major academic center, and who frequently gives blood to patients during surgery, I can't stress enough how important it is to keep our blood supply safe and plentiful, so we can continue giving life-saving blood transfusions.

### **Steven M. Frank M.D.**

Director, Johns Hopkins Health System Blood Management Program Director, Center for Bloodless Medicine and Surgery

Department of Anesthesiology/Critical Care Medicine Johns Hopkins Medical Institutions

## Basic Research Needs

Basic research needs include trauma-associated coagulopathy, optimization of transfusion therapy, and development of alternative transfusion products.

### *Transfusion in Pediatric Trauma Patients*

Trauma is a leading cause of death in children and young adults, but trauma-associated coagulopathy and its treatment are not well understood. Although we have made huge progress on the transfusion management of trauma patients, substantial gaps remain, including the best product, prehospital transfusion, and treatment in children (Kamyszek et al., 2019).

### *Platelet Transfusion and Cerebral Hemorrhage*

Platelet transfusions have proven detrimental in adults with intracerebral hemorrhage taking aspirin (Baharoglu et al., 2016) and in preterm neonates (Curley et al., 2019); however, we do not understand the best treatment of cerebral hemorrhage (stroke).

### *COVID-19–associated Coagulopathy and Endotheliopathy*

Other diseases where transfusion management and the underlying disease pathology are poorly understood include COVID-19–associated coagulopathy and endotheliopathy (Goshua et al., 2020). The mortality or life-long morbidity of both trauma and COVID-19–associated coagulopathy speaks to the urgency of research on these topics.

### *Transfusion Therapy for Individuals with Sickle Cell Disease or Other Health Disparities*

Research is urgently needed to optimize the transfusion therapy and develop innovative solutions because currently there is insufficient blood supply for those patients (DeBaun, 2020; Nickel, Margulies, Frazer, Luban, and Webb, 2020). Because of the COVID-19 pandemic, antigen-matched units are in severe shortage in parts of the country.

### *Development of Assays*

Research support is also needed for the development of assays to identify patients at highest risk of antibody formation and improved methods of antibody detection.

### ***Human-induced Pluripotent Stem Cells***

Human-induced pluripotent stem cells (iPSCs) represent an attractive source to generate in-vitro red cells, megakaryocytes, and platelets for transfusion support. While progress has been made in the past decade, challenges remain for generating terminally differentiated red cells and platelets, and at a scale that would be clinically relevant. Since iPSCs are amenable to genetic manipulation, these could provide a source of antigen-negative or human leucocyte antigen (HLA)-compatible cells for patients who are alloimmunized and for whom no donor red cell or platelet product is suitable. In-vitro–derived cells can also be manipulated to generate novel reagent red cells or platelets that would facilitate evaluation of red cell antigen or HLA/human platelet alloantigen (HPA) sensitization. Such efforts would be particularly beneficial to patients requiring chronic transfusion, including those with sickle cell disease, thalassemia, and leukemia.

## **Regulatory Needs**

### ***Adoption of Innovative Therapies Developed in Other Countries***

Innovation has been a hallmark of U.S. industry. The blood industry is no exception. While technology in transfusion medicine has advanced in other parts of the world, meaningful advances have decreased in the U.S. in the past decade. Multiple factors contribute to the decrease in the U.S., and the two most prominent ones are a lack of a coherent national blood policy and insufficient incentives for investment.

Countries with a national blood system and policy usually have a united approach to supplying blood for the public good and coordination to ensure well-executed studies and their resulting data influence blood policies. While the U.S. system is much more fragmented, a system that could evolve would focus on national policy first and then have the functions aligned accordingly.

Other factors that affect innovation in the U.S. blood industry include regulatory environment, industry consolidation, lack of objective clinical trials, fragmented distribution system, waste, obsolete reimbursement models, and lack of financial returns on risk capital because of uncertainty. Some examples might include buffy coat platelets and non DEHP ((di-(2-ethylhexyl) phthalate) blood bags. Although the buffy coat method has been shown to be superior to the platelet rich plasma method from both clinical and cost perspectives and has become a standard practice outside the U.S, public-private partnerships are needed to drive the adoption of the buffy coat method in the U.S. The second example is non-DEHP blood bags. The European Union has determined that DEHP is a potential carcinogen and mandated that it should be removed from plastic blood bags and tubing. However, the cost

and lack of financial return for removing DEHP from plastic blood bags and tubing preclude the U.S. blood industry from taking leadership on this issue. In both cases, a national blood policy is needed to offer incentives for blood centers to adopt the changes and for innovators to modify products that would benefit U.S. patients.

### ***Assessing the Impact of Regulatory Standards on Innovation***

An agile and flexible approval process, especially in the early days of a public health emergency, is needed to meet critical needs. Transparency of the approval process and collaboration between FDA and the blood industry could 1) improve the understanding of the challenges facing all stakeholders, and 2) enable all entities involved to focus efforts on removing barriers and finding solutions. The remarkable response by industry and FDA to COVID-19 illustrates what can be achieved when communication is clear (for example, about acceptable safety and tolerability of products) and when FDA and industry collaborate.

It is suggested that FDA foster innovation by using regulatory science in their processes for review of blood components, including a robust approach to communication with the blood industry regarding challenges that must be addressed.

The development of an FDA disaster/pandemic protocol is also suggested for swift implementation of FDA-authorized alternatives when HHS declares a public health emergency. Such a protocol, including effective, well-established policies, processes, and procedures, would provide a clear path to confidently respond to unexpected events with both the donor and the patient in mind.

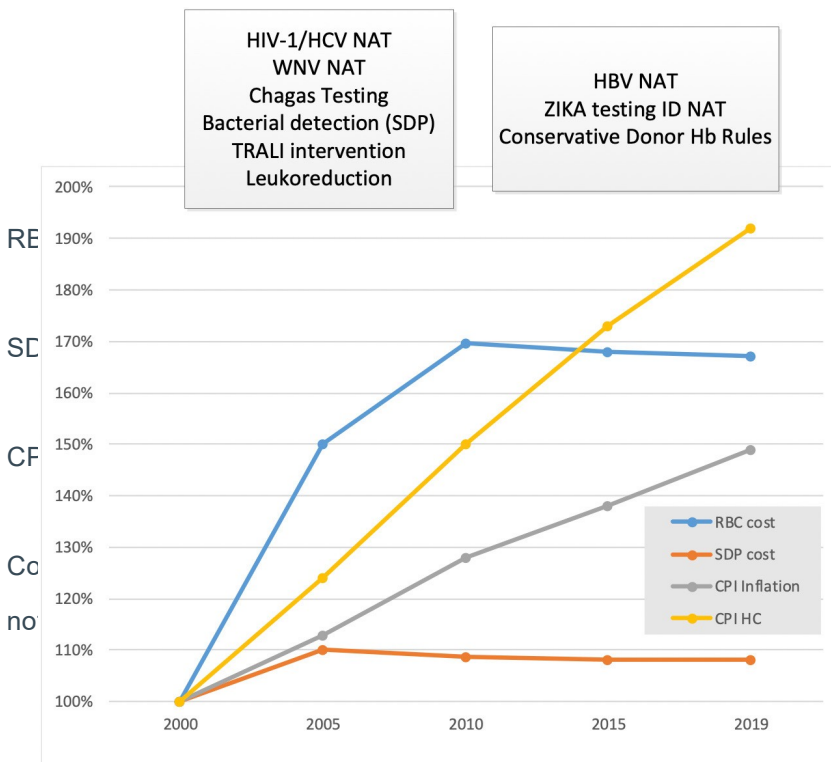
**Recommendation 6.2: Create and fund a blue-ribbon panel to address funding and reimbursement models to ensure a sustainable and innovative blood system responsive to current unmet medical needs as well as public health emergencies and other threats to the safety and availability of the blood supply and successful patient outcomes.**

### **Funding and Reimbursement Needs**

As outlined in Chapter 4 (Current Status of the U.S. Blood Supply), the current financial approach to reimbursement/payment for blood components is inadequate and does not relate to increased costs. The payment system for blood components needs to encourage public and private investments and enhance necessary improvements in safety. This must include the costs of innovation for implementing new mandated regulatory requirements for safety, for developing improved blood components, and for utilizing new blood therapies. The system must also include funding for blood centers to respond to and recover from public health emergencies so as to ensure operations without disruption.

Since 2000, there have been significant changes in requirements for blood components. The increased cost of provision has not been paralleled by appropriate increased reimbursement and was significantly lower than expected if adjusted by Consumer Price Index for Medical Care and Consumer Price Index Inflation. Figure 17 illustrates significant changes in blood component preparation and donor acceptability that have occurred since 2000. These additional safety and quality measures have not been accompanied by reciprocal increases in the acquisition costs for blood users; in contrary, the costs of blood components has remained virtually unchanged since 2010.

**Figure 17: Changes in Median Prices for Blood Components from Blood Centers to Hospitals**



Source: America’s Blood Center Price Surveys

The current model, which is primarily based on the reimbursement for transfused components to the final user, creates an incentive to negotiate the lowest price on delivery by the final user (for example, hospitals and clinics). This in turn shifts costs of blood component safety and quality to blood centers with ever-decreasing margins and the lack of investment in necessary improvements in infrastructure and research and development. The current financial status of blood centers is poor to extremely poor. The Advisory Committee on Blood and Tissue Safety and Availability, with help from the Biomedical Advanced Research and Development Authority (BARDA), ABC, and ARC, attempted to create a stress test scenario to evaluate how the current system would withstand any additional challenges. The results of this exercise are not available at this time; however, a quick analysis of tax forms submitted by the U.S. blood centers reveals a significant underfunding and undercapitalization.



Therefore, it is believed that the current financial approach to reimburse/pay for blood components is inadequate and does not relate to increased costs to ensure safety and availability of blood. Furthermore, any additional costs of new technologies are not reflected in pricing to incentivize their prompt implementation. The payment system for blood components needs to be completely overhauled to stimulate innovation, encourage public and private investments, and implement necessary improvements in safety.

There is no simple or quick solution to this problem. The creation of a blue ribbon panel, which could analyze and recommend the best and innovative reimbursement practices, would likely affect any future developments and investments in the field. There have been attempts in the past to address this issue (Advisory Committee on Blood and Tissue Safety and Availability, 2016; Fredrick, Berger, and Menitove, 2020); albeit, with no satisfying results, primarily due to regulation and complex relationships in payments for inpatient and outpatient services. However, some recommendations from these prior reports could serve as the starting point for the blue ribbon commission. Relevant recommendations from the ACBTSA have been included in Appendix E. If not addressed, the lack of innovative solution(s) in reimbursement for blood components will likely contribute to further deterioration of the current infrastructure and likely lead to inadequate preparedness to future challenges.

## Conclusion

The American public benefits from the safest blood supply in history and expects that the right blood at the right time, prescribed by informed experts in transfusion medicine, will always be there. It is our responsibility to ensure those needs are always met. Over the past decades, government, federal agencies, industry, blood centers, and the healthcare community worked together to achieve a safe and available blood supply. It is time to build upon this success and ensure the nation's blood system surmounts continuous emerging challenges through innovation and leads the world in improving patient outcomes.

The COVID-19 pandemic focused attention on the strengths and weaknesses of the U.S. blood system. The system responded rapidly, robustly, and reliably to the dramatic swings in the blood supply, from shortages to surpluses to shortages. It adapted to the dramatic redirection of venues for blood collection, from mobile blood drives to fixed-site locations. The system brought online a new product with life-saving potential, COVID-19 convalescent plasma, utilizing a public-private partnership model.

On the other hand, the pandemic exposed weaknesses that require remediation in order to address current needs and respond to future public health emergencies. These vulnerabilities include the following:

- Lack of current, real-time data for decision making.
- Uncertainty about modern business models for blood centers and appropriate remuneration for their services.
- Gaps in understanding of blood donor motivation to ensure adequate blood donations from current and future generations of blood donors.
- Barriers and an uncertain environment that stifles innovation and new technology adaptation.
- Ambiguity about the role of cost/benefit analyses in decision-making without compromising safety.

## Conclusion

We articulated solutions to these issues in our responses and recommendations related to the questions from Congress. Specifically, we request resources for the creation of task forces, blue-ribbon panels, and public-private partnerships that build on the accomplishments of the past; adequate capital investment for future infrastructure; and funding to achieve solutions that improve and sustain the U.S. blood system for current and future patient needs.

# Appendices

## Appendix A. Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019: Sec. 209. Report on Adequate National Blood Supply

Not later than 1 year after the date of the enactment of this Act, the Secretary of Health and Human Services shall submit to Congress a report containing recommendations related to maintaining an adequate blood supply, including—

1. Challenges associated with the continuous recruitment of blood donors (including those newly eligible to donate);
2. Ensuring the adequacy of the blood supply in the case of public health emergencies;
3. Implementation of the transfusion transmission monitoring system; and
4. Other measures to promote safety and innovation, such as the development, use, or implementation of new technologies, processes, and procedures to improve the safety and reliability of the blood supply.

## Appendix B. Committee and Working Group Membership

Dozens of individuals participated, either directly or indirectly, in the development of this report. The Subcommittee members express their gratitude to the subject matter experts for sharing their expertise and for members of the public, including patients, for sharing their perspectives, stories, and suggestions to help improve the quality of this report.

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# Appendices

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### Appendix C. Potential Future Studies for the Transfusion-Transmissible Infections Monitoring System (TTIMS)

#### Survey Data Collection

In addition to its current mandate of providing surveillance for U.S. blood safety related to HIV, HBV, and HCV, the current TTIMS DDCC and LRCC structure will support a wide range of future studies related to large volumes of representative blood collection organization blood component manufacturing data, targeted sampling/testing of extant blood donation samples, provision of well-defined survey and interview sampling frames for targeted and generalized survey data collection, and establishment and testing of targeted donor repositories.

1. Optimize donor survey methodology; what new tools/alternate methods are available, other than telephone, to improve our response rate? The lower than expected response rate for the risk factor interviews and the experience of other recent donor survey studies suggests that blood donors, and people in general, are increasingly less likely to respond to traditional methodologies. Other modalities such as interactive voice response (IVR) systems, online questionnaires, SMS systems or BOTs (computer-managed interaction involving “robots” without human interactions) should be considered. It would be important to have a carefully chosen control group and to bring in consultants with the requisite experience in the newer survey research methodologies.
2. Develop the capacity for donor compliance survey studies using the new modalities to assess, for example, undisclosed injection drug use (IDU), MSM, exchanging money or drugs for sex, or other deferrable behaviors.
3. Reassess approaches for rapid donor surveys (RapidDOS) using the new modalities and link this work to emerging infectious diseases (EID) studies as described below.

## Donor Health Studies

The functions of a new TTIMS Coordinating Center may include investigator- initiated studies implemented TTIMS-wide with a focus on donors, donor subpopulations, and donor experiences relevant to non-TTI aspects of blood manufacturing with a goal of improving donor safety and collection efficiency. Examples of possible TTIMS-wide initiatives include:

1. Identification, Assessment, and Evaluation of donor adverse events (donor hemovigilance).
2. Evaluation of donor iron stores and the impact of iron supplementation.
3. Consideration of acute donation reactions and possible preventive interventions.
4. Analysis of the impact of blood donation on young donors.
5. Expansion of TTIMS databases to capture other data, including deferrals, toxicology test results (for example, lead exposure), pre-donation hemoglobin values, and other measures of iron status. Analyses of these data could provide relevant findings that impact implementation of interventions, since the mitigation approaches taken by participating TTIMS organizations, and other U.S. blood collectors are different.
6. Assessment of commercial source plasma donors for biomarkers in relation to long-term and recent donation history. This is a long-needed area of study and could potentially be conducted by TTIMS through direct enrollment of source plasma donors.

## Manufacturing

Possible manufacturing studies include:

1. Multi-site clinical trial support for candidate devices used in the blood component manufacturing process.
2. Assessment of collection volume, frequency, iron in relation to donor age and gender
3. Evaluation of the impact of adoption of pathogen inactivation to changes in donor epidemiology (if any), and what changes may be acceptable for the donor history questionnaires (DHQ) or donation testing.



## Donor Recruitment

Possible donor recruitment studies include:

1. Investigation of donor knowledge, attitudes, behavior, studied through an accepted conceptual framework (barriers, incentives, peer factors, recruitment modes, etc.).
2. Social media-based research.
3. Assessment of collection dynamics and predictive modeling in relation to measurable variables, such as seasons, media events, social mood, and negative donation experiences.

## Emerging and Re-emerging Infectious Diseases (EID)

Establish the ability in real time to create a rapid response repository using the “walking repository” concept by building in a process where contemporary donor samples (both individual donation [ID] and mini-pools [MPs]) can be collected at will, as conditions emerge. This contrasts with a repository that could be built and stored for future use but with the downside that such a repository would be extremely costly and may not reflect, relative to geography or time, the emergence of a specific agent or donor epidemiologic changes.

A real-time program could be piloted for detection of arboviruses using donor samples from Puerto Rico and Florida with MPs collected during the active transmission season. Samples could be monitored by assays in development, including “arboplex” (DENV/CHIKV/ZIKV) nucleic acid testing (NAT) assays or assays for other flaviviruses. The collection of ID samples flanking epidemic periods could be evaluated for seasonal seroincidence, analogous to ongoing studies in Recipient Epidemiology and Donor Evaluation Study (REDS)-III and planned for REDS-IV-P in Brazil. Such a program would need to consider the need for dedicated repository space as well as requiring ongoing engagement and evaluation of metagenomic screening and multiplexed array-based technologies that are in development.

## Studies of Known Transfusion-Transmitted Infection (TTI)

Possible studies of known TTI include:

1. Ongoing surveillance, HIV, HBV, HCV incidence, prevalence
2. Exploration of the reasons for regional variation in prevalence/incidence observed in the first TTIMS contract cycle (for example, rates are significantly higher for HIV, HCV, and HBV markers in the Southeastern U.S.).
3. Investigation of the differences in yield between incidence methods (classic as recommended by Brambilla, Busch, Dodd, Glynn, and Kleinman [2017] and adopted by TTIMS) versus long-term methods used by ARC (extended length measurement); ARC use of 5 x 2-year periods comparing both methods have produced differing results. It will be necessary to carefully review Brambilla et al. (2017) variables used in modeling to determine possible root cause (this would be done as part of American Red Cross publication of their data). Such analyses may result in the need to consider other options of incidence calculations for TTIMS.
4. Development of HIV LAg avidity predictions of HIV recency and refinement of techniques.
5. Collection of data on the number of reentered MSM donors by participating centers as a subset of total collections and review associated marker prevalence.
6. Consideration of alternate methods of HIV, HCV and HBV incidence; IR = NAT yield/WP (Kuhns & Busch, 2006; Zou, Dodd, Stramer, Strong, & Tissue Safety Study Group, 2004).
7. Development of recency test for HBV and HCV infection. Are the methods recently developed/published by the John Hopkins University group (Boon et al., 2020; Lelie et al., 2017; Patel et al., 2016) using avidity-modified antibody maturation appropriately robust for our use, as we do for HIV recency based on the LAg assay? Or can we use S/CO ratios generated from Ab screening assays for donations that test HCV Ab+/NAT+ as a tool to measure recent infections similar to recent analyses for HIV screening assays based on wide dynamic range of chemiluminescent detection technologies.
8. Inclusion of HBsAg yield donors (HBV DNA pos/anti-HBc neg) in addition to HBV NAT yield to expand the yield of study of acute HBV-infected donors; interview all acute HBV-infected donors.
9. Assessment of PrEP/PEP and ARV use among donors. How are the performance of current donor screening and diagnostic NAT and serologic assays impacted by infected donors on PrEP or PEP or following the rapid initiation of ART? Is marker appearance/evolution suppressed when individuals who are on PrEP are nonadherent and become infected?

## Appendices

10. Development of serial sample reference panel from identified HIV, HCV, HBV yield cases.
11. Collection of data from donors/participants with HTLV infections since it is probable that changes to the HTLV algorithm (from testing all donations to only testing donors at their first presentation) will be suggested via publication moving forward; such changes have occurred in the U.K., the Netherlands, and Australia.
12. Collection of syphilis (STS) data from donors/participants to explore as a surrogate marker of high-risk sexual exposure. This would include all confirmed positives and use of RPR to define incident infections, and a proposal to interview all confirmed positives or the subset with incident infections for risk factors vs. data to support discontinuation.

## Appendix D. Transfusion Transmissible Risk

**Source:** Dodd, R.Y. Presentation to the Advisory Committee on Blood and Tissue Safety and Availability, August 26, 2020.

## Appendix E. Selected ACBTSA Recommendations

### November 2016 ACBTSA Recommendations

Federal oversight should proactively address the competing forces within the blood system. This includes:

- Ensuring appropriate financial remuneration for infrastructural support to maintain a sustainable and resilient blood supply
- Collecting data in a timely manner to help to drive policy and resource utilization
- Provide sufficient support for technological innovation with respect to resource sharing and institution of new safety measures as appropriate.

Specific Recommendations:

- Prioritize a review of these findings and develop policies to address the listed vulnerabilities in a timely and expeditious manner.
- Examine models of risk based decision making to inform future public policy to include all stakeholders in the vein to vein process from donor to patients and their families, and including all intermediaries, (e.g., blood centers, hospitals, clinicians, medical device developers).
- Develop mechanisms to encourage hospitals and blood centers to participate in data collection programs; this should include collection, utilization, and cost; the Secretary should convene a panel of stakeholders to suggest appropriate data elements.
- Explore the potential for direct payment to blood centers to cover the costs of the infrastructure required to maintain adequate supplies for the public good.
- Reduce regulatory uncertainty with respect to innovations to encourage investment in their development and implementation.

### September 2020 ACBTSA Recommendations

#### *Focus Area 1: Governance/Locus of Authority*

Recommendation: Establish a defined locus of authority for national blood and plasma policy, the Assistant Secretary for Health, coordinating with FDA, CDC, NIH, HRSA, ASPR, CMS, DoD, VA, and those non-government organizations that provide and transfuse blood and plasma products, and develop and implement a National Blood Policy inclusive of all blood and plasma products.

#### *Focus Area 2: National Disaster Planning/Business Continuity*

Recommendation: Develop and fund a comprehensive national disaster plan for the blood and plasma supply and include in National Recovery Framework to assure coordination between private and government sectors at the Federal and State levels.

Some key issues concerning this recommendation include:

- Convene stakeholders from federal agencies, industry, and healthcare experts to develop plan, including what Congressional funding may be required to implement and support the plan.
- Ensure that blood and plasma donation, processing and product distribution are designated as critical infrastructure and essential services.
- Perform an independent after-action review of blood/plasma community and HHS response to pandemic, focusing on blood supply adequacy.
- Define role, gaps and needs in disaster response of the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism, and provide funding, as needed, to fill gaps.
- Examine adequacy of current agreements that support disaster response activities between the private and government sectors, such as with HHS, DOD

### ***Focus Area 3: Supply Chain to Produce Blood Products***

Recommendation: Develop policies and provide funding to strengthen the resiliency of the blood and plasma supply chain in order to ensure product availability to hospitals during national emergencies, to include:

- Ensure blood and plasma center employees are considered essential personnel and are federally recognized with the same designation as critical healthcare workers during national emergencies and have priority access to vaccines and to supplies that are critical for blood collection and manufacturing, including personal protection equipment (PPE).
- Appoint a representative from the blood and plasma industry to federal committees or task forces responsible for allocation of critical supplies and transportation and logistics resources during national emergencies and give priority access to transportation and delivery systems for blood and plasma centers to assure continued operations in situations where infrastructure is disrupted.
- Provide funding and assign a task force to establish a 6-month distributed national stockpile of key supplies and devices that are essential to maintain a safe and available blood supply. The storage process and resource sharing of the stockpile will be managed and coordinated by blood and plasma industry representatives, thereby ensuring currently in-use and in-dated supplies.
- Work with manufacturers of plastics, testing reagents and ancillary supplies to identify specific U.S. product codes that could be manufactured in alternative manufacturing plants and proactively work with the FDA on functional flexibility resulting in FDA approval to continue to supply products that are critical to the U.S. blood supply chain from these alternative manufacturing plants.

## ***Focus Area 4: Blood and Plasma Donor Engagement, Growth, and Research***

Recommendation 4.1: Fund social science research to generate efficient and effective strategies to engage and retain younger and more diverse blood and plasma donors.

- Support public awareness and sustainable donor engagement studies including implementation and translational science.
- Evaluate the effectiveness of monetary and non-monetary incentives.
- Evaluate the implementation of evidence-based interventions designed to engage and retain blood and plasma donors.

Recommendation 4.2: In partnership with FDA, examine and revise policies that could increase the availability of blood and plasma donors and products

## ***Focus Area 5: Data Infrastructure Solutions***

Recommendation:

Establish, implement, and fund comprehensive, sustainable, minimally burdensome infrastructure that monitors and makes available real-time data on blood availability and utilization,

Building on current infrastructure and gap analysis, develop a plan for a hemovigilance and transfusion outcomes system and determine funding mechanism.

Key attributes of such an infrastructure include:

- Being rooted in legislation and/or regulation
- Promotes improved patient outcomes
- Ensures data confidentiality
- Minimizes reporting burden by key stakeholders
- Leverages existing electronic reporting platforms
- Captures data from the maximum number of blood centers and hospitals

## ***Focus Area 6: Innovation***

Recommendation 6.1: Establish a public-private partnership to proactively explore and develop policy solutions intended to encourage innovation, promote quality and efficiencies, and advance the continued safety and availability of the blood supply.

The goals of such a partnership applied to blood products could provide for the following:

- Utilize regulatory science in the development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated blood products.
- Benefit patients by speeding the rate of important new products reaching the market by developing sound scientific and policy approaches to reduce the size and duration of pre-market clinical trials.
- Reduce time and resources needed for product development, assessment, and



review. Utilize methods to allow rapid implementation of alternative approaches to supply blood product needs as exemplified in the response to past emergency situations such as hurricane Maria, other natural disaster scenarios, or situations involving specific military product needs.

- Establish early dialogue and coordination of clinical and development efforts with CMS and other government agencies regarding reimbursement policies and decision making to speed reimbursement programs and align with real costs as exemplified in the convalescent plasma program and funding of new screening tests for emerging pathogens at blood centers.
- Increase early discussion and collaboration between product developers and providers, regulatory scientists and decision makers as exemplified in the INTERACT program approach used by FDA for medical products.

Recommendation 6.2: Establish training and education workshops to instruct the general healthcare community on appropriate approaches and processes to use for regulatory approvals for the use of blood products (existing and new) under EUA, EAP and other appropriate approval mechanisms.

### ***Focus Area 7: Finance***

Recommendation: Identify and secure stable funding sources and mechanisms to support the national blood system in order to cover (but not be limited to) the following initiatives:

- Innovation that has the potential to improve the safety, efficacy, or reliability of the blood supply.
- Creation of redundant capacity in the blood system to reduce risk of blood product or critical supply shortages.
- Implementation of new mandated regulatory requirements that improve blood safety.
- Urgent financial needs of blood centers during national emergencies (e.g., the CARES Act).

## Appendix F. Acronyms and Abbreviations

<b>AABB</b>	Formerly the American Association of Blood Banks
<b>ABC</b>	America's Blood Centers
<b>ACBTSA</b>	Advisory Committee on Blood and Tissue Safety and Availability
<b>ARC</b>	American Red Cross
<b>ASH</b>	Assistant Secretary for Health
<b>ASPR</b>	Assistant Secretary for Preparedness and Response
<b>BCA</b>	Blood Centers of America
<b>CCP</b>	COVID-19 convalescent plasma
<b>CDC</b>	Centers for Disease Control and Prevention
<b>DoD</b>	U.S. Department of Defense
<b>FDA</b>	U.S. Food and Drug Administration
<b>HHS</b>	U.S. Department of Health and Human Services
<b>HRSA</b>	Health Resources and Services Administration
<b>NBCUS</b>	National Blood Collection and Utilization Survey
<b>NMDP</b>	National Marrow Donor Program
<b>NHSN</b>	National Healthcare Safety Network
<b>NIH</b>	National Institutes of Health
<b>OPTN</b>	Organ Procurement and Transplantation Network
<b>PHI</b>	Protected health information
<b>TTI</b>	Transfusion-transmissible infections
<b>TTIMS</b>	Transfusion-Transmissible Infections Monitoring System
<b>UNOS</b>	United Network for Organ Sharing

## Appendix G. References

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