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July 10, 2025

The Honorable Robert F. Kennedy, Jr.
Secretary
U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Submitted via https://www.regulations.gov

Re: Docket AHRQ-2025-0001: Request for Information (RFI): Ensuring Lawful Regulation and Unleashing Innovation to Make America Healthy Again

Dear Secretary Kennedy:

America's Blood Centers (ABC) is the national organization bringing together community-based, independent blood centers. Our member organizations operate more than 700 blood collection sites in more than 1,100 communities, providing close to 60 percent of the U.S., and a quarter of the Canadian, blood supply. These blood centers serve more than 150 million people and provide blood products and services to more than 3,500 hospitals and healthcare facilities across North America. All ABC U.S. members are licensed and regulated by the U.S. Food and Drug Administration (FDA).

HHS is seeking information on ways to deregulate the federal government, including the identification of regulations and guidance that impose undue burdens and significant costs on private parties that are not outweighed by public benefits. ABC appreciates the opportunity to provide comments and recommendations regarding unnecessary regulation that pose undue burdens on both FDA and blood centers.

Unnecessary regulation has at times decreased the availability of blood products while increasing costs without any commensurate increase in safety. Unnecessary and outdated regulations add operational complexity, limit innovation, or otherwise fail to enhance the safety and adequacy of the blood supply. Additionally, unnecessary regulation poses a significant burden on the FDA, ultimately generating unnecessary work for an agency. We encourage HHS to evaluate current and future regulations, and we have provided our recommendations on regulations and guidance that should be modified or repealed below.

Priority I: ABC Recommends Reducing Undue Burdens Imposed on Both FDA and Blood Centers by Amending FDA Guidance for Industry Regarding Licensing Requirements for Blood Centers

A. Background

Every two seconds, someone in America requires a blood transfusion, and each day, over 42,000 units of red blood cells, platelets, and plasma are used by patients. Blood centers frequently open additional sites

to meet the demand for blood products and ensure a safe and available blood supply is always available to meet patient needs.

However, as blood centers adapt to the needs of blood donors and the patients they serve, government regulations impose unnecessary and burdensome barriers to a safe and available blood supply. Outdated regulations currently govern the collection of automated (apheresis) blood products at new donation sites.

FDA regulations require licensed establishments to report changes to their approved biologics license applications (BLA) in accordance with 21 CFR 601.12. FDA's *Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods* provides guidelines specific to platelets collected by automated methods and resuspended in plasma, referred to as "Platelets, Pheresis," and includes requirements for reporting changes to an approved BLA specific to the manufacture of Platelets, Pheresis (also known as Apheresis Platelets). Under the Guidance, FDA's *Guidance for Industry: Recommendations for Collecting Red Blood Cells by Automated Apheresis Methods* provides guidelines specific to collecting single and double units of Red Blood Cells (RBC) as well as collection of co-components. Under both guidances, FDA states that the implementation of automated collection is a change that has substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a product, requiring the submission of a supplement to the blood center's BLA, and receipt of approval by FDA prior to interstate distribution of the product (21 CFR 601.12(b)).

As a result of these requirements, each time a new donation site is opened, a blood center must go through an extensive licensure process to add the new site to their existing Biologics License Application (BLA). This process can take more than a year, despite the new site using the same Standard Operating Procedures (SOPs), devices, and standardized staff training as their primary licensed facility. Additionally, as part of this licensure process, blood centers must provide two months of quality control data. This data must be submitted even though the medical device manufacturers are already required to perform mandatory validation testing to receive 510K clearance and approval for their devices, and blood centers must also conduct full validation of the collection process prior to implementing routine collections. Requiring two months of quality control data in addition to these validation requirements is duplicative, unnecessary, and burdensome, both for blood centers who must provide the data, and the FDA, who must review the data.

The substantial manufacturing steps required after collection, including infectious disease and bacterial detection testing, product modification, final labeling, and storage, all occur at the manufacturing site. The manufacturing site is typically the site holding the BLA for the manufacturing of all products collected by a blood center. With new locations opening quite frequently across the country, this unnecessarily delays the availability of blood for patients when and where it is needed and largely duplicates the review the FDA has already undertaken.

While these requirements may have been reasonable as new technology was established, they are no longer reasonable or necessary, and they impose undue burdens on blood centers and FDA. The safety history of the use of automated (apheresis) devices demonstrates that facilities can collect apheresis products at new fixed site locations, as well as mobile collection sites (e.g., a blood drive bus parked in a parking lot) without adversely impacting donor safety.

Due to this safety history, the need to ensure the availability of blood and blood components for patients, and the need for blood centers to be able to quickly fully utilize these additional collections, ABC recommends that FDA allow the implementation of all types of apheresis product collections at new fixed site locations, as a minor change, requiring only a description in the blood center's annual report. The implementation of apheresis product collections should be allowed as a minor change provided the

primary facility is already approved for the apheresis product they seek licensure for. While FDA always has the ability to inspect any licensed site, an inspection should not be required as a precursor to licensure.

B. Recommendation to Reduce Undue Burden and Significant Costs

Minimizing the duplicative data currently required by FDA and allowing the immediate implementation of all types of apheresis product collections at new fixed site locations would not only ensure a safe and available blood supply but also minimize the administrative burdens FDA currently faces.

C. Proposed Changes to FDA Guidance for Industry

To reduce the undue burdens associated with licensure requirements on both FDA and blood centers, ABC recommends the following:

i. Amend the FDA Guidance for Industry: Recommendations for Collecting Red Blood Cells by Automated Apheresis Methods as follows:

Section VI. Registration and licensing procedures for the manufacture of red blood cells collected by automated methods (p. 7). In the second paragraph of this section, insert the language italicized and bolded below:

"The implementation of automated RBC collection is a change that has substantial potential to have an adverse effect on the identity, strength, quality, purity or potency of a product. Blood establishments holding a biologics license application that intend to manufacture double RBC units and/or single unit of RBC plus platelets and/or plasma by automated methods must submit a supplement to their biologics license application and receive approval by FDA for each of these products prior to interstate distribution of the product [21 CFR 601.12(b)]. ***However, provided the blood establishment's primary facility is already approved for the automated apheresis product they seek licensure for, the implementation of automated RBC collection at the blood establishment's new fixed site locations is a minor change, requiring only a description in the blood center's annual report and need not receive approval prior to distribution of the product. [21 CFT 601.12(d)].*** Blood establishments that are approved to manufacture RBC using one manufacturer's device and wish to change to another manufacturer's device must also submit a supplement and receive approval prior to distribution of the product manufactured on the new device [21 CFR 601.12(b)]."

ii. Additionally, ABC recommends amending the FDA Guidance for Industry: Collection of Platelets by Automated Methods as follows:

Section X. Reporting changes to an approved biologics license application (BLA). A. Prior Approval Supplement (PAS): Changes Requiring Supplement Submission and Approval Prior to Distribution of the Product Made Using the Change (Major Changes) (21 CFR 601.12(b)) (p. 23). In the second bullet of this section, insert the language italicized and bolded below:

"Under 21 CFR 601.12(b), changes that have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product must be reported to FDA in a Prior Approval Supplement (PAS).

Under this standard, the following kinds of manufacturing changes would fall within this category, warranting submission of your request to implement the following changes to your approved BLA as a PAS:

• if you currently hold an unsuspended, unrevoked BLA to manufacture blood components other than Platelets, Pheresis, and you intend to manufacture and distribute Platelets, Pheresis under that license.

• if you are currently approved to manufacture Platelets, Pheresis at a specific facility, and you intend to manufacture Platelets, Pheresis at a different facility, not under an approved Comparability Protocol. To submit a request for a Comparability Protocol see below. ***However, provided the blood establishment's primary facility is already approved for the automated apheresis product they seek licensure for, the manufacture of Platelets, Pheresis at the blood establishment's new fixed site locations is a minor change, requiring only a description in the blood center's annual report and need not receive approval prior to distribution of the product. [21 CFR 601.12(d)]***"

Priority II: ABC Recommends Eliminating the Surface Antigen Testing Requirement for Hepatitis B.

A. Background

In addition to streamlining the licensure process, there are steps FDA can take to deregulate and streamline processes to support a robust and available blood supply and reduce undue burdens on blood centers. FDA should apply evidence-based decision making to its testing requirements to ensure testing burdens are justified by commensurate increases in safety and eliminating current FDA testing requirements that do not have appropriate safety justifications. We believe this will lead to the elimination of the hepatitis B surface antigen (HBsAg) testing requirement.

Hepatitis B is a liver infection that can result in acute or chronic disease. It is caused by the hepatitis B virus (HBV) and can be spread through bodily fluids, including blood. In 1970, to protect the blood supply and avoid transfusion transmission, the United States began testing donated blood for HBsAg, which is produced during active and chronic HBV infections. Testing for antibody to hepatitis B core antigen (anti-HBc) was voluntarily implemented in 1987, with licensed anti-HBc testing mandated in 1991. FDA Guidance requiring nucleic acid testing (HBV NAT) was finalized in October 2012.

Testing to reduce or eliminate the transfusion transmission of HBV is important and must be continued. While the HBsAg test represented the most advanced screening tool when introduced, current testing technology has rendered this test duplicative. Today's more sensitive and specific assays, specifically HBV NAT and anti-HBc, provide superior detection capabilities, making the continued reliance on HBsAg testing unnecessary. The continued inclusion of the HBsAg test does not further increase safety over the two remaining HBV tests and should be eliminated.

HBV NAT testing can detect infection up to 11 days sooner than when only HBsAg and anti-HBc had been used for this purpose.[1] Accordingly, the residual risk of HBV transfusion-transmission has dropped from approximately 1 in 200,000 units prior to the use of HBV-NAT to around 1 in 3 million units at this time.[2] In 2013, Stramer et al.'s analysis of HBV testing data from almost 13 million US-based donations

[1] Kleinman SH, Strong DM, Tegtmeier GGE, et al. Hepatitis B virus (HBV) DNA screening of blood donations in minipools with the COBAS AmpliScreen HBV test. Transfusion 2005; 45:1247-1257.
[2] Dodd R. Landscape of infectious disease risk. Advisory Committee on Blood and Tissue Safety and Availability. 2018.

demonstrated no confirmed HBV-infectious units containing HBsAg that would have been "missed" by routine testing for HBV-NAT and anti-HBc alone.[3] Dodd et al.'s extension of this analysis, performed on an additional 22.4 million donations and published in 2018, revealed the elimination of HBsAg screening would have a negligible deleterious impact – i.e., an increased risk of new HBV transfusion-transmissions of less than 1 per 4 million donations.[4] More recently, a study from the Netherlands further supports the view that HBsAg testing no longer enhances blood safety.[5]

Additionally, a study of the incremental cost-utility of NAT after implementation of serology screening has prompted the need for reevaluation of the current test strategy.[6] At an estimated cost of $1.00 to $1.50 per HBsAg test, this represents a cost of approximately $15MM to $22.5MM annually.[7]

B. Recommendation to Reduce Undue Burden and Significant Costs

The HBsAg testing requirement for hepatitis B virus for whole blood and blood components intended for transfusion should be removed. FDA was poised to eliminate this testing requirement in 2020, and the Blood Products Advisory Committee (BPAC) was scheduled to meet April 2-3, 2020 to discuss the discontinuation of the HBsAg requirement. However, the meeting was postponed, and when it ultimately occurred, it did not address the elimination of HBsAg. As a result, this test is still required. HBsAg testing is one of three tests currently required for hepatitis B virus (HBV). Each of these three tests was added as new testing technology became available, however, the need for the older technology test was not reexamined. The HBsAg test does not increase transfusion safety, is outdated, and incurs significant costs. Other required testing methods have proven to be highly effective in identifying HBV risk in donors for years. ABC recommends discontinuing HBsAg testing, with the retention of NAT and anti-HBc to detect acute, chronic, and occult HBV infections.

C. Proposed Changes to FDA Guidance for Industry

To reduce undue and unnecessary burdens, and the significant costs associated with the HBsAg testing requirement, ABC recommends revising the FDA Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components, Including Source Plasma, to Reduce the Risk of Transmission of Hepatitis B Virus as follows:

i. Reissue the Guidance with the removal of the HBsAg testing requirement for Whole Blood and blood components intended for transfusion.

Priority III: ABC Recommends the Alteration of HTLV-I/II Testing to One-Time Testing for Donors of Whole Blood and Blood Components Intended for Transfusion in the U.S.

[3]Stramer SL, Notari EP, Krysztof DE, et al. Hepatitis B virus testing by minipool nucleic acid testing: does it improve blood safety? Transfusion 2013; 53:2449-58.

[4] Dodd RY, Nguyen ML, Krysztof DE, et al. Blood donor testing for hepatitis B virus in the United States: is there a case for continuation of hepatitis B surface antigen testing? Transfusion 2018; 58:2166-70.

[5] van de Laar TJ, Hogema BM, Molenaar-de Backer MW, et al. Blood donor screening in the Netherlands: Universal anti-HBc screening in combination with HBV nucleic acid amplification testing may allow discontinuation of hepatitis B virus antigen testing. Transfusion 2021;1-9. https//doi.org/10.1111/trf.16420.

[6] Janssen, MP, van Hulst M, Custer B, et al. An assessment of differences in costs and health benefits of serology and NAT screening of donations for blood transfusion in different Western countries. Vox Sang 2017; 112(6):518-525.

[7] Katz LM and Sayers M. Donor screening for hepatitis B: hepatitis B surface antigen – a belt, suspenders, and another belt? Transfusion 2018; 58:2087-2091.

A. Background

Human T-lymphotropic virus types I and II (HTLV-I/II) are retroviruses transmitted from mother to child at birth and/or via breast milk, sexually (with more efficient transmission from male to female), and through intravenous drug use and other blood exposure. HTLV-I/II may also be transmitted via transfusion of cellular blood components but has not been demonstrated to be transmitted by plasma.

HTLV is a strict intraleukocytic agent. Therefore, leukoreduction is highly efficient at preventing transmission from cellular blood components containing residual lymphocytes. In addition to donor antibody testing, transfusion transmission mitigation strategies also include use of pathogen reduction technology (PRT) for platelet components. Lastly, transmission is markedly reduced or eliminated following refrigerated storage for approximately 10 days.

On March 25, 2025, ABC submitted a joint comment letter to FDA requesting the change to a one-time testing requirement. The letter contains additional information on relevant studies and supportive experience outside of the United States.

B. Recommendation to Reduce Undue Burden and Significant Costs

The HTLV-I/II antibody testing requirement at each donation of whole blood and blood components intended for transfusion should be revised based on: (1) the declining prevalence of HTLV-I/II infection in US blood donors; (2) the low incidence observed among US repeat blood donors; (3) the low likelihood of infection and disease in individuals receiving HTLV-I/II antibody-reactive Whole Blood and blood components, (4) the efficacy of leukoreduction in reducing the infectivity of HTLV-I/II antibody-reactive donations, and (5) the use of effective pathogen reduction technology (PRT) for some platelets.

C. Proposed Changes to FDA Guidance for Industry

To reduce undue and unnecessary burdens, and the significant costs associated with HTLV-I/II testing, ABC recommends revising the FDA Guidance for Industry: Use of Serological Tests to Reduce the Risk of Transfusion-Transmitted Human T-Lymphotropic Virus Types I and II (HTLV-I/II) as follows:

i. Reissue the Guidance to require one-time donor testing for antibodies to HTLV-I/II coupled with effective leukoreduction in donations of whole blood and blood components intended for transfusion.

Priority IV: ABC Recommends FDA Withdraw the Malaria Draft Guidance and Ensure there are no Requirements for Malaria Testing of Blood Donations at this Time.

A. Background

In January 2025, FDA published the Draft Guidance for Industry: Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria. On March 13, 2025, ABC submitted a joint comment letter to FDA. In the letter, we stated: "Until FDA performs real world modeling studies to determine the sensitivity of available tests, including studies performed in malaria-endemic locations, and including data on semi-immune donor populations, an option to continue the present TTM risk reduction questioning without testing is necessary to ensure any testing burden is justified by a commensurate increase in safety. We note that the current deferral policy is extremely effective, and testing requirements add significant financial costs for blood centers without providing a significant increase in safety. Furthermore, there is currently only one malaria test approved for screening of the blood supply. Without an alternative, supply

chain challenges could adversely impact blood availability. Therefore, we believe that FDA should ensure multiple tests are available prior to creating any new testing requirements."

B. Recommendation to Reduce Undue Burden and Significant Costs

To prevent undue burden and significant costs that would result from implementation of the malaria draft guidance, ABC strongly recommends that FDA withdraw the draft guidance.

C. Proposed Withdrawal of FDA Draft Guidance for Industry

ABC strongly recommends that FDA withdraw the malaria draft guidance and ensure there are no requirements for malaria testing of blood donations at this time.

Priority V: ABC Recommends Lowering the U.S. Platelet Content Requirement (PCR)

A. Background

To reduce unnecessary and burdensome regulation, support innovation and blood product availability, and increase platelet availability for patients, FDA should lower the U.S. PCR, the minimum number of platelets per unit, to expand platelet supply availability and align with international standards.

Platelets are cells in blood that form clots to help stop bleeding. They are used to stop or avoid massive bleeding for cancer patients, patients undergoing major surgery, and trauma victims. They are collected either as a part of whole blood donation or through platelet apheresis, the use of a special machine that separates platelets into a collection bag and returns all other blood components back to the donor.

When apheresis technology was initially adopted in 1972, the FDA set the minimum PCR of 3×10^{11} platelets per unit, which remains the current standard. This was not derived from clinical effectiveness studies but instead came from the average total number in a pool of platelets from six whole blood donations, which was the standard way platelets were provided before apheresis technology was available.

The United States (US) has a minimum PCR higher than Canada and most European Union (EU) nations (which range from 2.0 to 2.5×10^{11} platelets).[8] Harmonization of the US with EU minimum PCR will increase the number of platelet units available without negatively impacting patient care.

A lower PCR generally does not correlate with a patient needing more platelet transfusions. Clinical trials in the US, including the Platelet Dose Study (PLADO), and elsewhere have demonstrated acceptable clinical effectiveness of a lower PCR for the prevention of bleeding in thrombocytopenic hematology-oncology patients (patients who do not produce enough platelets because of their cancer or its treatment).[9] One apheresis platelet donation, if large enough, can be split into multiple units. By increasing the number of donations eligible to split, reduction of the PCR will allow blood collection facilities to increase the number of platelet units produced.[10] An analysis of two large blood center databases of 5,805

[8] EDQM. Guide to the preparation, use and quality assurance of blood components. 19th ed. Available at https://www.edqm.eu/en/blood-guide. Accessed 10 Feb. 2020.
[9] Shlichter SJ, Kaufman RJ, Assmann SF, et al. Dose of prophylactic platelet transfusions and prevention of hemorrhage. *N. Engl. J. Med* 2010; 362:600-13.
[10] Benjamin RJ, Katz L, Gammon RR, Stramer SL, Quinley E. The argument(s) for lowering the US minimum required content of apheresis platelet components. *Transfusion* 2019; 59: 779-88.

apheresis platelet units suggested this change in PCR had the potential for a 21 to 23 percent increase in platelet units produced, without changes to collection procedures.[11]

Regarding the impact on donors, a lower PCR would allow for a reduction in the number of platelets collected from some donors without reducing the platelet units available. Donors may experience shorter collection times. Longer collection times increase the risk of donor adverse events (AE),[12] and decrease donor satisfaction. Donors who suffer AE are less likely to return to donate, so the strategy of shorter collection times could reduce the risk of intermittent shortages by increasing donor satisfaction and donor retention.[13]

Regarding the impact on patients, the contemporary size of a platelet pool is four to six units (2.2 to 3.0 $x10^{11}$ platelets); with no appreciated impact on clinical efficacy. Platelets collected from whole blood donations have been safely used for transfusion both before and after apheresis platelets became available. Similarly, there are no differences in the rate of transfusion reactions. Most studies have concluded the equivalency in apheresis platelets and pooled platelets.[14,15]

While the research supports the safety and efficacy of a range of platelet dosages, reducing the minimum PCR to 2.5 x 10^{11} is a conservative approach which will increase platelet availability to address anticipated increased demand without compromising patient safety.

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce unnecessary and burdensome regulation, support innovation and blood product availability, and increase platelet availability for patients, FDA should reduce the minimum PCR from 3 x 10^{11}/unit to 2.5 x 10^{11}/unit to expand platelet supply availability and align with international standards.

C. Proposed Changes to FDA Guidance for Industry

As such, ABC recommends amending the FDA Guidance for Industry: Collection of Platelets by Automated Methods as follows:

i. Section VI. Validation of the collection process. D. Product performance qualification for component collection process (p. 10). "Actual platelet yield" bullet. Strike the language below as indicated, and insert the language italicized and bolded below:

"actual platelet yield (platelet count multiplied by the volume):

- determine actual platelet yield at collection.
- follow the platelet pre-donation count recommendations in section III.B.1., and set an appropriate target platelet yield as recommended by the automated blood cell separator device manufacturer to maximize the likelihood that each transfusable component contains ≥ ~~3.0 x 10^{11}~~ ***2.5 x 10^{11}*** platelets and the target collection type (single, double, triple) is achieved."

[11] Id.

[12] Id.

[13] Id.

[14] Whitaker BI, Rajbhandary, S, and Harris A. The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report, AABB, December 18, 2015.

[15] Tormey CA, Sweeney JD, Champion MH, Pisciotto PT, Snyder EL, Wu Y. Analysis of transfusion reactions associated with prestorage-pooled platelet components. Transfusion 2009; 49(6):1242-7. doi: 10.1111/j.1537-2995.2009.02128.x.

ii. Table 1, (p.13), Product performance qualification criteria for the platelet component collection process, row 2, actual platelet yield of transfusable component, recommended results:

Replace ≥ 3.0 x 10^{11} with ***2.5 x 10^{11}***

iii. Section VII. Quality assurance and monitoring. A. Standard operating procedures (SOPs) and recordkeeping. 2. Additional provisions applicable to SOPs (p. 16). "Labeling" bullet. R Strike the language below as indicated, and insert the language italicized and bolded below:

"Labeling:

- The final component volume stated on the label should be determined after removal of samples for platelet count determination, QC, and/or bacterial contamination testing.
- Platelets, Pheresis for transfusion should routinely contain > ~~3.0 x 10^{11}~~ ***2.5 x 10^{11}*** platelets. When special circumstances warrant their use, Platelets, Pheresis components containing less than ~~3.0 x 10^{11}~~ ***2.5 x 10^{11}*** platelets should be labeled with the actual platelet content."

iv. Section VII. Quality assurance and monitoring. C. Component testing. 2. QC monitoring (p. 20). "Transfusable Platelets, Pheresis components" bullet. Strike the language below as indicated, and insert the language italicized and bolded below:

"transfusable Platelets, Pheresis components ≥ ~~3.0 x 10^{11}~~ ***2.5 x 10^{11}*** platelets."

v. Section IX. Labeling (p. 22). Second bullet. Strike the language below as indicated, and insert the language italicized and bolded below:

"Platelets, Pheresis components for transfusion, containing less than ~~3.0 x 10^{11}~~ ***2.5 x 10^{11}*** platelets per storage container, should be labeled with the actual platelet content."

Priority VI: ABC Recommends Allowing Blood Centers to Convert Plasma from Transfusable to Further Manufacture Without Requiring Expiration

A. Background

FDA should allow blood centers to convert recovered plasma collected through apheresis from transfusable to further manufacture, without requiring expiration, for more effective blood inventory management and to avoid product wastage.

Blood centers collect blood through whole blood donation (volunteer donor's blood collected directly into a blood bag and the blood components are separated at the blood center); and apheresis (volunteer donor's blood collected through a machine that separates the blood components at the point of donation). Both methods employ identical donor screening and produce plasma for patient transfusion. Plasma derived from whole blood donations that is not needed for transfusion may be acquired by fractionators to create essential products such as Factor VIII concentrate, immunoglobulin, and albumin. Apheresis plasma is identical to whole blood plasma, yet the FDA requires apheresis plasma that is not transfused to expire before it can be used for fractionation. Expiration occurs one year from the date of collection. Expired plasma cannot be used for fractionation into protein therapy products for patients; instead, it may only be used to manufacture diagnostic products.

The United States blood supply depends on dedicated donors to provide a consistent source of blood components of the various blood types. Blood centers are experts in managing inventory to ensure that every donation that can be utilized is utilized with minimal wastage. However, it is never possible to exactly meet demand, while being prepared for any emergency, without some excess products. Additionally, hospital demand changes as the needs of their patients change. As a result, blood centers at times may have products not required for current transfusion needs. Donors intend their blood to be used to save a life or reduce the pain and suffering of others. Every blood component should be used for this purpose before it expires. In addition, using all components from one donor is the most cost-effective method of collecting and processing. At the same time, plasma fractionators that utilize plasma to manufacture medications would be able to utilize any excess plasma. As long as there is a surplus of transfusable plasma, recovered plasma should not be left to expire and risk being wasted, but instead should be used for life-saving therapeutics.

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce burdensome, unnecessary, and wasteful requirements, and for more effective blood inventory management, FDA should allow blood centers to convert plasma collected through apheresis to meet anticipated demand, from transfusable to recovered plasma for further manufacturing, without requiring expiration.

C. Proposed Changes to FDA Requirements

ABC recommends that FDA eliminate the current expiration requirement and allow blood centers to convert plasma collected through apheresis methods from transfusable to recovered plasma for further manufacturing.

Priority VII: ABC Recommends that FDA Allow Blood to be Held for Up to 24 Hours at Room Temperature Prior to Processing into Components

A. Background

FDA should allow blood to be held at room temperature for up to 24 hours prior to processing into components, in line with current evidence and international standards. Currently, to make platelets from whole blood, FDA requires the platelet concentrate to be separated within 4 hours of collection or within the timeframe that the blood bag's package insert indicates. In the U.S., the FDA has given clearance for up to 8 hours from collection (8 hour-hold) for the separation of platelet concentrates from whole blood.[16] However, for blood centers in the United States to practically implement alternative strategies for platelet collection, FDA should approve a 24-hour room temperature hold, as has been safely done in other jurisdictions.

Europe allows for a 24-hour hold without requiring refrigeration, as does Canada. In addition to the extensive real word data from Europe and Canada, studies show there is no significant issue with overnight hold of whole blood.[17,18] For blood centers in the United States to practically implement

[16] 21CFR640.24(b), eCFR :: 21 CFR 640.24 -- Processing.

[17] Lu FQ, Kang W, Peng Y, Wang WM. Characterization of blood components separated from donated whole blood after an overnight holding at room temperature with the buffy coat method. Transfusion 2011; 51: 2199-2207.

[18] van der Meer, P.F., Cancelas, J.A., Cardigan, R., Devine, D.V., Gulliksson, H., Sparrow, R.L., Vassallo, R.R., de Wildt-Eggen, J., Baumann-Baretti, B., Hess, J.R. and (2011), Evaluation of overnight hold of whole blood at room temperature before component processing: effect of red blood cell (RBC) additive solutions on in vitro RBC measures. Transfusion, 51: 15S-24S. https://doi.org/10.1111/j.1537-2995.2010.02959.x

alternative strategies for platelet collection, FDA must approve a 24-hour room temperature hold, as has been safely done in other jurisdictions.

In the United States, whole blood derived platelets are used to supplement platelet inventory. However, platelets cannot be refrigerated, and in many cases, 8 hours often does not allow enough time to separate platelets from whole blood to create platelet products, particularly when blood is collected at mobile collection sites that must return to the blood center for processing. With a more flexible 24-hour room temperature hold for whole blood, there would be more time to make platelet products, and more platelets in inventory for patients who need them.

For whole blood, when blood drives are held in rural areas, it is often impossible to return the blood for processing to the blood center within the 8-hour window. Additionally, the 8-hour hold requirement creates staffing issues at blood centers, as night staff must process blood that is collected in the evening. However, with a 24-hour hold, the blood would be processed by the daytime staff.

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce undue burdens associated with refrigeration requirements beyond 8 hours, and allow for the processing of more platelet products, and more platelets in inventory, FDA should allow blood to be held at room temperature for up to 24 hours prior to processing into components, in line with current evidence and international standards.

C. Proposed Changes to FDA Regulations

For the reasons noted above, 21 CFR 640.24(b) should be amended by striking the language below as indicated, and inserting the language italicized and bolded below to allow for a 24-hour hold of platelet concentrate:

> *"Immediately after collection, the whole blood or plasma shall be held in storage between 20 and 24 °C unless it must be transported from the collection center to the processing laboratory. During such transport, all reasonable methods shall be used to maintain the temperature as close as possible to a range between 20 and 24 °C until it arrives at the processing laboratory where it shall be held between 20 and 24 °C until the platelets are separated. The platelet concentrate shall be separated within ~~4[four]~~ **24** hours or within the timeframe specified in the directions for use for the blood collecting, processing, and storage system."*

Priority VIII. ABC Recommends that FDA Allow Source Plasma to be Held for Up to 24 Hours After Collection at Room Temperature Prior to Freezing

A. Background

Under current regulations (21 CFR 640.69 (b)), "immediately after filling, plasma intended for manufacturing into injectable products shall be stored at a temperature not warmer than -20 °C". This requirement is burdensome and unnecessary. The European standard allows for source plasma to be frozen within 24-hours of collection: "When obtained by plasmapheresis, plasma intended for the recovery of proteins that are labile in plasma is frozen by cooling rapidly at −30 °C or below as soon as possible and at the latest within 24 h of collection."[19] FDA should allow source plasma to be frozen up to 24 hours post collection, in line with international standards.

[19] European Pharmacopoeia 5.0, "Human Plasma for Fractionation," 01/2005:0853, corrected, p. 1746.

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce undue and unnecessary burdens, FDA should allow source plasma to be held at room temperature for up to 24 hours prior to freezing, in line with international standards. The 24-hour hold is more flexible for blood centers' operation, as they can use staff more efficiently in manufacturing plasma (e.g. they can batch plasma and freeze it all at the same time instead of one at a time as it is collected). Additionally, a 24-hour hold is more effective for blood inventory management.

C. Proposed Changes to FDA Regulations

To this end, ABC recommends amending 21 CFR 640.69 (b) by striking the language below, as indicated, and inserting the language italicized and bolded below to allow for a 24-hold of source plasma:

> **"**Storage. ~~Immediately after filling~~ ***Within 24 hours of filling***, plasma intended for manufacturing into injectable products shall be stored at a temperature not warmer than −20 °C, except for plasma collected as provided in § 640.74. Plasma intended for manufacturing into noninjectable products may be stored at temperatures appropriate for the intended use of the final product, provided these temperatures are included in the Source Plasma license application."

Priority IX: ABC Urges FDA to Modify the Criteria for Use of Cold-Stored Platelets (CSP)

A. Background

When published in 2023, the FDA Guidance for Industry: Alternative Procedures for Cold-Stored Platelets Intended for the Treatment of Active Bleeding when Conventional Platelets Are Not Available or Their Use is Not Practical allowed for extended use of cold-stored platelets from 3 to 14 days, a critical step forward in safely promoting increased availability and utilization of platelets for patients in need. With the newly available CHIlled Platelet Study (CHIPS data), the criteria for use of CSP should be updated to allow CSP to be used for any use, or at the discretion of the transfusing physician.

B. Recommendation to Reduce Undue Burden and Significant Costs

Particularly in rural areas, having a longer dated platelet product available when needed would significantly reduce waste of the general platelet supply, decrease costs associated with movement of products, and help ensure platelets are available when and where a patient needs them for any reason.

C. Proposal to Modify Criteria for Use of CSP

ABC urges FDA to quickly move to modify the criteria for use of CSP, based upon the data obtained from CHIPS. CHIPS has completed data collection and is expected to be published soon.

Priority X. ABC Recommends Reducing Undue Burdens Imposed on Blood Centers by Amending FDA Regulations to Allow a Physician's Designee to Perform Donor Physical Assessments for Blood Pressure and Pulse

A. Background

FDA regulation 21 CFR 630.10(f)(2) states that "the donor's systolic blood pressure must not measure above 180 mm of mercury, or below 90 mm of mercury, and the diastolic blood pressure must not measure above 100 mm of mercury or below 50 mms of mercury." However, a donor whose blood pressure measures "outside these limits may be permitted to donate only when the responsible physician examines the donor and determines and documents that the health of the donor would not be adversely affected by donating."

Similarly, 21 CFR 630.10(f)(4) states that a donor with a pulse that falls outside of the prescribed 50 and 100 beats per minutes "may be permitted to donate only when the responsible physician determines and documents that the health of the donor would not be adversely affected by donating."

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce undue and unnecessary burdens, FDA should allow a qualified physician's designee to perform a donor physical assessment and documentation for blood pressure and pulse, when a donor's measurements fall outside of the required measurements, to determine whether a donor is permitted to donate. Allowing a qualified physician's designee to perform these functions would maintain the health of the donor, while allowing the physician to perform other essential clinical and medical functions of blood collection and patient safety oversight. It is not necessary to call the physician for otherwise healthy donors with a pulse or blood pressure out of acceptable range. This donor safety issue has been handled well historically, and centers should be permitted to establish their standard operating procedures (which are subject to FDA review and approval) to evaluate these donors without physician approval at each donation. (eg. an otherwise healthy donor receiving beta blockers). Current requirements result in wasted donor and staff time and preventable loss of valuable blood products.

C. Recommended Changes to FDA Regulations

For the reasons noted above, ABC recommends that 21 CFR 630.10(f)(2) and 21 CFR 630.10(f)(4) be amended by inserting the language italicized and bolded below to allow an individual designated by the responsible physician to perform the task:

i. 21 CFR 630.10(f)(2)

> *"Blood pressure.* The donor's systolic blood pressure must not measure above 180 mm of mercury, or below 90 mm of mercury, and the diastolic blood pressure must not measure above 100 mm of mercury or below 50 mms of mercury. A donor with measurements outside these limits may be permitted to donate only when the responsible physician***, or a qualified individual designated by the responsible physician,*** examines the donor and determines and documents that the health of the donor would not be adversely affected by donating."

ii. 21 CFR 630.10(f)(4)

> *"Pulse.* The donor's pulse must be regular and between 50 and 100 beats per minute. A donor with an irregular pulse or measurements outside these limits may be permitted to donate only when the responsible physician***, or a qualified individual designated by the responsible physician,*** determines and documents that the health of the donor would not be adversely affected by donating."

Priority XI. ABC Recommends Reducing Undue Burdens Imposed on Both FDA and Blood Centers by Developing a Pre-Approved Variance Process for Operational Changes at Blood Centers

A. Background

FDA processes for variances are lengthy and burdensome, even for minor modifications. Under current alternative procedure regulations (21 CFR 640.120(a)):
"(a) The Director, Center for Biologics Evaluation and Research, may issue an exception or alternative to any requirement in subchapter F of chapter I of title 21 of the Code of Federal Regulations regarding

blood, blood components, or blood products. The Director may issue such an exception or alternative in response to:

(1) A written request from an establishment. Licensed establishments must submit such requests in accordance with § 601.12 of this chapter;

(2) An oral request from an establishment, if there are difficult circumstances and submission of a written request is not feasible. Establishments must follow up such oral request by submitting written requests under paragraph (a)(1) of this section within 5 working days."

B. Recommendation to Reduce Undue Burden and Significant Costs

A pre-approved variance process would not only remove unnecessary administrative burdens for blood centers, but also minimize the administrative burdens FDA currently faces.

C. Recommendation to Develop a Pre-Approved Variance Process

ABC recommends that FDA develop a pre-approved framework for commonly requested variances or alternative procedures to expedite innovation and pilot testing.

Priority XII. ABC Recommends that FDA Allow the Determination of Donor Eligibility within 24 Hours Before Collection

A. Background

FDA regulation 21 CFR 630.10(c) requires that blood centers "must determine donor eligibility on the day of donation." This means that a donor can fill out the donor questionnaire at 1:00 a.m. and donate at 11:00 p.m. that same day. However, the donor is not permitted to fill out the questionnaire at 11:00 p.m. and donate at 6:00 a.m. the next day. There is no reason for FDA to allow one and not the other. Many centers are moving to an internet computer assisted self-interview process, which allows a donor to answer the donor questionnaire before arriving at the blood center. Current requirements do not allow a donor to fully utilize this technology, resulting in loss of product and wasted donor and staff time.

B. Recommendation to Reduce Undue Burden and Significant Costs

To reduce undue burdens associated with the determination of donor eligibility, FDA should allow the determination of donor eligibility within 24 hours before collection.

C. Recommended Changes to FDA Regulations

For the reasons noted above, 21 CFR 630.10(c) should be amended by striking the language below as indicated, and inserting the language italicized and bolded below to allow for the determination of donor eligibility within 24 hours before collection:

"When must you determine the eligibility of a donor? You must determine donor eligibility ~~on the day of donation, and~~ ***within 24 hours*** before collection."

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ABC appreciates the opportunity to comment on the RFI. If you have any questions or require additional information, please contact Justine Coffey, Director of Regulatory Affairs and Public Policy (jcoffey@americasblood.org).

Sincerely yours,

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Chief Executive Officer