



November 27, 2023

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Proposed Rule: Medication Guides: Patient Medication Information (Docket No. FDA-2019-N-5959)

Dear Dr. Califf,

The Association for the Advancement of Blood & Biotherapies (AABB), America's Blood Centers (ABC), and the American Red Cross appreciate the opportunity to submit comments in response to the Food and Drug Administration's proposed rule entitled "Medication Guides: Patient Medication Information" (Docket No. FDA-2019-N-5959). Collectively, our organizations represent the nation's blood collection establishments, transfusion services, and transfusion medicine professionals.

Executive Summary

Our organizations commend FDA for its important work to ensure that patients have access to information that enables them to understand the risks and benefits of prescription medicines and to use them safely and effectively when dispensed in an outpatient setting. Additionally, our organizations support providing patients with information that helps them make better healthcare decisions, and that informs them about potential side effects, when to notify a provider, or when to follow-up with a provider after receiving a blood transfusion.

We encourage FDA to exclude blood and blood components from the PMI requirements because we have identified more efficient and effective options to deliver PMI, which can use the existing processes and framework to support the intended goals and outcome. Additionally, we believe FDA should exclude blood and blood components from PMI since (1) patients receive information on the risks associated with blood transfusions, and are provided with the ability to ask questions, decline transfusion or select alternative treatment options, through the informed consent process; (2) blood and blood components are *always* transfused by a healthcare professional; and (3) PMI for blood and blood components will not achieve the intended results of aiding in "preventing the introduction, transmission, or spread of communicable disease," because these elements for blood safety must be addressed through a well-established, extensive system of robust safety requirements by FDA and AABB prior to labeling for distribution.

Our organizations have included responses to FDA's specific questions related to potential PMI for blood and blood components, which can be used if the Agency decides to require PMI for blood and blood components. If FDA requires PMI for blood and blood components, we

recommend that FDA avoid creating new regulatory burdens by incorporating PMI into the existing process used to update the *Circular of Information for the Use of Human Blood and Blood Components*

FDA should exclude blood and blood components from the PMI requirements since the Agency's rationale for requiring PMI is not applicable to these products.

1. A PMI for blood and blood components would be duplicative of the information furnished to patients during the informed consent process and may confuse patients.

Informed consent is an integral part of providing medical care, including blood transfusions furnished to patients in the outpatient setting. Each provider has a unique consent process for blood transfusions, but in general patients receive information about the intervention, expected benefits, material risks, alternative options, when to contact their healthcare provider should they experience an adverse reaction, and are provided with the opportunity to ask questions and solicit answers from a healthcare provider. Patients are empowered with choices, including the ability to decline the therapy or select an alternative treatment option, and must make autonomous decisions. Finally, the consent process must be documented.¹

AABB's Circular of Information Task Force develops the FDA-required *Circular of Information for the Use of Human Blood and Blood Components* (hereinafter referenced as the *Circular*), the FDA-recognized extension of container labeling under 21 CFR 606.122. AABB's Task Force includes qualified representatives from the FDA, American Red Cross, America's Blood Centers, and the Armed Services Blood Program, who jointly develop updates to the *Circular* approximately every 2 years. By regulation, the *Circular* must be made available at distribution and wherever patients are transfused.² The *Circular* provides specific instructions for the administration and use of blood and blood components intended for transfusion. Additionally, the *Circular* details the risks and benefits associated with the transfusion of blood and blood components. Thus, blood collection establishments already make available to providers information that can be used during the informed consent process through the *Circular*.

Since the purpose of PMI documents for blood and blood components is to provide providers and patients with important safety information regarding "side effects and hazards" and directions for use of blood and blood components, the documents will overlap with the informed consent process for blood transfusions. Additionally, the documents have the potential to create confusion if the PMI for a specific blood component contains different information than a provider's informed consent materials for the same blood transfusion. The informed consent process is not uniform, and the information provided to patients will vary based on considerations unique to each patient. Some providers use generic blood transfusion informed consent materials that do not refer to specific blood components. Thus, patients may be confused

¹ Kaplan, A., Arinsburg, S, Puca, K and Coberly, E. Informed Consent for Blood Transfusion *available at* https://www.aabb.org/docs/default-source/default-document-library/resources/informed-consent-for-blood-transfusion.pdf?sfvrsn=b2ee9851_2 (February 23, 2023).

² An Acceptable Circular of Information for the Use of Human Blood and Blood Components, FDA Guidance for Industry (March 2022).

if they receive a PMI for platelets when they have been consented for a “blood transfusion.” If a PMI is simply appended to the documents provided during the informed consent process, patients may disregard the additional information as being superfluous.

2. Blood and blood components are always transfused by a healthcare professional.

FDA specifies that PMI “is intended to improve public health by providing patients with clear, concise, accessible, and useful written prescription drug product information delivered in a consistent and easily understood format to help patients use their prescription drug products safely and effectively.”³ This reasoning does not apply to blood or blood components since patients never self-administer these products; they are always transfused by a healthcare provider. Therefore, requiring PMI for blood and blood components will not contribute to achieving FDA’s goal for PMI.

3. A PMI for blood and blood components will not achieve the intended results of aiding in “preventing the introduction, transmission, or spread of communicable disease.”

FDA suggests that it has the authority to require a PMI for blood and blood components intended for transfusion on an outpatient basis because the Agency is authorized “to make and enforce regulations determined to be necessary to prevent the introduction, transmission, or spread of communicable disease into the United States or from one State or possession into any other State or possession.” Further, FDA reasons that “for blood and blood components intended for transfusion on an outpatient basis, the proposed requirement to include information on the risks associated with blood transfusion, including transfusion-transmitted infections, in PMI may aid in preventing the introduction, transmission, or spread of communicable disease.”

The high degree of safety of the U.S. blood supply is maintained through a comprehensive donor screening and testing process, clearly defined by FDA regulations and recommendations and AABB Standards, which includes (1) providing donors with educational materials; (2) the donor history questionnaires (DHQ) and related materials designed to assess both the safety of the donor and the blood collection; (3) a focused health exam, including hemoglobin screening and evidence of wellness at the time of donation; (4) donor blood testing for transfusion-transmitted infectious diseases; and (5) management of donation information, including soliciting post-donation information in the event the donor develops symptoms of infection after donation. Collectively, these steps establish multiple safety nets to prevent the introduction, transmission, and spread of communicable disease because they assess the blood donor and the donation.

Since a PMI for blood and blood components is intended for the recipient of a blood transfusion, it will not impact donor education, screening, testing, or information. Therefore, while a PMI for blood and blood components may include information about potential risks associated with certain transfusion-transmitted infectious diseases, it will not contribute to preventing the introduction, transmission, or spread of communicable disease.

³ 88 Fed. Reg. 35694, 35695 (May 31, 2023).

Despite the above reasons for excluding blood and blood components from the PMI requirements, if FDA decides to require PMIs for blood and blood components, AABB, America's Blood Centers and the American Red Cross provide the following responses to FDA's specific questions related to potential PMIs for blood and blood components.

1. Informational materials that are currently available to patients who receive blood or blood components for transfusion on an outpatient basis, including the adequacy of such information.

As mentioned above, all patients who receive blood transfusions in the outpatient setting of care are provided information during the informed consent process. The process varies significantly between providers, so it is not possible to evaluate the adequacy of the information provided to all patients. However, all hospital transfusion services have the *Circular* and can use this comprehensive resource to develop informed consent materials.

The informed consent process is intended to capture material information but is not comprehensive. For example, providers' informed consent processes often cover blood transfusions generally and tend to focus on information related to red blood cell transfusions. They may not refer to risks uniquely associated with specific blood components, such as bacterial risks associated with some platelet components that must be stored at room temperature. In some cases, the consenting provider may be a nurse who does not yet know what blood component a patient will be receiving.

2. The difference in the proposed requirements for applicants that FDA should consider in finalizing the rule (i.e., the requirement to submit PMI to FDA for approval).

As detailed above, our organizations encourage FDA to exclude blood and blood components from the PMI requirements. If FDA requires PMI documents for blood and blood components, AABB encourages FDA to incorporate PMI into the existing process used to update the *Circular* which includes support from FDA liaisons.

Specifically, a working group under the AABB Circular of Information Task Force could be charged with developing and maintaining the PMI documents for blood and blood components by leveraging information included in the *Circular* that must be reviewed and recognized as acceptable by FDA. During this process, the working group would identify and update PMI requirements for blood and blood components, in terms that are understood by patients and their families, as part of the formal submission to the Office of Blood Research and Review (OBRR) in CBER.

We encourage FDA to consider the PMI as addenda to the *Circular*. Therefore, the documents would be submitted to FDA for review with the next version of the FDA-recognized *Circular* through the longstanding, existing process. They would not be subject to a new or separate approval process. The PMI would be available to providers and the public as soon as the next update of the *Circular* is completed and formally accepted by FDA.

Notably, hospitals may receive and store blood components from more than one blood supplier. If each licensed blood establishment is required to disseminate PMI to hospitals, it would not be tenable for hospitals to manage different PMI appropriately with the overall inventory. This could lead to errors. Incorporating PMI as addenda to the *Circular* would address this concern.

3. The feasibility of industry jointly developing PMI documents for blood and blood components intended for transfusion on an outpatient basis and the timeframe needed to develop the documents.

As described under question 2, if FDA decides to require PMI documents for blood and blood components, the blood community can jointly develop the PMI documents by creating a subgroup of subject matter experts under the AABB Circular of Information Task Force and incorporating the PMI documents into the longstanding collaborative process used to develop the *Circular*. FDA envisions separate PMI documents for (1) whole blood; (2) red blood cells; (3) platelets; (4) plasma; and (5) Cryoprecipitated Antihemophilic Factor and it will take time and effort for subject matter experts to agree on the information to be included in each PMI document. We anticipate that the subgroup would develop the PMI documents during the process of updating the *Circular*.

As noted earlier, the FDA-approved *Circular* is updated approximately every 2 years (with interim updates posted to reflect new information) and posted on AABB's website with open access to providers and the public. Updates to PMI documents could be made more frequently. The documents would be available as soon as the next update of the formally recognized by FDA.

4. The electronic storage of PMI for blood and blood components on the FDA website <https://labels.fda.gov>.

If the FDA opts to mandate PMI documents for blood and blood components, AABB, ABC, and the American Red Cross advise against introducing additional regulatory burdens by mandating that these PMI details be electronically housed on the FDA website. Instead, we recommend maintaining the current and proven method used for the recognition of the industry-developed *Circular*. The PMI documents could serve as addenda to the *Circular*, and their distribution to providers can be facilitated through the existing dissemination system for the *Circular*.

5. Request for comments on the feasibility of blood transfusion services, as the authorized dispenser of blood and blood components, providing PMI to patients (or patients' agents) who are administered blood or blood components on an outpatient basis.

While blood transfusion services could make PMI available to consenting providers, they may not be able to provide the documents directly to patients or the patients' agents if they are not responsible for consenting or administering the blood or blood components. Unlike prescription medications, blood and blood components are not dispensed directly to patients by the transfusion services. Providers have different processes and procedures to obtain patients' informed consent prior to performing blood transfusions under the practice of medicine. Usually

the treating provider or his/her designee, rather than the blood transfusion service, obtains a patient's informed consent for a blood transfusion.

Additionally, providers define "medical intervention" differently for the purposes of the informed consent process for blood transfusions. For example, some providers may obtain consent prior to each transfusion, whereas other providers may have a consent process that covers multiple transfusions for patients who get multiple or frequent blood transfusions. It would be overly burdensome to require providers to give patients a PMI before every blood transfusion, when established informed consent processes and procedures do not necessarily require providers to obtain a patient's informed consent before each transfusion.

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Thank you for the opportunity to submit comments on the proposed rule and for soliciting feedback from the blood community on potential PMI requirements for blood and blood components.

Sincerely,

[signatures on file]

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