March 30, 2017

Division of Dockets Management (HFA–305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Submitted via http://www.regulations.gov
Re: Docket No. FDA–2016–D-4308, Labeling of Red Blood Cell Units With Historical Antigen Typing Results; Draft Guidance for Industry, 03 January 2017.

Dear Dockets Manager:

AABB, America's Blood Centers (ABC) and the American Red Cross (ARC) appreciate the opportunity to provide comments to the Food and Drug Administration (FDA) on the draft guidance titled "Labeling of Red Blood Cell Units With Historical Antigen Typing Results; Draft Guidance for Industry." These comments on the draft guidance were prepared by a working group comprised of member experts, including members of AABB's Regulatory Affairs Committee, and interested parties from ABC and the ARC.

Our organizations support the FDA's draft recommendations for labeling red blood cells with the results of historical antigen testing, consistent with the 30th Edition of the *AABB Standards for Blood Banks and Transfusion Services*, based on the adequacy of processes to ensure donor identification, as well as the accurate linkage of the donor to test results from at least two previous donations, without confirmation of the prior RBC antigen typing results on the current donation. The use of historical testing, as defined above, based on either serologic or molecular tests, is acceptable to determine non-ABO/Rh(D) RBC antigen types. This approach reduces unnecessary delays in patient care for transfusion recipients with clinically significant antibodies or a history of such antibodies. We have provided several recommendations for changes intended to improve the clarity and operational feasibility of the recommendations. We have two general comments. We suggest FDA refer to a donor's "predicted RBC phenotype" rather than "likely" phenotype. In addition, we suggest that the scope of recommendations of the draft guidance should not encroach on established practices within the area of transfusion services.

Our comments to specific draft recommendations are arranged in the following format:

> **Section** – language from draft guidance reprinted.
> **Recommendation or Request for Clarification** – recommendation or clarification request.

Rationale/Supporting Information – rationale in support of the recommendation /clarification request.

Section - III. Recommendations
B. Labeling RBC Units with Historical RBC Antigen Typing Results
When blood establishments use historical non-ABO/Rh(D) RBC antigen typing results for a subsequent donation by the same donor, the labeling of the RBC unit **should indicate that the results are historical** and whether the results were obtained using an unlicensed reagent or unapproved test. The transfusion service receiving the unit may use this information to determine whether additional confirmation of the typing is warranted.

We recommend the use of the container label or a tie-tag to convey historical RBC typing results, based on whether the historical testing was performed using licensed reagents/approved tests or unlicensed reagents/unapproved tests, respectively. See recommendations 2 and 3 below. In addition, FDA recommends the following for blood collection establishments to label RBC units with non-ABO/Rh(D) historical RBC antigen typing results:
1. You should use historical antigen typing results to label a unit only **if two previous separate donations from the donor were tested by your blood collection establishment** and antigen typing results were found to be concordant.

Recommendation- Our organizations have two recommendations for this section. First, all references to "historical" on the label and all related language should be remove from the recommendation.

Rationale- We disagree with this recommendation, as the requirement for the "historical" designation does not provide additional safety to the transfusion recipient, but adds to the complexity of labeling. This distinction also implies that two historical typing results are in some way inferior to, or might differ from, a single test on the current unit.

This recommendation creates additional concerns when applied to the recommendation for the use of eye-readable text on the affixed label (found in Section III. B. 2.), as discussed below. We otherwise support the recommendations in Section III. B. 1.

Recommendation- Second, members of our organizations are requesting clarification of any limitations on the test methods necessary to label RBCs where the draft guidance remains silent on the combination of methods for testing of the two donations. We suggest providing an affirmative statement in the final guidance that FDA considers labeling of RBCs based on any combination of serological and/or molecular methods to be an acceptable approach if test results are concordant and consistent with all other recommendations.

Rationale- The draft recommendations provide a detailed explanation of FDA's current thinking on certain aspects of testing. Given the absence of a specific statement on combining test methods, a clarification would prevent confusion and assure blood establishments that FDA considers labeling based on historical testing as acceptable without recommending a specific combination of test methods.

Section - III. Recommendations, B. 2.
You should place historical RBC typing results directly on the container label only if two concordant test results were obtained using licensed reagents or approved tests. If RBC antigen typing results are printed

directly on the container label, you should use a standard labeling format such as ISBT 128 or another format accepted by FDA to display the **results in eye-readable** text. ***The labeling format used should indicate that the typing results are historical.***

Recommendation- We wish to reiterate that the recommendation to indicate on the label that results are historical would be very onerous without providing any additional benefit to protect the safety of the transfusion recipient.

In addition, eye-readable text on the affixed label representing the various acceptable test options can be difficult to distinguish. FDA should carefully re-consider the small space available, the difficulty discerning differences in text, and variability in printer function, that could influence the quality of the bolded eye-readable text. We support the use of tie-tags in labeling.

Rationale- As previously stated, we support the labeling of RBCs as described in the draft guidance, except the recommendation that the format indicate the typing results are historical which implies that those results are inferior to or less reliable than one-time serological or molecular testing on that donation.

Because FDA recommends eye-readable text include a combination of historical and current testing, the eye-readable label will require some system of letters or characters for antigen profiles that may contain a mixture of current and historical antigen types. This text is already extremely small. There is concern that users will not be able to consistently and clearly distinguish small eye-readable text with historical results in the space available on the affixed label. We have conferred with ICCBBA to investigate this concern, and we believe that, in some instances, there might not be sufficient surface area present on current container labels, to assure our ability to comply with the addition of the extra information. We do not believe that blood centers or transfusion services are broadly capable of exploiting these structures at this time. In any event, an approach that relies on eye-readable methods on the affixed label, utilizing complex text, represents a step backward in transfusion safety.

AABB is an international, not-for-profit association representing individuals and institutions involved in the fields of transfusion medicine and cellular therapies. The association is committed to improving health through the development and delivery of standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership includes physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries and AABB accredits institutions in over 50 countries.

Founded in 1962, ABC is North America's largest network of community-based, independent blood programs. The network operates more than 600 blood donor centers providing over half 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. America's Blood Centers' U.S. members are licensed and regulated by the U.S. Food and Drug Administration. Canadian members are regulated by Health Canada.

The ARC shelters, feeds and provides emotional support to victims of disasters; supplies about 40 percent of the nation's blood; teaches skills that save lives; provides international humanitarian aid; and supports military members and their families. The Red Cross is a not-for-profit organization that depends on volunteers and the generosity of the American public to perform its mission. About 5.6 million units of whole blood are collected from roughly 3.3 million Red Cross volunteer donors, separated into 8 million transfusable blood products and supplied to approximately 2,700 hospitals and transfusion centers across the country for patients in need.

Thank you for the opportunity to offer these comments. We look forward to continuing to work with the FDA on patient and donor safety initiatives. Questions concerning these comments may be directed to SCarayiannis@aabb.org.

Sincerely,

Sharon Carayiannis
Director, Regulatory Affairs
AABB