CURRENT REGULATORY OPTIONS FOR COLLECTIONS FROM FEMALE BLOOD DONORS WITH HEMOGLOBIN LEVELS OF 12.0 – <12.5 g/dL

Toolkit for AABB Members

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1- Purpose of this Toolkit

In response to member questions and comments, AABB is posting this information to highlight regulatory options made possible in the May 2015 Donor Eligibility Final Rule, and AABB's slide presentation from the November 2016 BPAC.

This Toolkit is intended to supplement but not replace your review of the May 2015 Final Rule.

The toolkit identifies information in the May 2015 Final Rule which:

- Established a minimum Hemoglobin (HB) level 12.5 grams per deciliter (g/dL) of blood or a hematocrit value of 38 percent for female allogeneic donors
- **Recognized that "lower levels are also within the normal range for women."**
- **Authorized collection from female donors**
  - **"with levels no lower than 12.0 grams of hemoglobin per deciliter** of blood, or a hematocrit value no lower than 36 percent"
  - "provided that the establishment has taken additional steps to assure that the alternative standard is **adequate to assure donor safety, in accordance with a procedure that has been found acceptable for this purpose by FDA"**

The toolkit also provides information developed in 2016 by an AABB working group and their considerations which were presented by AABB at the request of FDA for the November 2016 BPAC.*

***** While the FDA approval process to collect blood from female allogeneic donors with hemoglobin levels no lower than 12.0 g/dL (as described in the final rule**) does not require a variance** under 21 CFR 640.120, a blood establishment has the option to submit a formal variance approval request under 21 CFR 640.120 to collect blood from male allogeneic donors with hemoglobin values below the minimum standard of 13 g/dL.

2- Regulatory Options and Flowcharts

This information, initially presented at the Nov 2016 Blood Products Advisory Committee Meeting, has been updated to identify the existing regulatory pathway:
REVISED: Management of Risk for Iron Deficiency In Female Blood Donors

3- Information on Blood Donation and Iron Health

In response to member feedback and requests, the AABB Donor Health and Safety Committee has developed this optional resource, "Information on Blood Donation and Iron Health," for use with Association Bulletin #17-02, "Updated Strategies to Limit or Prevent Iron Deficiency in Blood Donors." This tool, modeled after a similar document that accompanied Association Bulletin #12-03, may be considered by blood centers seeking additional information on the topic.

4- Excerpts from the May 2015 Final Rule

Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use

This Toolkit is intended to supplement but not replace your review of the May 2015 Final Rule.

Executive Summary, *Purpose of the Final Rule,* Summary of the Major Provisions of the Final Rule [pages 29843-44]

"Section 630.10(f) requires establishments to perform a limited physical assessment of the donor. This assessment must include donor temperature, blood pressure, pulse, minimum weight, condition of the skin at phlebotomy site and on arms, and hemoglobin or hematocrit levels. The rule maintains current requirements for hemoglobin and hematocrit levels for female donors, but since lower levels are also within the normal range for women, the rule would authorize collection from female donors with levels no lower than 12.0 grams of hemoglobin per deciliter of blood, or a hematocrit value no lower than 36 percent, provided that the establishment has taken additional steps to assure that the alternative standard is adequate to assure donor safety, in accordance with a procedure that has been found acceptable for this purpose by FDA. The rule raises the minimum standard for male donors from 12.5 grams of hemoglobin per deciliter of blood, or a hematocrit value that is equal to or greater than 38 percent, to 13 grams and 39 percent, respectively."

J. General Donor Eligibility Requirements (§ 630.10)

6. SECTION 630.10(F)

c. *Hemoglobin or hematocrit determination (§ 630.10(f)(3)).* [29867-68]

"At the July 2010 Blood Products Advisory Committee meeting, following the discussion of hemoglobin qualification standards and iron depletion in donors, the committee voted unanimously (10 yes votes, 0 no votes, 1 abstention) in support of raising the hemoglobin level for men, but did not support a change in the hemoglobin level for women (10 no votes and 1 abstention) (Ref. 44). The shortcomings of relying solely on hemoglobin measurement and the need to study measures to mitigate iron deficiency in blood donors were discussed at both meetings of the Blood Products Advisory Committee (Refs. 43, 44) and at the November 2011 Workshop (Ref. 46). After reviewing those discussions and the data presented at those meetings, we have decided to promulgate different standards for male and female donors, but not to alter the current 8 week interval between donations of Whole Blood and single donations of apheresis Red Blood Cells. Recognizing that research in this area continues and that data may be developed to support a change in donor hemoglobin standards, we have provided for greater flexibility in donor hemoglobin standards.

Section 630.10(f)(3)(i) now requires that allogeneic donors must have a hemoglobin level or hematocrit value that is adequate to assure donor safety. In addition, we establish minimum standards. The minimum standard established for female allogeneic donors in § 630.10(f)(3)(i)(A) is consistent with the current standard: A hemoglobin level that is equal to or greater than 12.5 grams per deciliter of blood, or a hematocrit value that is equal to or greater than 38 percent. However, we recognize that a lower hemoglobin/ hematocrit level is also within the normal range for female donors. Since hemoglobin levels are influenced by

the male hormone testosterone, female donors typically have lower hemoglobin levels than male donors. The fact that a female donor's hemoglobin/hematocrit level is lower than that of a male of similar age does not necessarily mean that the female donor has low iron stores, which the body uses to replace hemoglobin lost to blood donation (Refs. 47, 48). For this reason, in the preamble to the proposed rule we specifically requested comment on whether to permit collections from female allogeneic donors with a hemoglobin level of 12.0 grams per deciliter of blood or a hematocrit value of 36 percent. We are not establishing that minimum level at this time. However, § 630.10(f)(3)(i)(A) provides that an establishment may collect blood from female allogeneic donors who have a hemoglobin between 12.0 and 12.5 grams per deciliter of blood, or hematocrit value between 36 and 38 percent, provided that the establishment takes additional steps to assure that the lower value is adequate with respect to donor safety, in accordance with a procedure that has been found acceptable for this purpose by FDA. FDA has not yet recognized any such procedures, and awaits the development of data related to these issues. Conceivably, these steps might include a pre-donation measure of iron stores by means of a ferritin test, or iron replacement therapy and monitoring of iron stores. We have determined that standard collections from a donor with a hemoglobin level as low as 12.0 grams per deciliter of blood or hematocrit value of 36 percent would meet minimum potency levels based on calculated hemoglobin content."

Comments to FDA [29868]
Comment 67: "We received one comment supporting lowering the hemoglobin level for women and one opposing lowering the hemoglobin level for women. The comment supporting a lower minimum hemoglobin level stated that a hemoglobin level of 12.0 grams per deciliter of blood was normal for women, and allowing such donors to donate would improve blood availability. The comment opposing lowering the minimum hemoglobin level stated that this practice would make more women susceptible to anemia and iron deficiency."

FDA Response: "For female allogeneic donors, the current minimum hemoglobin/hematocrit levels remain the default minimum levels under this rule. In the event that an establishment takes additional steps that are adequate to assure donor safety an establishment may collect from female donors with normal, but lower, hemoglobin levels, between 12.0 and 12.5 grams per deciliter of blood, or a hematocrit value between 36 and 38 percent, provided the establishment has taken additional steps to assure that this alternative standard is adequate to ensure that the health of the donor will not be adversely affected due to the donation, in accordance with a procedure that has been found acceptable for this purpose by FDA. We have not yet found such a procedure adequate for this purpose. However, we recognize that, in the future, new data may support revised hemoglobin/hematocrit standards for female allogeneic donors, particularly if it becomes possible to measure other values, including iron stores, before donation. In determining or recognizing an alternative measure, FDA intends to consider other evidence related to donor health, including iron stores. Until then, establishments must follow the current standard for female allogeneic donors: A hemoglobin level of 12.5 grams per deciliter of blood or a hematocrit value of 38 percent."