Food and Drug Administration
Center for Biologics Evaluation and Review

SUMMARY MINUTES
114th Meeting of the BLOOD PRODUCTS ADVISORY COMMITTEE

November 17, 2016
Great Room, Building 31
FDA White Oak Campus
10903 New Hampshire Avenue
Silver Spring, MD 20903

Committee Members
Sridhar Basavaraju, M.D., FACEP #
Meera B. Chitlur, M.D.
Miguel Escobar, M.D.
John B. Holcomb, M.D., F.A.C.S. #
Susan F. Leitman, M.D. ##
Norma B. Lerner, M.D., M.P.H.
Thomas Ortel, M.D., Ph.D.
Margaret V. Ragni, M.D., M.P.H.
Robert J. Rees, MHA, MT(ASCP)
Sonja Sandberg, SB., Ph.D.
Christopher Stowell, M.D., Ph.D. #

FDA Participants
Anne Eder, M.D., Ph.D.
Orieji Illoh, M.D.
Peter Marks, MD., Ph.D.
Wendy Paul, M.D.
Emily Storch, M.D.

Temporary Voting Members
Gary Brittenham, M.D.
Alfred DeMaria, M.D.
Michael DeVan, M.D., F.C.A.P., CDR MC USN
Alain Joffe, M.D., M.P.H
Cassandra Josephson, M.D.
Laura Murray-Kolb, Ph.D.
Ingrid Rabe, MBChB, Mmed.
Jack Stapleton, M.D.

Guest Speakers
Ritchard Cable, M.D.
Sharon Carayiannis, MT(ASCP)HP
Christopher France, Ph.D.
Mindy Goldman, M.D.
Jed Gorlin, M.D., MBA.
Hany Kamel, M.D.
Joseph Kiss, M.D.
Bryan Spencer, M.P.H.

Acting Industry Representative
Toby Simon, M.D.

Acting Consumer Representative
Christopher Templin

Designated Federal Official
LCDR Bryan Emery M.A., B.S.N. USPHS

Committee Management Specialists
Joanne Lipkind
Rosanna Harvey

Did not attend
Acting Chair

The summary minutes for the November 17, 2016 meeting of the Blood Products Advisory Committee were approved on October 18, 2017.

I certify that I participated in the November 17, 2016 meeting of the Blood Products Advisory Committee and that these minutes accurately reflect what transpired.

/Signed/	/Signed/
Bryan Emery, LCDR	Susan Leitman., M.D.
Designated Federal Official	Acting Chair

The Acting Chair, Dr. Susan Leitman, called the 114th Meeting of the Blood Products Advisory Committee (BPAC) to order at 8:00 a.m. EST on November 17, 2016. The meeting was held in an open session. The Chair invited the members, temporary members, and participants seated at the table to introduce themselves. Dr. Peter Marks, Director of the Center for Biologics Evaluation and Research gave opening remarks to the public explaining the reorganization of the Office of Blood Research and Review and the formation of the Office of Tissues and Advanced Therapies. The Designated Federal Official (DFO) LCDR Bryan Emery made administrative remarks and read into the official record the conflicts of interest statement pertaining to the meeting participants. There were no waivers issued for the conflicts of interest for this meeting. After the conflicts of interest statement was read for the public record by the DFO, the Food and Drug Administration (FDA) and non-FDA speaker presentations began.

QUICK SUMMARY

Topic IA: Considerations for Iron Management in Blood Donors

FDA sought the advice of the Blood Products Advisory Committee on iron management in blood donors.

Dr. Wendy Paul from the FDA first introduced the topic and provided background to the committee on iron management and read the questions to the committee. This was followed by a presentation on iron deficiency in blood donors and results from the Reds-II Donor Iron Status Evaluation (RISE) study by Dr. Ritchard Cable of the American Red Cross. Dr. Joseph Kiss from the Institute for Transfusion Medicine presented the results of a on randomized clinical trial on oral iron supplementation after blood donation. Mr. Bryan Spencer of the American Red Cross presented the results of a randomized trial on strategies to reduce iron deficiency in blood donors. Dr. Mindy Goldman of the Canadian Blood Services spoke on iron deficiency and ferritin testing in Canadian blood donors. Last, Dr. Jed Gorlin of Innovative Blood Resources discussed a feasibility study on ferritin testing and iron supplementation.

Following the questions for the speakers, the Chair read the Open Public Hearing statement at the beginning of the Open Public Hearing. Three oral presentations were made during the Open Public Hearing by the blood industry. Dr. George Schreiber representing the Plasma Protein Therapeutics Association (PPTA), presented on iron deficiency in frequent plasma donors. Dr. Lou Katz of America's Blood Center spoke second about the need to address iron deficiency in frequent blood donors. Last, Dr. Steve Kleinman representing AABB, provided strategies to monitor, limit, or prevent iron deficiency in blood donors.

After the Open Public Hearing presentations, the committee began open committee discussion and voted on the questions for the committee.

During committee discussion, the Questions for the Committee originally presented by FDA were revised.

Topic IA: Questions for the Committee

1. Does the available scientific evidence support the need for routine monitoring of iron stores in the absence of iron supplementation in:

    a. All blood donors
    The Committee voted as follows: 9 yes votes; 5 no votes; 1 abstain

    b. Frequent donors (male and female)
    The Committee voted as follows: 14 yes votes; 1 no vote; 0 abstain

    c. Premenopausal female donors
    The Committee voted as follows: 14 yes votes; 0 no votes; 1 abstain

2. Does the available scientific evidence support the need for routine monitoring of iron stores with iron supplementation in:

    a. All blood donors
    The Committee voted as follows: 4 yes votes; 10 no votes; 1 abstain

    b. Frequent donors (male and female)
    The Committee voted as follows: 11 yes votes; 4 no vote; 0 abstain

    c. Premenopausal female donors
    The Committee voted as follows: 10 yes votes; 4 no votes; 1 abstain

3. Does the available scientific evidence confirm that iron supplementation in blood donors:
    a. Mitigates iron deficiency
    The Committee voted as follows: 14 yes votes; 1 no vote; 0 abstain

    b. Improves hemoglobin recovery
    The Committee voted as follows: 12 yes votes; 2 no votes; 1 abstain.
    One member who voted no commented that no evidence was presented at the meeting to demonstrate that iron supplementation in blood donors improved hemoglobin recovery.

4. Please comment on the feasibility of iron supplementation in consideration of:

    a. Potential adverse effects
    b. Adherence

    One member commented that in one study at her institution, 8-12% of donors had gastrointestinal adverse effects that resulted in the donors stopping supplementation. However, potentially severe adverse effects were not observed and there was never a case of accidental poisoning. She commented that there are more likely adverse effects of not giving iron.

With respect to adherence, one member commented that adherence depends on the message to the donor and active follow up by the center. Adherence was close to 70% at her institution.

One member comments that supplementation is a benefit even if there is not full adherence and different preparations of iron may have better tolerability.

Several members commented on the lack of communication between the blood center and the donor's physician, and recommended the blood centers provide a letter to the donor's physician.

One member commented that a multi-vitamin may be sufficient and more tolerable for donors.

Several members commented on potential communication strategies to relay messages to donors. One member commented that donors may not take the time to read educational materials and the messages should be communicated verbally in a 1:1 discussion. She suggested that a skilled nurse could communicate with donors in the canteen following donation.

Another member commented on the potential value of iron supplementation on cognitive functioning of teen donors.

5. Please comment on whether available scientific data support the effectiveness of the following methods for iron supplementation in blood donors:

    a. Educational material provided to the donor
    b. Iron supplements provided to the donor by the blood center

    The Committee members agreed that the data presented support the effectiveness of both strategies. One member commented that while the strategies were effective in clinical studies, demonstration studies are necessary to evaluate effectiveness in the donor setting.

6. Please comment on whether there are adequate data at this time in support of a strategy for increasing the minimum interdonation intervals for men and women, to prevent iron deficiency from blood donation without monitoring of iron storesThe Committee members commented that increasing the interdonation interval has not been demonstrated to be an effective method to prevent iron deficiency.

After the discussion questions were completed the committee took a brief lunch break. The BPAC reconvened in open session after lunch to discuss Topic IB.

Topic IB: Considerations for Blood Collections from Female Donors with Hemoglobin Levels between 12.0 -12.5g/dL or Hematocrit Values between 36-38%

FDA sought the advice of the Blood Products Advisory Committee on blood collections from female donors with Hemoglobin Levels between 12.0 -12.5g/dL or Hematocrit Values between 36-38%.

Dr. Orieji Illoh from the FDA introduced the topic and provided background to the committee on considerations for blood collections from such female donors to the committee. Sharon Carayiannis presented a proposed algorithm developed by AABB.

Following the presentations, the Committee asked questions of the speakers. There were not requests for presentations during the Open Public Hearing Session. The Committee immediately moved into open committee discussion and the Questions for the Committee.

1. **Topic IB: Questions for the Committee** Given that close to half of women with hemoglobin values between 12.0-12.5 g/dL will be iron deficient or iron depleted, please comment on the proposed procedures for collection of blood from female donors with hemoglobin values between 12.0-12.5g/dL:

    a. Collection of blood, ferritin testing, followed by 16-week deferral and iron supplementation if ferritin level is low.

        i. Collection of blood prior to obtaining ferritin test result
        ii. Proposed deferral period for females with low ferritin
        iii. Iron supplementation options

    b. Collection of blood, 6-month deferral, and iron supplements for 60 days. No ferritin testing.

        i. Collection of blood without prior knowledge of ferritin levels
        ii. Proposed deferral period
        iii. Iron supplementation options

The Committee members commented that the proposal (a) that includes ferritin testing is preferred. However, several Committee members opposed collecting blood prior to obtaining the results of the ferritin test, noting that the blood establishment would be collecting blood from a potentially iron deficiency female.

Members comments that at least 50% of female donors with hemoglobin values between 12.0-12.5g/dL would have iron deficiency based on the data presented.

One Committee member commented on anemia versus functional outcome, noting that young women may have functional issues in school or parenting.

Another member commented that without ferritin testing the blood centers may be supplementing donors with alpha thalassemia trait.

A member commented on the difference in accuracy between venous and capillary Hb measurements and noted that a measurement of 12 g/dL could really be 11.5 g/dL if obtained through capillary measurement.

Another member commented that hemoglobin values between 12.0-12.5g/dL are in the normal range for female and that obtaining ferritin values before collection is not practical because point of care testing is not available and donors are not likely to return.

One member commented that the proposal (b) without ferritin testing is not acceptable.

2. Please discuss any alternative procedures that FDA should consider to permit collection of blood from female donors with hemoglobin values between 12.0-12.5 g/dL.

   The Committee did not suggest alternative procedures, except that ferritin testing results should be obtained prior to collection.

After the discussion questions were completed the committee took a 15 minute break.

Topic II: Blood Collection and Adverse Events in Teenage (16-18 years) Blood Donors

FDA sought the advice of the Blood Products Advisory Committee on blood collection and adverse events in teenage blood donors.

Dr. Emily Storch from FDA introduced the topic and provided background to the committee on the topic. After the introduction, Dr. Anne Eder from the FDA gave a presentation on teen blood donation and adverse reactions. A presentation on the experience with mitigation strategies was then given by Dr. Hany Kamel of Blood Systems, Inc. Dr. Christopher France of Ohio University spoke on predicting and preventing syncopal and presyncopal reactions among young donors. Mr. Bryan Spencer representing the American Red Cross concluded the presentations by presenting results from the CHILL Study on iron loss and deficiency in teenage donors.

Following the questions for the speakers, the Chair read the Open Public Hearing statement during the start of the Open Public Hearing session. Three oral presentations were made during the Open Public Hearing. Dr. Lou Katz of America's Blood Center presented donation data according to the age of the donor. Allene Carr-Greer of AABB briefly discussed AABB's Donor Health and Safety Committee. Dr. Hany Kamel of Blood Systems, Inc. responded to concerns about iron deficiency in teenage donors.

The Committee moved into Open Committee Discussion and the Questions for the Committee after the Open Public Hearing session ended.

Topic II: Questions for the Committee

The Committee addressed the following questions:

1. Does the available evidence indicate that adverse reactions and injuries after blood donation in teenage donors is a notable enough concern to require intervention?

   The Committee voted as follows: 15 yes votes; 0 no votes; 0 abstain

2. Considering possible mechanisms to reduce the risk of adverse reactions and injuries in teenage blood donors:

   a. Does the available evidence support applying EBV <3500 ml as a means to mitigate donor reactions?
      The Committee voted as follows: 15 yes votes; 0 no votes; 0 abstain

   b. Do the available data indicate that applied muscle tension during or immediately after donation is effective to mitigate reactions?

The Committee voted as follows: 10 yes votes; 4 no votes; 1 abstain
The Chair suggested the Committee consider voting on the effectiveness of fluid and/or salt supplementation. However, the members commented that data was insufficient and it was difficult to separate the independent contributions of the fluid and salt.

3. Please comment on the need to ensure parental consent material contains adequate information on the increased risk of adverse reactions and injuries in teenage donors.

   One member commented that there is sufficient date to indicate that certain risks are present. Parents should be presented the risks and asked to provide consent.

   A member asked whether the federal government could require consent considering the variable requirements at the state level.

   One member commented on the logistics of obtain consent prior to the drive. Other members commented that this should be feasible since parental consent is required for many student activities (e.g. field trips). Also, blood establishments have successfully implemented consent in states where it is required.

   One member supported transparency with respect to the known risks of teen donation because, in part, some may view the risk higher than they are.

   One member was supportive of parental consent and noted that email and school websites can be effective mechanisms to communicate with the parents. Also, informed consent will provide parents with the opportunity to reduce risk, such as not permitting teen to drive following donation.

4. Considering available evidence related to iron deficiency in teenage blood donors:

   a. Does the available scientific evidence suggest that teenage blood donors are susceptible to developing iron deficiency?
      The Committee voted as follows: 15 yes votes; 0 no votes; 0 abstain.

   b. If so, please comment on possible interventions including:

      i. Further studies evaluating the effect of iron deficiency in teenage blood donors
      ii. Donor education
      iii. Iron management by ferritin testing, iron supplementation, or limiting donation frequency

   One member commented that long-term studies are needed to assess impact of iron deficiency on cognitive function.

   One member commented on the value of placebo-controlled study to control for confounding variables; another member questioned the ethics of such a study.

   One member commented that more studies are needed on iron deficiency in the absence of anemia.

Several members expressed concern about iron deficiency in teenagers in general, not just in blood donors. One member suggested that the results of the CHILL study should be published in a pediatric journal to raise awareness of the public health issue.

Several members commented that the information provided to teenage blood donors should be shared with parents and physicians.

One member commented that blood establishments should routinely assess ferritin in teen donors, regardless if hemoglobin levels. She also noted that limiting donation frequency is not the most impactful intervention.

Another member suggested capping donation frequency to 1-2 donations per year, noting that when combined with routine ferritin testing, donors should remain in good health. Oher members agreed.

One member commented that iron should be given when ferritin is low.

One member suggested integrating blood drives in the school health program, noting the opportunity for linkages to address issues of communication and education.

5. Please discuss whether there is enough associated risk in teenage donors to warrant restriction of the donor pool to individuals aged 18 years and over.

   The Committee commented that it is not necessary to restrict the donor pool provided interventions are implemented. The members commented that strategies to balance risks are available and should be implemented.

   One member commented that it is important to engage young donors and ensure they have a good and healthy experience.

The meeting was adjourned at 6 p.m.