FOOD AND DRUG ADMINISTRATION

Center for Biologics Evaluation and Research
116th Meeting of the Blood Products Advisory Committee
White Oak Conference Center
Great Room, Building 31
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 30, 2017

Committee Members
Meera B. Chitlur, M.D.#
Michael DeVan, M.D., F.C.A.P., CDR MC USN
Alfred DeMaria, 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.
Roger Lewis., M.D, Ph.D., FACEP
Thomas Ortel, M.D., Ph.D.
Robert J. Rees, MHA, MT(ASCP)
Sonja Sandberg, SB, Ph.D.
Christopher Stowell, M.D., Ph.D. (Acting Chair)
Kathleen Sullivan, M.D, Ph.D.
Jack Stapleton, M.D.

Temporary Voting Members
Mathew Arduino, MS., DrPH, PSHEA
Sridhar V. Basavaraju, M.D., FACEP
Karen Carrol, M.D.
Patricia Kopko, M.D.
Karen Quillen, M.D., MPH
David Stroncek, M.D.
Cliff Sullivan, M.D.

Designated Federal Official
LCDR Bryan Emery B.S.N. USPHS

Did not attend

FDA Participants
Salim Haddad, M.D.
Julia Lathrop, Ph.D.
Jason Liu, M.D., Ph.D.
Teresita Mercado, M.S., MT (ASCP)
Jennifer Scharpf, M.P.H
Sharmila Shrestha, M.B.A., MT (ASCP)

Guest Speakers
Steven Field, MBChB, MA
Carl McDonald, Ph.D., MSc., BSc.
Ralph Vassallo, M.D.
Kathleen Sullivan, M.D, Ph.D.
Jack Stapleton, M.D.

Consumer Representative
Judith Baker, DrPH. MHSA

Industry Representative
Susan Stramer, Ph.D.

Committee Management Specialists
Joanne Lipkind
Rosanna Harvey

These summary minutes for the November 30, 2017 meeting of the Blood Products Advisory Committee were approved on Dec 19, 2018.

I certify that I participated in the November 30, 2017, meeting of the Blood Products Advisory Committee and that these minutes accurately reflect what transpired.

Signed ___XXXXX_____
Bryan Emery, MA, BSN., LCDR
Designated Federal Official

Signed_____ XXXXXX_____
Christopher P. Stowell, M.D, Ph.D.
Acting Chair

The Acting Chair, Dr. Christopher Stowell, called the meeting of the Blood Products Advisory Committee to order at 8:00 a.m. EST on November 30, 2017. The meeting was held in an open session. The Chair invited the members, temporary members, and participants seated at the table to introduce themselves. 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.

QUICK SUMMARY

Topic I: Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

An introduction and overview of the topic was presented by Dr. Salim Haddad from the Division of Blood Components and Devices (DBCD), Office of Blood Research and Review (OBRR), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA). Jennifer Scharpf from OBRR presented a summary of the public comments on FDA's draft guidance document. This was followed by a presentation titled, "Platelet Bacterial Contamination Risk Mitigation: Another Successful Approach" by Dr. Ralph R. Vassallo of Blood Systems, Inc. Next, Dr. Carl McDonald of the United Kingdom, National Health Service Blood and Transplant spoke on the experience of the United Kingdom National Health Service, Blood and Transplant. Dr. Steven Field of the Irish Blood Transfusion Service concluded with a presentation titled, "Screening of Platelets for Bacterial Contamination: Experience of the Irish Blood Transfusion Service from 2005-20016."

After a short break and questions of the speakers, the committee reconvened for the Open Public Hearing (OPH) session and Dr. Stowell the Acting Chair, read the OPH statement. Eleven oral presentations were made during the OPH:

1. Dr. Michael Jacobs of Case Western University
2. Dr. Jessica Jacobson presented data for AABB
3. Dr. Peter Tomasulo represented BioMerieux
4. Dr. Anna Razatos represented Terumo BCT
5. Dr. Richard Benjamin represented Cerus Corporation

6. Dr. Arthur Bracey of Baylor St. Luke's Medical Center
7. Dr. Sarah Harm of the University of Vermont Medical Center
8. Dr. Neil Krueger presented for Oxford Immunotec
9. Dr. Louis Katz of the America's Blood Centers
10. Mr. Joe Sanders represented Verax Biomedical
11. Dr. Axel Stover of Fresenius Kabi USA

After lunch, the Committee reconvened and immediately began the Open Committee Discussion and voted on the questions before the committee.

The final questions addressed by the Committee are as follows:

1. Do the available data support 5-day storage of apheresis platelets without secondary testing if platelets are cultured no sooner than 24-36 hours post collection with a sampling volume of at least 3.8% of the collection?

   The committee voted as follows: 16 yes votes; 1 no vote, 0 abstain

2. Do the available data support the following measures to extend dating to day 7?

   a. Culture of apheresis platelets sampled no sooner than 36-48 hours after collection using a test volume of at least 16 ml per split without secondary testing.

   The committee voted unanimously as follows: 17 yes votes, 0 no votes, 0 abstain

   b. Repeat culture on Day 4 with a volume of 16 ml per component divided into an aerobic and anaerobic culture tube.

   The committee voted unanimously as follows: 16 yes votes, 0 no votes, 0 abstain

   Note: One member became ill and was not present during vote for question 2b.

3. Should primary testing of platelets with large volumes include the use of both anaerobic and aerobic culture systems?

   The committee voted unanimously as follows: 17 yes votes, 0 no votes, 0 abstain

The Committee paused for a short break to allow the Committee to reconfigure for the second topic discussion.

Topic II: Classification of Human Leukocyte Antigen, Human Platelet Antigen and Human Neutrophil Antigen Devices

FDA sought the advice of the Committee on the classification of human leukocyte antigen (HLA), human platelet antigen (HPA) and human neutrophil antigen (HNA) devices.

Dr. Julia Lathrop from the Division of Emerging Transfusion Transmitted Diseases (DETTD), OBRR, FDA introduced the topic and provided background information to the Committee on the classification of medical devices. This was followed by a presentation on the classification of HLA, HPA and HNA devices by Dr. Jason Liu and Mrs. Sharmila Shrestha of the Division of Blood Components and Devices (DBCD), OBRR, FDA.

After questions of the speakers, the floor was opened to the public for an Open Public Hearing. There were no requests for presentations. The committee immediately began the Open Committee Discussion.

After the Open Committee Discussion, the Questions for the Committee portion of the meeting began.

The final questions addressed by the Committee are as follows:

1. Following the review of relevant literature, medical device reports and recalls related to HLA, HPA and HNA devices, FDA has identified the following risks to health when these devices are used for transfusion, transplantation or disease diagnosis:

Patient injury or death due to:

- Poor graft survival or function due to transplantation of incompatible hematopoietic cells, tissue or organ.
- Graft rejection because of the transplantation of incompatible hematopoietic cells, tissue or organ.
- Graft-versus-host disease because of the transplantation of incompatible immune system cells.
- Incorrect or delayed diagnosis of medically related conditions or assessment of future risk of adverse outcomes because of incorrect HLA, HPA or HNA test results.
- Transfusion reaction (e.g. Transfusion Associated Lung Injury, Post Transfusion Purpura) due to incorrect HLA, HPA or HNA test results.
- Platelet refractoriness because of incorrect HLA or HPA typing or antibody detection results.

2a. Do you agree that this is a complete and accurate list of the risks to health presented by HLA, HPA and HNA devices?

The committee voted unanimously as follows: 14 yes votes, 0 no votes, 0 abstain

2b. If you disagree, please comment on what additional risks should be included or explain which, if any, of the risks listed are not part of the overall risk assessment of HLA, HPA and HNA devices.
N/A

3. Section 513 of the Food, Drug, and Cosmetic Act (FD&C Act) states:

A device should be **Class III** if:

- Insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance,

AND

- The device is life-supporting or life sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury

A device should be **Class II** if:

- General controls by themselves are insufficient to pro vide a reasonable assurance of safety and effectiveness.

AND

- There is sufficien t information to establish special controls to provide such assurance.

A device should be **Class I** if:

- General controls are sufficient to provide reasonable assurance of the safety and effectiveness,

OR

- Insufficient information exists to determine that general controls are sufficient or special controls can be established to provide a reasonable assurance of safety and effectiveness, but the device type is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health and does not present a potential unreasonable risk of illness or injury.

General controls may include:

- Prohibition against adulterated or misbranded devices,
- Good Manufacturing Practices (GMPs),
- Registration of manufacturing facilities,
- Listing of device types,
- Recordkeeping, etc.

a. FDA believes that general controls alone are not sufficient to provide a

reasonable assurance of safety and effectiveness for HLA, HPA and HNA devices.

i. Do you agree with this assessment?

The committee voted unanimously as follows: 14 yes votes, 0 no votes, 0 abstain

ii. If not, please discuss how general controls alone are sufficient to provide a reasonable assurance of safety and effectiveness for HLA, HPA and HNA devices.

N/A

b. Under the Federal Food, Drug, and Cosmetic Act, a device is potentially class III if it is "life-supporting or life-sustaining, or of substantial importance in preventing impairment of human health." FDA believes that HLA, HPA and HNA devices are not life- supporting or life-sustaining,

i. Do you agree with this assessment?

The committee voted as follows: 13 yes votes, 1 no votes, 0 abstain

ii. If not, please explain why HLA, HPA and HNA devices are life- supporting or life-sustaining.

No comments were made by the committee after voting.

c. Under the Federal Food, Drug, and Cosmetic Act, a device is potentially class III if it is "of substantial importance in preventing impairment of human health." FDA believes that HLA, HPA and HNA devices are of substantial importance in preventing impairment of human health.

i. Do you agree with this assessment?

The committee voted unanimously as follows: 14 yes votes, 0 no votes, 0 abstain

ii. If not, please explain why HLA, HPA and HNA devices are not of substantial importance in preventing impairment of human health.

N/A

d. Under the statute, a device is potentially class III if it presents a "potential unreasonable risk of illness or injury." Considering the risks and benefits of these devices, FDA believes that HLA, HPA and HNA devices present a potential

unreasonable risk of illness or injury. (Note that such a device may still be classified as class II if application of special controls would provide reasonable assurance of its safety and effectiveness.)

i. Do you agree with this assessment?

The committee voted unanimously as follows: 14 yes, 0 no votes, 0 abstain

ii. If not, please explain why HLA, HPA and HNA devices are not for a use which presents a potential unreasonable risk of illness or injury.

N/A

e. FDA believes sufficient information exists to establish special controls for HLA, HPA and HNA devices. FDA is proposing the following as special controls that would provide reasonable assurance of safety and effectiveness:

1) Premarket submissions must include detailed documentation of the following information:
   i. Device accuracy study using well-characterized samples representing as many targets as feasible.
   ii. Precision studies to evaluate possible sources of variation that may affect test results
   iii. Comparison studies to evaluate the device's performance compared to a predicate.
   iv. Specific information that address or mitigate risks associated with false positive antibody reactivity e.g., reactivity with denatured/cryptic epitopes, if applicable.
   v. Description of how the assay cut-off was established and validated as well as supporting data.
   vi. Documentation for device software, including, but not limited to, software requirement specifications, software design specification, e.g., algorithms, alarms and device limitations; hazard analysis, traceability matrix, verification and validation testing, unresolved anomalies, hardware and software specifications; electromagnetic compatibility and wireless testing.
   vii. For multiplex assays in which large numbers of probes and/or primers are handled during manufacturing process, premarket submissions should provide the design specifications that are in place to prevent incorrect reactivity assignment.
   viii. Description of a plan on how to ensure the performance characteristics of the device remain unchanged over time when new HLA, HNA or HPA alleles are identified, and/or reactivity assignments are changed from the assignments at the time the device was evaluated.

2) The device labeling must include:

i. A limitation statement that reads, "The results should not be used as the sole basis for making a clinical decision."
ii. A warning that reads "The use of this device as a companion diagnostic, has not been established."

f. Based on the information presented today, please discuss whether you believe that sufficient information exists to establish special controls that can provide a reasonable assurance of safety and effectiveness of HLA, HPA and HNA devices. If not, please explain why not.

The committee voted as follows: 12 yes votes, 1 no votes, 1 abstain

g. Do you agree that the list in e.1) is a sufficient and accurate list of the special controls needed to provide reasonable assurance of safety and effectiveness for HLA, HPA and HNA devices?

The committee voted as follows: 13 yes votes, 0 no votes, 1 abstain

If you disagree, please comment on what additional special controls are needed or explain which, if any, of the proposed special controls are not needed.

One member commented why she abstained from voting on this question.

h. Do you agree that the Agency's proposed classification for HLA, HPA and HNA devices as Class II with special controls will provide reasonable assurance of safety and effectiveness?

The committee voted unanimously as follows: 14 yes votes, 0 no votes, 0 abstain

If you disagree, please discuss why special controls are not adequate to assure safety and effectiveness of HLA, HPA and HNA devices.

N/A

After the discussion was completed, the Acting Chair, Dr. Christopher Stowell, adjourned

Additional information may be obtained from the transcript and the recording of the webcast of the meeting. The transcript and webcast are available at the following link:

https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm554807.htm