MEETING SUMMARY

AATB-FDA LIAISON COMMITTEE MEETING

Wednesday, December 4, 2013
Bethesda North Marriott Hotel and Conference Center
5701 Marinelli Road
North Bethesda, MD 20852
8 am – Noon

SUMMARY OF THE MEETING

I. Introductions (8:10 am)

Frank Wilton, American Association of Tissue Banks, opened the meeting and requested introductions for those attending. The following are the participants who were in attendance:

FDA PARTICIPANTS

Peter Marks, MD, PhD
Deputy Director
Office of the Director
Center for Biologics Evaluation and Research

Diane Maloney, JD
Associate Director for Policy
Office of the Director
Center for Biologics Evaluation and Research

Sherry Lard, PhD
Associate Director for Quality Assurance
Office of the Director
Center for Biologics Evaluation and Research

Kate Cook, JD
Regulatory Counsel
Office of the Director
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Celia M. Witten, MD, PhD
Director
Office of Cellular, Tissue and Gene Therapies
Center for Biologics Evaluation and Research
Stephanie Simek, Ph.D.
Deputy Director
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Kimberly Benton, PhD
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Ellen Lazarus, MD
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Wilson Bryan, MD
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Raj Puri, MD, PhD
Director
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Melissa Greenwald, MD
Human Tissue and Reproduction Branch
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Shyh-Ching Lo, PhD, MD
Director
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Office of Cellular, Tissue and Gene Therapies
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Theodore Stevens, MS
Associate Director for Information Management
Office of Cellular, Tissue and Gene Therapies
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Rachael Anatol, Ph.D.
Associate Director of Policy: New Legislation
Office of Cellular, Tissue and Gene Therapies
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Charlene Cho, JD, PhD
Regulatory Policy Analyst
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Mary Malarkey
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Office of Compliance and Biologics Quality
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Gilliam Conley
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Division of Inspections and Surveillance
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Robert Sausville
Director
Division of Case Management
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Faye Vigue
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Pauline Cottrell
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Manufacturers Assistance and Technical Training Branch
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AATB PARTICIPANTS

Bruce Stroever
President and Chief Executive Officer, MTF
Chair, Tissue Policy Committee

Debbie Dean
Executive Vice President, MiMedx

David Fronk
Vice President, Regulatory Affairs and Quality Assurance, CryoLife

Douglas Wilson
Vice President, LifeNet Health

Frances Harrison
Vice President, Regulatory Affairs and Quality Assurance, LifeCell

Frank Wilton
CEO, American Association of Tissue Banks

Jeffrey Sandler
Senior Vice President, Donor Services, Tissue Banks International

Kai Lo
Senior Director, Site Leader – Osteotech Operations, Medtronic Spine and Biologics

Kelly Snyder
Senior Director, GTP Quality Systems, DCI Donor Services

Kevin Cmunt
CEO, Gift of Hope
President, American Association of Tissue Banks

Lou Barnes
Executive Director, DCI Donor Services Tissue Bank

Mark Spilker
Vice President, R&D, QA, & Regulatory Affairs, MTF

Natika Calhoun
Senior Manager/Tissue Bank Director, Medtronic Spine & Biologics

Patty Malone
Director, Quality Assurance at Community Blood Center-Community Tissue Services

Parker H. “Pete” Petit
Chairman of the Board and Chief Executive Officer, MiMedx

Ricci Whitlow
Senior Vice President, Technical Operations, LifeCell
II. Introductory Remarks

Mr. Wilton, AATB, asked Dr. Witten if she had any opening comments. Dr. Witten commented on AATB’s follow up letter. She agrees that the brief information on the website are not necessarily clear, and it was helpful to understand that ambiguity when reviewing a recent AATB letter to the FDA regarding acellularization/decellularization.

III. Follow up to September 6, 2013 AATB-FDA meeting regarding HCT/P Biological Product Deviation Reports (BPDRs) and Tissue Recalls

Ms. Christrup, Hart Health Strategies gave an overview and a history of the Direct Recall Classification (DRC) process. She reviewed the FDA track and DRC. AATB appreciates modifications and updates to the DRC. She spoke about the inherent link between the eBPDR and notification/recall. Ms. Malarkey agreed about the presence of this link: a very small percentage of eBPDRs become recalls. Ms. Christrup spoke about problems with this inherent link. She gave examples of situations where a deviation has not resulted in a notification/recall, such as sample filtration and testing window. She reviewed the effect on donor screening recalls and discussed a proposed solution: requiring BPDR but not requiring a recall. This solution would be consistent with current guidance.

Ms. Malarkey: As a result of the last meeting, FDA has looked at processes to focus on those situations with systemic issues. The majority of recalls are blood recalls. DRCs were meant to streamline the process, and as a result, FDA is posting recalls in a much more timely fashion. Just because something was posted in 2012 doesn’t mean it occurred in 2012. FDA is looking at the donor screening issue. Technically, these products are HCT/P deviation reports, and eBPDR guidance doesn’t apply to these
products. FDA is considering new guidance for HCT/P—no timeframe yet, but they recognize there is a gap that needs to be filled. **Mr. Conley:** If you have specific questions about filing deviation reports, continue to use the contact you have been using.

IV. **Tissue Reference Group (related to acellularization/decellularization processes)**

**Mr. Spilker,** MTF, discussed the Tissue Reference Group and reviewed some recommendations regarding decellularization, most recently from July 2013. Though there is a disclaimer, AATB believes that acellularization/decellularization processes do not preclude a tissue from being a 361 product. **Dr. Witten:** There are examples on the web of decellularized tissues that are not precluded from being a tissue. But your letter raised good points. **Mr. Spilker:** We don’t want this to prevent the industry from innovative development. AATB requests that the TRG discontinue the practice of broad recommendations. AATB would like more detailed information in the confidential replies to the applicant. **Mr. Stroever,** MTF, gave an example of acellularized dermis. These recommendations are open to interpretation by insurers, hospitals, etc. as well.

**Dr. Witten** sees the need to consider this issue.

V. **Update on the draft Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)**

**Ms. Malone,** CTS, reviewed basic information regarding this draft guidance. She reviewed AATB’s concerns with the proposal. There is little evidence that HCT/Ps transmit WNV. She summarized an article published by the CDC this year. Without any evidence of risk, it doesn’t seem to follow the normal course for regulation. A tiered, risk-based approach is not being applied. There is also a lack of WNV testing in organs. It is unclear how this issue will affect the organ community. AATB also has concerns with the Novartis (Procleix) test and false positives and suggests further study and a public workshop.

**Dr. Witten** asked for these comments to be submitted to the docket. She asked for data regarding false positives. FDA had a workshop—there is a problem with the lack of data, but that doesn’t necessarily mean that there isn’t a problem. **Mr. Wilton:** Is the FDA aware of transmission evidence? **Dr. Greenwald:** The draft guidance discussed the medical literature evidence. It would be helpful for the tissue community to request other types of studies. **Dr. Witten:** It would be difficult to deal with shared donors with only testing some types of tissue. **Dr. Greenwald:** This isn’t the only area that we are different than organ donors with. **Mr. Stroever:** We only have a few data points (CDC, weight of numbers showing lack of transmission evidence). **Mr. Spilker:** We have established pathways within our organization to make this a pathway issue and not a donor eligibility issue. **Dr. Witten:** FDA won’t extend the comment period in order to wait for study results. Feel free to let us know about studies you are planning on performing.
Mr. Wilton: Are all WNV incidents reported to the CDC? Is there a comprehensive database? Dr. Greenwald: It is a voluntary submission database. Keep in mind that 80 percent of people don’t realize they have WNV. Mr. Brubaker asked Dr. Lo if his lab was involved in any WNV studies and Dr. Lo described that the CBER lab is not working on this; it is a very complex issue.

VI. Update on the Microbiological Surveillance Program and Process Validation Guidance Document

Mr. Brubaker, AATB, reviewed the AATB Guidance Document: Microbiological Surveillance Program and process validation. He discussed revisions to the final draft, and the creation of new terms for companion tissue, method suitability test, and Representative Sample Item Portion (RSIP). AATB added more examples and more references, but probably won’t finish answering comments until next spring.

VII. Update on the Effective Quality Assurance of the Donor Risk Assessment Interview (DRAI) Guidance Document

Mr. Brubaker also discussed the Effective Quality Assurance of the Donor Risk Assessment Interview (DRAI) Guidance Document. AATB would like comments on this one by the end of the year. AATB is still working to determine if this guidance is required to be implemented or only recommended. The AATB review process will take place in early 2014. He highlighted comments and reviewed revised recommendations including additions to Sampling Plan, examples, and corrective and preventative action.

Dr. Witten and Ms. Malarkey: We will need to look at this document and discuss it. Just because it is an audio record and not a written record doesn’t mean it’s not a record. Mr. Stroever: The origins of these recordings were more related to consent issues. Dr. Witten: Maybe our comments were unfortunately worded, but this is something we need to look at again. Explain what is it about retaining interviews that is problematic? Ms. Malarkey: Even if you enter a paper record electronically, you can’t get rid of the original. Mr. Stroever: This is a concurrent record – a recorded record of what is being written down, and often OPOs are double checking these within 30 days. AATB will help FDA reach out to OPOs and try to better understand why this is a burden.

VIII. Update on the Guidance for Industry and FDA Staff: Minimal Manipulation of Structural Tissue Jurisdictional Update (Jurisdictional Update)

Mr. Wilton reviewed the jurisdictional update issue and then asked if Dr. Witten had additional comments.

Dr. Witten: We would welcome any thoughts on the problematic lack of research infrastructure regarding tissues. Mr. Wilton: There has been discussion with Commissioner Hamburg regarding research collaboration. Mr. Brubaker gave an update on the TODES survey. We are communicating with 19 OPOs, 18 of which recover tissue. We are hoping for a data dump. Dr. Greenwald: The way in which the
test results are recorded and stored is different across the board – making it difficult to pull data into one place. It is also challenging to avoid data overlap in test results, because each donor has multiple donor IDs. She added that this study won't have the ability to do correlations between donor screening and test results. **Dr. Witten:** We need a more granular, detailed description of some of these issues and TODES. She would be interested in hearing from AATB more about ISBT-128. **Mr. Wilton:** It is an issue we continue to address. Multiple participants from the FDA stressed that science based comments to guidance are most helpful.

The meeting concluded.