FINAL Meeting Summary of the 13th Cell Therapy/FDA Liaison Meeting

October 19, 2016
Bethesda, MD

Host Organization:

Participating organizations: AABB, ASBMT, ASGCT, ASH, FACT, FDA/CBER/OTAT, ICCBBA, ISCT, SITC, USP

Meeting transcript prepared by Deborah Griffin.

The FDA CTLM Meeting was held October 19, 2016 at 12:30pm. The following topics were presented during the meeting with the agency. After a welcome from the ISCT NA LRA Designate, Olive Sturtevant, the participants in the room introduced themselves and their role within the stakeholder group or FDA.

PRESENTATION SESSION 1: NEED FOR DEFINITION OF CRITICAL QUALITY AND PRODUCT ATTRIBUTES FOR CELLULAR AND GENE THERAPY PRODUCTS TO ALLOW FOR COMPARABILITY THROUGHOUT CLINICAL DEVELOPMENT

Presentations by:

- ***Presentation 1a*: Michelle Myers, PhD (GSK, ASGCT)**
- ***Presentation 1b*: Thomas Finn, PhD (FDA OTAT)**

Both of the speakers defined CQA. M. Myers used a fictitious case study to demonstrate the process of defining and developing CQAs from an *ex vivo* gene therapy product, genetically modified, autologous CD34 positive cells, for a metabolic disorder. Two take-home messages were 1. To review assay robustness early in development and develop robust methods as early as possible and 2. To maintain retained samples from early in the development to test and retest after improvements to assays. An example of comparability studies was presented and a discussion of the challenges faced during the study process. T. Finn reviewed the terminology, delineating the difference between specifications, CQA, and lot release criteria. He also discussed the FDA's expectations when reviewing the data provided and how to develop criteria based on the data that the researcher has collected.

PRESENTATION SESSION 2: INTRODUCTION TO STANDARDS FROM THE FDA PERSPECTIVE (FDA WORKSHOP RECAP)

Presentation by:

- ***Presentation 2*: Judith Arcidiacono, MS (FDA OTAT)**

J. Arcidiacono briefly reviewed documentary standards and reference materials for cellular therapy and how they are being developed in several areas, such as USP, NIST, and ASTM.

PRESENTATION SESSION 3: NEED FOR REFERENCE STANDARDS FOR CELL AND GENE THERAPY

Presentations by:

- ***Presentation 3a (Vectors): Boro Dropulic, PhD, MBA (Lentigen, ASGCT)***
- ***Presentation 3b (CD34+): Ruud Hulspas, PhD (USP)***

B. Dropulic presented information about lentiviral vectors as a critical raw material, including variability, both in producing and in assaying. For this meeting, the speaker surveyed 24 senior members of ASGCT regarding reference standards and presented the responses to the group. The results of the survey indicate that the respondents generally believe that reference standards are a good idea, but it a challenge as well. R. Hulspas presented 3 topics: reproducibility and variability in preclinical research standards, standards and practices in Flow Cytometry, and a case study where standards are being applied in cellular therapy.

Discussion: Dr. Witten asked the M. Myers to review her Discussion Points slide. One of the topics that were discussed was how to design a comparability study when a manufacturing process is now going to be performed in a new, global, location. The FDA provided advice on how to transfer the manufacture of the product, how to determine variability, and other considerations. Another FDA speaker advised to determine how much variation can be tolerated.

The FDA asked B. Dropulic about the ASGCT survey and the next steps. B. Dropulic noted he will present the findings and discussion back to ASGCT to determine next steps.

PRESENTATION SESSION 4: NEED FOR DOCUMENTARY AND REFERENCE MATERIALS/STANDARDS FOR CELL AND GENE THERAPY AND HOW THE SCIENTIFIC COMMUNITY/INDUSTRY IS ADDRESSING THIS NEED; SCB

Presentation by:

- ***Presentation 4: Michael Mendicino, PhD (SCB, ISCT)***

The SCB's rationale and mission as a multi-stakeholder organization were presented, including the groups that the SCB is working with in order to accelerate standards development, outreach and coordination of workshops, and inter-laboratory studies after launch in early 2017. Cell characterization and Rapid Microbiological Methods were among the cell therapy priority topics presented.

PRESENTATION SESSION 5: RELEVANT COMMUNICABLE DISEASES IN HCT/PS (WNV AND ZIKA)

Presentations by:

- ***Presentation 5a: Phyllis Warkentin, MD (FACT)***

- ***Presentation 5b*: Michelle M. McClure, PhD (FDA OTAT)**

P. Warkentin discussed the recent guidelines concerning ZIKA, WNV and other emerging viruses, and the challenges that the community faces when labeling these products. The issue of incomplete donor screening and ineligible donors was brought up. The FDA clarified that if there is an identified communicable disease risk factor, the donor can be determined ineligible only after all of the required donor screening and testing is completed. If a risk factor is identified part way through but all the required screening and testing are not completed in accordance with the FDA regulations, then the donor eligibility is incomplete. Urgent medical need can be used if the donor eligibility determination is incomplete. M. McClure also discussed timing of donor testing and related information in the recently published WNV Guidance.

PRESENTATION SESSION 6: LABELING OF CELLULAR PRODUCTS WITH UNIQUE PRODUCT AND PATIENT IDENTIFIERS WHEN THE PRODUCTS ARE INTENDED FOR FURTHER MANUFACTURE BY A CONTRACT ORGANIZATION OR STUDY SPONSOR

Presentation by:

- ***Presentation 6*: Olive Sturtevant, MHP (ISCT)**

O. Sturtevant presented the near-misses that have occurred due to the removal of patient identifiers on products manufactured by the third-party manufacturers for industry-sponsored clinical trials. Labeling of cellular products requires patient information for administration to the patient. Industry sponsors are reluctant to include patient information on the products and work-arounds have been created.

Discussion: The FDA stated that this labeling issue described is not something that they can enforce. They mandate only that the manufacturers have a system that allows tracking of products to the recipient and vice versa. The requirements do not extend to the facilities that receive the products for administration. FDA then suggested that a community solution would be appropriate. A short discussion about testing, quarantine and import of products was held.

The meeting concluded at 3:43pm.