Biotechnology Industry Organization

February 23, 2015

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA–2014-D-1696: Minimal Manipulation of Human Cells, Tissues, and Cellular and Tissue-Based Products

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the Draft Guidance for Industry and FDA Staff entitled "Minimal Manipulation of Human Cells, Tissues, and Cellular and Tissue-Based Products" (HCT/P).

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products.

GENERAL COMMENTS:

BIO would like to commend the FDA on recognizing the need for additional clarity in this area, which will provide a common understanding and predictability that will continue to foster investment in these therapies. In particular, BIO applauds FDA for its helpful discussion of "original relevant characteristics" of structural and nonstructural tissues, as well as for the use of multiple examples.

BIO requests additional clarification as to whether any *in vitro* expansion of cells harvested from human tissue in culture constitutes more than minimal manipulation. Additionally, we welcome a more detailed discussion as to what enzymatic treatment or chemical treatment (other than sterilization or preservation) may be included within the term minimal manipulation, and what would be considered more than minimal manipulation.

BIO asks FDA, when it finalizes this guidance, to include examples relating to the use of human tissues for active wound healing, in light of the proliferation of human skin allografts entering the marketplace for this purpose over the last five years. Further policy clarification on this particular clinical area of use of allografts is necessary and will

1201 Maryland Avenue SW
Suite 900
Washington DC 20024
202.962.9200 P
202.488.6306 F
bio.org

be generally beneficial to Sponsors of both 361 HCT/P allografts and therapeutics approved under a Biologics License Application (BLA).

BIO also requests that FDA address the issue of HCT/Ps that may be structural tissues when marketed for straightforward mechanical properties, but are more properly viewed as nonstructural tissues when marketed for purposes that depend upon the tissue's biochemical activity. Manipulation that is "minimal" with respect to a tissue that is intended for structural use may not be "minimal" with respect to the same tissue if it is intended for a nonstructural use. We also suggest that FDA include clarifying language with its list of "examples of structural tissues" stating explicitly that any of these tissues may be nonstructural if used for other purposes and examples of manipulations that are "minimal" for structural tissues would not be applicable. (Alternatively or in addition, FDA could clarify that where a tissue has a structural role in the donor, marketing it for a nonstructural purpose in the recipient is not permitted under section 1271.10 because such a purpose would not constitute "homologous use.")

BIO recommends that FDA issue similar clarifying guidance for industry concerning the "homologous use" and "dependence on metabolic activity of living cells" criteria of section 1271.10, as BIO believes that there is widespread confusion in the allograft industry as to the meaning and appropriate application of these criteria.

Despite the important role served by these guidance documents, BIO respectfully requests that FDA take a more active role in ensuring that the Section 361 regulatory pathway is not used inappropriately to bring products to market that are effectively intended to function as cell therapy products without FDA premarket review. BIO therefore urges FDA to consider mandating the Tissue Reference Group (TRG) process or establishing a claims notification process for Section 361 tissues (similar to dietary supplements and food additive notifications), in order to bring order and regulatory discipline to the allograft marketplace.

BIO believes that the guidance does not impose or contain any sweeping changes to existing Agency policies or positions, but rather illustrates and clarifies the Agency's long-standing interpretations of the law. Based on prior TRG determinations and Agency pronouncements over the last several years in various untitled letters, it is clear that the draft guidance generally reflects the Agency's existing thinking on the application of the "minimal manipulation" criterion.

Finally, BIO believes that a potential notice-and-comment rulemaking process prior to FDA application of the interpretations announced in the guidance would be unnecessary and could inappropriately suspend the Agency's enforcement of existing regulations. We believe that any proposed delays will only complicate the enforcement landscape, as new products that do not meet the criteria of section 1271.10, but are marketed as Section 361 HCT/Ps continue to enter into the market.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Minimal Manipulation of Human Cells, Tissues, and Cellular and Tissue-Based Products" Draft Guidance. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)