ALLIANCE OF
WOUND CARE
STAKEHOLDERS
POWER THROUGH COLLECTIVE ADVOCACY

September 27, 2016

Ms. Leslie Kux
Associate Commissioner for Policy
Division of Dockets
Management (HFA-305),
Food and Drug Administration,
5630 Fishers Lane,
Rm. 1061,
Rockville, MD 20852

Re: FDA-2015-D-3581 for "Homologous Use of Human Cells, Tissues, and Cellular and Tissue-Based Products; Draft Guidance for Industry and FDA Staff

Submitted electronically at www.regulations.gov

Dear Ms. Kux:

On behalf of the Alliance of Wound Care Stakeholders, I am submitting the following comments in response to the FDA draft guidance document on "***Homologous Use of Human Cells, Tissues, and Cellular and Tissue-Based Products: Draft Guidance for Industry and Food and Drug Administration Staff*" (December 2015).** The Alliance is a nonprofit multidisciplinary trade association of physician medical specialty societies and clinical associations whose mission is to promote quality care and access to products and services for people with wounds through effective advocacy and educational outreach in the regulatory, legislative, and public arenas. Most of the Alliance clinical members use tissue products in their practices and thus have a vested interest in ensuring patient access to these important products – which may be in jeopardy based on the language contained in the guidance documents issued for comment.

The Alliance believes that the FDA correctly uses the term "basic function" when referring to the functions of the Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). This term is consistent with current regulatory and statutory language and is a more scientifically correct and appropriate term. However, we are baffled that the FDA would introduce a different term, "main function", when referring to the functions of the HCT/P in the draft minimal manipulation guidance document.

The notion that these tissues have a "main function" which determines whether a product is structural or non-structural conflicts with current regulation as well as the draft guidance document on homologous use. The conflict with the homologous use guidance is problematic as it is not possible to separate homologous use from minimal manipulation when considering whether or not a product is regulated as a 361 HCT/P (Human Cells, Tissues, and Cellular and Tissue-Based Products). The draft

5225 Pooks Hill Rd | Suite 627S | Bethesda, MD 20814
T 301.530.7846 | **C** 301.802.1410 | **F** 301.530.7946
marcia@woundcarestakeholders.org

homologous use guidance document accurately utilizes the term "basic function/functions" and we agree with that term. Tissue has more than 1 function and as such, the Alliance recommends that the FDA continue to utilize the term basic function and/or functions when determining whether a product is structural or non structural.

The Alliance also commends the FDA in recognizing that anatomical location, as well as basic function, determines homologous use and that anatomical location is not the sole determinant of homologous use. Finally, we commend the FDA for its recognition of the unique properties of dermis, which is separate from epidermis in terms of properties and function.

The Alliance however does have a couple of concerns with the draft homologous use guidance document.

First, the Alliance would like to state that regulations expressly do not separate the definition of homologous use depending on whether tissue is structural or non-structural. The FDA's **"presumption"** that homologous uses of structural tissue "generally" will be structural and homologous uses of nonstructural tissue "generally" will be non-structural is not technically correct. Tissue can be structural and nonstructural. One example is the use of split-thickness and dermal tissues and their function as a scaffold and biological modulator. A biological modulator is a material or substance derived from biological sources that influences processes such as wound healing. They act as a scaffold to support cell ingrowth and granulation tissue formation. They have receptors that permit fibroblasts to attach to the scaffold. They have the ability to act as a chemoattractant for endothelial cells and contain/protect growth factors useful in angiogenesis and matrix construction. This is an example of a tissue having both structural and non-structural characteristics. As such more clarity is necessary when discussing basic function/functions of both structural and non-structural tissue.

The second issue of concern relates to section 4.2 – Homologous Use of Amnion Tissue. The Alliance is concerned about how the narrow definition of homologous use for amnion tissue will impact its use for wound care. Section 4.2 states,

> *"The basic functions of amniotic membrane include serving as a selective barrier for the movement of nutrients between the external and in utero environment and to retain fluid in utero. An amniotic membrane product is used for wound healing of dermal ulcers and defects. This is not homologous use because wound healing of dermal lesions is not a basic function of amniotic membrane"*

However, there are many basic functions of amniotic tissue. The basic functions of placental tissue or amniotic membranes can include – preventing infection, rapid self-restoration, allowing free movement, a protective barrier and a cover. With or without maintenance of the donor cells, many of these basic functions are sustained and observed after placement in the recipient (even after removal of donor cells). By utilizing most of the basic function or functions within the definition of placental tissue a clinician can apply placenta-derived tissues as part of a good wound care treatment for a variety of wound types and severities as we described earlier and this tissue type should be used for wound healing. The FDA had even stated in the past that amnion may be used for wound healing

when cytokines were present—meaning that it was not decellularized. As such, the Alliance recommends that the FDA continue to permit amnion in their homologous use considerations.

Conclusion

The concepts of Minimal Manipulation and Homologous Use are so interrelated that while it is appropriate to have separate guidance documents for each, there must be consistency between the two documents. Each of the guidance documents should provide specific detail in order to give greater clarity and guidance - this does not occur in these particular documents. In fact, many examples that were previously provided have been eliminated. More importantly, there are too many significant new requirements within the minimal manipulation document that not only conflict with the homologous use guidance document, but they conflict with current regulatory language. The FDA should work with stakeholders to develop an appropriate guidance document that is consistent with current regulatory language and actually provides guidance and clarity to existing regulations.

The Alliance appreciates the opportunity to provide CMS with our comments. If you require additional information or have any questions, please do not hesitate to contact me.

Sincerely,

Marcia Nusgart R. Ph

Marcia Nusgart, D.Ph.
Executive Director