Human Cells, Tissues, and Cellular and Tissue-Based Products – FDA Draft Guidances

04-16-15 • alert • katherine leibowitz

If your company is involved in the human tissue space, please note that FDA recently issued three draft guidances relating to human cells, tissues, and cellular and tissue-based products ("HCT/Ps"). HCT/Ps require FDA premarket review as a drug, device or biologic unless they meet the four criteria set forth in 21 CFR 1271.10(a):

The HCT/P

– is minimally manipulated;

– is intended for homologous use only;

- doesn't involve combining the cells or tissues with another article; and

- either doesn't have a systemic effect and doesn't depend on the metabolic activity of living cells for its primary function or has a systemic effect or depends on the metabolic activity of living cells for its primary function and is for autologous use or allogeneic use in a first-degree or second-degree blood relative or is for reproductive use.

HCT/Ps that meet these four criteria are regulated solely under Section 361 of the Public Health Services (PHS) Act and 21 CFR 1271 (referred to as "361 HCT/Ps"). FDA does not require premarket review for 361 HCT/Ps because it does not view them as drugs, devices or biologics.

While manufacturers generally prefer their HCT/Ps to be designated as a 361 HCT/P due to the lighter regulatory obligations, the Minimal Manipulation (see #1 below) and Adipose Tissue (see #2 below) draft guidances suggest that FDA is narrowing the field of HCT/Ps that could qualify as 361 HCT/Ps. Importantly, rather than reviewing minimal manipulation on a case-by-case basis, FDA would create a presumption of minimal manipulation unless the manufacturer could show otherwise. Further, these two draft guidances define key regulatory terms that had been previously undefined and include numerous, detailed examples. Manufacturers hoping to avoid premarket review should carefully

confirm that their HCT/Ps qualify as 361 HCT/Ps in light of what appears to be a more stringent regulatory environment.

Set forth below are some general comments about each draft guidance.

1. ## Minimal Manipulation:

   In December 2014, FDA released draft guidance setting forth recommendations for meeting the "minimal manipulation" criterion in 21 CFR 1271. As mentioned above, minimal manipulation is one of the four criteria that must be met to be considered a 361 HCT/P (thereby avoiding FDA premarket review). The draft guidance is entitled, "Minimal Manipulation of Human Cells, Tissues, and Cellular- and Tissue-Based Products; Draft Guidance for Industry and Food and Drug Administration Staff."

   The draft guidance would supersede the FDA "Guidance for Industry and FDA Staff: Minimal Manipulation of Structural Tissue Jurisdictional Update" dated September 2006. The draft guidance is intended for manufacturers, health care providers and FDA staff.

   FDA explains that it released the draft guidance in response to request from stakeholders for clarification regarding the "minimal manipulation" criterion in Section 1271.10(a)(1). The draft guidance contains examples of HCT/Ps that are and are not minimally manipulated. It also contains general principles that can be applied to development of future HCT/Ps. The guidance notes that if information does not exist to show that the "processing" meets the definition of "minimal manipulation," then FDA would consider the processing to be "more than minimal manipulation," which means the HCT/P would require premarket review. Thus, FDA would impose an obligation on the manufacturer to show that the HCT/P is not minimally manipulated, and if it could not, then the product would be subject to FDA premarket review. This presumption would likely narrow the field of HCT/Ps that would qualify as 361 HCT/Ps.

2. ## Adipose Tissue HCT/Ps:

   In December 2014, FDA released draft guidance intended to help determine whether HCT/Ps derived from adipose tissue are subject to FDA premarket review requirements. The draft guidance is entitled, "Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) from Adipose Tissue: Regulatory Considerations; Draft Guidance for Industry."

   It is intended for sponsors, clinicians, and other establishments that manufacture and use HCT/Ps from adipose tissue.

   The draft guidance discusses whether an HCT/P from adipose tissue meets the four criteria required to qualify as a 361 HCT/P (thereby avoiding FDA premarket review). It is presented in Q & A format and sets forth examples of HCT/Ps from adipose tissue as well as the regulatory pathway for each example.

3. ## Adverse Reactions:

The most recent draft guidance, released February 20th, is entitled, "Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271."

This draft guidance would replace a 2005 guidance on how to report adverse reactions relating to 361 HCT/Ps. This draft guidance would supplement the 2011 guidance entitled, " Guidance for Industry: Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)."

The draft guidance addresses manufacturer regulatory obligations to investigate and report adverse reactions involving communicable diseases related to a 361 HCT/P that the manufacturer made for distribution. It would not apply to non-reproductive HCT/Ps, HCT/Ps regulated under 21 CFR 1270 or health professionals who deal with HCT/Ps.

As with the 2005 guidance that it would replace, the draft guidance is in Q & A format. It also contains a new section on Adverse Event Investigation that addresses information that should be reviewed.

If you have any questions or would like more information about these developing issues, please contact the following:

KATHERINE LEIBOWITZ
1-610-896-5788
Katherine.Leibowitz@LeibowitzLawTeam.com