FDA's "Same Surgical Procedure" Draft Guidance Could Stifle Use of Autologous Stem Cell Therapies


By Areta Kupchyk

The use of autologous stem cell therapies to treat medical diseases and conditions may be subject to regulation by the U.S. Food and Drug Administration (FDA) if the stem cells are not returned to the patient in the “same surgical procedure.” FDA’s proposed definition of “same surgical procedure,” published in “Draft Guidance for Industry: Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception” (draft guidance) in October 2014, received little attention from medical practitioners and patients. By the end of the comment period in December 2014, only 36 comments had been submitted to FDA, approximately 17 each from practitioners and patients. These comments overwhelmingly opposed FDA’s proposal. FDA has four options: (1) re-open the comment period; (2) revise the guidance and offer another opportunity for comment; (3) revise and finalize the guidance; or (4) finalize the guidance as written. FDA is under no deadline to act. Comments still may be submitted.

Autologous stem cells fall under FDA’s regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps) that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Prior to 2005, FDA regulated HCT/Ps as conventional medical products, such as drugs or medical devices, under the Federal Food, Drug, and Cosmetic Act (FDCA), or as biologics under Section 351 of the Public Health Service Act (PHSA). However, after exhaustive deliberation between 1997 and 2005, rather than require substantial evidence of effectiveness and safety data before marketing, FDA “down” regulated certain HCT/Ps to prevent the introduction, transmission, and spread of communicable diseases under the authority of Section 361 of the PHSA and the regulations found in 21 C.F.R. Part 1271 (Part 1271). Under 21 C.F.R. § 1271.10(a), HCT/Ps will be exempt from preapproval requirements if they meet the following four criteria:

1. The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer’s objective intent;
3. The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and

4. Either:
   i. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
   ii. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
      a. Is for autologous use;
      b. Is for allogeneic use in a first-degree or second-degree blood relative; or
      c. Is for reproductive use.

FDA carved out several exceptions from any FDA oversight. In recognition of certain procedures performed within the practice of medicine, FDA included an exception for “an establishment that removes HCT/P’s from an individual and implants such HCT/P’s into the same individual during the same surgical procedure.” FDA explained in its 1997 “Proposed Approach to Regulation of Cellular and Tissue-Based Products,” that in such a case, the “communicable disease risks, as well as the safety and effectiveness risks, would generally be no different than those typically associated with surgery.” The use of autologous stem cells to treat certain conditions or diseases could fall within this exception.

In its draft guidance, FDA stated that same surgical procedure could include rinsing, cleansing, sizing, labeling, and storage, but the entire procedure, from removal to implantation, must be done in the same facility because shipping to or performing the procedure in a second facility raises the possibility of contamination and cross-contamination.

Under certain circumstances, FDA proposed to permit certain procedures performed over several days to qualify for the exception so long as no processing or manufacturing steps are performed other than rinsing, cleansing, labeling, and storage.

FDA offered the following examples of procedures that would qualify for the same surgical procedure exception:

   a. Craniotomy with subsequent implantation of the bone flap to reverse the cranial defect.
   b. Parathyroidectomy with subsequent implantation of a portion of the tissue to preserve parathyroid function.

If a procedure performed at a hospital does not qualify as the same surgical procedure, the hospital would be required to register and comply with the HCT/P requirements under Part 1271. Hospitals could then be subject to FDA inspection. If FDA determines that the autologous stem cells have been more than minimally manipulated or used for a non-homologous purpose, they would be regulated as a biological product under the FDCA and the PHSA and subject to preapproval submissions demonstrating safety and substantial evidence of effectiveness.
In response to the draft guidance, physicians commented that FDA was overreaching into the practice of medicine. Requiring registration would place an undue burden on hospitals, especially trauma centers. Many comments gave examples of procedures that could fall outside the narrow exception unless explicitly identified in the guidance. For example, when a patient in an accident needs a craniotomy and skull flap removal, the skull flap typically is shipped to another facility for repair. Sometimes the re-implantation also is performed at another facility. Another common processing step is centrifugation, which physicians have employed safely for many years.

Although the 60-day comment period has closed, practitioners, hospitals, patients, and any other interested person may submit comments to FDA at any time. FDA is under no obligation to consider late-filed comments before finalizing a draft guidance; however, if finalization is not imminent, late-filed comments still could influence FDA’s actions.

Comments may be submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Comments should reference the full title of the draft guidance document and request consideration before finalization.

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