

# Overview on the Regulation of Cellular Therapies in Aesthetic Medicine



## **Background**

The Aesthetic Stem Cell Society (ASCS) is made up of plastic surgeons, facial plastic surgeons, oculoplastic surgeons, dermatologists, and researchers both in this country as well as internationally. The purpose of the Society is to advance and support the medical community's understanding and lawful use of stem cells for the purpose of aesthetic medicine and be an advocate for patient safety and quality of medical care regarding such use.

In 2016 the ASCS established a Multi-Specialty Task Force comprised of representatives from various medical specialty societies including the American Academy of Dermatology, the American Academy of Facial Plastic and Reconstructive Surgery, the American Society for Aesthetic Plastic Surgeons, the American Society of Ophthalmic Plastic and Reconstructive Surgery, and the American Society for Dermatologic Surgery. The purpose of this Multi-Specialty Task Force was to monitor and contribute to the FDA guidance development process regarding stem cells. The Multi-Specialty Task Force submitted written comments to the draft guidance. Members of the Multi-Specialty Task Force attended hearings held by the FDA for public comment regarding proposed guidance documents. Following the issuance of final guidance documents, the Multi-Specialty Task Force met with officials of the FDA to provide a Briefing on the present state of stem cell use in aesthetic medicine. This Briefing took place in December 2018.

The Multi-Specialty Task Force has become concerned with the confusion surrounding the use of cellular therapies in aesthetic medicine. This misinformation, and in cases disinformation, have been too prevalent amongst practitioners. In earlier 2019, the Multi-Specialty Task Force decided to prepare a document addressing regulatory issues for cellular therapy in aesthetic medicine. Below follows information on that topic that the Multi-Specialty Task Force hopes will be beneficial to the aesthetic medicine community.

## **Authority**

Use of cellular therapies in aesthetic medicine is subject to regulation from multiple authorities. The FDA has taken the lead in providing oversight and guidance in this area. In November 2017, the FDA released Guidance for Industry, "Same Surgical Procedure Exception under 21 CFR 1271.15(b) Questions and Answers Regarding the Scope of Exception" and "Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologues Use." These two (2) documents provide the agency's current thinking on certain regulatory provisions that apply in the field of aesthetic medicine. The FDA is actively engaged in enforcement. Actions have been brought in both California and Florida relating to stem cell clinics.

Enforcement actions have not been limited to the FDA. State of Attorneys General Offices have also been active in recent months. The New York State Office of the Attorney General has brought an action against a stem cell clinic. Most recently, the Illinois Attorney General Office

has announced its attention to become active in this area. The Multi-Specialty Task Force anticipates more action by Attorneys General Offices in the future.

The Federal Trade Commission has also brought an action against an entity for false representations in various advertisements relating to stem cell treatments. The FTC acted because they found claims made in advertisements were not substantiated by scientific literature.

In April 2018, the Federation of State Medical Boards released its “Regenerative and Stem Cell Practices” guidelines. This document provides guidance to State Medical Boards regarding the use of stem cells and other cellular therapies by physicians. The Multi-Specialty Task Force believes that this document is a prelude to Medical Boards oversight of cellular therapies.

Taken as a whole, these authorities are increasingly active in regulating cellular therapies. Each has its specific scope and interest. The Multi-Specialty Task Force anticipates greater oversight of practitioners using cellular therapies.

### **Medical Devices**

Medical devices used in both preparation and administration of cellular therapies come under the jurisdiction of the FDA. Medical devices are categorized into one of three classes, based on the degree of risk they present. Depending on the medical device classification, a device may require premarket clearance or premarket approval before it is marketed in the U.S. Medical devices are cleared or approved by FDA with a specific intended use, which may not be consistent with a physician’s utilization of the device for a particular patient or clinical indication. A practitioner should confirm that any medical devices being used have the appropriate FDA premarket authorization for the specific intended use.

There is also a process by which medical device manufacturers are "registered" and medical devices are “listed” with the FDA. FDA acceptance of an establishment registration, assignment of a registration number, and medical device listing does not constitute a determination that an establishment is in compliance with applicable rules and regulations or that a medical device is cleared or approved by the FDA. Medical devices which are only listed with the FDA (but not cleared, approved, or "exempt") would generally require an FDA Investigational Device Exemption (IDE) for therapeutic use.

### **Stem Cells**

The variety of sources and therapeutic uses for stem cells are numerous. Stem cell therapies are regulated by FDA under its regulatory framework for HCT/Ps. Human cells, tissues, or cellular or tissue-based products (HCT/Ps) are articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. FDA has implemented a tiered, risk-based approach to the regulation of HCT/Ps. Under the authority of Section 361 of the Public Health Service (PHS) Act, FDA established regulations that set forth the types of HCT/Ps that do not require premarket approval, and the registration,

manufacturing, and reporting steps that must be taken to prevent the introduction, transmission, and spread of communicable disease by these HCT/Ps. These regulations can be found in [21 CFR Part 1271](#).

In 21 CFR 1271.10(a), the regulations identify the criteria for regulation solely under section 361 of the PHS Act and 21 CFR Part 1271. An HCT/P is regulated solely under section 361 of the PHS Act and 21 CFR Part 1271 if it meets all of the following criteria (21 CFR 1271.10(a)): it is minimally manipulated, it is intended for homologous use only, it is not combined with another article (with some limited exceptions), and it does not have a systemic effect on the recipient and is not depending upon the metabolic activity of living cells for its primary function, or if it does, it is intended for homologous use or use by a first or second degree blood relative.

HCT/Ps that meet all of the criteria in 21 CFR 1271.10(a) are regulated solely under section 361 of the PHS Act and 21 CFR 1271, and no FDA premarket review is required. If an HCT/P does not meet the criteria set out in 21 CFR 1271.10(a), the HCT/P is regulated as a drug, device, and/or biological product under the Federal Food, Drug and Cosmetic Act (FD&C Act), and/or section 351 of the PHS Act (42 U.S.C. 262), and applicable regulations, including 21 CFR 1271, and premarket review is required.

Applying the criteria above, all allogeneic stem cell therapies are regulated as drugs and/or biological products under the FD&C Act and/or section 351 of the PHS Act. In order to lawfully market a biological product, a biologics license must be in effect (PHS Act) (42 U.S.C. 262(a)). Such licenses are issued only after a determination by FDA that the establishment and the biological product(s) meet applicable requirements to ensure the continued safety, purity, and potency of such products (21 CFR 601.2(d)). For clinical studies of investigational drug products, an IND application must be in effect in accordance with the FD&C Act (21 U.S.C. 355(i)) and FDA regulations (21 CFR part 312 and 21 CFR 601.21).

There have been questions raised to ASCS as to autologous derived stem cell therapies. The FDA's position is that anything beyond rinsing, cleansing, sizing, or shaping would generally not allow an autologous HCT/P to remain such HCT/P. Because adipose derived cells require chemical or mechanical processing to extract, establishments manufacturing such products do not meet FDA's same surgical procedure exception and the products fail to meet the criteria at 21 CFR 1271.10(a) so they are regulated as drugs and biological products under the FD&C Act and section 351 of the PHS Act and require premarketing review and approval.

In addition, most stem cell therapies are intended for nonhomologous use. For example, adipose derived stem cells which are used for hair growth or collagen rejuvenation would be considered nonhomologous use. It is clear that any use of stem cells for regenerative or aesthetic purposes would need to be administered under an FDA IND.

### **Amniotic Fluid**

At present, the FDA has not licensed any uses for the amniotic fluid. Amniotic fluid is not regulated by FDA as an HCT/P and the regulations in 21 CFR Part 1271 do not apply. Instead, it is generally regulated by FDA as a drug, device, and/or biologic requiring premarket review and approval. At present, an Investigational New Drug application (IND) would be required for all therapeutic uses of amniotic fluid.

### **Cord Blood**

Cord blood is regulated by FDA under its regulatory framework for HCT/Ps. Cord blood therapies for aesthetic uses are generally allogeneic. An Investigational New Drug application (IND) would be required for any therapeutic use of allogeneic cord blood.

### **Platelet Rich Plasma**

FDA has not licensed any Platelet Rich Plasma (PRP) products for any specific indications. Depending on a variety of factors including the intended use(s) of such products, they may be subject to regulation by FDA as biological products and drugs under the Public Health Service Act and Federal Food, Drug and Cosmetic Act.

If a medical device is labeled or promoted for manufacturing PRP for the purpose of administering the device output to a patient, then the device would require FDA approval or clearance for that use prior to marketing in the U.S.

### **Conclusion**

Cellular therapies in aesthetic medicine are evolving at a rapid pace. Organizations like the Federation of State Medical Board and the FDA have attempted to provide clear guidance to aesthetic medicine practitioners in recent years. Because of dynamic nature area of this medicine, physicians are cautioned to confirm their actions are compliant with both state and federal regulations. Further, questions and inquiries may be directed to Michael J. Sacopulos, Executive Director of the ASCS at [msacopulos@medicalriskinstitute.com](mailto:msacopulos@medicalriskinstitute.com) or to the FDA at: [Industry.Biologics@fda.hhs.gov](mailto:Industry.Biologics@fda.hhs.gov).