**UNITED STATES DISTRICT COURT**
**SOUTHERN DISTRICT OF FLORIDA**

Case No. 0:18-cv-61047-UU

UNITED STATES OF AMERICA,

Plaintiff,

v.

US STEM CELL CLINIC, LLC, *et al*.,

Defendants.
_____/

**ORDER ON MOTIONS FOR SUMMARY JUDGMENT**

THIS CAUSE is before the Court upon Plaintiff's Motion Summary Judgment ("Plaintiff's Motion"), D.E. 42, and Defendants' Motion for Summary Judgment ("Defendants' Motion" and together with Plaintiff's Motion, the "Motions"). D.E. 41. The Court has reviewed the Motions, the pertinent portions of the record and is otherwise fully advised in the premises. For the reasons discussed *infra*, Plaintiff's Motion is GRANTED and Defendants' Motion is DENIED.

## I. Factual Background

Unless otherwise indicated, the following facts are undisputed.

### A. Defendants and their Operations

Defendants[1] US Stem Cell Clinic, LLC (the "Clinic") and US Stem Cell, Inc. are Florida corporations. D.E. 42-1 ¶¶ 1-2; D.E. 50-1 ¶¶ 1-2. The Defendants are engaged in the business of providing a therapeutic treatment in which a patient's adipose tissue (fat) is extracted, processed to isolate certain stem cells, and injected back into the same patient to treat a range of neurological, autoimmune, and orthopedic illnesses. D.E. 42-1 ¶¶ 5-8; D.E. 50-1 ¶¶ 5-8. Defendant Kristin

[1] Although Theodore Gradel was initially listed as a Defendant, he has since entered into a consent agreement and is no longer party to this case. *See* D.E. 47; D.E. 62.

Comella ("Comella") is the Chief Scientific Officer of both the Clinic and US Stem Cell, Inc. D.E. 26 ¶ 22.

B. Stromal Vascular Fraction & Defendants' Procedure

Adipose tissue is a connective tissue composed of clusters of adipocyte cells (fat cells), surrounded by a reticular fiber network, interspersed with blood vessels and white blood cells. D.E. 42-1 ¶¶ 11-12; D.E. 50 ¶¶ 11-12; D.E. 42-4 ¶ 23; D.E. 45-5 at 6. Adipose tissue also contains stem cells including stromal and vascular stem cells known as the "stromal vascular fraction." ("SVF"). *Id.*

At the Clinic, Defendants utilize a multi-step procedure to separate the SVF from the other component cells of the adipose tissue. First, healthcare professionals working for Defendants extract a patient's adipose tissue via a "tumescent liposuction" procedure. D.E. 42 ¶ 9; D.E. 50-1 ¶ 9. Then, a "cell wash solution" is added to the extracted adipose tissue to remove blood cells. D.E. 45-2 at 8. This cell wash solution is purchased from manufacturers outside of Florida and is labelled "not for human therapeutic use." D.E. 50-1 ¶ 16; D.E. 53-1 at 10. Next, a solution containing a collagenase enzyme is added to the adipose tissue; this digests the collagen and fiber network connecting the cells in the adipose tissue. D.E. 1 ¶ 10; D.E. 26 ¶ 10; D.E. 42-4 ¶ 19. The enzyme solution is purchased from a manufacturer located outside of Florida. *Id.*; D.E. 53-1 at 18-19. Next, the tissue and enzyme mixture is centrifuged for five minutes, which separates the adipocytes and other components from the SVF. D.E. 42-4 ¶ 19; D.E. 45-2 at 8, 23-24. Then, to further isolate the SVF from the enzymatically-digested components of the adipose tissue, the mixture is filtered via a strainer, which allows only the SVF to pass through. D.E. 42-4 ¶ 19; D.E. 45-2 at 8, 25-26. The mixture is then centrifuged again to concentrate it and is combined with a platelet-rich plasma solution or saline. D.E. 42-4 at 8; D.E. 45-2 at 31. This solution, now

composed almost exclusively of SVF, is transferred to a syringe to be injected into the patient on the same day it is extracted. *Id.*

C. Marketing

Defendants make numerous claims about the health benefits of their SVF therapy. Defendants assert that the SVF therapy can treat neurological, autoimmune, orthopedic and degenerative diseases, including, *inter alia*, Parkinson's disease, Amyotrophic Lateral Sclerosis ("ALS"), lung disease, heart disease, and diabetes. D.E. 50-1 ¶ 24. Defendants also claim that their SVF therapy has "proven to be a better alternative for people facing debilitating conditions such as COPD [chronic obstructive pulmonary disease], Degenerative Disc Disease, Osteoarthritis and many others where traditional medicine falls short . . . ." D.E 43-1. These claims have been made in brochures, websites, YouTube videos, and other media. D.E. 50-1 ¶¶ 23, 25, 26.

D. FDA Inspections

Plaintiff, the United States Food and Drug Administration (the "FDA") inspected the Clinic over the course of six different visits from October 22, 2015 through December 7, 2015, and another seven visits between April 10, 2017 and May 11, 2017. D.E. 50-1 ¶¶ 29-30; D.E. 45 ¶¶ 13-17. The results of these inspections were memorialized in two "Form FDA-483's," detailing observations made by FDA inspectors regarding the SVF therapy. Among these observations were that: Defendants had not established a system for monitoring environmental conditions to prevent contamination during aseptic processing of the SVF, Defendants did not test the SVF for objectionable microorganisms, and that the label for the SVF did not contain indications for use, dosage, routes of administration or side effects. D.E. 50-1 ¶¶ 20, 32-33, 44; D.E. 53-17; D.E. 53-18.

Comella responded to the FDA on December 28, 2015, and May 16, 2017, asserting that Defendants were not required to comply with FDA regulations because the businesses were subject to statutory exceptions including, most importantly, the "same surgical procedure exception" contained in 21 C.F.R. § 1271.15(b). D.E. 45 ¶¶ 15, 18. On August 24, 2017, the FDA issued a warning letter to Defendants, re-iterating that during the inspections, FDA investigators had found the Clinic to be non-compliant with FDA regulations and disagreeing with Comella's assertions that Defendants were exempt from the FDA's adulteration and misbranding regulations. D.E. 43-8. The FDA warned that failure to take corrective action could lead to regulatory actions without further notice. *Id.* On August 29, 2017, Comella responded to the warning letter, disputing the FDA's findings and re-iterating that the Clinic was exempt from FDA regulation. D.E. 45 ¶ 20; D.E. 26 ¶ 52.

## II. Legal Standard

Summary judgment is authorized only when the moving party meets its burden of demonstrating that "the pleadings, depositions, answers to interrogatories and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56. When determining whether the moving party has met this burden, the Court must view the evidence and all factual inferences in the light most favorable to the non-moving party. *Adickes v. S.H. Kress & Co.*, 398 U.S. 144, 157 (1970); *Rojas v. Florida*, 285 F.3d 1339, 1341-42 (11th Cir. 2002).

The party opposing the motion may not simply rest upon mere allegations or denials of the pleadings; after the moving party has met its burden of proving that no genuine issue of material fact exists, the non-moving party must make a showing sufficient to establish the existence of an essential element of that party's case and on which that party will bear the burden of proof at trial."

*See Celotex Corp. v. Catrett*, 477 U.S. 317 (1986); *Poole v. Country Club of Columbus, Inc.*, 129 F.3d 551, 553 (11th Cir. 1997); *Barfield v. Brierton*, 883 F.2d 923, 933 (11th Cir. 1989).

If the record presents factual issues, the Court must not decide them; it must deny the motion and proceed to trial. *Envntl. Def. Fund v. Marsh*, 651 F.2d 983, 991 (5th Cir. 1981). Summary judgment may be inappropriate even where the parties agree on the basic facts, but disagree about the inferences that should be drawn from these facts. *Lighting Fixture & Elec. Supply Co. v. Cont'l Ins. Co.*, 420 F.2d 1211, 1213 (5th Cir. 1969). If reasonable minds might differ on the inferences arising from undisputed facts, then the Court should deny summary judgment. *Impossible Elec. Techs., Inc. v. Wackenhut Protective Sys., Inc.*, 669 F.2d 1026, 1031 (5th Cir. 1982); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986) ("[T]he dispute about a material fact is 'genuine' . . . if the evidence is such that a reasonable jury could return a verdict for the nonmoving party.").

Moreover, the party opposing a motion for summary judgment need not respond to it with evidence unless and until the movant has properly supported the motion with sufficient evidence. *Adickes*, 398 U.S. at 160. The moving party must demonstrate that the facts underlying the relevant legal questions raised by the pleadings or are not otherwise in dispute, or else summary judgment will be denied notwithstanding that the non-moving party has introduced no evidence whatsoever. *Brunswick Corp. v. Vineberg*, 370 F.2d 605, 611-12 (5th Cir. 1967). The Court must resolve all ambiguities and draw all justifiable inferences in favor of the non-moving party. *Liberty Lobby, Inc.*, 477 U.S. at 255.

## III. Analysis

### A. Regulatory Framework

This case turns on the interpretation of the Food, Drug, and Cosmetic Act (the "FDCA"), 21 U.S.C. § 301 *et seq*., the Public Health Service Act (the "PHSA"), 42 U.S.C. § 201 *et seq*., and the regulations promulgated thereunder. 21 C.F.R § 1271. Accordingly, before turning to the parties' claims, the Court briefly lays out the regulatory context for their arguments.

#### i. FDCA

The FDCA regulates "drugs," which the FDCA defines as, *inter alia*, "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1)(B). The FDCA prohibits taking any act with respect to a "drug" "if such act is done while such article is held for sale . . . after shipment in interstate commerce and results in such article being adulterated or misbranded." 21 U.S.C. § 331(k) (emphasis added).

A drug is "adulterated" under the FDCA if, *inter alia*, the methods used for its manufacture, processing, packing or holding do not conform to current good manufacturing practice ("CGMP"). 21 U.S.C. § 351(a)(1)(B). With respect to this action, the procedures that constitute CGMP are codified at 21 C.F.R. § 211. A drug is "misbranded" under the FDCA if, *inter alia*, its labeling[2] lacks "adequate directions for use." 21 U.S.C. § 352(f)(1).

#### ii. PHSA

##### 1. Generally

The PHSA regulates "biological products." It defines a "biological product" as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein . . . or analogous product . . . applicable to the prevention, treatment, or cure of a

[2] The FDCA defines labeling as all written matter "upon any article or any of its containers or wrappers, or accompanying such article." 21 U.S.C. § 321(m).

disease or condition of human beings." 42 U.S.C. § 262(i). Section 351 of the PHSA prohibits the delivery or introduction of any "biological product" into interstate commerce unless there is a "biologics license" in effect for the product and the product is properly labelled. 42 U.S.C. § 262(a). Section 361 of the PHSA permits the FDA[3] to make regulations "necessary to prevent the introduction, transmission, or spread of communicable diseases" into the United States. 42 U.S.C. § 264(a). Pursuant to this authority, the FDA separately promulgated regulations for human cells, tissues, or cellular or tissue-based products ("HCT/P's") at 21 C.F.R. Part 1271. 21 C.F.R. § 1271; 42 U.S.C. § 264.

2. HCT/P's - Section 351 and Section 361 HCT/P's

The parties do not dispute that the SVF is an HCT/P. *See* D.E. 41-1 at 16; D.E. 42-4 at 7. However, the PHSA distinguishes between two types of HCT/P's. One type of HCT/P's is known as "Section 361 HCT/P's." 21 C.F.R. § 1271.1. Section 361 HCT/P's are exclusively regulated by Section 361 of the PHSA, regardless of whether the HCT/P would also constitute a "drug" under the FDCA or a "biological product" under Section 351 of the PHSA. 21 C.F.R. §§ 1271.1(b), 1271.10. Thus, a manufacturer of Section 361 HCT/P's is not subject to the requirements of Section 351 of the PHSA or the FDCA. *Id.*; 21 C.F.R. § 1271.10(a). To qualify as a Section 361 HCT/P, the subject HCT/P must meet four criteria, including whether it is intended for "homologous use." *Id.* If the HCT/P does not meet these criteria, it is considered a "Section 351

[3] Although the text of the PHSA grants this authority to the Surgeon General, the Office of Surgeon General was abolished on June 25, 1966, and all of its functions were transferred to the Secretary of Health, Education, and Welfare, now the Secretary of Health and Human Services ("HHS"), by the 1966 Reorganization Plan No. 3, 42 U.S.C. § 202. The authority of the HHS Secretary was delegated to FDA. *See FDA Staff Manual Guide*, vol. II, § 1410.10 (listing delegations of authority), *available at* https://www.fda.gov/media/81983/download (last visited May 20, 2019).

HCT/P," and is regulated as a "biological product" and/or a "drug" under the FDCA. 21 C.F.R. § 1271.1(b)(2); 21 C.F.R. § 1271.20.

3. Same Surgical Procedure Exception

Separately, the FDA promulgated the "same surgical procedure" exception, exempting certain establishments from FDA regulation[4] if the "establishment . . . removes HCT/P's from an individual and implants such HCT/P's into the same individual during the same surgical procedure." Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447, 5449 (Jan 19, 2001); 21 C.F.R. § 1271.15(b).

On October 23, 2014, the FDA issued a draft guidance document, which it finalized on November 17, 2017. *Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception* (Nov. 2017), *available at* https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM419926.pdf (last accessed: May 20, 2019) (the "Guidance"). The Guidance "represents the current thinking of the [FDA] on this topic," and was not promulgated pursuant to notice-and-comment rulemaking. *Id.* In the Guidance, the FDA specifically addressed the meaning of "such HCT/P's" as used in the same surgical procedure exception:

> An HCT/P remains "such HCT/P" when it is in its original form. Generally, the only processing steps that will allow an HCT/P to remain "such HCT/P" are rinsing, cleansing, sizing, and shaping.

[4] The same surgical procedure exception in 21 C.F.R. § 1271.15(b) only expressly exempts manufacturers from Part 1271. *See* 21 C.F.R. § 1271.15(b) ("You are not required to comply with the requirements of this part . . . ."). However, in draft guidance, the FDA stated that "Part 1271 recognizes exceptions from the requirements of 21 CFR Part 1271. Typically, this would mean that products and establishments that meet one of these exceptions are not subject to FDA regulation." *Same Surgical Procedure Exception under 21 C.F.R. § 1271.15(b): Questions and Answers Regarding the Scope of the Exception, Draft Guidance for Industry* at 7 (Oct. 2014), *available at* https://wayback.archive-it.org/7993/20170404000725/https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM419926.pdf (last accessed May 20, 2019). In addition, the parties agree that if the same surgical procedure exception applies, then the SVF is not subject to FDA regulation under PHSA or the FDCA. D.E. 55 ¶ 15. Accordingly, the Court does not consider whether the SVF would be subject to regulation under the FDCA if the same surgical procedure exception applied.

Guidance at 5. The FDA also clarified that certain surgical procedures such as "autologous skin grafting" and "coronary artery bypass surgery" would be considered exempt from regulation under the same surgical procedure exception. *Id.* However, other procedures, such as isolating stem cells from adipose tissue, "would typically cause the adipose tissue to no longer be 'such HCT/P' and the establishment would generally not be considered to qualify for the exception under 21 CFR 1271.15(b)." *Id.* at 8.

iii. Overlapping Regulatory Regimes

In sum, there are three regulatory scenarios that could apply to Defendants. First, Defendants could be exempt from FDA regulation under the "same surgical procedure exception." Second, if the same surgical procedure exception does not apply, and if the SVF meets all four criteria to be considered a Section 361 HCT/P, then it is subject to exclusive regulation under Section 361 of the PHSA. Third, if the SVF does not meet these criteria, then the SVF is a Section 351 HCT/P and is subject to regulation under both the PHSA as a "biological product" and, if it is a "drug," the FDCA. With the regulatory framework in mind, the Court now turns to the parties' arguments.

B. Parties' Grounds for Summary Judgment

The FDA argues that there is no genuine dispute that the same surgical procedure exception does not exempt Defendants from FDA regulation, the SVF is not a Section 361 HCT/P, and the SVF is an adulterated and misbranded "drug" under the FDCA. *Id.* Accordingly, the FDA seeks summary judgment that the SVF is an adulterated and/or misbranded "drug" under the FDCA and an injunction preventing Defendants from further violating the statute. Defendants move for summary judgment on the sole issue of whether they are exempt from FDA regulation under the same surgical procedure exception. D.E. 41-1.

As the parties cross-move for summary judgment on the same surgical procedure exception, and a ruling favoring Defendants on this issue would be dispositive, the Court begins by addressing whether the exception applies to Defendants as a matter of law. Because the Court finds that as a legal matter, the exception is inapplicable, the Court then turns to whether the SVF is a Section 361 HCT/P, whether it is an adulterated or misbranded drug under the FDCA, and whether the FDA is entitled to an injunction.

C. Same Surgical Procedure Exception

i. Generally

21 C.F.R. § 1271.15(b) provides that an establishment is not subject to FDA regulation if it is "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." § 1271.15(b). Thus, in order to qualify for the "same surgical procedure exception," four elements must be met: (1) the product must be an HCT/P; (2) the HCT/P must be removed from and implanted in the same individual; (3) the process must occur during the same surgical procedure; and (4) the HCT/P that is implanted must be "such HCT/P."

ii. The Same Surgical Procedure Exception Does Not Apply

1. "Such HCT/P" is Unambiguously Not HCT/P that is "like or similar" HCT/P Removed from the Patient

The parties do not dispute that the SVF is an HCT/P. *See* D.E. 41-1 at 16; D.E. 42-4 at 7; 21 C.F.R. § 1271.3(d). The parties also do not dispute that the SVF is removed from and implanted in the same individual during the same surgical procedure. *See* D.E. 41-1 at 17; D.E. 45-5 at 2; D.E. 42-4 ¶ 24. Rather, the parties dispute whether the SVF that is implanted into the patient constitutes "such HCT/P's" removed from that patient. 21 C.F.R. § 1215.15(b).

The meaning of "such HCT/P's" within § 1271.15(b) presents an issue of regulatory interpretation, which is a question of law for the Court. *See Arevalo v. U.S. Attorney Gen.*, 872 F.3d 1184, 1187 (11th Cir. 2017). The first question the Court must decide is whether "such HCT/P's" as used in § 1271.15(b) unambiguously supports either party's interpretation. *See Belt v. EmCare, Inc.*, 444 F.3d 403, 408 (5th Cir. 2006) ("First, we ask whether the regulation is ambig[uous] with respect to the specific question considered.") (quotation omitted) (alteration in original). If so, then its unambiguous meaning controls. *See Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944); *Robinson v. Shell Oil Co.*, 519 U.S. 337, 340 (1997).

Initially, Defendants argue that "such HCT/P's" unambiguously means HCT/P's that are "like or similar" the HCT/P's removed from the patient. D.E. 41-1 at 19. As Defendants see it, the SVF implanted into the patient is "such HCT/P's" because it consists merely of cells separated from the adipose tissue extracted from the patient. *Id.* The FDA argues that the adipose tissue is "such HCT/P's" because "such HCT/P's" unambiguously refers to the HCT/P extracted from the patient that is still "in its original form," having only been subjected to minor "rinsing, cleansing, sizing and shaping." D.E. 42; D.E. 49.

To determine the meaning of "such HCT/P," the Court must look to the statutory or regulatory definition of the term, the ordinary meaning of the term, and its meaning in the broader context of the regulatory scheme. *Robinson*, 519 U.S., at 340-41. Here, "such HCT/P" is not defined in 21 C.F.R. § 1271 or elsewhere in the PHSA. Accordingly, the Court turns to the "ordinary, everyday meaning" of "such." *Schwarz v. City of Treasure Island*, 544 F.3d 1201, 1214 (11th Cir. 2008).

According to Defendants, the ordinary meaning of "such" is not "identical," but "relatedness" or "of the same class, type or sort." D.E. 41-1 at 12 (citing *Such*, THE MERRIAM-

WEBSTER DICTIONARY, https://www.merriam-webster.com/dictionary/such (last visited May 20, 2019)). On the other hand, the FDA maintains that the ordinary meaning of "such" in the legal context refers to an antecedent: "[t]hat or those; having just been mentioned." D.E. 49 (citing *Such*, BLACK'S LAW DICTIONARY (7th ed. 1999)); *see also United States v. Bowen*, 100 U.S. 508, 513 (1879) (interpreting statutory phrase "all such pensioners" to refer to antecedent subset of pensioners referenced in statutory text); *Such*, THE MERRIAM-WEBSTER DICTIONARY, https://www.merriam-webster.com/dictionary/such (last visited May 20, 2019) (including among the definitions of such: "of the character, quality, or extent previously indicated or implied"). Thus, in the FDA's view, "such" refers to the antecedent HCT/P in its original form.

The Court agrees with the FDA's interpretation. While the dictionary definitions could support both parties' interpretations, the word "such" must be read in the context of the sentence in which it appears. *See Food & Drug Admin. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000). The sentence contains no descriptions which would distinguish "such HCT/P's" from the antecedent HCT/P, thereby defining the "type or kind" of HCT/P to which the subsequent HCT/P could compare. Absent such descriptions, there are simply no criteria to limit what could constitute HCT/P's "of the same class, type or sort." Consequently, Defendants' proposed interpretation would create ambiguity whereas the FDA's construction is simple and straight forward, as well as consistent with the dictionary definitions and the context in which the words appear. Accordingly, the Court finds that the term "such HCT/P's" that are implanted into the patient does not unambiguously refer to HCT/P's that are "like or similar" the HCT/P's removed from the patient. Rather, the text of § 1271.15(b) unambiguously supports the FDA's interpretation, that "such HCT/P's" refers to the antecedent HCT/P removed from the patient in its original form.

2. § 1271.15(b) is Ambiguous as to the Subject HCT/P

Anticipating that the Court might conclude from the text of the regulation that "such HCT/P's" refers to the antecedent HCT/P removed from the patients, Defendants propose an alternative construction: that the comparative unit of HCT/P, to which "such HCT/P's" refers is the SVF that was extracted from the patient, not the adipose tissue. D.E. 50 at 9-14; *see also* D.E. 41-1 at 10 n.5.[5] As Defendants explain it, the SVF implanted into the patient is "such HCT/P" removed from the patient because those SVF cells remain largely unchanged from the SVF cells in the adipose tissue extracted from the patient. *See* D.E. 50 at 13 ("Because the SVF was unchanged from the time it was removed from the body (as part of the adipose tissue) until it was put back into the body it remains "in the form removed from the body."). The FDA counters that "such HCT/P's" implanted into the patient unambiguously refers to the HCT/P's that were removed from the patient in their original form, which in this case is the adipose tissue. D.E. 59 at 7-8. Therefore, if adipose tissue is the HCT/P removed from the patient, then adipose tissue must be implanted back into the patient for the exception to apply. D.E. 49 at 8.

The Court disagrees with both parties that § 1271.15 is unambiguous in this respect; the text is completely silent with respect to the particular unit of comparison between the HCT/P removed and implanted; in this case, adipose tissue or the SVF. Accordingly, § 1271.15(b) is "ambiguous with respect to the precise question we must answer:" whether "such HCT/P's" refers to all "such HCT/P's" removed from the patient in their original form or the HCT/P's extracted from the adipose tissue and implanted into the patient. *See United States v. Phifer*, 909 F.3d 372, 382 (11th Cir. 2018).

[5] Defendants argue that the FDA's opposition to this interpretation is reliant upon the Guidance. For reasons discussed *infra*, the Court is not persuaded by this argument. *See infra* pp. 15-16.

### 3. The FDA's Interpretation is Entitled to Deference

#### a. Standard

"[W]hen a regulation is ambiguous, we defer to the promulgating agency's interpretation of that regulation, unless its construction is 'plainly erroneous or inconsistent with the regulation.'" *Phifer*, 909 F.3d at 382 (quoting *Auer v. Robbins*, 519 U.S. 452, 461 (1997)). The Court must uphold an agency's interpretation of its regulations so long as it "reflect[s] the agency's fair and considered judgment on the matter in question." *Auer*, 519 U.S. at 461. The agency's interpretation must be given deference even if "even if [the agency's] interpretation is not 'the best or most natural one by grammatical or other standards.'" *Sierra Club v. Johnson*, 436 F.3d 1269, 1274 (11th Cir. 2006) (quoting *Legal Envtl. Assistance Found., Inc. v. EPA*, 276 F.3d 1253, 1262 (11th Cir.2001)) (alteration in original) (other quotations omitted). This is true "even if the agency's interpretation appears for the first time in a legal brief in the very litigation at issue." *Phifer*, 909 F.3d at 383 (citation omitted).

#### b. Parties' Arguments

In their motion, Defendants argue that the FDA is improperly using this action to enforce its Guidance as if it were a legally binding legislative rule and that therefore the FDA's interpretation of the same surgical procedure exception is not due deference. The FDA responds that its interpretation of the exception is not based on the Guidance; rather, it is consistent with § 1271.15(b), the FDA's long-held interpretation of the regulation, its regulatory history, compliance efforts and communications with Defendants. The FDA further argues that the Guidance has no legal effect and therefore it had no legal obligation to undergo notice-and-comment rulemaking procedures under the Administrative Procedure Act ("APA"), 5 U.S.C. § 1001 *et seq*., before its issuance because it is not a legislative rule. The Court agrees with the FDA.

c. The FDA's Interpretation is not Plainly Erroneous or Inconsistent

As a substantive matter, the FDA's interpretation on its face is neither "plainly erroneous" nor inconsistent with § 1271. *Auer*, 519 U.S. at 461. Other than arguments already discussed with regard to ambiguity, Defendants do not argue that the FDA's interpretation of the same surgical procedure exception is facially inconsistent or otherwise plainly erroneous, and the Court apprehends no independent grounds for so concluding. *See United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948) ("A finding is 'clearly erroneous' when . . . the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed.").[6]

Defendants argue however, that the FDA's interpretation is not entitled to deference because it "pronounces an entirely new position," contradicting twenty years of FDA regulatory thinking on the same surgical procedure exception. D.E. 41-1 at 21; *Christopher v. SmithKline Beecham Corp*., 567 U.S. 142, 155 (2012) (explaining that *Auer* deference is unwarranted where an "agency's interpretation conflicts with a prior interpretation" or is a *post hoc* rationalization "advanced by an agency seeking to defend past agency action against attack.") (quotation omitted). In support, Defendants point to the FDA's first proposal on regulating HCT/P's in which the FDA stated:

> the agency would not assert any regulatory control over cells or tissues that are removed from a patient and transplanted back into that patient during a single surgical procedure.

[6] Each party argues that the other's interpretation is absurd. Defendants argue that the FDA's interpretation is absurd because under its interpretation, cells could never qualify for the exception because they are always removed from a larger substance, even though the definition of "HCT/P" includes cells. D.E. 50 at 12. The Court does not agree. The FDA has addressed this issue by excluding many cells from the definition of HCT/P, such as "cell factors," "minimally manipulated bone marrow," "cells derived from animals" and "blood components." 21 C.F.R. § 1271.3(d)(1)-(8). In contrast, the FDA argues that Defendants' interpretation is absurd because it creates an exception that swallows the rule: under Defendants' interpretation, an establishment that extracts any HTC/P component from a patient, no matter how minute and no matter how processed and extracted, and implants that same component back into the patient would be exempt from FDA regulation. The Court agrees with the FDA that this is an untenable result. *See Spokane & Inland Empire R.R. v. United States*, 241 U.S. 344, 350 (1916) ("[E]xceptions from a general policy which a law embodies should be strictly construed.").

> The communicable disease risks, as well as the safety and effectiveness risks, would generally be no different than those typically associated with surgery.

Proposed Approach to Regulation of Cellular and Tissue-Based Products, FDA Dkt. No. 97N-0068, *available at* http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM062601.pdf (last accessed: May 20, 2019) (emphasis added) (the "1997 Proposed Approach").

Similarly, Defendants maintain that no limitation was imposed a year later in 1998, when the FDA published the proposed rule. *See* Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. 26744, 26748 (May 14, 1998) (the "1998 Rule"). According to Defendants, it was not until the FDA first proposed the Guidance in 2014 that the FDA indicated that it would limit the same surgical procedure exception to establishments that implant "such HCT/P's" that remain in their original form. D.E. 41-1 at 20-21.

The Court does not find Defendants' argument persuasive. First, even if the FDA were advancing a novel interpretation of the same surgical procedure exception, "a novel interpretation of its longstanding . . . regulations . . . alone is not a reason to refuse deference." *Talk Am., Inc. v. Michigan Bell Tel. Co.*, 564 U.S. 50, 64 (2011).[7] Second, the Court agrees with the FDA that its current interpretation is not inconsistent with any prior interpretations of § 1271 or the same surgical procedure exception.

[7] Defendants do not argue that this allegedly novel interpretation of the same surgical procedure exception is a violation of their procedural due process rights under the Fifth Amendment, and as such the Court does not consider it other than to briefly note that such an argument would be unavailing. *See Fils v. City of Aventura*, 647 F.3d 1272, 1284 (11th Cir. 2011) ("District courts cannot concoct or resurrect arguments neither made nor advanced by the parties.").

The FDA explains that since it began regulating HCT/P in the 1997 Proposed Approach, it has consistently indicated that HCT/P not in its original form would be subject to FDA regulation. D.E. 49 at 11-13. For example, in the 1997 Proposed Approach, the FDA explained that "cells and tissues that were manipulated extensively, combined with non-tissue components, or were to be used for other than their normal functions would be regulated . . . ." 1997 Proposed Approach (emphasis added). Additionally, in the proposals and rules discussing the same surgical procedure exception, the FDA provided illustrations of surgical procedures that would qualify for the exception. In each case, all of the HCT/P removed from the patient was implanted into that patient in its original form, indicating the limited type of removal and implantation encompassed by the same surgical procedure exception. For example, in the 1997 Proposed Approach, the FDA stated: "Autologous cells and tissues collected and transplanted in a single surgical procedure (e.g., skin or vein grafts) would not be subjected to any regulatory requirements." *Id.* at 20 (emphasis added). In the 1998 Rule, the FDA further explained that a surgeon removing "a saphenous vein from a patient for use in a later coronary bypass in the same patient" would fall under the same surgical procedure exception. *See* Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. at 26748; D.E. 49 at 12-13. Similarly, when the FDA later promulgated the final rule regulating HCT/P in 2001, it explained that procedures that modified the HCT/P from its original form would be excluded from the same surgical procedure exception:

> so long as the hospital does not engage in any other activity encompassed with in [sic] the definition of "manufacture," the hospital would not be required to register or comply with the other provisions to be codified in part 1271. For example, if the hospital expanded the cells or tissues, it would not meet the terms of the [same surgical procedure] exception.

Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. at 5449 (emphasis added).

The examples above demonstrate that the FDA's current interpretation of the same surgical procedure exception does not conflict with § 1271 or its regulatory history. Rather, the FDA has historically interpreted the same surgical procedure exception as limited to those procedures in which the HCT/P removed from the patient is implanted back into that patient in its original form, with minimal processing.[8] *See Gardebring v. Jenkins*, 485 U.S. 415, 430 (1988) (explaining that the Court must defer to the agency's interpretation unless an "alternative reading is compelled by the regulation's plain language or by other indications of the [agency's] intent at the time of the regulation's promulgation.").

Moreover, "[b]road deference is all the more warranted when, as here, the regulation concerns 'a complex and highly technical regulatory program,' in which the identification and classification of relevant 'criteria necessarily require significant expertise and entail the exercise of judgment grounded in policy concerns.'" *Thomas Jefferson Univ. v. Shalala*, 512 U.S. 504, 512 (1994) (quoting *Pauley v. BethEnergy Mines, Inc.*, 501 U.S. 680, 697 (1991)). Determining which HCT/P transplant procedures are exempt from FDA regulation undoubtedly requires significant expertise and the FDA's determination is "grounded in policy concerns" reflective of the FDA's mandate under Section 361 of the PHSA to "make and enforce such regulations as . . . are necessary to prevent the introduction, transmission, or spread of communicable diseases" 42 U.S.C. § 264(a),

[8] Defendants argue that the FDA's interpretation, as set out in the Guidance, is internally inconsistent because it defines "such HCT/P" as HCT/P in its "original form," but permits "rinsing, cleansing, sizing, or shaping" of the HCT/P, which would alter the "original form" of the HCT/P. Guidance at 5. According to Defendants, this means that "such HCT/P's" must refer to the HCT/P that is implanted into the patient. D.E. 50 at 17. But the rinsing and other procedures expressly identified by the FDA do not change the original form of the HCT/P. The Guidance describes these steps as "limited handling." *Id.* at 7. The FDA also provides defining examples of rinsing, sizing, and shaping, that would not alter the original form of the HCT/P, such as dilation to size a vascular graft in coronary bypass surgery, and examples of impermissible cleansing, such as centrifugation for cell isolation. Guidance at 6. Thus, Defendants' argument fails.

and its mandate under the FDCA to ensure that drugs are "safe and effective for use." 21 U.S.C. § 301 *et seq*. The FDA has consistently limited the same surgical procedure exception to procedures in which all such HCT/P removed from the patient is implanted back into the patient because the more a procedure modifies an HCT/P from its original form, the higher the risk of spreading communicable disease and the more regulation is required. Indeed, in the 1997 Proposed Approach, the FDA overtly explained that this was the rationale behind the same surgical procedure exception:

> The agency would not assert any regulatory control over cells or tissues that are removed from a patient and transplanted back into that patient during a single surgical procedure. The communicable disease risks, as well as safety and effectiveness risks, would generally be no different from those typically associated with surgery.

1997 Proposed Approach at 12 (emphasis added). In the 1998 Rule, the FDA further clarified that the same surgical procedure exception would not apply to otherwise qualified procedures that could increase the risk of the spread of disease:

> As the potential risk posed by a product increases, so will the level of oversight afforded that product . . . Storage in the same location as other human cellular or tissue-based products gives rise to concerns about the spread of infectious disease and would be considered beyond the bounds of the [same surgical procedure] exception.

Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. at 26745-26748 (emphasis added).

Similarly, when the FDA promulgated the final rule it stated, "[t]he regulation now being finalized forms the foundation for a regulatory program that will further the goal of preventing the transmission of communicable disease." Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. at 5449 (emphasis added).

Emphasizing its historical consistency, the FDA restated this regulatory philosophy in 2014 and in 2017 when it issued the Guidance:

> In sum, FDA's view is that autologous cells or tissues that are removed from an individual and implanted into the same individual without intervening processing steps beyond rinsing, cleansing, sizing, or shaping, raise no additional risks of contamination and communicable disease transmission beyond that typically associated with surgery.

*Same Surgical Procedure Exception under 21 C.F.R. § 1271.15(b): Questions and Answers Regarding the Scope of the Exception, Draft Guidance for Industry* at 3 (Oct. 2014), *available at* https://wayback.archive-it.org/7993/20170404000725/https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM419926.pdf (last accessed May 20, 2019); Guidance at 3 (emphasis added).

Thus, the FDA's interpretation herein aligns with the FDA's historical regulatory thinking; procedures like Defendants', in which all of the same HCT/P is not re-implanted into the patient, involve a higher risk of communicable disease and other safety concerns and are therefore subject to FDA regulation. To be sure, prior to 2014, the FDA had never expressly stated that to qualify for the same surgical procedure exception, the HCT/P implanted into the patient had to be all "such HCT/P" in the original form in which it was removed from the patient. But, its current interpretation plainly is not inconsistent with the same surgical procedure's regulatory history and is solidly grounded in the FDA's mandate under the FDCA and § 361 of the PHSA to prevent the spread of communicable diseases and otherwise ensure safety. Accordingly, the Court finds that it is entitled to deference. *See Cathedral Candle Co. v. U.S. Intern. Trade Comm'n*, 400 F.3d 1352, 1364 (Fed. Cir. 2005) ("While [the agency's] interpretation is by no means compelled by the language of the regulation, it is not contrary to the express terms of the regulation, nor is it at odds

with the purposes served by the regulation . . . [It] is reasonable and is therefore binding on us.") (citation omitted); *Long Island Care at Home, Ltd. v. Coke*, 551 U.S. 158, 170 (2007) ("[W]e concede that the Department may have interpreted these regulations differently at different times in their history . . . But as long as interpretive changes create no unfair surprise . . . the change in interpretation alone presents no separate ground for disregarding the Department's present interpretation."); *see Kennedy v. Plan Adm'r for DuPont Sav. & Inv. Plan*, 555 U.S. 285, 296 n.7 (2009) (holding that the Department of Labor's interpretation of ERISA was entitled to *Auer* deference even though its position had changed over time and its current position was presented for the first time in an *amicus* brief); *cf. Summit Petroleum Corp. v. U.S. E.P.A.*, 690 F.3d 733, 746 (6th Cir. 2012) (finding the EPA's interpretation of regulation was not entitled to *Auer* deference because the EPA's interpretation of the regulation at issue required a test that it explicitly rejected in notice and comment rulemaking and was directly contradicted by earlier guidance).

d. The Guidance is not a Legislative Rule

Finally, with respect to the "same surgical procedure" exception, the Court rejects Defendants' argument that this case should be dismissed because it depends improperly on the enforceability of the Guidance, which was not subjected to the APA's notice-and-comment requirements. D.E. 41-1 at 18-30; *see Appalachian Power Co. v. E.P.A.*, 208 F.3d 1015, 1024 (D.C. Cir. 2000) ("It is well-established that an agency may not escape the notice and comment requirements . . . by labeling a major substantive legal addition to a rule a mere interpretation."); *see also Gen. Elec. Co. v. E.P.A.*, 290 F.3d 377, 385 (D.C. Cir. 2002) (explaining that legislative rules that are not promulgated pursuant to notice and comment rulemaking must be vacated under the APA). What Defendants fail to appreciate, however, is that even if the FDA intends to enforce the Guidance in this case, its prosecution of the case is not procedurally improper and does not

warrant dismissal because the FDA's interpretation of the "same surgical procedure" exception, as articulated herein, does not depend on the Guidance, is not plainly erroneous or facially inconsistent with the regulation and is historically consistent with the FDA's interpretation. In other words, in the absence of the Guidance, the FDA has the authority to bring this enforcement action under the PHSA and FDCA and to oppose the Defendants' claim to the exemption. *See* 42 U.S.C. § 262(j); 21 U.S.C. § 332(a); *Am. Min. Cong. v. Mine Safety & Health Admin*., 995 F.2d 1106, 1112 (D.C. Cir. 1993) (concluding that rule was interpretive because "in the absence of the rule there would . . . be an adequate legislative basis for enforcement action or other agency action to confer benefits or ensure the performance of duties . . . ."). And its interpretation of the exemption is entitled to deference. *Auer*, 519 U.S. 452; *Talk Am., Inc*. 564 U.S. at 64 (explaining that even if an agency's interpretation is a "novel interpretation of its longstanding . . . regulations . . .novelty alone is not a reason to refuse deference.").

In any event, the Guidance is not a disguised legislative rule, as Defendants contend. The distinction between "legislative rules," which are subject to rigorous notice-and-comment rulemaking procedures and "interpretive rules," which are not, turns primarily on whether the rule has binding legal effect. 5 U.S.C. § 553; *see Nat'l Min. Ass'n v. McCarthy*, 758 F.3d 243, 252 (D.C. Cir. 2014). Courts make this assessment by considering the agency's characterization of the guidance and whether the agency has applied the guidance as binding on the parties. *McCarthy*, 758 F.3d 243. The FDA characterizes the Guidance as informational. As the FDA points out, the Guidance is presented in a "question and answer" format, advising the public of the FDA's interpretation of 21 C.F.R. § 1271.15(b):

> We . . . are issuing this guidance to provide you, tissue establishments and healthcare professionals, with our current thinking on the scope of the exception set forth in Title 21 of the Code of Federal Regulations (CFR) Part 1271, specifically the exception set forth in 21 CFR 1271.15(b).

Guidance at 1 (emphasis added); *see Perez v. Mortg. Bankers Ass'n*, 135 S.Ct. 1199, 1204 (2015) ("[T]he critical feature of interpretive rules is that they are 'issued by an agency to advise the public of the agency's construction of the statutes and rules which it administers.'") (quoting *Shalala v. Guernsey Mem'l Hosp.*, 514 U.S. 87, 99 (1995)).

Nonetheless, Defendants argue that the Guidance operates as a legislative rule because, as employed by the FDA in this case, it establishes a "binding norm" and lacks words connoting that compliance with the Guidance is optional, such as "should" or "may." D.E. 41-1 at 26; *see Cmty. Nutrition Inst. v. Young*, 818 F.2d 943, 946 (D.C. Cir. 1987) ("[C]ourts are to give far greater weight to the language actually used by the agency; we have, for example, found decisive the choice between the words 'will' and 'may.'") (citations omitted). This argument fails for the obvious reason that the questions, answers, and interpretations in the Guidance do not command the parties or impose any obligations; rather, almost every answer contains the qualifiers "typically," "generally" or "in general." *cf. Appalachian Power Co.*, 208 F.3d at 1023 (holding rule was legislative because "the entire Guidance, from beginning to end—except the last paragraph—reads like a ukase. It commands, it requires, it orders, it dictates."); *McCarthy*, 758 F.3d at 253 (finding that EPA final guidance was not a legislative rule because it was "devoid relevant commands."); *cf. Am. Bus Ass'n v. United States*, 627 F.2d 525, 532 (D.C. Cir. 1980) (holding statement was legislative rule because it "repeatedly says and implies 'the Commission will;' it nowhere says or implies 'the Commission may.'").

Defendants further argue that the Guidance is a legislative rule because it has a substantive impact on how stem cell clinics operate. D.E. 41-1 at 30. But again, contrary to Defendants' argument, the Guidance by its terms provides both the public and the FDA with substantial discretion in how to comply with § 1271.15 and is expressly not binding on the FDA or the public:

> This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

Guidance at 1 (emphasis added); *see Brock v. Cathedral Bluffs Shale Oil Co*., 796 F.2d 533, 537 (D.C. Cir. 1986) ("An agency pronouncement is not deemed a binding regulation merely because it may have 'some substantive impact,' as long as it 'leave[s] the administrator free to exercise his informed discretion.'") (quoting *Guardian Fed. Sav. & Loan Ass'n v. Federal Sav. & Loan Ins. Corp*., 589 F.2d 658, 666, 668 (D.C. Cir. 1978)) (alteration in original). Contrary to Defendants' assertions, "[t]his is not a case in which the guidance document signals that the agency 'will not be open to considering approaches other than those prescribed' therein." *Sierra Club v. Envtl. Prot. Agency*, 873 F.3d 946, 952 (D.C. Cir. 2017) (quoting *Gen. Elec. Co.*, 290 F.3d at 384).

The FDA's description of the legal effect of the Guidance emphatically reinforces this conclusion. As noted *supra*, the very first page contains a text box, conspicuously set apart from the other text, expressly providing that the Guidance "is not binding." Guidance at 1. The next page begins with "[the] FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities." *Id.* at 2 (emphasis added). Further, *every page* of the Guidance contains a bolded header, stating: "**Contains Nonbinding Recommendations**." *Id.* (emphasis in original); *see McCarthy*, 758 F.3d at 253 (explaining that guidance was not legislative rule because the disclaimers "run throughout the document."). While the FDA's own characterization of the Guidance's legal effect is not dispositive, the Court gives "some, albeit 'not overwhelming,' deference to an agency's characterization of its [Guidance]." *Young*, 818 F.2d at 946 (quotation omitted); *see also Cement Kiln Recycling Coal. v. E.P.A.*, 493 F.3d 207, 228 (D.C. Cir. 2007) ("[A]n agency's pronouncement that a document is non-binding will not make it so

where there is evidence—or practice—to the contrary . . . But the Coalition points to no such evidence here, and we have previously relied on similar disclaimers as relevant to the conclusion that a guidance document is non-binding.") (citations omitted) (emphasis added).

In conclusion, the Guidance is not, by its terms or by the FDA's interpretation, "legally binding" and, even if the FDA considered it as such, it would be irrelevant to the disposition of this action. *See United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1322 (D.C. Cir. 2014) ("Appellants claim that the FDA seeks to give legal effect to a statement that was not promulgated through formal rule-making procedures . . . Our decision, however, is based on, and gives effect to, the Part 1271 Regulations, not the preamble. Appellants' procedural challenge to the preamble is therefore irrelevant."). Congress has delegated to the FDA substantial discretion in the regulation of drugs and biological products, its interpretation of § 1271.15(b) is neither facially inconsistent nor otherwise plainly erroneous and is historically consistent with the FDA's position regarding the regulation of HCTP's. Therefore, the FDA's interpretation of the same surgical procedure exception in 21 C.F.R. § 1271.15(b) is entitled to deference under *Auer*.[9] 519 U.S. 452. Under this interpretation, "such HCT/P" implanted into the patient refers to all of the HCT/P removed from the patient in its original form, subject to limited handling. As Defendants' SVF therapy extracts adipose tissue, but only implants the SVF into the patient, after subjecting it to a specific and complex multi-step procedure, the HCT/P is no longer in its original form. Thus, the same surgical procedure exception does not and cannot apply to Defendants as a matter of law, and they are therefore subject to FDA regulation. As this is the sole issue on which Defendants move for

[9] The Court is aware that *Auer* has faced skepticism and that the Supreme Court recently heard oral argument in *Kisor v. Wilkie*, 139 S. Ct. 657, 202 (2018), which may eviscerate the doctrine. However, until the Supreme Court overturns *Auer*, it remains binding precedent and the Court must apply it as such.

summary judgment, the Court denies Defendants' Motion and grants the FDA's Motion on this issue.

D. Regulation of the SVF Under the PHSA - SVF as HCT/P

i. The SVF is not a Section 361 HCT/P

The next issue is whether the SVF is only subject to regulation under § 361 of the PHSA or whether the SVF is subject to regulation under § 351 of the PHSA and the FDCA. An HCT/P that meets all four of the criteria in 21 C.F.R § 1271.10(a) is not regulated under the FDCA. Instead, it is exclusively regulated under § 361 of the PHSA. 21 C.F.R. § 1271.10. The Court focuses its inquiry on one of these criteria, whether the HCT/P is intended for homologous use, because the issue is dispositive. *See* § 1271.10(a) ("[T]he HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent.").

1. Homologous Use

21 C.F.R. § 1271.3(c) defines "homologous use" as "the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor." § 1271.3(c) (emphasis added). The parties renew their dispute as to whether the subject HCT/P refers to the HCT/P removed from the patient or the HCT/P implanted into the patient; i.e. the adipose tissue or the SVF. However, the Court need not resolve this ambiguity because regardless of whether the HCT/P refers to adipose tissue or SVF, there is no genuine dispute that Defendants do not intend the HCT/P removed from the patient to perform the same basic function when implanted into the patient.[10]

[10] Section 1271.10(a) is silent as to the subject HCT/P and is therefore ambiguous. *Phifer*, 909 F.3d at 382. As Defendants' only challenge to the FDA's interpretation is a conclusory argument that it is based on another improper guidance document, the Court defers to the FDA's interpretation: the subject HCT/P is the adipose tissue removed from the patient. *See* D.E. 50 at 16; *Auer*, 519 U.S. at 461. Under its interpretation, the FDA argues that the SVF is not exclusively intended for homologous use because when implanted into the patient, it does not perform the same basic "cushioning and support" function of the adipose tissue extracted from the patient. D.E. 42 at 23; D.E. 42-4 ¶

To make this determination, 21 C.F.R. § 1271.10(a) refers the Court to "the labeling, advertising, [and] other indications of the manufacturer's objective intent." The FDA correctly notes that Defendants market and advertise the SVF for the treatment of "various neurological, autoimmune, orthopedic, and degenerative medical conditions and/or diseases, including but not limited to Amyotrophic Lateral Sclerosis ("ALS"), Parkinson's disease, spinal cord injuries, stroke, traumatic brain injury, chronic obstructive pulmonary disease ("COPD"), lung disease, and diabetes." D.E. 1 ¶ 7; D.E. 26 ¶ 7; *see also* D.E. 43-3 at 11-12 (advertising that Defendants' treatment can "reduce the deterioration of nerve cells, restore cell function and contribute to anti-inflammatory processes."). In response, Defendants vaguely assert that they intend the SVF to perform the same basic regenerative function before and after the procedure. *See* D.E. 50 at 18. But Defendants do not and cannot argue that providing a regenerative function in the donor is the same basic function as restoring cell function, contributing to anti-inflammatory processes, and otherwise treating this litany of illnesses in the recipient. *See* D.E. 50 at 18. Accordingly, there is no genuine dispute that the SVF is not intended solely for homologous use under § 1271.10(a) as a matter of law and therefore the SVF is not a "Section 361 HCT/P." *See* Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. at 5458 ("We continue to consider nonhomologous use to be a meaningful indicator that regulation

32. Defendants do not dispute this, but argue that the adipose tissue also performs a regenerative function in the patient before being extracted, which Defendants intend to provide by implanting the SVF into patients. *See* D.E. 50-1 ¶ 11; D.E. 55 ¶ 13; D.E. 50 at 18; D.E. 45-2. Section 1271.10(a) is ambiguous as to whether "homologous use" encompasses HCT/P's intended to perform at least one of the basic functions of the HCT/P removed from the patient or whether the HCT/P must perform all of the basic functions of the HCT/P removed from the patient. Neither party discusses this ambiguity, but the FDA's argument implicitly interprets homologous use as encompassing only HCT/P that performs all of the same basic functions in the recipient as in the donor. For reasons discussed *supra*, the Court defers to the FDA's interpretation. *See supra* pp. 17-27; *Auer*, 519 U.S. at 461. Accordingly, the fact that the SVF performs the same regenerative function as a constituent part of the adipose tissue does not equate to homologous use. As Defendants do not argue that the SVF they implant into a patient also provides the cushioning function of adipose tissue, *see* D.E. 50 at 18, there is no genuine dispute that the SVF is not intended solely for homologous use.

solely under section 361 of the PHS Act is not sufficient. For example, promotion of an HCT/P for an unproven therapeutic use, such as curing cancer, would clearly make it inappropriate to regulate the HCT/P solely under section 361 of the PHS Act and the regulations that will be in part 1271.").

E. Regulation of the SVF Under the FDCA – SVF as Drug

HCT/P's that are not exclusively regulated by Section 361 of the PHSA are regulated under both Section 351 of the PHSA and, if they are a "drug" under the FDCA. 21 C.F.R. § 1271.1(b)(2). The FDCA prevents the taking of any action with respect to a "drug" "if such act is done while such article is held for sale . . . after shipment in interstate commerce and results in such article being adulterated or misbranded." 21 U.S.C. § 331(k) (emphasis added).[11] Other than arguments already addressed regarding the same surgical procedure exception, Defendants have provided nothing in the way of evidence or argument to rebut any of the FDA's claims that the SVF should be regulated under the FDCA. *See* D.E. 41-1; D.E. 50. Accordingly, the Court only briefly reviews whether the FDA has met its burden of demonstrating that there is no genuine dispute that the SVF is an adulterated and misbranded drug under the FDCA.

i. The SVF is a Drug

The FDCA defines a "drug" as *inter alia*, "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1)(B); *see also Whitaker v. Thompson*, 353 F.3d 947, 953 (D.C. Cir. 2004) (explaining that under the

[11] 21 U.S.C. § 321(g)(1)(A), (D) includes "articles intended for use as a component of [a drug]" within the definition of "drug" under the FDCA. Courts have interpreted "held for sale" as meaning any use beyond personal consumption. *See, e.g., United States v. Evers*, 643 F.2d 1043, 1050 (5th Cir. 1981) (explaining that "held for sale" covers situations in which the drugs are held by a retailer, wholesaler, or even a physician who distributed the drugs). As such, there is no dispute that components of the SVF are shipped in interstate commerce or that the SVF is "held for sale" by Defendants. D.E. 50-1 ¶¶ 14, 16, 18, 19; *see United States v. Bacto–Unidisk*, 394 U.S. 784, 798, (1969) (explaining that Congress' intent was that the FDCA's "coverage be as broad as its literal language indicates.")

FDCA the "classification of a substance as a 'drug' turns on the nature of the claims advanced on its behalf."). Relying on the same marketing used to demonstrate that the SVF is not intended for homologous use, the FDA argues that it is undisputed that Defendants market their SVF as intended to cure and/or treat numerous diseases. D.E. 42 at 11-12. Defendants do not dispute this contention. D.E. 1 ¶ 7; D.E. 26 ¶ 7. Accordingly, as the SVF is intended for use in the treatment of, *inter alia*, Parkinson's disease, stroke, and lung disease in humans, the Court agrees with the FDA that the SVF is a drug under the FDCA and subject to its adulteration and misbranding provisions. *See, e.g.*, D.E. 50-1 ¶ 25 (explaining that Defendants' brochure markets the SVF as "proven to be a better alternative for people facing debilitating conditions such as . . . Degenerative Disc Disease, Osteoarthritis and many others where traditional medicine falls short . . . .").

ii. The SVF is Adulterated

A drug is "adulterated" under the FDCA if, *inter alia*, the methods used for its manufacture, processing, packing or holding do not conform to CGMP. 21 U.S.C. § 351(a)(1)(B). The CGMP is codified at 21 C.F.R. § 211. Among the many requirements of CGMP are that the drug must be aseptically processed, that the manufacturer has a system in place for monitoring environmental conditions, and "there shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms." 21 C.F.R. § 211.42(c)(10)(iv); 21 C.F.R. § 211.165(b).

The FDA argues that Defendants do not follow CGMP in manufacturing and processing the SVF. In support, the FDA points to the Form FDA-483's issued after the FDA's inspections of Defendants' facilities from April 10 to May 11, 2017. D.E. 42 at 15-16. While Defendants dispute some of the findings from these inspections, they do not dispute that as of the date of the inspection, they did not perform bioburden testing of their SVF to test for the presence of objectionable

microorganisms. D.E. 50-1 ¶ 33. Defendants also do not dispute that as of the date of the inspection they had not established a system for monitoring environmental conditions to prevent contamination during aseptic processing. D.E. 50-1 ¶ 44. The FDA argues that these failures constitute violations of CGMP because Defendants do not perform appropriate laboratory testing on the SVF to ensure it is free of objectionable microorganisms and do not have "a system for monitoring environmental conditions [during] aseptic processing." 21 C.F.R. § 211.165(b).

As Defendants do not challenge these claims, *see* D.E. 50; D.E. 42, the Court concludes that as of the date of the inspections, Defendants' SVF processing, packaging, and holding methods did not conform to the CGMP and the SVF is therefore adulterated. 21 U.S.C. § 351(a)(1)(B); *see United States v. Radix Labs., Inc.*, 963 F.2d 1034, 1038 n.4 (7th Cir. 1992) ("If a drug is not manufactured in conformity with CGMP it is adulterated."); *see Regenerative Scis., LLC*, 741 F.3d at 1323 ("[I]t is undisputed that appellants' facilities, methods, and controls for processing the Mixture violated federal manufacturing standards in numerous respects. Therefore, the Mixture is *per se* adulterated . . . ."); *United States v. 789 Cases, More or Less, of Latex Surgeons' Gloves, an Article of Device*, 799 F. Supp. 1275, 1287 (D.P.R. 1992) ("A device is adulterated, as a matter of law, if there is a single instance of failing to conform to the GMP regulations.").

iii. The SVF is Misbranded

A drug is "misbranded" under the FDCA if, *inter alia*, its labeling lacks "adequate directions for use." 21 U.S.C. § 352(f)(1). The FDA defines "adequate directions for use" as "directions under which the layman can use a drug safely and for the purposes for which it is intended." 21 C.F.R. § 201.5. Among other things, failure to specify or explain the: "uses for which [the] drug is intended," "quantity of dose, including usual quantities" and "route or method of

administration or application" for a drug may render directions for use inadequate. 21 C.F.R. § 201.5.

The FDA argues that the SVF is "misbranded" because its labelling lacks indications for use, dosages, routes of administration or side effects. D.E. 50-1 ¶ 20. According to the 2017 FDA inspection report, "the final SVF product label includes the patient's name on a syringe written in permanent marker [and] . . . there is no written procedure for final product labeling." D.E. 53-1 at 39. Defendants do not dispute this fact and offer no counterargument. D.E. 50-1 ¶ 20. Accordingly, as there appear to be no directions under which a layman can safely use the SVF for its intended purpose, the Court agrees that the FDA is entitled to summary judgment as to whether the SVF is misbranded. 21 C.F.R. § 201.5.

F. The FDA is Entitled to an Injunction

Lastly, the Court must determine if the FDA is entitled to an injunction. The FDA seeks a statutory injunction pursuant to 21 U.S.C. § 332(a) to prevent Defendants from "doing any act" with respect to the SVF in violation of 21 U.S.C. § 331(k). Defendants also seek authorization pursuant to the injunction, to inspect Defendants' business and records to ensure continuing compliance with the terms of the injunction.

Unlike a private party seeking an injunction, the FDA need not show that it would suffer irreparable harm if the injunction were not granted. *See Gresham v. Windrush Partners, Ltd.*, 730 F.2d 1417, 1423 (11th Cir. 1984). Instead, the FDA must demonstrate a "reasonable likelihood of further violations in the future" to obtain injunctive relief. *Regenerative Scis., LLC*, 741 F.3d at 1325. In making this determination, Courts review "[1] whether a defendant's violation was isolated or part of a pattern, [2] whether the violation was flagrant and deliberate or merely

technical in nature, and [3] whether the defendant's business will present opportunities to violate the law in the future." *Id.* (quotations omitted) (alterations in original).

The Court agrees with the FDA that there is a reasonable likelihood that Defendants will continue to violate the FDCA. Defendants' violations of the FDCA are not isolated; they have continuously performed the SVF therapy in noncompliance with CGMP as evidenced by the continued violations found in the Form FDA-483's in 2015 and 2017. D.E. 50-1 ¶¶ 29-30; D.E. 45 ¶¶ 13-17. Moreover, the violations are not merely technical; when confronted with the warning letter and Form FDA-483's informing them of their noncompliance, Defendants responded not by bringing their practice into conformity with CGMP, but by arguing that they were exempt from FDA regulation. D.E. 45 ¶ 20; D.E. 26 ¶ 52. Lastly, the Defendants' business will undoubtedly present opportunities to violate the FDCA in the future as there is no indication that they have now complied with CGMP or adequately labelled their product. Defendants offer no challenge to these arguments, and as such, the Court concludes that the FDA is entitled to an injunction under 21 U.S.C. § 332(a).[12]

## IV. Conclusion

For the reasons discussed *supra*, it is

[12] Defendants also make various arguments asserting that their SVF therapy is regulated by the Florida Board of Medicine and are therefore sufficiently regulated. D.E. 50 at 6-7. But, whether the SVF therapy is also regulated by the Florida Board of medicine is irrelevant; the issue is whether the SVF is regulated under the PHSA and/or FDCA. *See United States v. Regenerative Scis., LLC,* 878 F. Supp. 2d 248, 261 (D.D.C. 2012), *aff'd*, 741 F.3d 1314 (D.C. Cir. 2014) ("Where, as here, a product meets the definition of "drug" under the FDCA, it comes under the ambit of this law and is thus subject to its provisions. This is true even if its regulation will affect the practice of medicine. Consequently, Defendants' argument that the cell product cannot be regulated by the FDA because the Regenexx™ Procedure constitutes the 'practice of medicine' is unavailing.").

ORDERED AND ADJUDGED that Defendants' Motion, D.E. 41, is DENIED, and the FDA's Motion, D.E. 42, is GRANTED. The Court will separately enter judgment in favor of the FDA pursuant to Federal Rule of Civil Procedure 58. It is further

ORDERED AND ADJUDGED that the case is CLOSED for administrative purposes. All hearings are CANCELLED; all other pending motions are DENIED AS MOOT.

DONE AND ORDERED in Chambers at Miami, Florida, this _3rd_ day of June, 2019.

URSULA UNGARO
UNITED STATES DISTRICT JUDGE

copies provided: counsel of record