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CALIFORNIA STEM CELL TREATMENT CENTER, INC., CELL SURGICAL NETWORK CORPORATION, ELLIOT B. LANDER, M.D. and MARK BERMAN, M.D.

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

EASTERN DIVISION

UNITED STATES OF AMERICA,

Plaintiff,

v.

CALIFORNIA STEM CELL TREATMENT CENTER, INC., a California corporation, CELL SURGICAL NETWORK CORPORATION, a California corporation, and ELLIOT B. LANDER, M.D., MARK BERMAN, M.D., individuals,

Defendants.

CASE NO. 5:18-CV-01005-JGB-KK

Hon. Jesus G. Bernal
Riverside, Courtroom 1

DEFENDANTS' OPPOSITION TO PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT

Hearing:
Date: December 9, 2019
Time: 9:00 a.m.
Dept. Courtroom 1

Action Filed: May 9, 2018
Trial Date: February 11, 2020

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I. INTRODUCTION

This is a case about the intersection between a person's fundamental right to control his own body, including the cells that comprise it, a surgeon's ability to perform a medical procedure with informed consent of his patient, and a regulatory agency's attempt to bar access to a safe surgical procedure. The Government's summary judgment motion should be denied because it applies an incorrect legal framework to disputed facts.

Specifically, the Government claims that Defendants do not meet the Same Surgical Procedure Exemption ("SSP Exemption") because the surgical procedure at issue removes adipose (fat) tissue from a patient, but only reinjects the stem cells found within the tissue, and the stem cells themselves are altered during the procedure. But Defendants dispute the government's primary factual assertion that the stem cell material placed into a patient during the surgical procedure is not the same material that was removed. Further, Defendants offer concrete evidence, including expert opinion, that the stem cells placed into a patient are not materially altered during the procedure.

In addition to the factual dispute as to the underlying science and evidence, instead of looking to the plain language of the SSP Exemption, the Government attempts to enforce substantive changes to the exemption promulgated by a 2017 Guidance document requiring that the material be in its "original form" to qualify for the SSP Exemption. But the Supreme Court recently clarified the substantial burden a government agency must meet to obtain deference for its interpretation of regulations, including guidance documents. *Kisor v. Wilkie*, 139 S.Ct. 2400 (2019). Defendants dispute the underlying material facts as to whether the stem cells are altered and object to the reference to the guidance documents as the authority on what constitutes an exemption instead of the plain language of the statute such that summary judgment must be denied.

Moreover, the Government's attempt to regulate surgery is unconstitutional as Defendants' procedure does not affect interstate commerce and is not shipped in interstate commerce. The Government's attempt to tether its regulatory authority to the fact that Defendants use materials that were shipped in interstate commerce as part of the procedure falls short. If true, every surgical procedure would comprise interstate commerce, because a scalpel is shipped in interstate commerce. But the Government ignores that its express authority is limited to articles *after* shipment in interstate commerce. Because the stem cells themselves are not shipped in interstate commerce, FDA's attempt to regulate the procedure is unconstitutional.

Lastly, the Government seeks a permanent injunction for two additional procedures that Defendants stopped performing well before the initiation of this lawsuit. Thus, the Government lacks Article III standing to pursue injunctive relief regarding Defendants' former SVF/Vaccinia procedure, which has not been performed since August 2017, or the ACS Expanded Cell procedure, which has not been performed since December 2017.

For each of the foregoing reasons, the Government's Motion must be denied so Defendants can be afforded their Constitutional right to defend themselves against these claims on the merits at trial.

II. BACKGROUND FACTS

A. What is a Stem Cell?

Cells are the smallest and most basic functional structural units in the human body. Additional Material Fact ("AMF") No. 1. Every organ and tissue in the human body is comprised of cells. AMF No. 2. Surgeons routinely work on both tissues and cells that make up tissues. AMF No. 3. Surgery universally involves dissection (separation) of tissues and now technologically has evolved to the point where surgeons can isolate individual cells. AMF No. 4. Dissected tissues and

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cells can then be surgically relocated and re-purposed to other parts of the patient's body in the operating room. AMF No. 5.

Cal. Stem Cell's SVF Surgical Procedure involves the relocation of a patient's own SVF cells during a single, rather simple outpatient surgical procedure, performed at a Cal. Stem Cell clinic by a licensed healthcare professional. AMF No. 6. This procedure is simple, indeed among the simplest ones known for cell isolations (paralleling those for isolation of blood cells), and does not change the biological properties of the adipose cells and adipose tissue that were intended for the purpose of repair and regeneration. AMF No. 7. As its name sounds, SVF, or stromal vascular fraction, is the naturally occurring cellular part of the adipose tissue that does not contain the adipocytes (fat cells). AMF No. 8. SVF itself contains a population comprised of multiple cell types naturally found in adipose (fat) tissue; these include mesenchymal stem cells, hematopoietic cells, lymphocytes, early (progenitors) and mature lineage stages of endothelial cells, pericytes (also called peri-vascular cells), smooth muscle cells, and fibroblasts (also called stroma) among other cells. AMF No. 9.

SVF's mesenchymal stem cells, particularly those found in connective tissue (the "reticular interstitium") surrounding all organs and infiltrating all fat in the body, are regenerative cells promoting healing and the regeneration of new tissues. AMF No. 10. These mesenchymal stem cells are well known for producing paracrine signals (signaling factors released to neighboring cells) that confer regenerative functions. AMF No. 11. These cells provide regenerative and supportive effects through factors released into the tissues and referred to as "paracrine signals", ones delivered to neighboring cells. AMF No. 12. Those functions include regenerative tissue repair and healing, insulation, metabolic properties and energy storage, modulation of immune reactions and complex endocrine properties. AMF No. 13.

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SVF is also known to have progenitor cells that actually operate as stem cells depending upon the environment in which they are placed. AMF No. 14. These cells have evolved over the millennia to provide their activities and are the natural sources of paracrine signals that provide regulation of or amelioration of some conditions. AMF No. 15. Their relevance is to every type of tissue in the body. AMF No. 16.

Importantly, adipose tissue has the highest number of regenerative cells of any tissue in the body by weight. AMF No. 17. In fact, regeneration and repair (rather than cushioning) are among the most important functions of adipose tissue and likely why there are 100-1000 times more repair cells (stem/progenitor cells) found in adipose tissue than in an equivalent volume of bone marrow. AMF No. 18. Indeed, abdominal omental fat is called the "policeman of the abdomen" and long before it was known that fat naturally contains a treasure trove of regenerative cells, medical students were taught in basic general surgery that the omental fat accelerates healing. AMF No. 19. A general surgeon wraps omental fat around a surgical bowel anastomosis to accelerate healing and prevent infection (not as a cushion). AMF No. 20.

B. Defendants' SVF Surgical Procedure

Drs. Berman and Lander are Board Certified surgeons that have been performing medical operations for decades. AMF Nos. 21 & 22. Dr. Berman is an internationally recognized expert on fat transfer surgeries. In 2010, Defendants began offering the SVF Surgical Procedure to patients in the United States. AMF No. 23. This SVF procurement procedure is currently deployed under ten active Institutional Review Board ("IRB") investigational protocols. AMF No. 24.

These surgeons perform the SVF Surgical Procedure during a single outpatient procedure at a California Stem Cell Treatment Center surgical clinic located in California. AMF No. 25. The Defendants' SVF Surgical Procedure involves collecting a patient's cell population naturally contained in a patient's

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own adipose tissue and relocating that cell population back into the same patient (an "autologous use"). AMF No. 26; *see also* Dkt. No. 55-64 (Declaration of Carolyn Yong) at ¶ 30 ("CSCTC SVF . . . [is] for autologous use.").

During the SVF Surgical Procedure, the licensed physician collects the patient's SVF cells, using a technique called "mini-liposuction via subdermal local anesthesia"—which permits the liposuction of the SVF, along with the fat issue that contains it, through use of local, rather than general, anesthesia. AMF No. 27. Many of the cellular products are mechanically separated from the adipose tissue during the liposuction procedure, which is common in all surgeries. AMF No. 28. To free up even more cellular products, the physician then uses surgical tools—namely, collagenase enzymes and a centrifuge device—to isolate the SVF cell population by removing the adipocyte (fat) cells. AMF No. 29. The SVF is then suspended in a sterile saline solution, after which it is relocated back into the patient's body. AMF No. 30. In short, the SVF Surgical Procedure is an autologous use surgery that involves the collection and relocation of SVF cells that previously existed in the patient's body. Indeed, all of the cells in SVF already exist in the body's circulation. This procedure simply allows an increased quantity of the optimal healing stem cells to be added to specific areas (e.g. joints) or the general circulation.

In the case of Cal. Stem Cell's SVF Surgical Procedure, the stromal and vascular cells taken out of the patient in the performance of the procedure are the same cells that are put back into the patient. AMF No. 31. Importantly, the abovementioned surgical techniques employed by Cal. Stem Cell involve relocation of the very same SVF cell population that *previously existed* in the patient's body, not the creation or manufacture of any new "product" for introduction into the body. AMF No. 32. This is referred to as an autologous cell transplant: cells from a donor are given back to the same donor. AMF No. 33.

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Moreover, unlike manufactured drugs, the SVF Surgical Procedure does not require Cal. Stem Cell to produce any cellular- or tissue-based product to uniform specifications for strength, quality and purity. AMF No. 34. While safety and efficacy considerations require that drug products be manufactured in a uniform manner for use in various patients, uniform processing is not necessary (nor for that matter feasible) with the SVF Surgical Procedure. AMF No. 35. Rather, the cell population used in the SVF Surgical Procedure is unique to each patient, including the specific stem cell count. AMF No. 36. The outcomes of the SVF Surgical Procedure are also uniquely based on the patient's own tissue and cannot be replicated across patients or even with the same patient at different times. AMF No. 37. Unlike drug products which are provided based on an established effective dose, the patient's own stem cells function to effect repair of damaged tissues in the body. AMF No. 38. As noted above, these are the cells primarily involved with functional cellular repair and thus healing – something no drug can do.

C. The Equipment Defendants Use For The SVF Surgical Procedure Is Regulated Independently By FDA And Appropriate For Surgeons' Use In Surgery

Collagenase is used in the SVF Surgical Procedure to help separate the tissue's various cell types into a cell suspension enabling the elimination of adipocytes by the simple method of removing floating cells, those containing fat globules – a process that enriches the SVF cells, the source of paracrine signals that offer regenerative and repair effects. AMF No. 39. Importantly, the collagenase enzyme affects the extracellular matrix components in the connective tissue infiltrating the fat (reticular interstitium), a complex mixture of insoluble components (collagens, adhesion proteins, proteoglycans) that hold together the primary cell types present in adipose tissues: stem/progenitors and mature cells of lineages of stromal cells, vascular cells and adipocytes (fat) cells. AMF No. 40. The collagenase does not, however, break down adipose tissue (fat) since that

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would require lipase–a different enzyme. AMF No. 41. The collagenase also does not digest any of the cells found in the fat or in the SVF. AMF No. 41. Nor does it alter the cells. AMF No. 42. Indeed, one scientific publication has concluded that the exact type of collagenase used in the SVF procedure has no impact on the viability of the SVF cells, yield of cells, and, most significantly, the ability of the cells to differentiate. AMF No. 43. Moreover, the relevant regenerative characteristics of the cells are not changed by the collagenase.

Likewise, Cal. Stem Cell's use of an FDA 510(k)-cleared centrifuge helps clean and, with simple filtration techniques, size the SVF so that only the desired SVF components are available for relocation back into the patient. AMF No. 62. Notably, centrifugation is used in numerous surgical procedures, including bone marrow aspirate for regenerative purposes where the device's effect in separating cells and tissue does not subject these procedures to FDA regulation.[1] AMF No. 44.

Finally, it is critical to note that the surgical tools used by Cal. Stem Cell to wash and separate the SVF cells from the adipocyte cell fraction do not change the physical form of the SVF cells. AMF No. 45. The stromal and vascular cells remain unchanged from their original cellular forms. Further, recent publications establish that these cells have *not* been altered in any substantive way to change them from their naturally occurring state (i.e. they have the same DNA, same cell type, same flow cytometry markets and no evidence of introduction of any chemicals that would change their significant character). AMF No. 46.

[1] Note that the stem cells isolated from fat and connective tissue contained within bone marrow are the same regenerative cells that are isolated from adipose. *See* AMF No. 48. Bone marrow actually contains a fair amount of adipose tissue and is essentially isolated in a similar way as adipose tissue. AMF Nos. 49, 50.

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D. The FDA Historically *Has Not* Regulated Procedures Like Defendants' SVF Surgical Procedure

Despite the Government's arguments to the contrary, the FDA's authority to regulate what an individual does with his or her own cells or tissues is significantly narrow. Indeed, the FDA has long declined to exercise broad regulatory authority over a person's own cells. Prior to the late 1990s, the FDA—which has existed since 1906—exerted little or no regulatory control over human cellular and tissue-based products, even those that might constitute "drugs" or "biologic products." Then, in 1997, for the first time, through a guidance document, the FDA proposed to expand its authority to reach human cells, tissues, cellular- and tissue-based products ("HCT/Ps"). Proposed Approach to Regulation of Cellular and Tissue-Based Products (Feb. 1997) [2] (the "1997 Proposal").

Recognizing that it was venturing into new territory, the FDA made clear that its newly-claimed authority would be limited:

> 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 the safety and effectiveness risks, would generally be no different than those typically associated with surgery. *Id.* at 12 (emphasis added);
>
> and
>
> [a]utologous[3] use of cells and tissues harvested and transplanted in a single surgical procedure would be subject to ***no FDA oversight.*** *Id.* at 15 (emphasis added).

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[2] *Available at*: http://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/tissue/ucm062601.pdf

[3] Autologous use means "the implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered." 21 C.F.R. § 1271.3(a).

The FDA followed its 1997 guidance statement with a proposed regulation. Again, the FDA limited its reach when it reaffirmed its intent to exempt from this regulatory scheme those procedures involving the removal of HCT/Ps from an individual where those HCT/Ps were then implanted, transplanted, infused, or transferred into the same individual in a 1998 proposed rule establishing registration and listing requirements for HCT/Ps. 63 Fed. Reg. 26744, 26748 (May 14, 1998) (the "1998 Proposal").

Ultimately, in 2001, the FDA codified its limited regulatory authority at 21 C.F.R. Part 1271. The rule, which is the key rule in this case, exempts from any FDA regulation:

> [A]n establishment that removes HCT/P's from an individual and implants such HCT/P's into the same individual during the same surgical procedure.

21 C.F.R. § 1271.15(b) (the "SSP Exemption"). Somehow, more than ten years after this new rule allowing for limited FDA oversight of a person's own cells was promulgated, the FDA arbitrarily changed its mind and decided that it wished to expand its regulatory reach. FDA, however, did not attempt to amend the regulation itself, or propose a new regulation that would be subjected to the regulatory approval requirements of the Administrative Procedure Act. In 2014, the FDA released a draft guidance document. This draft guidance proposed to interpret the SSP Exemption to exclude surgical procedures that would otherwise qualify for exemption by requiring that the patient's transplanted HCT/P be implanted in its "original form," which is very narrowly defined and limits the types of surgical procedures that would fall within the SSP Exemption.[4] The Guidance was finalized in 2017.[5]

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[4] FDA's Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception Draft Guidance (Oct. 2014).

[5] *FDA Guidance For Industry: Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception* (the "2017 Guidance"), *available at* www.fda.gov/media/89920/download.

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The FDA's interpretation, a surprising reversal of course after more than a decade of non-regulation, is the result of an arbitrary and creeping expansion of its regulatory reach, meaning that the FDA is now seeking to exert its regulatory authority over the practice of medicine, including surgical procedures, such as Defendants' SVF Surgical Procedure, which involve nothing more than the relocation of a patient's very own cells.

III. LEGAL STANDARD ON SUMMARY JUDGMENT

Under Federal Rule of Civil Procedure 56, summary judgment should only be granted if the pleadings, the discovery and disclosure materials on file, and any affidavits show that there is no genuine issue as to any material fact and that the movant is entitled to judgment as a matter of law. A material fact is one that may affect the outcome of the case. *Anderson v. Liberty Lobby Inc.*, 477 U.S. 242, 248 (1986). Importantly, "[e]xpert opinion evidence is itself sufficient to create a genuine issue of disputed fact sufficient to defeat a summary judgment motion." *Thomas v. Newton Int'l Enters.*, 42 F.3d 1266, 1270 (9th Cir. 1994).

On a motion for summary judgment, "the judge's function is not ... to weigh the evidence and determine the truth of the matter but to determine whether there is a genuine issue for trial." *Anderson*, 477 U.S. at 249. In conducting this inquiry, a court must view the facts and the reasonable inferences drawn from them "in the light most favorable to the party opposing the motion." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986). "[P]apers supporting the movant are closely scrutinized whereas the opponent's are indulgently treated." *U.S. v. W. Elec. Co.*, 337 F.2d 568, 575 (9th Cir. 1964).

The movant bears the initial burden of demonstrating the absence of a genuine issue of material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). Only once the moving party shows the absence of genuine issues of material fact must the non-moving party go beyond the pleadings and identify facts showing a genuine issue for trial. *Id.* at 324.

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Where the moving party attempts to move for summary judgment on the ground that the non-moving party's affirmative defense lacks merit, such as the Government's claim that Defendants do not fall within certain exceptions to the FDCA, the moving party bears the burden of production and persuasion. *Nissan Fire & Marine Ins. Co., v. Fritz Cos.*, 210 F.3d 1099, 1102 (9th Cir. 2000). To meet that burden, the moving party must either negate an essential element of the defense or make a showing that the non-moving party does not have sufficient evidence on an essential element of that defense. *Id.*

IV. ANALYSIS

A. The Government is Inappropriately Attempting to Regulate Surgery

Pursuant to the Federal Food, Drug and Cosmetics Act, the FDA has the authority to regulate drugs (21 U.S.C. § 321), and pursuant to the Public Health Service Act (42 U.S.C. § 201), the authority to regulate biological products. For all of the reasons discussed here, Defendants' SVF Surgical Procedure is neither of these. Instead, Defendants are simply physicians who are practicing medicine and performing surgery. And, as courts have recognized, the FDA generally does not regulate doctors – particularly those using office-based drugs or biologicals for the sole use of their patients. *Amarin Pharma, Inc. v. FDA*, 119 F. Supp. 3d 196, 200 (S.D.N.Y. 2015). Indeed, allowing the FDA to expand its regulatory authority to encompass the Defendants' activities would be to allow the FDA to regulate not only an individual's private relationship with his/her physician, but also the individual's use of his/her body and medical decisions. *See Roe v. Wade*, 410 U.S. 113 (1973). These are activities that implicate fundamental rights of privacy and bodily autonomy. *See Griswold v. Connecticut*, 381 U.S. 479, 485 (1965). Thus, to hold that the FDA can regulate the SVF Surgical Procedure as if the SVF cells were a saleable commodity ignores the fundamental and constitutional differences between drugs and an individual's right to control her body.

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Moreover, Defendants' SVF Procedure is patently distinct from traditional pharmaceutical drug production. The stereotypical pharmaceutical drug has a chemical composition that does not vary over time, and this uniformity makes it easy for the FDA to treat the drug uniformly with respect to production, inspection, labeling and, thus, sales. In comparison, the stem cells that Defendants remove from a patient for later reinsertion lack this uniformity, and thus cannot be mass-produced or effectively labeled and sold. And, significantly, unlike traditionally manufactured pharmaceutical drugs, the SVF—like the BRCA1 and BRCA2 genes at issue in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013)—cannot be patented because they are naturally-occurring human body parts that are a "product of nature and not patent eligible merely because it has been isolated." *Id.* at 579. Thus, applying a regulatory regime crafted to oversee the pharmaceutical drug industry to naturally-occurring stem cells simply makes no practical sense; especially where the SVF is the sole property of the patient, could never be made the same way twice, and could never be sold.

Finally, it is established law that a physician can use FDA-approved drugs and medical devices for non-FDA approved ("off label") uses. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001). And, here, Defendants are using FDA-approved drugs and medical devices in a medical procedure involving the isolation and re-insertion of a patient's own cells. Thus, at a minimum, the Defendants' actions are protected as lawful "off-label" uses of FDA-approved drugs and medical devices. Accordingly, Defendants have not violated the law.

B. Plaintiff Cannot Meet its Burden to Demonstrate that There Is No Triable Issue Of Fact Regarding The Application Of The Same Surgical Procedure Exemption

Although the Government is correct that Defendants ultimately bear the burden to *prove at trial* that the SSP Exemption applies to exempt their SVF Surgical Procedure from regulation by the FDA, the Government has not, and

cannot, meet its burden on summary judgment—to demonstrate that no material factual dispute exists regarding whether Defendants' SVF Surgical Procedure is regulated under the FDCA as a "drug." FDA's own regulations explicitly exclude from any FDA regulatory authority an "establishment that removes HCT/Ps from an individual and implants such HCT/P's into the same individual during the same surgical procedure." 21 C.F.R. § 1271.15(b). While Defendants strongly believe their SVF Surgical Procedure meets this exemption, and look forward to presenting their full defense on the merits at trial, the analysis is riddled with material disputed facts requiring a denial of the Government's Motion.

1. Defendants' SVF Surgical Procedure Indisputably Satisfies the First Three Elements of the SSP Exemption

To qualify for exemption from FDA regulation, assuming the FDCA applies at all, the procedure first must involve HCT/Ps, which the regulation defines as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." 21 C.F.R. § 1271.3(d). Here, the parties do not dispute that the SVF cells are HCT/Ps. AMF No. 47; *see also* Dkt. No. 55-64 (Yong Decl.) at ¶ 18 ("Adipose derived stromal vascular fraction (SVF), such as found in CSCTC SVF . . . is an HCT/P.").

Second, the procedure must involve an autologous use—*i.e.*, the procedure must involve transplanting HCT/Ps into the same patient from whom the HCT/Ps were removed. Again, there is no dispute that the Defendants' SVF Surgical Procedure is an autologous procedure as it involves transplanting the SVF cell population back into the same individual from whom the SVF cells originated. AMF No. 26.

Third, the entire surgical procedure must occur during a single sitting. Here, the Defendants' entire SVF Surgical Procedure takes place within a single surgical procedure in a single facility on a single day. Again, neither of the parties disputes this fact. AMF No. 6.

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2. There Is A Battle Of The Experts Regarding Whether Defendants' SVF Surgical Procedure Satisfies The Final Element Of The SSP Exemption

The fourth and final element of the SSP Exemption requires that the HCT/Ps that are removed from the patient must remain "such HCT/Ps" when transplanted back into the patient. 21 C.F.R. § 1271.15(b). The ultimate question for the trier of fact following a full presentation of evidence is whether the HCT/P removed from the patient during the SVF Surgical Procedure is unaltered when transplanted back into the patient. There are two fundamental disputed issues in connection with this analysis, each of which providing a basis to deny the Government's Motion: (1) what is the appropriate unit of comparison, tissue or cells; and (2) are the cells transplanted back into the patient altered.

a. Plaintiff's Proposed Unit of Comparison For Determining Whether "Such HCT/P" Is Implanted Violates Basic Statutory Construction

Plaintiff erroneously asserts that Defendants do not qualify for the SSP Exemption because they remove adipose (fat) tissue, but inject SVF cells back into the patient. Motion at 25-26. Plaintiff argues that Defendants, therefore, do not implant back into the patient "such HCT/P" that was removed. *Id.* Such an over simplistic view of the SVF Surgical Procedure and the FDA's regulatory scheme is unsupportable and falls apart based on a plain reading of the regulation.

HCT/P stands for "Human Cells, Tissues, or Cellular or Tissue-Based Products." *See* 21 C.F.R. § 1271.3. Obviously, cells – separate and apart from the tissue in which those cells are found – are an important aspect of this definition. More importantly, a cell is always a component of something else; a cell can only be removed from a patient along with that something else, such as tissue. AMF No. 2. To put that cell back into the patient, it must be isolated in some way from the tissue that surrounds it. *Id.*

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Under Plaintiff's approach, which is disputed, a "cell" can never be subject to the SSP Exemption because tissue (or some other part of the body containing more than cells) must first be removed to isolate that cell. By rendering the "C" in HCT/Ps nonexistent, the FDA's interpretation violates the well-established canon of interpretation that every word in a regulation must be given force and effect.[6] *TRW Inc. v. Andrews*, 534 U.S. 19, 31 (2001) ("It is 'a cardinal principle of statutory construction' that 'a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant.'" (citing *Duncan v. Walker*, 533 U.S. 167, 174 (2001)); *see also Cooper Indus., Inc. v. Aviall Servs., Inc.*, 543 U.S. 157, 166 (2004) (finding that party's "reading [of a statute] would render part of the statute entirely superfluous, something [the Court is] loath to do."); *accord Nat'l Ass'n of Home Builders v. Defenders of Wildlife*, 551 U.S. 644, 669 (2007).

Because the term "cells" is a necessary component of the regulatory definition of "human cells, tissues, and cell- and tissue-based products," it must be given effect. The only possible interpretation of the phrase "such HCT/Ps" that gives effect to each word in the term requires that the appropriate unit of comparison is the HCT/Ps put back into the patient, which in this instance are the SVF cells. At the very least, there is a triable issue of fact regarding whether the SVF cells are the "such HCT/P" removed during the SVF Surgical Procedure.

b. There Is A Material Dispute Regarding Whether SVF Cells Are Significantly Altered

The parties' experts disagree on whether the SVF cells are altered during the SVF Surgical Procedure, the critical inquiry whether "such HCT/P" is implanted during the procedure, which itself demands that the Court deny this Motion.

[6] Canons of construction applicable to statutes apply with equal force to regulations. *Karczewski v. DCH Mission Valley LLC*, 862 F.3d 1006, 1016 (9th Cir. 2017).

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For the reasons discussed above, the appropriate assessment for determining whether the HCT/Ps at issue in the Defendants' SVF Surgical Procedure remain "such HCT/Ps" is whether the SVF cells removed from the patient are sufficiently similar to the SVF cells implanted back into that same patient. Here, the SVF cells isolated and removed from the patients are not materially altered during the SVF Surgical Procedure. AMF Nos. 40-43.

During the SVF Surgical Procedure, the physician performing the procedure uses a collagenase enzyme to breakdown binding collagen proteins in order to separate the SVF cells from the adipose tissue. AMF No. 29. And, scientific studies indicate that the collagenase only affects the collagen matrix of the adipose tissue—not the SVF cells—and therefore does not impact or damage the SVF cells. AMF Nos. 40-43.[7] And, as Dr. Reid explained, "the collagenase enzyme affects only the extracellular matrix components . . . [and] does not . . . break or digest any cells and nor does it alter the cells." AMF Nos. 40-42. Scientific studies that specifically assessed SVF cells indicate that the collagenase only affects the collagen matrix of the adipose tissue—not the SVF cells—and also does not impact or damage the SVF cells. AMF Nos. 40-43. Indeed, as the Plaintiff's expert acknowledges, the SVF cells are simply isolated and removed from the patient's body. Dkt. No. 55-64 (Yong Decl.) at ¶¶ 31–32.

The Government's expert, however, attempts to dispute Dr. Reid's expert opinions and supporting scientific articles, positing that the SVF cells are altered by the collagenase. *Id.* at ¶ 50. The two studies on which the Government relies (Autengruber and Ford), however, are inapposite and only serve to underscore the parties' factual dispute. *Id.* For example, the study conducted by Dr. Autengruber involved the incubation of spleen cells in collagenase, followed by centrifugation

[7] There is also mechanical separation of SVF cells during the liposuction procedure. AMF No. 28. One's own damaged cells either provide useful "exosome" material or can simply be filtered through one's normal organs just like any other devitalized cells from any surgical or injurious occurrence.

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and resuspension in a "highly enriched" medium that was further supplemented with penicillin, streptomycin, and fetal calf serum. *Id.* at ¶ 50 & n.38 (A. Autengruber, M. Gereke, G. Hansen, C. Henning, D. Bruder, *Impact of enzymatic tissue disintegration on the level of surface molecule expression and immune cell function*, European J. of Microbiology & Immunology, 2(2):112–20 (2012)). Clearly, this varies greatly from the SVF Surgical Procedure, which involves adipose-derived SVF cells and resuspension in simple saline. AMF Nos. 27, 30. Similarly, the study conducted by Dr. Ford involved the incubation of central nervous system cells—not adipose-derived SVF cells. Dkt. No. 55-64 (Yong Decl.) at ¶ 50 & n.37 (AL Ford, E. Foulcher, AL Goodsall, JD Sedgwick, *Tissue digestion with dispase substantially reduces lymphocyte and macrophage cell-surface antigen expression*, J. of Immunological Methods, 194(1):71-5 (1996)). Significantly, however, the Government's expert, Dr. Yong, does not even attempt to explain how a study involving different types of cell or a different resuspension medium is applicable to the Defendants' SVF Surgical Procedure protocol. Neither the Autengruber study nor the Ford study should be relied upon to draw any conclusions regarding the impact of collagenase on adipose-derived SVF cells that are re-suspended in simple saline.

Thus, at a minimum, material disputed facts exist regarding whether the SVF Surgical Procedure changes the SVF cells and, thus, whether the procedure converts the SVF cells into a new substance that would disqualify the SVF from constituting "such HCT/Ps." The fact that this issue requires a resolution of conflicting expert opinion itself dooms this Motion. Accordingly, the Government has not met its burden to demonstrate that no material disputed facts exist regarding whether the SSP Exemption applies, and the Government's Motion for Summary Judgment should be denied.

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c. The Government's Reliance on the Southern District of Florida's Decision in US v. US Stem Cell, Inc. Is Misplaced

In its Motion, the Government repeatedly relies on a decision from the United States District Court for the Southern District of Florida in *United States v. US Stem Cell, Inc.*, Case No. 18-61047, Dkt. No. 73 (S.D. Fla. June 3, 2019) ("*US Stem*"), as if to suggest that the same result is a foregone conclusion here. Not so. First, the Southern District of Florida's decision is an unpublished decision issued by a court outside of the Ninth Circuit. Moreover, the deadline to appeal the decision has not passed, so that order is not yet final. And most significantly, the decision itself cautioned that "[t]he Court is cognizant of the fact that stem cell treatments and products are rapidly evolving, but every such treatment and product is unique and whether they constitute 'drugs,' or 'biological products' subject to FDA regulation under the FDCA and PHSA, respectively, requires independent consideration." *US Stem*, Dkt. No. 82 at 2 (S.D. Fla. June 25, 2019).

Further, the *US Stem* court's order adopted the FDA's interpretation promulgated by the 2017 Guidance, which as discussed in Section IV.C below, is not entitled to any deference and is improper under the recent U.S. Supreme Court decision in *Kisor*, 139 S.Ct. 2400.

Finally, the facts at issue in this case significantly differ from those at issue in *US Stem*. Most prominently (in addition to the numerous other factual issues addressed throughout this Opposition), Defendants Berman and Lander are board-certified surgeons performing a surgical procedure, whereas the persons responsible for conducting the SVF procedure in *US Stem* were not licensed physicians. Whether or not Drs. Berman and Lander qualify for the SSP Exemption has a critical differentiating fact given they are surgeons. Accordingly, the *US Stem* action has no precedential or persuasive value in this Court, and this Court is not bound by the *US Stem* decision.

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C. The FDA's Arbitrary Newly-Rendered Interpretation of the SSP Exemption Is Not Entitled to Deference

Recognizing that it cannot prevail based on a plain reading of the SSP Exemption, the Government resorts to relying on the FDA's self-serving interpretation of the Exemption set forth in FDA's 2017 Guidance. Specifically, the Government argues that only HCT/Ps whose "original form" is unaltered constitute "such HCT/Ps" under the SSP Exemption (i.e. the adipose (fat) tissue removed must be implanted). Mtn. at 25–26. This position is not supported by any regulation, but only in the FDA's non-binding 2017 Guidance document. *See id.* (quoting "original form" requirement language); Dkt. No. 55-64 (Yong Decl.) at ¶ 27 ("Thus, in order to qualify for the [SSP] exception, an establishment must implant into the same individual the HCT/P in its original form.").

As an initial matter, the FDA, through the Government's position here, is attempting to enforce *substantive* changes to the SSP Exemption that did not go through the proper notice and comment period, as required by the Administrative Procedures Act. *See Azar v. Allina Health Services*, 139 S.Ct. 1804, 1810-11 (2019) (substantive regulatory changes must comply with the APA notice and comment requirements). The Government's purported requirement that the "original form" must be implanted is not found in the regulation and substantively changes the analysis, as discussed above.

Moreover, this Court should disregard the 2017 Guidance in analyzing the SSP Exemption because the 2017 Guidance, which substantively changes the regulation, is not entitled to any deference. The Supreme Court in *Kisor*, 139 S.Ct. at 2414-18, recently clarified that deference is unwarranted in certain circumstances, including (1) where the regulation in question is plainly unambiguous, (2) where the agency's new position is unreasonable, or (3) where the agency's new position conflicts with its prior position, thus creating an "unfair surprise" to a regulated party. *See also Christopher v. Smithkline Beecham Corp.*,

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567 U.S. 142, 155 (2012); *Christiansen v. Harris Cnty.*, 529 U.S. 576, 588 (2000). Because all three circumstances are present, this Court should disregard the FDA's improper attempt to expand its regulatory authority and instead apply the plain language of the SSP Exemption.

1. The FDA's Interpretation of the SSP Exemption Is Not Entitled to Deference Because the Exemption is Unambiguous On Its Face

This Court should decline to defer to the FDA's attempts to substantively change the applicability of the SSP Exemption. Through the 2017 Guidance, and now its position in this litigation, the FDA seeks to limit the application of the SSP Exemption by adding an additional requirement that the HCT/Ps remain in their "original form." This language, however, is not included anywhere in the regulation. And, as the *Kisor* Court recently re-emphasized, "the possibility of deference can arise only if a regulation is genuinely ambiguous." *Kisor*, 139 S.Ct. at 2414; *see also Christiansen*, 529 U.S. at 588 ("The regulation in this case, however, is not ambiguous . . . . To defer to the agency's position would be to permit the agency, under the guise of interpreting a regulation, to create *de facto* a new regulation."). Accordingly, as discussed in Section IV.B above, because the plain language of the SSP Exemption is unambiguous—and unambiguously applies to exempt Defendants' SVF Surgical Procedure from regulation by the FDA, the FDA's improper exercise of regulatory authority should not be permitted to stand and certainly does not warrant deference.

Additionally, the Government has not made any showing that the SSP Exemption itself is ambiguous such that deference to regulatory interpretation would be appropriate. Instead, the Government simply adopts the FDA's position as set forth in the 2017 Guidance as if it were already a part of the SSP Exemption. This is improper and the Supreme Court has repeatedly rebuked such efforts. *See Azar*, 139 S.Ct. at 1816; *see also Kisor*, 139 S.Ct. at 2414.

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2. Even if the SSP Exemption Were Ambiguous, the FDA's Interpretation of the SSP Exemption Is Not Entitled to Deference Because it is Unreasonable

Even if the regulation were ambiguous (it is not), the FDA, through this litigation, seeks to enforce its 2017 Guidance that promulgated a patently unreasonable interpretation of the plainly unambiguous SSP Exemption—an interpretation that is, thus, not entitled to deference. *Kisor*, 139 S.Ct. at 2415 ("If genuine ambiguity remains, moreover, the agency's reading must still be 'reasonable.'").

As discussed in Section IV.B above, the Government improperly seeks to amend the regulation to remove any reference to cells, and instead analyze only whether the same tissue that was removed was implanted into the patient. That is unreasonable. *Turtle Island Restoration Network v. Dep't of Commerce*, 878 F.3d 725, 735 (9th Cir. 2017) (rejecting U.S. Fish and Wildlife Service's interpretation of 50 C.F.R. § 21.27 in part because "[t]he FWS's approach to the regulation renders the majority of its text superfluous."); *cf. Ma v. Sessions*, 907 F.3d 1191, 1198 (9th Cir. 2018) (upholding an agency's interpretation as "reasonable" in part because "[t]o hold otherwise would render [part of a statute] superfluous.").

Further, the Government's selective enforcement against Defendants is belied by its non-regulation of substantially similar practices that would run afoul of its unreasonable interpretation of the SSP Exemption. For example, the FDA allows the use of certain stem cells extracted from bone marrow even though the cells are essentially identical to the cells found in adipose tissue. AMF No. 48. Yet, adipose tissue also exists in bone marrow. AMF No. 49. Like the SVF Surgical Procedure, when bone marrow is subjected to centrifugation, the stem cells are isolated and the leftover adipose tissue is discarded. AMF No. 50.

Another example, the FDA does not currently regulate the routine intra-operative use of autologous fat to repair dural defects. AMF No. 51. Dura is brain

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lining that occasionally gets damaged in neurosurgery, which can result in loss of fluid from around the brain. AMF No. 52. Some surgeons are isolating autologous fat from around the patient's umbilical area, crushing that fat with a "Spence Cranioplastic roller" to transform it into a thin foil on a separate table in the operating room, and returning that "foil" to the patient during the same procedure to repair the brain's lining. AMF No. 53. This is far more processing of the tissue than Defendants' SVF Surgical Procedure, yet exempted from FDA regulation.

Yet another example, vein or artery graft are often used for coronary artery bypass surgery. AMF No. 54. The vein is harvested and processed to prepare it for other surgical uses than what it was intended for, but just like the SVF, it is a naturally occurring substance, and not subject to FDA regulation. AMF No. 55.

Because the FDA's interpretation runs afoul of the Supreme Court's holding in *Kisor*, this Court should decline to defer to the FDA's position. *Kisor*, 139 S. Ct. at 2415; *see also Perez v. Mortg. Bankers Ass'n*, 135 S. Ct. 1199, 1207 (2015). Instead, the Court should simply apply the plain language of the SSP Exemption to the Defendants' SVF Surgical Procedure and, accordingly, exclude it from FDA regulation. Application of such arbitrary interpretation of FDA regulations could result in hundreds of surgeries potentially falling under the purview of the FDA and such surgeries declared illegal.

3. FDA's Interpretation Should Not Be Granted Deference Because It Constitutes an Unfair Surprise to Defendants

Lastly, the FDA's interpretation of "such HCT/Ps" under the 2017 Guidance should not be afforded *Kisor* deference because it pronounces an entirely new position regarding the applicability of the SSP Exemption—a position that directly contradicts twenty years of FDA pronouncements on the issue and results in "unfair surprise" to Defendants and others providing autologous SVF surgical therapies. As the *Kisor* Court found, a "court may not defer to a new interpretation, whether or not introduced in litigation, that creates 'unfair surprise'

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to regulated parties." *See Kisor*, 139 S.Ct. at 2417-18 (citing *Long Island Care at Home, Ltd. v. Coke*, 551 US 158, 170 (2007)); *see also Christopher*, 567 U.S. at 155–56 (stating that when regulated parties are unfairly surprised by an interpretation, that interpretation is not entitled to deference).

As detailed above, until 1997, FDA exerted little to no regulatory control over human cellular and tissue-based products. Then, in 1997, FDA introduced Guidance providing that:

> 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 the safety and effectiveness risks, would generally be no different than those typically associated with surgery.

1997 Proposal at 12 (emphasis added).[8] Accordingly, the SSP Exemption was promulgated in 2001 based upon the 1997 Guidance. 21 C.F.R. § 1271.15(b). This regulation has not been amended since its promulgation.

Physicians and surgeons have relied upon this regulatory exemption in the ordinary course of their medical practice, including Defendants here, as surgery is not regulated by the FDA. In fact, in 2010, Defendants began performing the SVF Surgical Procedure, based in large part on the unambiguous position of the FDA that a same day surgical procedure such as the SVF Surgical Procedure would not be subjected to FDA regulations. The SVF Surgical Procedure was clearly exempt under the 1997 Guidance, which was the foundation for the SSP Exemption.

Importantly, Defendants have been successfully performing point of care investigative deployment of autologous adipose SVF since 2010 and through CSN since 2012. Defendants have collected an abundance of data, developed IRB approved protocols and maintain medical malpractice insurance for every member

[8] The 1997 Guidance recognized that same surgery transplant of cells or tissue would not carry a risk of communicable disease greater than general surgery. One of the FDA's roles is to prevent the transmission of communicable disease.

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of the CSN network. As Defendants have lower rates of complications than any pharmaceutical drug product and numerous patients (including themselves, their colleagues and their families) that have come to rely on such HCT/P therapy; it would be patently unfair to force them to stop their SVF procedure after 9 years of positive and safe responses.

Yet, the 2017 Guidance, which pronounced the FDA's new definition of "such HCT/Ps," undoubtedly, on its face, constitutes an "unfair surprise" to Defendants as it directly conflicts with the FDA's longstanding position regarding the applicability of the SSP Exemption. This 2017 Guidance marked a significant change of course in regulating same day surgical procedures. Based on the 1997 Guidance, FDA ***would not*** regulate cells that are removed from a patient and implanted back into that patient during a single surgical procedure. 1997 Proposal at 12. Now, under the 2017 Guidance, a procedure such as Defendants' SVF Surgical Procedure would not be exempt because it seeks to implant cells, which as discussed above, must begin with the removal of tissue.

Moreover, the FDA's enforcement of the 2017 Guidance, through the Government's position here, is an illegal attempt to substantively change the SSP Exemption without complying with the APA. *See Azar*, 139 S.Ct. at 1810-11. The FDA itself recognized that its new position was a drastic departure from its prior position. FDA informed the public, including Defendants, that they would have a three-year grace period (until December 2020) to determine how best to regulate procedures involving HCT/Ps.[9] Clearly, the FDA did not wait for that three-year period to end for the defendants, even though the defendants are one of the few organizations that had actually been working with the FDA on a real IDE application through the Center for Biological Evaluation and Research.

[9] *See* Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use (December 2017), at 21, *available at* www.fda.gov/media/109176/download.

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Accordingly, this Court should deny deference to the FDA's 2017 Guidance, disregard the 2017 Guidance's improper and overreaching expansion of the FDA's regulatory authority, apply the plain unambiguous language of the SSP Exemption to exclude the Defendants' SVF Surgical Procedure from regulation by the FDA, and deny the Government's Motion for Summary Judgment.

D. The FDA's Attempt To Enforce Its Newly-Rendered Interpretation of the SSP Exemption Is Unconstitutional

The FDA's interpretation of the SSP Exemption is also unconstitutional because it attempts to extend federal regulation to an article that does not affect interstate commerce, as required by the Commerce Clause, U.S. Const. art. I, § 8, cl. 3, and that is not shipped in interstate commerce, as defined by the FDCA, 21 U.S.C. § 321(b).

Federal law governing economic activity is constitutionally limited to activities that affect interstate commerce. Although the definition of interstate commerce has expanded over the last century to include intrastate activities that have a substantial effect on interstate commerce, the unifying concept behind this expansion has been that the activity in question involved a fungible commodity. Thus, the difference between the commodity used intrastate and the commodity that traveled across state lines was indistinguishable. For example, wheat grown for personal use affected interstate commerce because, had the farmer not grown the wheat, she would have bought the wheat from the interstate market. *Wickard v. Filburn*, 317 U.S. 111, 128 (1942). Because wheat is a fungible commodity, the effect of forbidding the regulation of the wheat would "undercut the regulation of the interstate market in that commodity." *Gonzales v. Raich*, 545 U.S. 1, 19 (2005) (applying *Wickard* to marijuana); *see also Nat'l Fed'n of Indep. Bus. v. Sebelius*, 567 U.S. 519, 561 (2012) (explaining that the Court in *Raich* denied an exception to marijuana grown for home consumption because "marijuana is a fungible commodity" (Roberts, C.J.)).

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The SVF Surgical Procedure does not involve a fungible commodity nor an interstate market. As the Government concedes, the SVF Surgical Procedure involves the use of a patient's own cells in one surgical procedure performed in one office. The cells are unique to the individual and do not leave the location of the procedure. There is no other market for the cells. To the extent the SVF Surgical Procedure uses products that travel in interstate commerce, they are not the necessary ingredient. Rather, the SVF cells stay in one location during the entire procedure. There is no interstate market for the SVF cells.

Because the SVF cells are not shipped in interstate commerce, the FDA's interpretation not only exceeds the scope of the Commerce Clause, but it also exceeds the FDA's statutory authority. *See 62 Cases, More or Less, Each Containing Six Jars of Jam v. United States*, 340 U.S. 593, 600 (1951) ("In our anxiety to effectuate the congressional purpose of protecting the public, we must take care not to extend the scope of the statute beyond the point where Congress indicated it would stop."); *see Panama Ref. Co. v. Ryan*, 293 U.S. 388, 430 (1935) ("[T]here are limits of delegation which there is no constitutional authority to transcend."). Section 331(k) prohibits "any . . . act with respect to a food, drug, device, tobacco product, or cosmetic, if such act is done while such article is held for sale (whether or not the first sale) ***after shipment in interstate commerce*** and results in such article being adulterated or misbranded." 21 U.S.C. § 331(k) (emphasis added). The FDCA defines "interstate commerce," as "(1) commerce between any State or Territory and any place outside thereof, and (2) commerce within the District of Columbia or within any other Territory not organized with a legislative body." 21 U.S.C. § 321(b). Because the article must be ***shipped*** in interstate commerce, rather than merely affect interstate commerce, the scope of the FDCA does not reach to the full extent of the Commerce Clause. Indisputably, the SVF cells are not shipped in interstate commerce.

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The FDA has falsely suggested that by using crystalloids manufactured from outside the state, the cells have been adulterated and now comprise a product of interstate commerce. This is factually inaccurate from a surgical standpoint because it is not possible to perform surgery without the use of fluids such as crystalloids, and it would suggest every surgeon that isolates, removes or transfers any tissues to cure, treat, diagnose or mitigate a condition for their patient is creating interstate commerce.

Finally, the uniqueness of the SVF cells presents further constitutional implications. The FDA is seeking to regulate not only an individual's private relationship with her physician, but also the individual's use of her body and medical decisions. These are not a "'class of activities' that have a substantial effect on interstate commerce." *Gonzales*, 545 U.S. at 17. Rather, these are activities that implicate fundamental rights of privacy and bodily autonomy. *See Griswold*, 381 U.S. at 485. To hold that the FDA can regulate the SVF Surgical Procedure as if the SVF cells were any other commodity ignores the fundamental and constitutional difference between drugs shipped in interstate commerce and an individual's right to control his/her own body and the cells and tissues therein.

E. The Government's Analysis Of The Minimal Manipulation Standard Is Irrelevant To This Dispute

For each of the reasons above, Defendants' SVF Surgical Procedure is not regulated by the FDA. The Government's attempts to regulate the SVF Surgical Procedure as a biological product under the PHS Act are equally unavailing, as the procedure is exempted from *all* FDA oversight. 21 C.F.R. § 1271.15.

However, the Government has misconstrued the applicable regulations to create a straw man argument that Defendants' SVF Surgical Procedure is more than "minimally manipulated" and therefore fails to meet a different "exemption" from FDA regulations. Motion at 27-29. As the FDA knows, if an HCT/P does not qualify for the SSP Exemption, the HCT/P may be regulated solely under the

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PHS Act, and not the full FDCA, if it meets the Minimal Manipulation test. *See* 21 C.F.R. § 1271.10; *see also* 2017 Guidance, at 4 ("[i]f an establishment meets the exception in [SSP Exemption] . . . the establishment need not consider whether that HCT/P meets the [Minimal Manipulation Exemption]."). If neither the SSP Exemption (complete exemption from FDA regulations) nor the Minimal Manipulation test (where an HCT/P would be subjected to more lenient regulations) apply, then a HCT/P is considered a drug, device, or biological product and subject to regulation under the full FDCA. 21 C.F.R. § 1271.20.

The critical error by the Government is the purpose of the Minimal Manipulation test. If Defendants establish that the SVF Surgical Procedure meets the Minimal Manipulation test, then the SVF Surgical Procedure ***would be*** regulated by the FDA. 21 C.F.R. § 1271.10. This is contrary to Defendants' position, which is that its SVF Surgical Procedure is not subject to FDA oversight or regulation at all because it meets the SSP Exemption (as FDA itself concedes is the appropriate analysis once the SSP Exemption is met). While Defendants believe that they would satisfy the Minimal Manipulation test, establishing that exemption that would subject the SVF Surgical Procedure to FDA regulation under the PHS Act. Defendants do not wish to bring themselves under the authority of the FDA and, thus, the Government's analysis regarding the Minimal Manipulation Exemption is irrelevant and should be disregarded.

V. THE GOVERNMENT LACKS STANDING TO PURSUE INJUNCTIVE RELIEF REGARDING THE SVF/VACCINIA AND EXPANDED CELL TREATMENTS

Article III standing requires a present case or controversy, and it is well-settled that "[p]ast exposure to illegal conduct does not in itself show a present case or controversy regarding injunctive relief . . . ." *Lujan v. Defenders of*

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Wildlife, 504 U.S. 555, 564 (1992).[10] The Ninth Circuit has explained that to satisfy the standing requirements under *Lujan*, a plaintiff seeking prospective injunctive relief "must demonstrate that he has suffered or is threatened with a concrete and particularized legal harm, coupled with a sufficient likelihood that he will again be wronged in a similar way." *Bates v. United Parcel Serv., Inc.*, 511 F.3d 974, 985 (9th Cir. 2007) (citations and quotations omitted); *see also Chapman v. Pier 1 Imports (U.S.) Inc.*, 631 F.3d 939, 946 (9th Cir. 2007) (en banc) (citations and quotations omitted) (holding a plaintiff "must demonstrate a real and immediate threat of repeated injury in the future" for Article III injunctive relief standing). The party asserting the claim has the burden of establishing these elements. *Chandler v. State Farm Mut. Auto. Ins. Co.*, 598 F.3d 1115, 1122 (9th Cir. 2010). A plaintiff must demonstrate standing separately for each form of relief sought. *Los Angeles v. Lyons*, 461 U.S. 95, 109 (1983) (notwithstanding the fact that plaintiff had standing to pursue damages, he lacked standing to pursue injunctive relief). Standing is examined at "the commencement of the litigation." *Friends of the Earth, Inc. v. Laidlaw Envtl. Servs., Inc.*, 528 U.S. 167, 189 (2000).

To pursue injunctive relief, a plaintiff must show that he is "realistically threatened by a *repetition* of the violation." *Gest v. Bradbury*, 443 F.3d 1177, 1181 (9th Cir. 2006). The mere fact that a plaintiff has alleged a past wrong does not mean there is likelihood of future injury. *Freeman v. ABC Legal Servs, Inc.*, 877 F. Supp. 2d 919, 926-27 (N.D. Cal. 2012). Although past wrongs can be evidence of a "real and immediate threat of repeated injury," they do not "in themselves amount to [a] real and immediate threat of injury necessary to make out

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[10] Defendants acknowledge that the Government has Article III standing under *Lujan* and does not need to establish the general requirements for standing to bring an action. *See Consumer Fin. Protection Bureau v. Gordon*, 819 F.3d 1179, 1187 (9th Cir. 2016). However, the Government is still required to make a showing that it has standing to pursue injunctive relief, i.e. that there is a showing that the defendants' conduct is likely to recur. *Id.* at 1197-98.

a case or controversy." *Bates*, 511 F.3d at 985 (citations and internal quotations omitted). When the defendant no longer wishes, or is no longer able, to engage in the challenged activity, a prayer for injunctive relief is moot. *See Already, LLC v. Nike, Inc.*, 568 U.S. 85, 92-95 (2013) (voluntary unconditional and irrevocable covenant not to sue was sufficiently broad to ensure no further trademark infringement actions between the parties).

The Government has not met its burden of establishing standing to pursue injunctive relief regarding the SVF/Vaccinia nor the ACS Expanded Cell therapies. To the contrary, the Government's own evidence establishes that it lacks any such standing because those therapies have not been utilized since well before the filing of this litigation.

Regarding the SVF/Vaccinia, the procedure is only possible if Defendants have access to the FDA licensed ACAM2000 vaccine. AMF No. 56. As the Government acknowledged, FDA (through the United States Marshalls) seized all ACAM2000 in StemImmune's possession on August 25, 2017 AMF No. 57. For clarity, this action was not filed until nearly nine months later, on May 9, 2018. *See* Compl. Thus, Defendants have not and, because the government controls distribution of ACAM2000, could not have performed the SVF/Vaccina procedure during the pendency of this action, and definitely not as of the commencement of this action. AMF No. 58. Moreover, Defendants have no interest in performing the SVF/Vaccinia procedure in the future absent appropriate regulatory approval. AMF No. 59.

Regarding the ACS Expanded Cell procedure, Defendants likewise ceased performing this procedure following notice from the FDA, well prior to the filing of this action. Defendants ceased performing the ACS Expanded Cell procedure as of December 2017. AMF No. 60. While Defendants maintained that the SVF Surgical Procedure is not subject to FDA regulation (resulting in the instant lawsuit containing myriad disputed facts to be resolved at trial), Defendants complied with

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FDA's position regarding the ACS Expanded Cell procedure.[11] Again, Defendants have no interest in performing the ACS Expanded Cell procedure in the future absent appropriate regulatory approval. AMF No. 61. The only procedure Defendants wish to continue performing, and the only procedure performed immediately prior to and during the pendency of this litigation, is the regular SVF Surgical Procedure. Thus, the Government has failed to establish standing to pursue injunctive relief as to the SVF/Vaccinia and ACS Expanded Cell procedures.

VI. CONCLUSION

For the foregoing reasons, Defendants respectfully request that this Court deny the Government's Motion for Summary Judgment.

Dated: August 9, 2019

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[11] It should be noted, Defendants had an IRB approved safety study and had validated the safety and by virtue of their data, the efficacy, of the ACS Expanded Cells with plans of an IND with this supportive data.