IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

UNITED STATES OF AMERICA,	) Civil Action No. 1:10-CV-01327-RMC
	)
Plaintiff,	)
	)
v.	)
	)
REGENERATIVE SCIENCES, LLC, et al.,	)
	)
Defendants.	)

PLAINTIFF'S MOTION TO DISMISS DEFENDANTS' COUNTERCLAIMS

The United States of America, plaintiff and counterclaim defendant, moves this Court to dismiss Defendants' Counterclaims pursuant to Federal Rules of Civil Procedure 12(b)(1) and 12(b)(6). The grounds for this motion are set forth in the memorandum of points and authorities attached to this motion.

DATED this 7th day of January, 2011.

Respectfully submitted,

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MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFF'S MOTION TO DISMISS DEFENDANTS' COUNTERCLAIMS

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HISTORY

INTRODUCTION

In this suit, the United States seeks to enjoin a Colorado corporation, Regenerative Sciences, LLC ("RS LLC"), and three of its owner-employees (collectively, "Defendants") from continuing to manufacture and distribute a cultured cell product in violation of the Federal Food, Drug, and Cosmetic Act ("FDCA"). In particular, the Complaint alleges that Defendants' cultured cell product is a drug that is adulterated because it is not manufactured in accordance with current good manufacturing practice ("CGMP") in that, among other things, Defendants do not test it for sterility or for the presence of endotoxins (which can cause fever) or mycoplasma (a type of bacteria that can be pathogenic in humans) before transporting it to a clinic for injection into patients. The Complaint further alleges that the cultured cell product is misbranded because its labeling does not bear adequate directions for use and its label does not contain the statement "Rx only." The government has filed a separate motion for summary judgment on these issues.

With their Answer, Defendants filed eight Counterclaims against the government that challenge the United States Food and Drug Administration's ("FDA") authority to regulate Defendants' manufacture and distribution of the cultured cell product. Counterclaims I, II, III, and VII argue that FDA has acted beyond the scope of its authority in seeking to regulate what they self-servingly characterize as the "practice of medicine." The cultured cell product Defendants make falls squarely within the FDCA's definition of a "drug," and there is no language in the FDCA to suggest that Congress intended to exempt such products from the statute's adulteration and misbranding provisions. Moreover, although FDA's long standing policy is that the agency does not regulate the practice of medicine – meaning once FDA has approved a drug for one use, the agency will not object if a physician chooses to prescribe the

drug for another (unapproved) use for her patients – FDA's practice of medicine policy has no application to a drug, such as Defendants' cultured cell product, that has ***not been approved for any use***. As a result, all of Defendants' Counterclaims based on FDA's purported lack of authority to regulate the "practice of medicine" fail as a matter of law.

Counterclaims IV, V, and VI challenge, on various theories, an example FDA provided in the preamble to a regulation regarding how the agency interpreted a term in the codified language. Counterclaims IV and V contend that the preamble statement is arbitrary and capricious, and Counterclaim VI alleges that the statement is a legislative rule that was promulgated without notice and comment in violation of the APA. The inclusion of an example in a preamble is not final agency action subject to arbitrary and capricious review. Nor is it a rule of any kind, let alone a legislative rule subject to notice and comment requirements. Accordingly, none of these Counterclaims states a claim upon which relief can be granted.

Counterclaims II, IV, V, and VI should be dismissed for the additional reason that they allege procedural deficiencies in a rule that FDA issued more than six years before Defendants filed their Counterclaims. Thus, the statute of limitations bars all of those claims.

Defendants' final claim, Counterclaim VIII, alleges that FDA's regulatory scheme for cells and tissues set forth in 21 C.F.R. Part 1271 is *ultra vires* because Part 1271 was issued under FDA's authority to promulgate regulations to prevent the transmission of communicable diseases and, in Defendants' view, their autologous[1] product carries no risk of spreading disease.

[1]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). Allogeneic use refers to the implantation, transplantation, infusion, or transfer of

Defendants' argument discounts the scope of the broad authority delegated to FDA under the Public Health Service Act ("PHSA"), 42 U.S.C. § 264(a), and ignores FDA's determination that, regardless of whether the human cells, tissues, and cellular or tissue-based products (as defined in 21 C.F.R. § 1271.3(d)) are intended for autologous or allogeneic use, the manufacturing process needs to be controlled to prevent the transmission of communicable diseases.

For all of these reasons and the reasons discussed below, Defendants' Counterclaims should be dismissed.

STATEMENT OF FACTS

RS LLC is a Colorado corporation that is owned *in part* by physicians licensed to practice medicine in Colorado. Answer ¶¶ 4-7.[2] According to Defendants, RS LLC "owns" a procedure called the "Regenexx Procedure," which it licenses to the Centeno-Schultz Clinic. Counterclaims ¶¶ 3-4.

As part of the Regenexx Procedure, RS LLC receives bone marrow or synovial fluid and blood samples that have been recovered from a patient at the Centeno-Schultz Clinic. *Id*. ¶ 5. RS LLC isolates what it describes as mesenchymal stem cells ("MSCs") from the bone marrow or synovial fluid, expands the cells using growth factors from the patient's blood (e.g., platelet lysate) and reagents (e.g., Dulbecco's Modified Eagle's Medium), and combines them with other

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human cells or tissue into an individual other than the individual from whom the cells or tissue were recovered.

[2]Defendants First Amended Answer ("Answer") and its Counterclaims appear in the same document (Dkt #15-1), both starting with paragraphs numbered 1. To avoid confusion, we cite the two portions of the document separately.

drug products (such as heparin and doxycycline). Answer ¶ 11. The process of expanding the cells typically takes two to three weeks and involves multiple steps in which the cells are centrifuged (with certain cell and plasma layers then removed) and then placed in culture media in an incubator, thereby causing the cells to divide and expand in number. *Id.* When the cells expand to a certain point, they are exposed to an enzyme, trypsin, which digests some of the proteins on the surface of the cells and causes the cells to detach from the plastic flask in which they were contained. *Id.* RS LLC then harvests the detached cells, treats them with media to stop the action of the trypsin, washes them with fresh media, and either puts the cells into other flasks for further expansion, prepares them for cryo-preservation, or prepares them for injection. *Id.* Ultimately, after one or more cell passages[3] (and, in some cases, following cryo-preservation), RS LLC places the expanded cells, along with a drug product that has been shipped in interstate commerce and other additives, into syringes. *Id.* RS LLC then transports the syringes to the Centeno-Schultz Clinic, where, according to Defendants, the cells are "placed back into the patient's injured area (i.e., knee, hip, rotator cuff), typically 4-6 weeks after they were removed" and they "begin to repair the patient's degenerated or injured area." Counterclaims ¶ 10.

We refer to the article RS LLC transports to the Clinic for injection into patients as RS LLC's "cultured cell product." The cultured cell product has not been approved by FDA for any

[3]Each cycle of detaching the cells with trypsin, and then putting them into new flasks is termed a cell passage.

use. Answer ¶¶ 20-21, 25. Defendants admit that they promote the Regenexx procedure[4] to treat various orthopedic conditions and injuries. Counterclaims ¶ 10. For example, their Regenexx pamphlet states, "The Regenexx procedure is safe and can often prevent the need for surgery," and lists the following conditions and diseases as "candidates" for the procedure: "Patients with non-healing bone fractures"; "Osteoarthritis of the knee, hip, ankle, shoulder, hands"; "Chronic bulging lumbar disc"; "Injuries to the meniscus, rotator cuff"; "Avascular Necrosis of the shoulder, hip"; and "Chronic Bursitis." Answer ¶ 16.a; *see also id.* ¶ 16.b. (admitting claims on RS LLC's website). Indeed, in their pleadings, Defendants describe the Regenexx Procedure as a "treatment of orthopedic injuries and arthritis." Counterclaims ¶ 14; *see also id.* ¶ 10.

STATUTORY AND REGULATORY FRAMEWORK

I. THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

As noted above and explained in our accompanying Motion for Summary Judgment, the Complaint alleges that Defendants' cultured cell product is an adulterated and misbranded drug under the FDCA. Complaint ¶¶ 16-17, 30-39. The FDCA gives FDA broad authority to regulate the manufacture, labeling, and distribution of drugs. An "article" is a drug if it is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or is "intended to

[4]The cultured cells are responsible for the Regenexx procedure's alleged treatment effect. *See*, *e.g.*, Counterclaims ¶¶ 5, 10 (explaining the "Regenexx procedure" and how the cells are "placed back into the patient's injured area" and "***[t]he stem cells then begin to repair the patient's degenerated or injured area***.") (emphasis added); *see also Regenerative Sciences v. FDA*, Civ. No. 1:10-cv-01055-RMC (D.D.C.) Complaint (Dkt. No. 1) ¶¶ 11, 14-15 (RS LLC alleges that the Regenexx procedure "is for the treatment of orthopedic injuries and arthritis," and the "[p]rocedure requires the removal of stem cells and other tissue from a donor patient, the expansion of the stem cells, and ***the placement of the stem cells in the same patient for the treatment of the patient's degenerated or injured area of the body***.") (emphasis added).

affect the structure or any function of the body . . . ." 21 U.S.C. § 321(g)(1)(B)&(C). Thus, whether any particular article is a drug depends on its "intended use." *See Whitaker v. Thompson*, 353 F.3d 947, 953 (D.C. Cir. 2003); *Action on Smoking and Health v. Harris*, 655 F.2d 236, 239 (D.C. Cir. 1980); *United States v. Travia*, 180 F. Supp. 2d 115, 118 (D.D.C. 2001).

The "intended use" of a product refers, in turn, "to the objective intent of the persons legally responsible for the labeling of drugs," which is "determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives . . . ." 21 C.F.R. § 201.128; *Action on Smoking and Health*, 655 F.2d at 239 (observing that "it is well established that the 'intended use' of a product, within the meaning of the [FDCA], is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source") (internal citations omitted); *Estee Lauder, Inc. v. FDA*, 727 F. Supp. 1, 2 (D.D.C. 1989) ("Courts have held that the decision as to whether a product is a drug depends on its 'intended use,' which can be determined from objective evidence such as the product's current and past containers, instructions, and advertisements.").

The FDCA "deems" drugs to be adulterated and misbranded if they do not comply with the requirements in 21 U.S.C. §§ 351, 352, and 353(b)(4). Of particular relevance in this enforcement action, section 351(a)(2)(B) deems a drug to be adulterated if it is not manufactured in compliance with CGMP, section 352(f)(1) deems a drug to be misbranded if its labeling does not bear adequate directions for use, and section 353(b)(4) deems a prescription drug to be

misbranded if, at any time prior to dispensing, the label fails to bear, at a minimum, the symbol "Rx only." It is a violation of the FDCA, *inter alia*, to do any act while a drug is held for sale after shipment (of the drug or one of its components) in interstate commerce that results in the drug being adulterated or misbranded. *See* 21 U.S.C. § 331(k).

II. THE PUBLIC HEALTH SERVICE ACT

As explained in the accompanying Motion for Summary Judgment, FDA also regulates biological products under the PHSA, 42 U.S.C. § 262. A "biological product" includes any "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product . . . , applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i). A product may be both a drug and a biological product. *See*, *e.g.*, *CareToLive v. von Eschenbach*, 525 F. Supp. 2d 952, 957 (S.D. Ohio 2007); *United States v. Loran Medical Systems, Inc.*, 25 F. Supp. 2d 1082, 1084 (C.D. Cal. 1997) (cell product made from neonatal rabbit and human fetal cells was a drug and a biological product). A product that has been licensed under the PHSA is not required also to have an approved new drug application under the FDCA; in every other respect, however, the FDCA applies, including the provisions applicable to adulteration and misbranding of drugs. 42 U.S.C. § 262(j).

In a separate provision, the PHSA grants FDA broad authority to issue regulations to prevent the transmission of communicable diseases. Section 361(a) of the PHSA, 42 U.S.C. § 264(a), provides:

> The Surgeon General, with the approval of the Secretary, is ***authorized to make and enforce such regulations as in his judgment are necessary to prevent the***

> ***introduction, transmission, or spread of communicable diseases*** from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgment may be necessary.

42 U.S.C. § 264(a) (emphasis added). This authority has been delegated to FDA.[5]

III. FDA'S REGULATION OF CELLULAR PRODUCTS

In the late 1980's and early 1990's, scientists developed innovative methods to manipulate and use human cells and tissues for therapeutic uses. In response to these developments, in 1993, FDA outlined its regulatory approach to products intended for use in somatic cell and gene therapies. *See* Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products; Notice, 58 Fed. Reg. 53248 (Oct. 14, 1993) (hereafter, "Somatic Cell Therapy Notice"). FDA explained that the agency's existing statutory authorities are sufficiently broad to encompass the new somatic cell and gene therapies that were being investigated and developed. *Id.*

In the Somatic Cell Therapy Notice, the agency defined "somatic cell therapy products" as "autologous . . ., allogeneic . . ., or xenogeneic (i.e., inter-species) cells that have been propagated, expanded, selected, pharmacologically treated, or otherwise altered in biological

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[5]The statute grants this authority to the Surgeon General, with the approval of the Secretary. The Office of Surgeon General was abolished by section 3 of 1966 Reorg. Plan No. 3, eff. June 25, 1966, 80 Stat. 1610, and all of its functions were transferred to the Secretary of Health, Education, and Welfare (now Secretary of HHS)) by section 1 of 1966 Reorg. Plan No. 3, set out under 42 U.S.C. § 202. The HHS Secretary's authority has been delegated to FDA. *See* FDA Staff Manual Guide 1410.10.1.A.3.

characteristics ex vivo [i.e., outside the body] to be administered to humans and applicable to the prevention, treatment, cure, diagnosis, or mitigation of disease or injuries." *Id.* at 53249. The agency stated that cellular products intended for use as somatic cell therapy are biological products under the PHSA and drugs under the FDCA and explained that cells intended for use as somatic cell therapy would be subject to, *inter alia*, the PHSA's licensure requirement when they are "manipulated in a way that changes the biological characteristics of the cell population (e.g., by expansion, selection, encapsulation, activation, or genetic modification as a part of gene therapy . . . .)." *Id.* at 53249-50.

In 1997, FDA announced a new proposed approach for regulating human cells, tissues, and cellular or tissue-based products ("HCT/Ps"). *See* Proposed Approach to Regulation of Cellular and Tissue-Based Products, FDA Dkt. No. 97N-0068 (Feb. 28, 1997) ("Proposed Approach") (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM062601.pdf); *see also* Proposed Approach to Regulation of Cellular and Tissue-Based Products; Availability and Public Meeting, 62 Fed. Reg. 9721 (Mar. 4, 1997) ("Proposed Approach FR Notice"). FDA explained that the potential uses for such products are too diverse for a one-size-fits-all regulatory approach. Proposed Approach at 9.

In developing this new approach, FDA identified the principal public health concerns and attendant regulatory issues associated with the use of HCT/Ps, focusing on several questions, including: How can the transmission of communicable disease be prevented?; What processing controls are necessary, e.g., to prevent contamination that could result in an unsafe or ineffective

product, and to preserve integrity and function so that products will work as they are intended?; and How can clinical safety and effectiveness be assured? Proposed Approach at 9.[6] FDA differentiated cells and tissues and their uses by their risk relative to each of the public health concerns, to enable the agency to provide only that level of oversight relevant to each of the individual areas of concern. *Id.*; Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products; Proposed Rule, 63 Fed. Reg. 26744, 26745 (May 14, 1998).

Although FDA is authorized to apply all of the requirements in the FDCA and the PHSA to every product that meets the definition of a drug and/or biological product, the agency opted for a tiered, risked-based approach to regulate HCT/Ps that would provide only the degree of government oversight necessary to protect the public health. Proposed Approach at 6-7; *see also* Proposed Approach FR Notice, 62 Fed. Reg. 9721. To implement this new tiered approach, FDA issued, through notice and comment rulemaking, several regulations under its communicable disease authority under section 361 of the PHSA, 42 U.S.C. § 264.[7]

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[6]One of the factors FDA considered particularly relevant to these questions is the extent of processing the cells undergo. For example, the agency noted, *inter alia*, that "[i]mproper handing . . . can allow cells or tissues to become contaminated (e.g., bacterial contamination during collection, processing, storage, or transplantation, or cross contamination from other contaminated tissues)." Proposed Approach at 15. The agency also explained that clinical safety and effectiveness concerns depend in part on the extent of manipulation of the cells or tissues. *Id.* at 11.

[7]*See* Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447 (Jan. 19, 2001) ("Registration Rule"); Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, 69 Fed. Reg. 29785 (May 25, 2004) ("Donor Eligibility Rule"); Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and

FDA determined that some HCT/Ps could be effectively regulated solely by controlling the infectious disease risks they present. Such products are regulated only under the agency's HCT/P regulations (21 C.F.R. Part 1271) – that is, they are not subject to the premarket approval requirements (of safety and efficacy) for drugs, devices, and biological products in the FDCA and the PHSA. Such products are sometimes referred to as "361 HCT/Ps," after the communicable disease provision in section 361 of the PHSA, 42 U.S.C. § 264.[8] All other HCT/Ps (as defined in 21 C.F.R. § 1271.3(d)) are regulated as drugs, devices, and/or biological drugs because they present a greater degree of risk. Registration Rule, 66 Fed. Reg. at 5450.

An HCT/P is regulated solely under section 361 of the PHSA (42 U.S.C. § 264) and the regulations in 21 C.F.R. Part 1271 if it meets several criteria, one of which is that it be "minimally manipulated." 21 C.F.R. § 1271.10(a). Products that are more than "minimally manipulated" or that fail to meet any of the remaining criteria in section 1271.10 remain subject to the provisions of the FDCA and the PHSA, including the adulteration, misbranding, and premarket approval requirements. 21 C.F.R. § 1271.20; Registration Rule, 66 Fed. Reg. at 5456.[9]

Enforcement, 69 Fed. Reg. 68612 (Nov. 24, 2004) ("CGTP Rule").

[8]FDA determined that due to "their nature as derivatives of the human body, all human cellular and tissue-based products pose a potential risk of transmitting communicable diseases." *See*, *e.g.*, CGTP Rule, 66 Fed. Reg. at 1508, 1509 (Jan. 8, 2001).

[9]The HCT/P regulation, 21 C.F.R. § 1271.15, also identifies exceptions – that is, circumstances under which an establishment is not required to comply with 21 C.F.R. Part 1271. None of the exceptions in 21 C.F.R. 1271.15 is applicable to RS LLC's cultured cell product.

STANDARD AND SCOPE OF REVIEW

I. REVIEW UNDER THE ADMINISTRATIVE PROCEDURE ACT

Defendants' Counterclaims are premised on perceived violations of the Administrative Procedure Act. *See* Counterclaims ¶ 1. The APA entitles "[a] person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action . . . to judicial review thereof." 5 U.S.C. § 702. However, courts may review only "final agency action for which there is no other adequate remedy in a court." 5 U.S.C. § 704. Under the APA, an agency decision shall not be set aside unless the court finds that the agency's conclusions are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," *id*. § 706(2)(A), or "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," *id.* § 706(2)(C).

To determine whether an agency has acted within or outside the bounds of its authority, a reviewing court will look to the agency's enabling statute. *See, e.g., Univ. of D.C. Faculty Ass'n/NEA v. D.C. Fin. Responsibility & Mgmt. Assistance Auth.*, 163 F.3d 616, 620 (D.C. Cir. 1998).

The arbitrary and capricious standard of review in 5 U.S.C. § 706(2)(A) is highly deferential to the agency. *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971). Indeed, "[t]here is a presumption in favor of the validity of administrative action." *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 216 (D.D.C. 1996) (citing *Ethicon, Inc. v. FDA*, 762 F. Supp. 382, 386 (D.D.C. 1991)). The reviewing court must consider whether the agency's decision was based upon consideration of the relevant factors and whether there has

been a clear error of judgment. *Overton Park*, 401 U.S. at 416. But "under this narrow scope of review, '[t]he court is not empowered to substitute its judgment for that of the agency.'" *Bristol-Myers Squibb*, 923 F. Supp. at 216 (quoting *Overton Park*, 401 U.S. at 416); *see also Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 13, 18 (D.D.C. 2008) ("it is not enough for the agency decision to be incorrect – as long as the agency decision has some rational basis, the court is bound to uphold it."). In determining whether the agency's decision was rational and based on relevant factors, the administrative record compiled by the agency should serve as the "focal point for judicial review." *Camp v. Pitts*, 411 U.S. 138, 142 (1973).

II. FDA'S LEGAL INTERPRETATIONS AND SCIENTIFIC JUDGMENTS ARE ENTITLED TO DEFERENCE

Defendants' Counterclaims challenge FDA's interpretation of a statute that FDA is charged with implementing, FDA's interpretation of regulations that the agency issued through notice and comment rulemaking, and FDA's evaluation of scientific data within its area of expertise. Well-established precedent dictates that this Court give deference to FDA in each of these contexts.

The Supreme Court's decision in *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984), and its progeny set forth a two-step framework for reviewing an administrative agency's interpretation of its statute. Under *Chevron* step 1: "First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Id.* at 842-43. *Chevron* step 2 applies when Congress has not directly addressed the issue or has done so ambiguously. In that

event, the Court may not "simply impose its own construction on the statute," but rather must determine whether the agency's construction is based on a permissible interpretation of the statute. *See id.* at 843; *id.* at 843-44 & n.11 (in case of ambiguity, the court must uphold the agency's interpretation if its construction is permissible under the statute; a court need not conclude that the agency's construction was the only one it permissibly could have adopted or even the reading the court would have reached); *Barnhart v. Walton*, 535 U.S. 212, 218 (2002) (reviewing court must decide: (1) whether the statute unambiguously forbids agency interpretation, and (2) whether the agency interpretation exceeds the bounds of the permissible); *Anna Jaques Hosp. v. Sebelius*, 583 F.3d 1, 5 (D.C. Cir. 2009).

Moreover, when a court is evaluating an agency's interpretation of its own regulations, the agency is entitled to "substantial deference." *Thomas Jefferson Univ. v. Shalala*, 512 U.S. 504, 512 (1994); *United States Air Tour Ass'n v. FAA*, 298 F.3d 997, 1005 (D.C. Cir. 2002); *see also Novartis Pharms. Corp. v. Leavitt*, 435 F.3d 344, 349 (D.C. Cir. 2006) ("We have held on a number of occasions that FDA interpretations of the [FDCA] receive deference, as do its interpretations of its own regulations unless plainly erroneous or inconsistent with the regulations.").

Finally, when, as here, an agency's decisions are based on evaluation of scientific information within the agency's area of scientific or technical expertise, its decisions are traditionally accorded heightened deference. *See Am. Wildlands v. Kempthorne*, 530 F.3d 991, 1000 (D.C. Cir. 2008). Courts "review scientific judgments of the agency 'not as the chemist, biologist, or statistician that [they] are qualified neither by training nor experience to be, but as a

reviewing court exercising [its] narrowly defined duty of holding agencies to certain minimal standards of rationality.'" *Troy Corp. v. Browner*, 120 F.3d 277, 283 (D.C. Cir. 1997) (quoting *Ethyl Corp. v. EPA*, 541 F.2d 1, 36 (D.C. Cir. 1976)).[10]

ARGUMENT

I. DEFENDANTS' COUNTERCLAIMS BASED ON FDA'S ALLEGED LACK OF AUTHORITY TO REGULATE THE "PRACTICE OF MEDICINE" SHOULD BE DISMISSED

Four of Defendants' eight Counterclaims assert that FDA lacks the authority to regulate what they characterize as the "practice of medicine." Defendants ask this Court to declare that RS LLC's "Regenexx medical procedure" constitutes the practice of medicine and is beyond the jurisdiction of FDA. They also seek to enjoin FDA's implementation of the HCT/P rule. *See*, *e.g.*, Counterclaims ¶¶ 47-69, 98-103 (Counts I, II, III, and VII).

Defendants' practice of medicine claims are legally deficient, on a number of grounds. Although Defendants self-servingly cast this dispute as being about FDA's regulation of a medical ***procedure***, FDA is actually seeking to regulate the ***manufacture*** of a ***drug product by a corporation*** and its employees. Defendants' claims offer no explanation of how a corporation – one owned by physicians and non-physicians (Answer ¶¶ 4-7) – and its laboratory director, could possibly be engaged in the practice of medicine. In any event, Defendants' Answer and Counterclaims admit all of the facts necessary to establish that RS LLC's cultured cell product

[10]Such deference has repeatedly been applied in cases involving FDA. *See, e.g., Serono Labs.*, *Inc. v. Shalala*, 158 F.3d 1313, 1320-21 (D.C. Cir. 1998); *Henley v. FDA*, 77 F.3d 616, 621 (2d Cir. 1996); *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995); *Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 142 (3d Cir. 1987).

falls squarely within FDA's jurisdiction. Moreover, even though FDA has explained that it does not regulate the "practice of medicine," Defendants' conduct does not fall within that term as the FDCA, FDA, and the courts have defined it. As a result, all of Defendants' practice-of-medicine based claims should be dismissed.

A. Defendants' Answer and Counterclaims Admit the Facts that Vest FDA with Jurisdiction Over the Cultured Cell Product

Defendants' challenge to FDA's authority to regulate their manufacture of the cultured cell product should be dismissed for failure to state a claim upon which relief may be granted. Whether the FDCA provides jurisdiction over cultured cell products like the one manufactured by RS LLC is, first and last, a question of statutory construction, and it is axiomatic that the proper construction of a statute must begin with the statutory language. *Barnhart v. Sigmon Coal Co., Inc.*, 534 U.S. 438, 450 (2002); *see also United States v. Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969) (regarding the definition of drug, "Congress fully intended that the [FDCA's] coverage be as broad as its literal language indicates").

As discussed in greater detail *supra* at 5-6, the FDCA broadly defines "drug" as an "article" that is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or is "intended to affect the structure or any function of the body of man or other animals." 21 U.S.C. § 321(g)(1)(B)&(C). This statutory definition is a term of art and whether any particular article meets that definition depends on its "intended use." 21 C.F.R. § 201.128; *Whitaker*, 353 F.3d at 953; *Action on Smoking and Health*, 655 F.2d at 239; *supra* at 6.

Defendants' Answer and Counterclaims admit the critical facts that fix their product's status as a drug under the FDCA. By their own description, Defendants send the cultured cell

product that results from the manufacturing process described *supra* at 3-4 to the Clinic to be injected into patients to treat orthopedic conditions and arthritis. Counterclaims ¶¶ 10, 14-15. Defendants likewise admit that their promotional materials describe the Regenexx procedure as a treatment for a variety of orthopedic conditions. Answer ¶ 16.b. Thus, the "intended use" of the cultured cell product that RS LLC and its employees place into a syringe at the end of the manufacturing process is beyond question to treat a variety of diseases and to affect the structure and function of the body. Defendants' cultured cell product is therefore a drug under the FDCA.

B. Congress Did Not Exempt Drugs Made by Physicians from the FDCA's Adulteration and Misbranding Provisions

Defendants maintain that, "Congress has clearly precluded the FDA from asserting jurisdiction to regulate the practice of medicine." Counterclaims ¶ 53; *see also id.* ¶¶ 58, 67, 101. This argument is baseless and thus, not surprisingly, Defendants' Counterclaims do not cite any provision in the FDCA or other authority to support their contention.

1. Congress Did Not Exclude Defendants' Product from the FDCA

Congress did not exclude articles manufactured by physicians from the definition of "drug," from the FDCA's adulteration and misbranding provisions, from the premarket approval requirement for "new drugs," from the statute's "prohibited acts," or from its enforcement tools. *See* 21 U.S.C. §§ 321(g)&(p), 331, 332, 333, 334, 351, 352 & *passim*. If Congress had, for example, intended for physicians to be able to manufacture drugs that are exempt from the drug adulteration provisions – which specify, *inter alia*, that a drug is adulterated if it is not manufactured in accordance with CGMP; if it "consists in whole or in part of any filthy, putrid, or decomposed substance"; and "if it has been prepared, packed, or held under insanitary

conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health." (*see* 21 U.S.C. § 351(a)) – there should be strong textual evidence of such an exemption. There is none. To the contrary, the two provisions in the FDCA that specifically address physicians who make drugs for their patients – 21 U.S.C. § 360(g)(2) and 374(a)(2)(B) – make clear that, in Congress' view, drugs manufactured by physicians are subject to the FDCA.[11]

FDA's consistent and long-standing position is that the agency generally will not interfere with a physician prescribing ***lawfully marketed products*** for uses other than those for which they are approved, licensed, or cleared by FDA. In other words, if a drug is approved by FDA to treat

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[11]Under 21 U.S.C. § 360(g)(2), "practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in the course of their professional practice," are exempted from the FDCA's registration requirement in 21 U.S.C. § 360(b). Under 21 U.S.C. § 374(a)(1)&(2)(B), FDA may inspect any establishment (including a physician's office) where drugs are "manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction," but its authority to review records is more limited with respect to licensed practitioners "who manufacture, prepare, propagate, compound, or process drugs . . . solely for use in the course of their professional practice" than with more traditional manufacturers. Neither section suggests that an article that otherwise meets the definition of a drug in 21 U.S.C. § 321(g) is outside the scope of the FDCA simply because a physician made it, and attempts to read a broader "practice of medicine" exemption into the FDCA based on these provisions have been consistently rejected. *See United States v. Algon Chem., Inc*., 879 F.2d 1154, 1161 (3d Cir. 1989) (rejecting attempt to read a "practice of medicine" exemption into the FDCA based on 21 U.S.C.§§ 360(g) and 374(a)(2), the court explained "the medical practitioner exemptions by their terms afford no more than the right to be free from inspection and registration requirements when veterinarians and other practitioners compound medicine with legally acquired materials, not the right to acquire unapproved drug substances"); *Cowan v. United States*, 5 F. Supp. 2d 1235, 1240 (N.D. Okla. 1998) ("the 'medical practice exemption' referenced by Plaintiff is a very limited exemption from the registration requirements of the FDCA. Plaintiff's assertion that this exception provides a broad-based exemption to all physicians from the requirements of the [FDCA] is incorrect.").

diabetes and a physician opts to prescribe that drug to her patient to treat leukemia, FDA would consider that prescription for a new use of an approved drug to be the "practice of medicine" and would not interfere.[12]

Nevertheless, FDA has an indisputable role in regulating the manufacture, labeling, and distribution of drugs, *see*, *e.g.*, 21 U.S.C. §§ 321(g)&(p), 331(a)-(d) & (k), 351, 352, 355. The agency's role in determining the availability of therapeutic products inevitably affects the options available to practitioners seeking to use or prescribe those products. Courts have consistently rejected any notion that the FDCA's legislative history suggests a broad loophole for the practice of medicine. Indeed, in rejecting a district court's conclusion that "'it was not the purpose of the [FDCA] to involve the agency in the practice of the healing arts,'" the Seventh Circuit explained,

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[12]*See* Citizen Petition Regarding the Food and Drug Administration's Policy on Promotion of Unapproved Uses of Approved Drugs and Devices; Request for Comments, 59 Fed. Reg. 59820, 59821 (Nov. 18, 1992) ("[O]nce a [drug] ***product has been approved*** for marketing, a physician may prescribe it for uses or in treatment regimens of patient populations that are not included in approved labeling.") (emphasis added); New Drug, Antibiotic, and Biologic Drug Product Regulations; Final Rule, 52 Fed. Reg. 8798, 8803 (March 19, 1987) ("it was clearly the intent of Congress in passing the [FDCA] Act that FDA not regulate the practice of medicine, which the agency has consistently viewed as including the use by physicians of marketed drugs for unlabeled indications in 'the "day-to-day" treatment of patients. ***Once a drug product has been approved for marketing, a physician may, in treating patients, prescribe the drug for uses not included in the drug's approved labeling***. Control of the practice of medicine in these cases is primarily exercised through State laws affecting medical licensing and practice and through products liability-law.") (emphasis added); Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the FDA, 37 Fed. Reg. 16503 (Aug. 15, 1972) ("Although it is clear that Congress did not intend the [FDA] to regulate or interfere with the practice of medicine, it is equally clear that it ***did intend that the [FDA] determine those drugs for which there exists substantial evidence of safety and effectiveness and thus will be available for prescribing by the medical profession***, and additionally, what information about the drugs constitutes truthful, accurate, and full disclosure to permit safe and effective prescription by the physician.") (emphasis added).

> ***If not that, however, what does the statute do? Congress gave the FDA comprehensive powers to license the manufacture of drugs and limit their sales. To regulate drugs is to be 'involved' in the 'practice of the healing arts.'*** True, the Senate report that accompanied the original statute in 1935 said that the bill was 'not intended as a medical practices act and [would] not interfere with the practice of the healing art[s]', S. Rep. No. 361, 74th Cong., 1st Sess. 3 (1935), but the statute has undergone much amendment since then, including a complete over-haul in 1962. Phrases such as the one in the 1935 Senate report--not repeated in 1962--never meant more than that medical licensure and discipline would continue to be the states' business; states, not the FDA, would decide whether (for example) physicians had selected wisely from among methods of treatment. The full quotation, redacted by [the defendant] and the district court, makes the point: the statute is "not intended as a medical practices act and [would] not interfere with the practice of the healing art by chiropractors and others". So states set medical qualifications, and practitioners who do not use drugs (i.e., chiropractors) may go on as before. ***Nothing in the history or structure of the Act permits drugs deemed ineffective or dangerous by the FDA to be available for use***. *United States v. Rutherford*, 442 U.S. 544, 61 L. Ed. 2d 68, 99 S. Ct. 2470 (1979).

See United States v. 9/1 Kg. Containers, 854 F.2d 173, 176 (7th Cir. 1988) (emphasis added); *accord United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981) ("[W]hile the [FDCA] was not intended to regulate the practice of medicine, it was obviously intended to control the availability of drugs for prescribing by physicians."); *Algon Chem*., 879 F.2d 1154 (holding that "practice of medicine" policy did not permit veterinarians to compound drugs from components they could not legally obtain); *Loran Medical Systems*, 25 F. Supp. 2d at 1087 ("The court disposes quickly of defendants' argument that the FDA's exercise of authority over the Cell Product is an attempt to regulate the practice of medicine – an area traditionally left to the states. While the [FDCA] was not intended to regulate the practice of medicine, it was obviously intended to control the availability of drugs for prescribing by physicians. The court has already determined that the Cell Product is a drug. Accordingly, the FDA has the authority to regulate its use.") (internal citation and quotation omitted); *Cowan*, 5 F. Supp. 2d 1235 (adopting magistrate

judge's report and recommendation rejecting argument that "practice of medicine" exception permits physician to treat AIDS patient with an experimental drug developed by the physician).

The FDCA's sole use of the term "practice of medicine," in the medical device context, shows Congressional ratification of ***FDA's*** view of that term. In 1997, Congress amended the FDCA to add 21 U.S.C. § 396, which states:

> Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer ***any legally marketed device*** to a patient for any condition or disease within a legitimate health care practitioner-patient relationship. . . .

Any contention that Congress precluded FDA from enforcing the FDCA's requirements regarding premarket approval of unapproved new drugs and prohibitions on causing the adulteration and misbranding of drugs that are made from components that have moved in interstate commerce is simply incorrect.

2. Defendants' Practice of Medicine Claims Should Be Dismissed

Counterclaim I rests upon the unsupported contention that FDA cannot regulate RS LLC's manufacture of the cultured cell product because Congress precluded FDA from regulating the practice of medicine.[13] Counterclaims ¶¶ 53-54 and page 21. This assertion is

[13]Ignoring the text of the FDCA, Defendants turn to a provision in the Colorado Medical Practice Act, C.R.S. § 12-36-106, which defines the "practice of medicine" very broadly in order to delineate what conduct triggers the requirement to hold a medical license. *See* C.R.S. § 12-36-106(2). Indeed, the Colorado statute's definition of the "practice of medicine" includes simply holding oneself out to be a physician. *See* C.R.S. § 12-36-106(1)(d). There is, however, nothing in the text or structure of the FDCA to suggest Congress intended this or any other ***state*** statute to be used to define the scope of ***FDA's*** authority. Indeed, the notion that Congress intended to limit the scope of the broad remedial provisions of the FDCA in a manner that varies from state to state, based on different definitions of the "practice of medicine" – without a word in the FDCA to indicate this intent – is untenable. Defendants' claimed exception to the "drug"

demonstrably incorrect for the reasons discussed above.

Counterclaims III and VII similarly contend that 21 C.F.R. Part 1271 is *ultra vires* because, Defendants argue, ***the regulation*** "grants authority to FDA to regulate the practice of medicine," which, according to Defendants, Congress never permitted FDA to do. Counterclaims ¶ 64-67 and page 24 (Count III); Counterclaims ¶ 101 and page 29 (Count VII).[14] In the same vein, Counterclaim II contends that 21 C.F.R. Part 1271 is arbitrary and capricious because "FDA lacks the authority to regulate the practice of medicine" and the agency thus acted arbitrarily in concluding that HCT/P regulation does not infringe on the practice of medicine.

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definition based on the "practice of medicine" is a request for a disfavored implied exemption, and should be rejected at step 1 of the *Chevron* framework. *See United States v. Rutherford*, 442 U.S. 544, 552 (1979) (unanimously rejecting request from terminally ill patients to imply an exception to the FDCA's premarket approval requirement for new drugs, the Court explained "Only when a literal construction of a statute yields results so manifestly unreasonable that they could not fairly be attributed to congressional design will an exception to statutory language be judicially implied."); *see also Carter v. Welles-Bowen Realty, Inc.*, 553 F.3d 979, 985 (6th Cir. 2009) ("According to 'traditional canons of statutory interpretation, remedial statutes should be construed broadly to extend coverage and their exclusions or exceptions should be construed narrowly.'") (quoting *Cobb v. Contract Transport, Inc.*, 452 F.3d 543, 559 (6th Cir. 2006)); *Bacto-Unidisk*, 394 U.S. at 798 ("remedial legislation such as the [FDCA] is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health").

[14]Counterclaim III presents a more narrow challenge, contending that the definition of "HCT/P" in 21 C.F.R. § 1271.3(d) is *ultra vires* because it includes articles intended for autologous (as well as allogeneic) use. Defendants allege that this regulation grants FDA the authority to regulate the practice of medicine, "which was never authorized by Congress." Counterclaims ¶¶ 64-67. As already shown, because RS LLC's product is, without question, intended to treat or mitigate disease and to affect the structure or function of the body, it is a drug under 21 U.S.C. § 321(g). The statutory definition of drug is broad and unqualified and does not distinguish between articles intended for autologous versus allogeneic use. Defendants' suggestion that there is an exception from the "drug" definition for autologous products lacks any basis in the statutory language. Defendants' argument therefore should be rejected at step 1 of the *Chevron* framework.

Counterclaims ¶¶ 57-60. For the reasons stated above, RS LLC's product is clearly a drug under 21 U.S.C. § 321(g)(1)(B)&(C), and, because there is no "practice of medicine" exception in the statute for Defendants' product, the Counterclaims that challenge 21 C.F.R. Part 1271 based on "practice of medicine" arguments fail to state a claim.

Moreover, Counterclaims II, III, and VII (as well as the remaining Counts which seek to enjoin FDA's application of 21 C.F.R. Part 1271) misapprehend the nature and purpose of the HCT/P rule. As the agency explained in the Registration Rule, ***"Our ability to regulate an HCT/P as a drug, device, and/or biological product derives from the [FDCA] and section 351 of the [PHSA] [42 U.S.C. § 262]***, authorities that are distinct from our authority to issue regulations to prevent the transmission of communicable disease under section 361 of the [PHSA]." 66 Fed. Reg. at 5456 (emphasis added); *see also* Somatic Cell Therapy Notice, 58 Fed. Reg. 53248.

FDA did not attempt to enlarge the scope of its authority over products like the cultured cell product through promulgation of the HCT/P rule. Quite the contrary. Rather than subjecting all HCT/Ps to all of the regulatory requirements in the FDCA and PHSA because those products meet the definition of a "drug" and a "biological product," FDA issued the HCT/P rule to establish a tiered, risk-based system of regulation whereby it would apply only the degree of government oversight necessary to protect the public health. Proposed Approach at 6; Proposed Registration Rule, 63 Fed. Reg. at 26745. In other words, ***FDA opted to apply less regulation to HCT/Ps that meet the criteria in 21 C.F.R. § 1271.10 than it could have under its statutory authorities***. Because there is no "practice of medicine" exception in the statute for Defendants'

product, their contention that the HCT/P regulatory scheme impermissibly grants FDA authority precluded by Congress misses the mark entirely. Even if this Court were to invalidate and enjoin application of 21 C.F.R. Part 1271, as Defendants request, FDA's enforcement action against Defendants should still proceed because FDA's authority to regulate Defendants derives from the FDCA and PHSA.

For all of these reasons, Counterclaims I, II, III, and VII should be dismissed.

II. COUNTERCLAIMS REGARDING THE DEFINITION OF MINIMAL MANIPULATION

Three of Defendants' Counterclaims raise procedural objections to the FDA's assertion in the preambles to the proposed and final Registration Rule that expansion of cells in culture constitutes more than minimal manipulation. Specifically, Counterclaim IV alleges that the preamble statements "imposed a per se rule which provides that any expansion of stem cells constitutes more than minimal manipulation of the cells" but that FDA violated the APA by failing to explain how expansion of the cells alters the relevant biological characteristics of the cells and failing to share the scientific research collected by the agency on that issue. Counterclaims ¶¶ 73-77. Counterclaim V similarly alleges that, even before FDA made these statements in the preambles, the agency was aware that "ample science existed [which proved] that expansion of stem cells in culture did not alter the relevant biological characteristics of the cells," but FDA failed to consider the relevant science. *Id.* ¶¶ 83-87. Counterclaim VI asserts that "FDA's statement that expansion of stem cells in culture does not constitute minimal manipulation was a legislative rule" that was issued "without the use of legislative rulemaking procedures" in violation of the APA. *Id.* ¶¶ 93-96.

None of these Counterclaims states a claim upon which relief may be granted. They object to *an example* of how FDA interpreted the term "minimal manipulation" with respect to a particular factual scenario: expansion of cells in culture. That example is neither a legislative rule subject to the APA's notice and comment requirement nor final agency action subject to APA review.

A. Counterclaim VI Should be Dismissed Because The Preamble's "Cell Expansion" Example is Not a Legislative Rule

Defendants contend that "FDA's statement that expansion of stem cells in culture does not constitute minimal manipulation was a legislative rule" and ask this Court to enjoin implementation of 21 C.F.R. Part 1271 "pending compliance with the notice and comment provisions of the [APA] . . . ." Counterclaims ¶¶ 94 and pages 28-29. Defendants have again missed the mark. FDA's preamble example is not a legislative rule that requires notice and comment rulemaking.

Under the APA, the publication of notice and opportunity for comment are only required for a limited subset of agency pronouncements. Rulemaking is necessary for "legislative" or "substantive" rules, but not for "interpretive rules" or "general statements of policy." 5 U.S.C. § 553(b)(3)(A) & (d). A rule is "legislative" only when the "agency intends to create new law, rights, or duties." *Gen. Motors Corp. v. Ruckelshaus*, 742 F.2d 1561, 1565 (D.C. Cir. (1984).

In contrast, "interpretive rules are those that merely clarify or explain existing laws or regulations." *Nat'l Med. Enters., Inc. v. Shalala*, 43 F.3d 691, 697 (D.C. Cir. 1995). Similarly, a "policy statement announces the agency's tentative intentions for the future." *Brock v. Cathedral Bluffs Shale Oil Co.*, 796 F.2d 533, 537 (D.C. Cir. 1986) (quoting *Pac. Gas & Elec. v. FPC*,

506 F.2d 33, 38 (D.C. Cir. 1974)). Moreover, an agency pronouncement does not become a substantive rule where, as here, it merely "supplies crisper and more detailed lines than the authority being interpreted." *Am. Mining Cong. v. Mine Safety & Health Admin.*, 995 F.2d 1106, 1112 (D.C. Cir. 1993).

In *American Mining Congress*, the D.C. Circuit identified four criteria that indicate a rule is legislative (none of which is present in this case): (1) in the absence of the rule, no legislative basis would exist for an enforcement action; (2) the agency has published the rule in the Code of Federal Regulations ("CFR"); (3) the agency explicitly invoked its general legislative authority to pass the rule; (4) the rule effectively amends a prior legislative rule. 995 F.2d at 1112.[15]

Regardless of whether the preamble example[16] is characterized as an interpretive rule, a policy statement, or not a "rule" at all, it is certainly not a ***legislative*** rule. In the proposed and final Registration Rule, FDA included "minimal manipulation" as one of the criteria for determining whether an HCT/P would qualify for regulation solely under section 361 of the PHSA, and defined "minimal manipulation" of cells and nonstructural tissues as "processing that

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[15] Similarly, in *Cement Kiln Recycling Coalition v. EPA*, 493 F.3d 207 (D.C. Cir. 2007), the court described the factors for distinguishing legislative rules from policy statements (in the context of the Resource Conservation and Recovery Act) as "(1) the Agency's own characterization of the action; (2) whether the action was published in the Federal Register or Code of Federal Regulations; and (3) whether the action has binding effects on private parties or on the agency." *Id.* at 226-27.

[16] The regulation defines minimal manipulation for "cells or nonstructural tissues" as "processing that does not alter the relevant biological characteristics of cells or tissues." 21 C.F.R. § 1271.3(f)(2). This language was included in the proposed Registration Rule, 63 Fed. Reg. at 26754, and was not changed in the final rule, 66 Fed. Reg. at 5467. Thus, there can be no question that the actual codified language was the subject of notice and comment rulemaking.

does not alter the relevant biological characteristics of cells or tissues." *See* 21 C.F.R. §§ 1271.3(f)(2), 1271.10(a)(1); Proposed Registration Rule, 63 Fed. Reg. 26754; Registration Rule, 66 Fed. Reg. at 5467. In the preamble to the final rule, the agency shared its thinking regarding the interpretation of "minimal manipulation":

> At this time, examples of HCT/P's that we consider to be minimally manipulated include those that have been subjected to the following procedures: Density gradient separation; selective removal of B-cells, T-cells, malignant cells, red blood cells, or platelets; centrifugation; cutting, grinding, or shaping; soaking in antibiotic solution; sterilization by ethylene oxide treatment or irradiation; cell separation; lyophilization; cryopreservation; or freezing. ***We do not agree that the expansion of mesenchymal cells in culture or the use of growth factors to expand umbilical cord blood stem cells are minimal manipulation***.

66 Fed. Reg. at 5457 (emphasis added); *see also* Proposed Registration Rule, 63 Fed. Reg. at 26748.

Although the codified definition of minimal manipulation is a legislative rule, the examples in the preambles are most assuredly not. FDA retains the discretion to assess each situation individually and the flexibility to further develop its approach to the codified definition of "minimal manipulation" as science and circumstances evolve.

Further, none of the indicia of rulemaking identified in *American Mining Congress* apply to the preamble statements: 1) in their absence, FDA has the same authority granted by the FDCA and the codified rules, 21 U.S.C. §§ 301-399b; 21 C.F.R. Part 1271; 2) the preamble examples were not published in the CFR; 3) although FDA invoked its legislative authority to issue the rule itself, it did not invoke its legislative authority in offering these examples; and 4) the statements did not amend a prior legislative rule. *See Am. Mining Cong.*, 995 F.2d at 1112. Nor do the preamble statements have a "binding effect" on private parties or the agency.

See id.; *Cement Kiln,* 493 F.3d at 226-27. Indeed, FDA prefaced its description of the example in the preamble to the final rule with "At this time" - underscoring the importance of making individual determinations in the context of current scientific understanding. Registration Rule, 66 Fed. Reg. at 5457. The statements likewise do not impose any new obligations or requirements beyond the requirements set forth in the regulations themselves, and, as discussed above, 21 C.F.R. Part 1271 is itself ***less burdensome*** than the FDCA or section 351 of the PHSA.

Because the challenged preamble statements are not a legislative rule that requires notice and comment rulemaking under the APA, Counterclaim VI fails to state a claim as a matter of law and should be dismissed.

B. Counterclaims IV and V Should Be Dismissed Because the Preamble Statements Are Not Final Agency Action Subject to APA Review

In Counterclaim IV, Defendants allege that the "cell expansion" preamble statements are arbitrary and capricious because FDA "never explained why any expansion of stem cells in culture does not constitute minimal manipulation" or why it "alters the relevant biological characteristics of the cells" and failed to share the "scientific research . . . on the issue" with the "interested public." Counterclaims ¶¶ 75-77. Counterclaim V alleges that "ample science existed" and "was made available to FDA both prior and subsequent to FDA's promulgation of the definition of minimal manipulation" showing that "expansion of stem cells in culture did not alter the relevant biological characteristics of the cells." Counterclaims ¶¶ 85-86. FDA's alleged "failure to consider the relevant science is arbitrary and capricious." *Id.* ¶¶ 87-88.

The most obvious problem with these claims is that they do not present the Court with a reviewable agency action. Under the APA, this Court may review only "final agency action for

which there is no other adequate remedy in a court." 5 U.S.C. § 704. To qualify as "final" within the meaning of the APA, an action must meet two requirements: First, it "must mark the consummation of the agency's decision-making process – it must not be of a merely tentative or interlocutory nature. . . . [S]econd, the action must be one by which rights or obligations have been determined, or from which legal consequences will flow." *Bennett v. Spear*, 520 U.S. 154, 177-78 (1997) (internal citations and quotations ommitted). Here, the challenged preamble statements meet neither of those requirements.

First, the examples given in the preambles reflected the agency's judgment about particular conduct at a particular moment in time. From the time it announced the Proposed Approach, however, the agency recognized that developing science may change the agency's view about what type of processing alters the relevant biological characteristics of the cells:

> As additional information is generated about procedures in the 'more-than-minimal-manipulation' category, the agency intends to consider them to be in the 'minimal-manipulation' category when clinical data and experience show that the procedure does not alter the biological characteristics of the cells or non-structural tissue, or the relevant structure-related characteristics of structural tissue. This flexibility will permit product processing that has been found not to affect the pertinent characteristics of the product to be subjected to a lower level of regulation.

Proposed Approach at 17. Consistent with this appreciation that its views could change over time, in the preamble to the proposed Registration Rule, the agency stated,

> Examples of manipulation not considered minimal, ***based on current scientific knowledge***, include cell expansion, encapsulation, activation, and genetic modification. FDA recognizes that the subsequent accumulation of clinical data and experience about a particular process may demonstrate that it does not alter the original relevant characteristics of the cells or tissue, and the ***agency will consider this information in determining whether a procedure should be considered minimal as opposed to more-than-minimal manipulation***.

63 Fed. Reg. at 26748-26749 (emphasis added).

FDA likewise prefaced the final rule's preamble discussion of examples of what does and does not constitute more than minimal manipulation "At this time." Registration Rule, 66 Fed. Reg. at 5457. Consequently, the examples offered in the preambles cannot be properly characterized as the "consummation of the agency's decision-making process."

Moreover, the preamble examples do not impose any requirements or obligations on the Defendants.[17] Indeed, Defendants apparently did not alter their conduct based on the statements, because, as discussed in our Motion for Summary Judgment, they continued to manufacture a product made from expanded cells without adhering to the requirements in the FDCA. *See*, *e.g.*, Pl.'s Mot. for Summary Judgment at 14-17, 26-35. Nor do the statements claim to carry the force of law. *See* 21 C.F.R. § 10.85(d)&(j) (noting that statements in preambles do not establish legal requirements).[18]

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[17]In the enforcement action, FDA is submitting a declaration explaining why RS LLC's processing of the cells in its cultured cell product does not meet the definition of minimal manipulation in 21 C.F.R. § 1271.3(f)(2).

[18]Although FDA previously took the position than an advisory opinion could be final agency action, *see* 21 C.F.R. § 10.45(d), FDA's current view is that advisory opinions (including statements in preambles) cannot legally bind the agency and are not final agency action. *See* Administrative Practices and Procedures; Advisory Opinions and Guidelines; Proposed Rule, 57 Fed. Reg. 47314 (Oct. 15, 1992) (proposing to amend, *inter alia*, 21 C.F.R. § 10.45 because, "Under the proposed revisions to §§ 10.85 and 10.90, advisory opinions and guidelines would "not bind the agency" and would not "create or confer any rights, privileges, or benefits for or on any person."). Further, as noted above, FDA's advisory opinions "may be used in administrative or court proceedings to illustrate acceptable and unacceptable procedures or standards, but not as a legal requirement." 21 C.F.R. § 10.85(j).

Because the challenged preamble statements are not final agency action, they cannot be challenged under the APA. 5 U.S.C. § 704. As a result, Counterclaims IV and V should be dismissed.

III. DEFENDANTS' PROCEDURAL CHALLENGES TO THE HCT/P RULE ARE TIME BARRED

The United States enjoys sovereign immunity, and thus Congress can set the conditions under which the United States may be sued. *United States v. Mitchell*, 463 U.S. 206, 212 (1983) ("It is axiomatic that the United States may not be sued without its consent and that the existence of consent is a prerequisite for jurisdiction."). One such condition is a statute of limitations. Defendants' APA claims are governed by the "catch-all" statute of limitations set forth in 28 U.S.C. § 2401(a), which provides "Except as provided by the Contract Disputes Act of 1978, every civil action commenced against the United States shall be barred unless the complaint is filed within six years after the right of action first accrues. . . ." *See Harris v. FAA*, 353 F.3d 1006, 1009 (D.C. Cir. 2004) ("Unless another statute prescribes otherwise, a suit challenging final agency action pursuant to section 704 must be commenced within six years after the right of action first accrues. 28 U.S.C. § 2401(a)"); *Wong v. Doar*, 571 F.3d 247, 262-63 (2d Cir. 2009) (applying § 2401(a) to APA challenge); *Cedars-Sinai Med. Ctr. v. Shalala*, 177 F.3d 1126 (9th Cir. 1999) (same).[19]

[19] The D.C. Circuit has not resolved whether the statute of limitations in 28 U.S.C. § 2401(a) is jurisdictional. *See Harris*, 353 F.3d at 1013 n.7 (noting uncertainty about whether § 2401(a) is jurisdictional but not resolving the issue); *Felter v. Norton*, 412 F. Supp. 2d 118, 122 (D.D.C. 2006) (reviewing D.C. Circuit case law on whether 28 U.S.C. § 2401(a) is jurisdictional and concluding that for claims that "do not have an analogue in private litigation" the "running of the statute of limitations is an absolute jurisdictional bar subject to a motion to dismiss under

In determining when a cause of action accrues, the D.C. Circuit has distinguished between substantive and procedural challenges to regulations. In the context of an enforcement action, a party may raise a substantive challenge (i.e., that a regulation is unconstitutional, *ultra vires*, or based on a misconstruction of the statute) based on when the statute is applied to the claimant, but any "attack on the ***procedural genesis*** of" a regulation outside the statute of limitations period is time barred. *JEM Broadcasting Co. v. FCC*, 22 F.3d 320 (D.C. Cir. 1994) (discussing the 60 day limitations period in the Hobbs Act, the court explained "[C]hallenges to the *procedural lineage of agency regulations*, whether raised by direct appeal, by petition for amendment or rescission of the regulation ***or as a defense to an agency enforcement proceeding***, will not be entertained outside the 60-day period provided by statute.") (second emphasis added). "[I]n a procedural challenge, it is the manner in which the regulation was adopted which is in issue; the content or substance of the regulation is irrelevant." *Utu Utu Gwaitu Paiute Tribe v. Dept. of Interior*, 766 F. Supp. 842, 844 (E.D. Cal. 1991) (citing *Sierra Club v. Penfold*, 857 F.2d 1307, 1315 (9th Cir. 1988)).

In the case of claimed procedural error in the promulgation of a regulation, final agency action occurs upon issuance of the regulation. *Wong*, 571 F.3d at 262-63 (§ 2401(a) barred challenge for failure to issue regulation in accordance with APA's notice and comment requirement; statute of limitations began to run when regulation was issued even though it had only recently been applied to claimant); *Cedars-Sinai Med. Ctr. v. Shalala*, 177 F.3d at 1129

Rule 12(b)(1)"). As a result, Plaintiff moves to dismiss these claims under both Rule 12(b)(1) and Rule 12(b)(6).

("[A] cause of action challenging procedural errors in the promulgation of regulations accrues on the issuance of the rule."); *JEM Broadcasting*, 22 F.3d at 326 ("We have held unequivocally that when a party complains of an agency's failure to provide notice and comment prior to acting, it is that failure which causes 'injury'; and interested parties are 'aggrieved' by the order promulgating the rules. Moreover, the failure to provide notice and comment is a ground for complaint that is or should be fully known to all interested parties at the time the rules are promulgated.") (internal citation omitted); *Alabama v. Shalala*, 124 F. Supp. 2d 1250, 1270 (M.D. Ala. 2000) (claim of procedural deficiency in promulgating OMB Circular accrued when the Circular was published in Federal Register; APA challenge to its application in action to disallow costs paid to Alabama by federal government was barred by statute of limitations).

Requiring procedural challenges to be initiated within the limitations period serves the goal of ensuring prompt review of regulations: "Congress has 'determined that the agency's interest generally lies in prompt review of agency regulations,' and 'we accord heavy weight to that view.' We place a high value on finality in administrative processes, for finality 'conserves administrative resources and protects the reliance interests of regulatees who conform their conduct to the regulations.'" *JEM Broadcasting*, 22 F.3d at 325 (internal citations omitted); *accord Cedars-Sinai*, 177 F.3d at 1129 ("it is clear that the cause of action arises under the [APA] to challenge the manner in which the policy was announced. As such, the cause accrued at the time of that announcement. . . .[S]uch a rule is necessary so that regulations are not indefinitely subject to challenge in court. Accepting the [plaintiffs'] argument and allowing suit whenever a regulation was administered by a federal agency 'would virtually nullify the statute of

limitations for challenges to agency orders.'") (internal citation omitted).

The final Registration Rule, which defined "HCT/P" and "minimal manipulation," and identified "minimal manipulation" as a factor for determining whether an HCT/P would be regulated as a drug, biologic or device versus as a 361 HCT/P, was published in January 2001, more than six years before Defendants' filed their Counterclaims (or any of their other actions against FDA). *See* Registration Rule, 66 Fed. Reg. 5447 (Jan. 19, 2001). As a result, any claims based on procedural defects in that Rule are time barred.

Counterclaims II, IV, V, and VI raise several procedural challenges to the Registration Rule. In Counterclaim VI, Defendants allege that FDA's definition of "minimal manipulation" is a legislative rule that was not issued through notice and comment rulemaking procedures and is therefore invalid. Counterclaims ¶¶ 90-97. As part of the requested relief in Counterclaim VI (as well in Counterclaims II, IV, and V), Defendants ask the Court to enjoin implementation of 21 C.F.R. Part 1271 "pending compliance with the notice and comment provisions of the [APA]." *Id.* at 28-29. Charges that an administrative agency failed to comply with the notice and comment provisions of the APA are a "common procedural challenge" to an administrative regulation, and are therefore barred if raised more than six years after publication of the rule. *Utu Utu Gwaitu Paiute Tribe*, 766 F. Supp. at 844 (citing *Chemical Waste Management v. EPA*, 869 F.2d 1526 (D.C. Cir. 1989)); *see also Cedars-Sinai Med. Ctr.*, 177 F.3d at 1129 (holding that procedural claim that agency failed adhere to notice-and-comment rulemaking provisions of APA was barred by six-year statute of limitations applicable to actions for judicial review of agency regulations).

In Counterclaims II, IV, and V, Defendants contend FDA failed to consider or explain several factors in issuing the Registration Rule, thus rendering the HCT/P regulation arbitrary and capricious.[20] These claims address the manner in which the Registration Rule was promulgated rather than substance of the rule itself, and therefore are also barred by the statute of limitations as procedural challenges that accrued at the time the regulation was published. *Massachusetts Mfg. Extension Partnership v. Locke*, ---- F. Supp. 2d ----, 2010 WL 2679835 *8 (D.D.C.) (July 7, 2010) (holding that claim that "in-kind contribution cap" regulation was arbitrary and capricious because NIST "never provided an explanation for the cost cap" was barred six years after the final rule was published); *see Citizens Alert Regarding The Environment v. EPA*, 102 Fed. Appx. 167, 168 (D.C. Cir. 2004) (holding that claim that EPA had acted "arbitrarily and capriciously" in approving Pennsylvania's program for disbursing federal grant money to individual wastewater disposal projects was barred, under 28 U.S.C. § 2401, six years after EPA approved the program); *see also Big Horn Coal v. Temple*, 793 F.2d 1165, 1169-70 (10th Cir. 1986) (J. Barrett concurring) (stating that statute of limitations period began to run

[20]In Counterclaim II, Defendants contends that in the "one occasion" that FDA addressed whether the HCT/P regulations impermissibly infringed upon the practice of medicine (in the preamble to the final Registration Rule), the agency acted arbitrarily by failing to "consider any factors relevant to the practice of medicine" and failing to "explain what data relevant to the practice of medicine it relied upon." Counterclaims ¶¶ 56-61. Counterclaim IV alleges that "FDA's definition of 'minimal manipulation' is arbitrary and capricious," *id.* ¶ 78, because FDA "has never explained how or why expansion of stem cells in culture alters the relevant biological characteristics of the stem cells" and "does not constitute minimal manipulation," *id.* ¶ 75-76, and because "FDA has never shared with the interested public the scientific research collected by the agency on the issue of whether any (or what type of) expansion of stem cells in culture alters the relevant biological characteristics of the stem cells." *Id.* ¶ 77. In Counterclaim V, Defendants assert that "FDA never considered the available science relevant to the issue of 'minimal manipulation.'" *Id.* ¶ 87.

on a "procedural challenge" to regulation as being "arbitrary and capricious" when the rule was promulgated, and that "[t]he purpose of these time limits is to impart finality into the administrative process, thereby conserving administrative resources and protecting the reliance interests of those who might conform their conduct to the administrative regulation . . . . This purpose is not only undermined by considering petitions to review filed after the time period has expired, but also when a final agency rule is collaterally challenged in a subsequent agency action. Therefore, absent exceptional circumstances [when the agency's rule is 'constitutionally infirm or outside the agency's statutory authority'], I would not consider collateral procedural challenges to final agency actions after the time limit for the courts to review procedural challenges has expired.") (citing *Natural Resources Defense Council v. NRC*, 666 F.2d 595, 602 (D.C. Cir. 1981)).

IV. COUNTERCLAIM VIII SHOULD BE DISMISSED

In Counterclaim VIII, Defendants allege that "FDA's entire regulatory scheme governing stem cells is *ultra vires* as it purports to give the FDA the authority to regulate the autologous use of stem cells which carries no risk of spreading communicable disease from foreign countries into the States or possessions, or from one State or possession into any other State or possession." Counterclaims at 30. Defendants' argument ignores FDA's determination that, regardless of whether cells or tissue are intended for autologous or allogeneic use, the manufacturing process for all HCT/Ps must be controlled to prevent the transmission of communicable diseases.

As noted, a reviewing court will look to the agency's enabling statute to determine whether the agency has acted within or outside the bounds of its authority. *See, e.g., Univ. of D.C. Faculty Ass'n/NEA.*, 163 F.3d at 620. The enabling statute's grant of authority at issue here is exceedingly broad. As discussed above, section 361 of the PHSA, 42 U.S.C. § 264(a), authorizes FDA to "make and enforce such regulations ***as in [the agency's] judgment are necessary*** to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession." (emphasis added). Moreover, because section 361 of the PHSA is remedial legislation aimed at protecting the public health, it is entitled to liberal construction. *See*, *e.g.*, *Bacto-Unidisk*, 394 U.S. at 798.

Pursuant to this broad delegation of power, FDA has considerable discretion in determining whether regulations are necessary to prevent the spread of communicable diseases. FDA determined that due to "their nature as derivatives of the human body, ***all human cellular and tissue-based products pose a potential risk of transmitting communicable diseases***." *See*, *e.g.*, CGTP Rule, 66 Fed. Reg. at 1509 (emphasis added); Proposed Donor Eligibility Rule, 64 Fed. Reg. at 52,698 (All HCT/Ps "pose some risk of carrying pathogens that could cause disease in recipients and family members or other close contacts of recipients, health care personnel, and other handlers of tissue.").

FDA invoked section 361 to issue the three rules that comprise 21 C.F.R. Part 1271. First, the Registration Rule, 66 Fed. Reg. 5447, codified at 21 C.F.R. Part 1271, Subpart B, requires manufacturers of HCT/Ps to register and list their HCT/Ps with FDA. That regulation

forms the foundation for a regulatory program designed to prevent the transmission of communicable disease. 66 Fed. Reg. at 5449. Second, the Donor Eligibility rule requires tissue establishments to evaluate donors of cells and tissues, through screening and testing, to reduce the transmission of infectious diseases through transplantation of HCT/Ps. *See* 21 C.F.R. 1271 Subpart C; 69 Fed. Reg. at 29787. Third, the current good tissue practice ("CGTP") rule establishes requirements for HCT/Ps related to recovery, donor screening, donor testing, processing, storage, labeling, packaging, and distribution to "prevent the introduction, transmission, or spread of communicable diseases by HCT/Ps (e.g., by ensuring that the HCT/Ps do not contain communicable disease agents, that they are not contaminated, and that they do not become contaminated during manufacturing)." 21 C.F.R. § 1271.150(a); *see* CGTP Rule, 69 Fed. Reg. at 68613-14, 68621; *see generally* 21 C.F.R. Part 1271 Subpart D.[21]

The purpose of the donor screening and testing requirements in subpart C is to prevent a recipient from receiving cells or tissues from a donor who has a communicable disease. *See, e.g.*, Donor Eligibility Proposed Rule, 64 Fed. Reg. at 52,713 (explaining that an important benefit of the rule is protection of the recipient from transmissible diseases). The agency tailored the regulation's donor testing and screening requirements to the degree of risk posed by the product. *Id.* at 52697. Because "autologous use of cells raises lesser communicable-disease concerns than does allogeneic use," Proposed Approach at 13, the regulations do not require manufacturers to determine the eligibility of donors for cells or tissues for autologous use. 21 C.F.R.

[21]Communicable diseases include, but are not limited to, those transmitted by viruses, bacteria, fungi, parasites, and transmissible spongiform encephalopathy agents. 21 C.F.R. § 1271.150(a).

§ 1271.90(a)(1). Instead, FDA requires that cells and tissues be labeled "FOR AUTOLOGOUS USE ONLY" if stored for autologous use. 21 C.F.R. § 1271.90(b)(1). In addition, the regulations provide that if an establishment removes HCT/Ps from an individual and "implants such HCT/Ps into the same individual during the same surgical procedure," then the establishment is not regulated as a drug, biological product, or device under the FDCA and PHSA ***or*** under Part 1271. 21 C.F.R. § 1271.15(b).

In sharp contrast, cells and tissues for autologous use and allogeneic use are equally subject to the communicable disease risk posed by the manufacturing process. The processing of cells and tissues involves multiple steps, including, among others, recovering cells from a donor, transporting the cells in a container to a facility, processing the cells using reagents and equipment, storing cells in freezers and other containers, labeling, and transplanting the cells into the donor. *See* 21 C.F.R. § 1271.3(e) (defining "manufacture"). During all of these steps, regardless of whether the cells or tissues are for autologous or allogeneic use, they are susceptible to, *inter alia*, improper labeling, a mix-up with other cells, contamination, cross-contamination, and accidental exposure to communicable disease agents. *See, e.g.,* 21 C.F.R. § 1271.190(c) (listing the types of concerns the CGTP rules are designed to prevent); 21 C.F.R. § 1271.150(a).[22]

In FDA's judgment, the risks of communicable disease transmission introduced by these manufacturing steps makes regulation of HCT/Ps, including those for autologous use, necessary

[22]Defendants' Counterclaims illustrate that the risk of contamination during manufacturing is not theoretical. They explain that, in the "rare occurrence that microbial contamination has been observed" in their "patient samples," RS LLC discards the cells and follows sterilization protocols. Counterclaims ¶ 7.

to prevent the spread of communicable diseases.[23] Because improperly handled HCT/Ps put recipients (including when the donor and recipient are the same individual), the recipients' family members and close contacts, health care personnel, and other handlers of the HCT/Ps at risk of contracting and transmitting disease, each step involved in the manufacture of the HCT/P "needs to be appropriately controlled." CGTP Rule, 69 Fed. Reg. at 68,613.

Given the broad authority vested in FDA to issue regulations to prevent the transmission of communicable disease and FDA's considered determination that the regulations in 21 C.F.R. Part 1271 are necessary to prevent the transmission of communicable diseases, Defendants' contention that the HCT/P regulatory scheme is *ultra vires* is erroneous and should be dismissed.

Finally, the relief Defendants seek here has no bearing on "FDA's continued efforts to regulate Regenerative's medical practice," *see* Counterclaims ¶ 111, or the government's authority to pursue an enforcement action regarding Defendants' adulteration and misbranding of the cultured cell product. Even if this Court were to conclude that 21 C.F.R. § 1271.3(d)'s

[23] *See, e.g.*, CCTP Final Rule, 69 Fed. Reg. at 68,613 ("Errors in labeling, mixups of testing records, failure to adequately clean work areas, and faulty packaging are examples of improper practices that could produce a product capable of transmitting disease to its recipient."); *id*. ("[I]mproper handling of an HCT/P can lead to bacterial or other pathogenic contamination of the HCT/P, or to cross-contamination between HCT/Ps, which in turn can endanger recipients."); *id*. at 68,630 ("Use of a contaminated or otherwise defective supply or reagent in the manufacture of an HCT/P could lead to such problems as the introduction of a disease agent . . . ."); *see also* Proposed Approach at 12 ("For example, an infected product could cross-contaminate other cellular or tissue-based products stored in the same liquid nitrogen freezer, or could contaminate processing equipment, which, if not properly treated, could contaminate other tissue processed with that equipment. If contaminated tissue is not properly tested or labeled, health care workers as well as patients may be put at risk."); *id.* ("*[F]or both autologous and allogeneic settings*, the use of cellular or tissue-based products that are banked, transported, or processed in facilities with other cellular or tissue-based products increases the risk of transmission of communicable disease . . . ." (emphasis added)).

definition of HCT/P must be limited to allogeneic products because FDA is without authority to regulate autologous products under section 361 of the PHSA, that conclusion would not affect FDA's authority to regulate Defendants' cultured cell product under the FDCA because, as discussed, it is clearly a drug under 21 U.S.C. § 321(g)(1)(B)&(C). *See supra* at 16-17. Instead, such a conclusion would simply eliminate the regulatory pathway for autologous products that (unlike the product at issue here) meet the criteria in 21 C.F.R. § 1271.10(a) to be regulated solely under 21 C.F.R. Part 1271.

CONCLUSION

For all of these reasons, the government respectfully requests that this Court grant this motion and dismiss all of Defendants' Counterclaims with prejudice.

DATED this 7th day of January, 2011.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on the 7th day of January, 2011, the undersigned caused a true and correct copy of the above-entitled Plaintiff's Motion to Dismiss Defendants' Counterclaims, and attached memorandum of points and authorities, to be served via the District Court's Electronic Filing System upon counsel of record for the defendant as follows:

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