

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,)	
403 Summit Boulevard)	
Suit 201)	
Broomfield, Colorado 80021,)	
)	
CHRISTOPHER J. CENTENO, M.D.)	
403 Summit Boulevard)	
Suit 201)	
Broomfield, Colorado 80021,)	
)	
JOHN R. SCHULTZ, M.D.)	
403 Summit Boulevard)	
Suit 201)	
Broomfield, Colorado 80021, and)	
)	
MICHELLE R. CHEEVER,)	
403 Summit Boulevard)	
Suit 201)	
Broomfield, Colorado 80021, and)	
)	
Individuals,)	
)	
Defendants.)	

DEFENDANTS’ ANSWER, AFFIRMATIVE DEFENSES AND COUNTERCLAIMS

COME NOW, the Defendants, REGENERATIVE SCIENCES LLC (“Regenerative”), CHRISTOPHER J. CENTENO, M.D. (“Dr. Centeno”), JOHN R. SCHULTZ, M.D. (“Dr. Schultz”) and MICHELLE R. CHEEVER (“Ms. Cheever”), by and through undersigned counsel, and file their answer, affirmative defenses and counterclaims. In support thereof, Defendants respectfully state as follows:

ANSWER TO THE PLAINTIFF'S COMPLAINT

1. Admit, but deny the ultimate conclusions included in this paragraph.
2. Admit.
3. Admit.
4. Admit the first two sentences of this paragraph. Deny the third sentence.
5. Admit.
6. Admit the first sentence. Deny the second sentence.
7. Admit the first sentence. Admit the second sentence, but deny the second sentence to the extent that it infers that Ms. Cheever is the person most responsible for the day-to-day operations of the Regenerative Sciences Laboratory. Deny the third sentence. Admit the fourth sentences, as Ms. Cheever participated in the drafting of the laboratory procedures, but deny that she drafted the procedures alone, deny that she alone is responsible for the procedures being followed by Regenerative's employees, and affirmatively allege that the laboratory director reports to the medical director. Admit the fifth sentence, and allege that such equity ownership comes by way of stock options granted but not yet exercised.
8. Admit.
9. Deny.
10. Deny the first sentence, as the Defendants do not manufacture a cultured cell product. Admit the second sentences. Deny the third sentence, as the Defendants do not manufacture a cultured cell product.
11. Admit the first five sentences. Admit the sixth sentence, but deny that Regenerative engages in any distribution activities.

12. Admit the first sentence, but deny that the Defendants manufacture a cultured cell product. Admit the language of the regulation included in the second sentence, but deny that Chapter 1271 of Title 21 of the Code of Federal Regulations, or any of its individual regulations, applies to the practice of medicine or was lawfully promulgated.

13. Deny the first sentence, as the Defendants do not manufacture a cultured cell product. Admit the second sentence, but deny that the Defendants manufacture a cultured cell product. Deny the third sentence, as the Defendants do not manufacture or distribute a cultured cell product.

14. Admit the language of the statute, but deny that the statute governs the practice of medicine.

15. Admit the language of the regulation, but deny that the regulation governs the practice of medicine.

16. Deny.

a. Admit the contents of Regenerative promotional material, but deny that this promotional material renders Regenerative a drug manufacturer.

b. Admit the contents of Regenerative promotional material, but deny that this promotional material renders Regenerative a drug manufacturer.

17. Deny the first sentence, as the Defendants do not manufacture a cultured cell product. Deny the second sentence.

18. Deny that there have been no adequate and well-controlled studies performed on Regenerative's medical procedure. Deny that the Defendants manufacture a cultured product. Deny that Defendants' medical procedure is not safe or effective for any orthopedic (or any other) indication.

19. Deny.

20. Admit, but deny that the Defendants manufacture a “cultured cell product,” and deny that an NDA is required for Defendants medical procedure.

21. Admit, but deny that the Defendants manufacture a “cultured cell product,” and deny that an IND is required for Defendants medical procedure.

22. Admit the language of the statute, but deny that the statute governs the practice of medicine.

23. Deny.

24. Admit.

25. Admit, but deny that the Defendants manufacture a “cultured cell product,” and deny that a BLA is required for Defendants medical procedure.

26. Admit the language of the regulations, but deny that the regulations were lawfully adopted or that the regulations govern the practice of medicine.

27. Admit the language of the regulations, but deny that the regulations were lawfully adopted or that the regulations govern the practice of medicine.

28. Admit the language of the regulations in the first two sentences, but deny that the regulations were lawfully adopted or that the regulations govern the practice of medicine. Deny the third sentence as FDA has never “explained” that expansion of cells in culture does not qualify as minimal manipulation.

29. Deny the first sentence. Admit the second sentence, but deny that the Defendants manufacture a product. Deny the third sentence.

30. Admit the language of the statute, but deny that 21 U.S.C. § 351 is applicable to the Defendants’ medical practice.

31. Admit the first sentence. Admit the second sentence, but deny that CGMP is somehow applicable to the Defendants' medical practice. Admit the third sentence. Deny the first clause of the fourth sentence.

a. Admit, but deny that 21 C.F.R. § 211.113 or 21 C.F.R. § 610.12 are applicable to the Defendants' medical practice. Affirmatively allege that the Defendants perform a medical procedure within the bounds of good medical practices as governed by the law of State of Colorado.

b. Admit, but deny that 21 C.F.R. § 211.165(b) is applicable to the Defendants' medical practice. Affirmatively allege that the Defendants perform a medical procedure within the bounds of good medical practices as governed by the law of the State of Colorado.

c. Admit, but deny that 21 C.F.R. § 211.160(b) is applicable to the Defendants' medical practice. Affirmatively allege that the Defendants perform a medical procedure within the bounds of good medical practices as governed by the law of the State of Colorado.

d. Admit, but deny that 21 C.F.R. § 211.165(a) is applicable to the Defendants' medical practice. Affirmatively allege that the Defendants perform a medical procedure within the bounds of good medical practices as governed by the law of the State of Colorado.

e. Admit, but deny that 21 C.F.R. § 211.42(c)(10)(iv) is applicable to the Defendants' medical practice. Affirmatively allege that the Defendants perform a medical procedure within the bounds of good medical practices as governed by the law of the State of Colorado.

32. Admit the first sentence. Admit the second sentence, but deny that CGMP is applicable to the Defendants' medical practice. Admit the third and fourth sentences.

a. Admit, but deny that 21 C.F.R. § 211.160(b) is applicable to the Defendants' medical practice.

b. Admit, but deny that 21 C.F.R. § 211.165(a) is applicable to the Defendants' medical practice.

c. Admit, but deny that 21 C.F.R. § 211.113(b) or 21 C.F.R. § 610.12 is applicable to the Defendants' medical practice.

d. Admit, but deny that 21 C.F.R. § 211.165(b) is applicable to the Defendants' medical practice.

e. Admit, but deny that 21 C.F.R. § 211.42(c)(10)(iv) is applicable to the Defendants' medical practice.

f. Admit, but deny that 21 C.F.R. § 211.113(b) is applicable to the Defendants' medical practice.

g. Admit, but deny that 21 C.F.R. § 211.42(c)(10)(v) is applicable to the Defendants' medical practice.

h. Admit, but deny that 21 C.F.R. § 211.42(c)(10)(iii) is applicable to the Defendants' medical practice.

33. Deny.

34. Deny the first sentence. Deny the second sentence, as the Defendants do not manufacture cultured cell products. Admit the third sentence. Admit the fourth sentence, but deny that Defendants engage in any distribution activities. Affirmatively allege that Regenerative's laboratory provides services exclusively to Regenerative's medical clinic, the

very location where Regenerative's licensed physicians treat their patients using autologous stem cell therapies.

35. Deny.

36. Deny.

37. Deny.

38. Deny.

39. Deny.

40. Admit the first sentence, but deny the existence of a "cultured cell product."

Admit the language of the federal register notice included in the second sentence, but deny that it was lawfully issued.

41. Admit the first sentence, but allege that the Plaintiff itself has explained that the "untitled" letter issued to Regenerative was "tentative" and without "a direct legal effect on Regenerative;" *see* 21 C.F.R. § 10.85(k). Admit the second sentence, but allege that the Plaintiff itself has explained that the issuance of a list of inspectional observations "does not constitute final agency action and has no immediate impact on a party." Admit the third sentence, and affirmatively allege that the Defendants are engaged in the practice of medicine, and that Regenerative responded on numerous occasions to FDA in a good faith attempt to address the issues raised by FDA at the close of the 2009 inspection.

42. Admit the first sentence, but allege that the Plaintiff itself has explained that the issuance of a list of inspectional observations "does not constitute final agency action and has no immediate impact on a party." Admit the second sentence, but allege that the Plaintiff itself has explained that the issuance of a list of inspectional observations "does not constitute final agency action and has no immediate impact on a party." Deny the third sentence. Admit the fourth

sentence, but deny that counsel's statements were made "instead" of Regenerative's commitments to adapt itself consistent with the observations made by FDA at the close of the February/April 2009 inspection. Admit the fifth sentence, and affirmatively allege that Regenerative responded on numerous occasions to FDA in a good faith attempt to address the issues raised by FDA at the close of the 2009 and 2010 inspections.

43. Deny.

44. Deny.

AFFIRMATIVE DEFENSES

I. The Defendants are engaged in the practice of medicine as defined by the law of State of Colorado. The federal government lacks the authority to regulate the practice of medicine in Colorado or any other state, as this authority has been reserved to the States by the Tenth Amendment of the U.S. Constitution. Any FDA regulations which purport to regulate the practice of medicine are *ultra vires* and unconstitutional.

II. The Defendants treat their patients in the ordinary course of their state-regulated medical practice. As such, the Defendants are statutorily exempted from regulation by the Plaintiff.

III. The Defendants are engaged in the practice of medicine as defined by law of the State of Colorado and treat their patients in a one-on-one basis exclusively at Regenerative's medical clinic in Broomfield, Colorado. As such, the Defendants do not affect interstate commerce and the federal government lacks the authority to regulate the Defendants' medical practice.

IV. The Defendants are engaged in the practice of medicine as defined by the law of the State of Colorado. The Defendants' treatment of their patients using autologous stem cell therapies does not constitute the distribution of a product.

V. The Defendants are engaged in the practice of medicine as defined by the law of the State of Colorado. The Defendants' manipulation of their patients' bodies does not constitute the manufacturing of a product.

VI. FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, is *ultra vires* as it purports to grant jurisdiction to the Plaintiff – i.e. to regulate the practice of medicine – which was never authorized by Congress.

VII. FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, is *ultra vires* as it purports to grant jurisdiction to the Plaintiff – i.e. to regulate stem cells used for an autologous purpose in a medical procedure – which was never authorized by Congress.

VIII. FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, is arbitrary and capricious as it was enacted without giving due consideration to the science relevant to HCT/Ps.

IX. FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, is arbitrary and capricious as it was enacted without explaining to the interested public the science relied upon by the agency in promulgating the regulations.

X. The FDA's definition of "minimal manipulation" is a legislative rule not issued through notice and comment rulemaking procedures and is therefore invalid.

COUNTERCLAIMS

Defendants/Counterclaimants REGENERATIVE SCIENCES LLC (“Regenerative”), CHRISTOPHER J. CENTENO, M.D. (“Dr. Centeno”), JOHN R. SCHULTZ, M.D. (“Dr. Schultz”) and MICHELLE R. CHEEVER (“Ms. Cheever”), by and through undersigned counsel, respectfully represent as follows:

Jurisdictional Allegations

1. This Court has subject matter jurisdiction over these counterclaims pursuant to:
 - a. 5 U.S.C. §§ 704 and 706(2)(C) of the Administrative Procedures Act (“APA”) because the FDA exceeded its statutory authority by enacting a regulation (21 CFR § 1271.3(d)) designed to do regulate more than that authorized by Congress in the Public Health Service Act (42 USC § 201, *et seq.*), and using that *ultra vires* regulation for purposes of regulating the Plaintiff’s medical practice;
 - b. 5 U.S.C. § 553 *et seq.* and § 706(2)(D) because the FDA enacted and is enforcing regulations without following the notice and rule making procedures mandated by the APA;
 - c. 28 U.S.C. § 2201 as Plaintiff seeks declaratory judgments finding that the Regenexx procedure constitutes the practice of medicine and is beyond the scope of FDA’s regulatory authority; that FDA lacks the statutory authority to regulate the practice of medicine; that FDA’s enforcement activities to date have been arbitrary and capricious; and that 21 CFR § 1271.3(d) is *ultra vires*;
 - d. 28 U.S.C. § 1331 as this matter arises under the Constitution and laws of the United States.
2. Venue is proper in this District pursuant to 28 U.S.C. § 1391(e).

STATEMENT OF FACTS

Introduction

3. Regenerative, by and through physicians licensed to practice medicine in the State of Colorado, performs a non-surgical procedure for patients suffering from moderate to severe joint, muscle, tendon or bone pain due to injury or other conditions. This procedure is known as the “Regenexx[®] Procedure” and is performed in the CentenoSchultz Clinic, located in Broomfield, Colorado.

4. Drs. Centeno and Schultz are the majority shareholders of Regenerative; Regenerative owns the Regenexx Procedure, and licenses it to the clinic for the exclusive use of Regenerative.

5. The Regenexx[®] Procedure begins with a licensed physician taking a small bone marrow sample from the back of a patient’s hip through a needle. Blood samples are also taken from a vein in the patient’s arm. These samples are then sent to the Regenerative laboratory which is also in Broomfield, Colorado, just a few miles from the Clinic where the mesenchymal stem cells (MSCs) are isolated from the bone marrow and then grown to greater numbers. This process uses the natural growth factors found in the patient’s blood to grow the MSCs.

6. After approximately 2 weeks, the expanded stem cells are sent to the University of Colorado affiliated Colorado Genetics Laboratory for testing. This is performed with every patient and is to ensure that the cells have not lost or gained abnormal genetic material which would render them unusable as part of good medical practices. If the cells do not pass this quality test, the attending physician is notified and the cells are not used in patients.

7. Additionally, multiple quality tests are performed on every patient sample at Regenerative’s laboratory including cell grading and surveillance of microbial contamination. If

cells are observed that do not pass these quality criteria, they are discarded rather than used in patients. Also, on the rare occurrence that microbial contamination has been observed, the cells are discarded and the lab is instructed by the medical director to follow sterilization protocols appropriate for good medical practices.

8. Furthermore, random cell surface testing using flow cytometry and random outside bacterial and pathogen testing is performed to ensure that the patient cells meet the accepted medical standards as "mesenchymal stem cells" and to ensure that the laboratory is following good medical practices. For example, no outside patient sample sent for routine, random quality checks has ever shown evidence of unknown or undetected pathogen contamination.

9. In addition to these routine safety procedures, Regenerative has on multiple occasions retained independent third party auditors to inspect its lab facilities and hold it to reasonable guidelines for a medical practice processing autologous tissues. As part of this continuous quality improvement program, Regenerative has frequently made improvements to its facilities to promote patient safety as part of its medical practice.

10. Once the cells pass quality assurance testing, they are placed back into the patient's injured area (i.e. knee, hip, rotator cuff), typically 4-6 weeks after they were removed. The stem cells then begin to repair the patient's degenerated or injured area. The repair process usually takes between 3-6 months but many patients demonstrate marked improvement within 1-3 months.

11. The Regenexx® Procedure and the activities of the Clinic constitute the practice of medicine, which is outside the FDA's regulatory authority, and solely regulated by the several states.

12. The “practice of medicine” is defined by the laws of the State of Colorado, in pertinent part, as follows:

(1) For the purpose of this article, "practice of medicine" means:

(a) Holding out one's self to the public within this state as being able to diagnose, treat, prescribe for, palliate, or prevent any human disease, ailment, pain, injury, deformity, or physical or mental condition, whether by the use of drugs, surgery, manipulation, electricity, telemedicine, the interpretation of tests, including primary diagnosis of pathology specimens, images, or photographs, or any physical, mechanical, or other means whatsoever;

(b) Suggesting, recommending, prescribing, or administering any form of treatment, operation, or healing for the intended palliation, relief, or cure of any physical or mental disease, ailment, injury, condition, or defect of any person with the intention of receiving therefor, either directly or indirectly, any fee, gift, or compensation whatsoever;

...

(e) Performing any kind of surgical operation upon a human being;

C.R.S. § 12-36-106.

13. The Regenxx[®] Procedure is performed only by physicians lawfully licensed to practice medicine in the State of Colorado.

14. The Procedure is exclusively for the treatment of orthopedic injuries and arthritis.

15. The Procedure requires the removal of stem cells and other tissue from a patient, the growth of the stem cells to greater numbers outside of the patient’s body, and the placement of the stem cells back into in the patient for the treatment of the patient’s degenerated or injured area of the body. Regenerative operates the facilities that performs these functions and does so exclusively for the Centeno Schultz Clinic for the Regenxx procedure.

16. Once implanted back into the patient, the stem cells used in the Regenexx[®] Procedure perform the same basic function or functions that they performed before being removed.

17. Regenerative is not engaged in the manufacturing of drugs or biological products. The stem cells used in the Regenexx[®] Procedure are not drugs, but human tissue, no different than any other body part, and used exclusively for the patients from whom they were withdrawn.

18. Rather than being a drug manufacturer, Regenerative is engaged in the practice of medicine as defined by the laws of the State of Colorado, and the Regenexx[®] Procedure involves merely the *in vivo* use of a patient's own stem cells for the treatment of an injury.

19. Regenerative does not sell or distribute any product or stem cells in interstate commerce.

Procedural Posture

20. On or about August 5, 2008, Regenerative received a letter dated July 25, 2008 from FDA's Office of Compliance and Biologics Quality concerning Regenerative's Regenexx[®] Procedure. In that letter, the FDA alleged that Regenerative was promoting the use of stem cells under conditions that caused the cells to be drugs under section 201(g) of the Federal Food, Drug and Cosmetic Act (FDCA) and biological products as defined in section 351(i) of the Public Health Service Act (PHSA).

21. In that same letter, the FDA further alleged that the stem cells utilized in the Regenexx[®] Procedure were drugs which were not the subject of an approved biologics license application ("BLA") or investigational new drug application ("IND") and may therefore have been unlawful. Further, on July 25, 2008, the very date on which the FDA purportedly sent its letter to Regenerative, but eleven days before Regenerative actually received it, the FDA posted

its letter on its website (www.fda.gov) and thereby made the letter available to the public. Regenerative was given no opportunity to respond to the FDA's letter prior to the letter being published by the FDA on the World Wide Web.

22. On August 12, 2008, counsel for Regenerative sent the FDA a Petition for Stay of Action pursuant to 21 C.F.R. §10.35 requesting that all information in the petition for stay of action be withheld from public disclosure. On August 19, 2008, the FDA responded to counsel stating that FDA was in receipt of the petition for stay of action filed on behalf of Regenerative. FDA assigned the petition a docket number and accepted the petition for filing but did not indicate whether it would agree to the action requested.

23. On August 25, 2008, counsel for Regenerative sent FDA a separate legal opinion, citing cases, statutes, regulations and FDA policy which demonstrated that the agency's allegations in its July 25, 2008 letter were both legally and factually flawed. On October 3, 2008, the FDA formally denied Regenerative's Petition for Stay of Action, refused to remove the July 25, 2008 letter from the FDA's public website, and denied Regenerative's request that the Petition for Stay of Action be withheld from public disclosure.

24. Almost seven months later, on February 23, 2009, the FDA initiated an inspection of Regenerative's medical facilities. That inspection lasted approximately seven weeks, and concluded on April 15, 2009, when the FDA issued a Form 483 to Regenerative indicating that, according to the FDA, Regenerative was manufacturing biological drugs in a facility that did not meet the standards of federally regulated biological drug manufacturers. Also on April 15, 2009, the FDA warned Regenerative that its (Regenerative's) failure to comply with the terms of the Form 483 could lead to the issuance of a warning letter, seizure, injunction, criminal prosecution, and the disqualification of Regenerative's licensed physicians as clinical investigators.

25. While the inspection was ongoing, Regenerative sued the FDA in the United States District Court for the District of Colorado. Regenerative's suit alleged, *inter alia*, that FDA's regulatory scheme defining and regulating the autologous use of stem cells was *ultra vires*. On April 29, 2009, the FDA filed its motion to dismiss, and the District Court entered its order dismissing Regenerative's lawsuit on ripeness grounds on March 26, 2010.

26. The FDA's efforts to regulate Regenerative's medical practice continued shortly after the District Court dismissed Regenerative's lawsuit. On June 2, 2010, the FDA visited the Plaintiff for purposes of conducting an exhaustive inspection of the Plaintiff's medical clinic. FDA's inspection of Regenerative's medical clinic lasted for roughly two weeks and cost Regenerative nearly \$20,000 in personnel time.

27. The 2010 inspection concluded with an exit interview between FDA and Regenerative on or about June 16, 2010. During the exit interview, FDA issued a Form 483 to Regenerative which, like the April 15, 2009 Form 483 and June 2, 2010 Notice of Inspection, identified Regenerative as a drug manufacturer. This Form 483 also listed a number of alleged compliance deficiencies at Regenerative's medical facilities only applicable to large-scale drug manufacturers.

28. Likewise, during the June 16, 2010 exit interview, FDA advised Regenerative that the decision was made by FDA *before the inspection even began* that Regenerative was a drug manufacturer and that that decision could not be challenged. Moreover, FDA advised Regenerative that the failure to remedy the observations contained in the Form 483 could lead to the issuance of a warning letter, Cease and Desist Letter, civil penalties, and/or a judicial injunction to compel compliance under threat of closure and criminal prosecution.

29. On June 22, 2010, Regenerative challenged in this Court, in Case No. 10-cv-01055, FDA's finding that Regenerative was a drug manufacturer in Case No. 10-cv-01055. That case, however, was stayed by the Court upon the agreement of the parties that all of the issues raised therein, as well as all of the issues raised in the District of Colorado, would be litigated in this case.

The Regulatory Scheme at Issue in this Case

30. The FDA alleges that the stem cells used in Regenerative's autologous stem cell therapy are drugs and biological products.

A. Biological Products

31. The FDA regulates biological products generally, and HCT/Ps specifically, pursuant to authority vested in the FDA by Congress at 42 U.S.C. § 264(a). That statute provides in pertinent part as follows:

The Surgeon General, with the approval of the Administrator [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.

32. The Regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations, which purport to regulate HCT/Ps, were promulgated by FDA pursuant to 42 U.S.C. § 264(a).

33. In order to assert that the stem cells used in Regenerative's autologous stem cell therapy are biological products, FDA alleges that the stem cells are HCT/Ps as defined by 21 C.F.R. § 1271.3(d), and that such stem cells are "more than minimally manipulated" as defined by 21 C.F.R. § 1271.10.

34. FDA defines HCTPs, in pertinent part, as follows: “articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.” 21 CFR § 1271.3(d).

35. This definition does not distinguish between whether the “human recipient” is receiving the HCTP from another person (i.e. a “donor”) or whether the “human recipient” is receiving the HCTP from himself.

36. As such, this definition, which is included among a chapter of regulations (21 CFR § 1271.1, *et seq.*) governing how, why, and to what extent the FDA regulates HCTPs, allows the FDA to regulate even those human cell-based and tissue-based articles which are removed from a patient and then replaced back into the same person.

37. Consequently, 21 CFR § 1271.3(d) grants authority to the FDA – i.e. to regulate the practice of medicine – which was never authorized by Congress. 21 CFR § 1271.3(d) is consequently *ultra vires*.

38. FDA purports to regulate all HCT/Ps, regardless of how they are to be used. Thus, to the extent that this regulatory scheme purports to grant FDA the authority to regulate the practice of medicine, this entire regulatory scheme is *ultra vires*.

39. FDA purports to regulate all HCT/Ps, regardless of how they are to be used. Thus, to the extent that this regulatory scheme purports to grant FDA the authority to regulate stem cells which carry no risk of spreading communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession, this entire regulatory scheme is *ultra vires*.

40. FDA regulates certain HCT/Ps under sections 351 and 361 of the PHS Act and other HCT/Ps solely under section 361 of the PHS Act. In order to be regulated solely under section 361 of the PHS Act, the conditions outlined in 21 C.F.R. § 1271.10(a) must be met.

41. In this case, FDA alleges that Regenerative's medical practice is regulated under sections 351 and 361 of the PHS Act because the stem cells used in the procedure are more than minimally manipulated. As it relates to stem cells, "minimal manipulation" is defined as "processing that does not alter the relevant biological characteristics of cells..." 21 C.F.R. § 1271.3(e)(2).

42. FDA has never explained how or why expansion alters the relevant biological characteristics of cells or otherwise constitutes "more than minimal manipulation."

43. In 1998, FDA stated that it "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." However, as it relates to the expansion of stem cells, the FDA has not done so.

44. Despite questions from the public on the issue, FDA has never explained how a physician's expansion of autologous stem cells constitutes the manufacturing of a biological product as opposed to the practice of medicine.

B. Drugs

45. In order to assert that the stem cells used in Regenerative's autologous stem cell therapy are drugs, FDA alleges that they are intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease or intended to affect the structure or any function of the body.

46. However, despite questions from the public on the issue, FDA has never explained how a physician's expansion of autologous stem cells constitutes the manufacturing of a drug as opposed to the practice of medicine.

CLAIMS FOR RELIEF

I. The Regenxx™ Medical Procedure Constitutes the Practice of Medicine and is Beyond the Scope of the FDA's Regulatory Authority and Jurisdiction.

47. Defendants/Counterclaimants repeat and reallege the foregoing as though fully alleged herein.

48. The Regenxx™ medical Procedure is performed by physicians lawfully licensed to practice medicine in the State of Colorado.

49. The Regenxx™ medical Procedure is performed only in the State of Colorado.

50. The "practice of medicine" is defined by the law of the State of Colorado, in pertinent part, as follows:

(1) For the purpose of this article, "practice of medicine" means:

(a) Holding out one's self to the public within this state as being able to diagnose, treat, prescribe for, palliate, or prevent any human disease, ailment, pain, injury, deformity, or physical or mental condition, whether by the use of drugs, surgery, manipulation, electricity, telemedicine, the interpretation of tests, including primary diagnosis of pathology specimens, images, or photographs, or any physical, mechanical, or other means whatsoever;

(b) Suggesting, recommending, prescribing, or administering any form of treatment, operation, or healing for the intended palliation, relief, or cure of any physical or mental disease, ailment, injury, condition, or defect of any person with the intention of receiving therefor, either directly or indirectly, any fee, gift, or compensation whatsoever;

...

(e) Performing any kind of surgical operation upon a human being;

C.R.S. § 12-36-106.

51. A licensed physician's use of HCT/Ps for an autologous purpose, in the normal course of the physician's medical practice as recognized by the State in which the physician is licensed to practice, constitutes the Practice of Medicine and is not regulated by FDA under the authority of the PHSA or the FDCA.

52. A licensed physician's expansion of stem cells for an autologous purpose, in the normal course of the physician's medical practice as defined by the laws of the state in which the physician is licensed to practice, constitutes the Practice of Medicine and is not regulated by FDA under the authority of the PHSA or the FDCA.

53. Congress has clearly precluded the FDA from asserting jurisdiction to regulate the practice of medicine. In light of Congress's intent, the FDA's assertion of jurisdiction over the practice of medicine is precluded.

54. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Defendants/Counterclaimants respectfully request that this Honorable Court **a)** enter a judicial decision pursuant to 28 U.S.C. § 2201 *et.seq.* declaring that the RegenexxTM medical Procedure constitutes the Practice of Medicine which is beyond the jurisdiction of the FDA; **b)** enjoin the FDA from regulating the RegenexxTM medical Procedure; **c)** assess costs and attorneys' fees; and **d)** grant such other relief that the Court may deem just and proper.

II. FDA's decision that the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations do not infringe upon the practice of medicine was arbitrary and capricious.

55. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

56. The FDA has on one occasion publicly addressed the question of whether the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations infringe on the practice of medicine; *see* 66 Fed.Reg. 5452 (Jan. 19, 2001).

57. At that time, the FDA stated that its regulations do not infringe upon the practice of medicine.

58. The FDA lacks the authority to regulate the practice of medicine.

59. The FDA did not consider any factors relevant to the practice of medicine in making its determination.

60. The FDA did not explain what data relevant to the practice of medicine it relied upon in making its determination.

61. The FDA's determination that the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations do not infringe upon the practice of medicine was arbitrary and capricious.

62. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Defendants/Counterclaimants, respectfully requests that this Honorable Court a) enter a judicial decision pursuant to 28 U.S.C. § 2201 *et.seq.* declaring that the FDA

promulgated the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations in a manner that was arbitrary and capricious and that the regulations therefore are invalid; **b)** grant the Defendants/Counterclaimants injunctive relief, enjoining implementation of the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations pending compliance with the notice and comment provisions of the Administrative Procedure Act; **c)** vacate the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations and mandate that the FDA reissue the regulations under a notice of proposed rulemaking followed by a full 60 day notice and comment period; **d)** award the Defendants/Counterclaimants attorneys' fees and costs in accordance with law; and **e)** grant such other and further relief as the Court deems necessary or appropriate.

III. 21 C.F.R. § 1271.3(d) is *ultra vires*.

63. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

64. FDA defines HCTPs, in pertinent part, as follows: “articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.” 21 CFR § 1271.3(d).

65. This definition does not distinguish between whether the “human recipient” is receiving the HCTP from another person (i.e. a “donor”) or whether the “human recipient” is receiving the HCTP from himself.

66. As such, this definition, which is included among a chapter of regulations (21 CFR § 1271.1, *et seq.*) governing how, why, and to what extent the FDA regulates HCTPs, allows the FDA to regulate even those human cell-based and tissue-based articles which are removed from a patient and then replaced back into the same patient.

67. Consequently, 21 CFR § 1271.3(d) grants authority to the FDA – i.e. to regulate the practice of medicine – which was never authorized by Congress.

68. 21 CFR § 1271.3(d) is *ultra vires*.

69. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Regenerative respectfully requests that this Honorable Court a) enter a judicial decision, pursuant to 28 U.S.C. § 2201 *et seq.*, declaring 21 CFR § 1271.3(d) to be *ultra vires*; b) enjoin the FDA from regulating the RegenexxTM medical Procedure; c) assess costs and attorneys' fees; and d) grant such other relief that the Court may deem just and proper.

IV. The FDA's definition of "minimal manipulation" is arbitrary and capricious because the science upon which it was based has never been shared with the interested public.

70. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

71. 21 C.F.R. § 1271.10 provides that stem cells which are more than "minimally manipulated" will be regulated under Sections 351 and 361 of the FDCA.

72. 21 C.F.R. § 1271.3(f) defines the minimal manipulation of cells as "processing that does not alter the relevant biological characteristics of cells..."

73. The FDA has stated that expansion of stem cells in culture does not constitute minimal manipulation; *see* 66 Fed.Reg. 5457 (Jan. 19, 2001); *see also* 63 Fed.Reg. 26744 (May 14, 1998).

74. The FDA has never imposed an expansion threshold. Instead, the FDA has imposed a per se rule which provides that any expansion of stem cells constitutes more than minimal manipulation of the cells.

75. The FDA has never explained why any expansion of stem cells in culture does not constitute minimal manipulation.

76. The FDA has never explained how or why any expansion of stem cells in culture alters the relevant biological characteristics of the stem cells.

77. The 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.

78. The FDA's definition of "minimal manipulation" is arbitrary and capricious.

79. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Defendants/Counterclaimants, respectfully requests that this Honorable Court **a)** enter a judicial decision pursuant to 28 U.S.C. § 2201 *et.seq.* declaring that the FDA promulgated the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations in a manner that was arbitrary and capricious and that the regulations therefore are invalid; **b)** grant the Defendants/Counterclaimants injunctive relief, enjoining implementation of the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations pending compliance with the notice and comment provisions of the Administrative Procedure Act; **c)** vacate the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations and

mandate that the FDA reissue the regulations under a notice of proposed rulemaking followed by a full 60 day notice and comment period; **d)** award the Defendants/Counterclaimants attorneys' fees and costs in accordance with law; and **e)** grant such other and further relief as the Court deems necessary or appropriate.

V. The FDA's definition of "minimal manipulation" is arbitrary and capricious because it was issued without consideration of all relevant factors.

80. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

81. 21 C.F.R. § 1271.10 provides that stem cells which are more than "minimally manipulated" will be regulated under Sections 351 and 361 of the FDCA.

82. 21 C.F.R. § 1271.3(f) defines the minimal manipulation of cells as "processing that does not alter the relevant biological characteristics of cells..."

83. The FDA has stated that expansion of stem cells in culture does not constitute minimal manipulation; *see* 66 Fed.Reg. 5457 (Jan. 19, 2001); *see also* 63 Fed.Reg. 26744 (May 14, 1998).

84. The FDA has never imposed an expansion threshold. Instead, the FDA has imposed a per se rule which provides that any expansion of stem cells constitutes more than minimal manipulation of the cells.

85. However, even prior to the time that FDA originally promulgated its definition of "minimal manipulation," ample science existed proving that the expansion of stem cells in culture did not alter the relevant biological characteristics of the cells.

86. Such science was made available to FDA both prior and subsequent to FDA's promulgation of the definition of "minimal manipulation."

87. In promulgating the definition of “minimal manipulation,” FDA never considered the available science relevant to the issue of “minimal manipulation.”

88. The FDA’s definition of “minimal manipulation” is arbitrary and capricious.

89. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA’s continued efforts to regulate Regenerative’s medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Defendants/Counterclaimants, respectfully requests that this Honorable Court **a)** enter a judicial decision pursuant to 28 U.S.C. § 2201 *et.seq.* declaring that the FDA promulgated the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations in a manner that was arbitrary and capricious and that the regulations therefore are invalid; **b)** grant the Defendants/Counterclaimants injunctive relief, enjoining implementation of the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations pending compliance with the notice and comment provisions of the Administrative Procedure Act; **c)** vacate the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations and mandate that the FDA reissue the regulations under a notice of proposed rulemaking followed by a full 60 day notice and comment period; **d)** award the Defendants/Counterclaimants attorneys’ fees and costs in accordance with law; and **e)** grant such other and further relief as the Court deems necessary or appropriate.

VI. The FDA’s definition of “minimal manipulation” is a legislative rule not issued through notice and comment rulemaking procedures and is therefore invalid.

90. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

91. 21 C.F.R. § 1271.10 provides that stem cells which are more than “minimally manipulated” will be regulated under Sections 351 and 361 of the FDCA.

92. 21 C.F.R. § 1271.3(f) defines the minimal manipulation of cells as “processing that does not alter the relevant biological characteristics of cells...”

93. The FDA has stated that the expansion of stem cells in culture does not constitute minimal manipulation; *see* 66 Fed.Reg. 5457 (Jan. 19, 2001); *see also* 63 Fed.Reg. 26744 (May 14, 1998).

94. The FDA’s statement that expansion of stem cells in culture does not constitute minimal manipulation was a legislative rule.

95. The FDA’s statement that expansion of stem cells in culture does not constitute minimal manipulation was issued without the use of legislative rulemaking procedures.

96. The FDA’s ruling that the expansion of stem cells in culture does not constitute minimal manipulation was promulgated in violation of the APA.

97. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA’s continued efforts to regulate Regenerative’s medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Defendants/Counterclaimants, respectfully requests that this Honorable Court **a)** enter a judicial decision pursuant to 28 U.S.C. § 2201 *et.seq.* declaring that the FDA promulgated the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations in a manner that was violative of the APA and that the regulations therefore are invalid; **b)** grant the Defendants/Counterclaimants injunctive relief, enjoining implementation of the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations pending

compliance with the notice and comment provisions of the Administrative Procedure Act; **c)** vacate the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations and mandate that the FDA reissue the regulations under a notice of proposed rulemaking followed by a full 60 day notice and comment period; **d)** award the Defendants/Counterclaimants attorneys' fees and costs in accordance with law; and **e)** grant such other and further relief as the Court deems necessary or appropriate.

VII. The FDA's entire regulatory scheme governing stem cells is *ultra vires* as it purports to give the FDA the authority to regulate the practice of medicine.

98. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

99. FDA defines HCTPs, in pertinent part, as follows: "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." 21 CFR § 1271.3(d).

100. FDA purports to regulate all HCT/Ps, regardless of how the cells are used, and regardless of whether the cells are used by a licensed physician in the ordinary course of the physician's treatment of a patient; *see* 21 C.F.R. § 1271.10.

101. As such, FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, purports to grant authority to the FDA – i.e. to regulate the practice of medicine – which was never authorized by Congress.

102. Chapter 1271 of Title 21 of the Code of Federal Regulations is *ultra vires*.

103. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As

examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Regenerative respectfully requests that this Honorable Court a) enter a judicial decision, pursuant to 28 U.S.C. § 2201 *et seq.*, declaring 21 CFR § 1271.3(d) to be *ultra vires*; b) enjoin the FDA from regulating the RegenexxTM medical Procedure via; c) assess costs and attorneys' fees; and d) grant such other relief that the Court may deem just and proper.

VIII. The 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.

104. Defendants/Counterclaimants repeat and reallege the foregoing as if fully alleged herein.

105. FDA drafted the regulations found at Chapter 1271 of Title 21 of the Code of Federal Regulations pursuant to authority provided by Congress to FDA at 42 U.S.C. § 264(a).

That statute provides as follows:

The Surgeon General, with the approval of the Administrator [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.

106. FDA defines HCTPs, in pertinent part, as follows: "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." 21 CFR § 1271.3(d).

107. FDA purports to regulate all HCT/Ps regardless of whether the cells are withdrawn from a patient by a licensed physician and then administered back into that same patient; *see* 21 C.F.R. § 1271.10.

108. As such, FDA's regulatory scheme, which is found at Chapter 1271 of Title 21 of the Code of Federal Regulations, purports to grant authority to the FDA to regulate the use of stem cells which carry no risk of spreading communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession.

109. To the extent that Chapter 1271 of Title 21 of the Code of Federal Regulations purports to regulate stem cells which carry absolutely no risk of spreading communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession, Chapter 1271 of Title 21 of the Code of Federal Regulations exceeds the authority granted to the FDA by Congress at 42 C.F.R. § 264(a).

110. Chapter 1271 of Title 21 of the Code of Federal Regulations is *ultra vires*.

111. Regenerative has suffered and continues to suffer irreparable harm as a result of the FDA's continued efforts to regulate Regenerative's medical practice in this way. As examples, Regenerative has suffered significant financial loss, severe reputational damage through multiple FDA public statements, and loss of key employees and business relationships.

WHEREFORE, Regenerative respectfully requests that this Honorable Court a) enter a judicial decision, pursuant to 28 U.S.C. § 2201 *et seq.*, declaring 21 CFR § 1271.3(d) to be *ultra vires*; b) enjoin the FDA from regulating the RegenexxTM medical Procedure; c) assess costs and attorneys' fees; and d) grant such other relief that the Court may deem just and proper.

Dated this 27th Day of August, 2010.

CERTIFICATE OF SERVICE

I certify that I will electronically file the foregoing with the Clerk of the Court using the CM/ECF system on this 27th day of August, 2010, thereby causing it to be served upon all counsel of record.

/s/

William Coffield, Esq.

Bar No.: 431126

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