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Cultured Stem Cells—Court Rules on the Regenexx Case

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As discussed in our prior K&L Gates Alert, "Cultured Stem Cells for Autologous[1] Use: Practice of Medicine or FDA Regulated Drug and Biological Product?", in 2010 the Food and Drug Administration ("FDA") brought an action against Regenerative Sciences, LLC ("Regenerative") to permanently enjoin the company from using the Regenexx™ procedure to process mesenchymal stem cells ("MSC") for the treatment of various orthopedic conditions. On July 23, 2012, the United States District Court for the District of Columbia ruled in favor of FDA and granted its motion for summary judgment and permanent injunction against the use of the Regenexx procedure. This case has been closely watched by those involved in stem cell research and commercialization because of the many legal and practical questions it raises as to the regulation of human cells, tissues, and cellular and tissue-based products ("HCT/Ps") in humans. We provide a brief summary below.

Regulatory Background

Human stem cell treatments and associated products are regulated by the FDA under the authority of the Federal Food, Drug, and Cosmetic Act ("FDCA") and the Public Health Services Act ("PHSA"). As discussed in greater detail in our previous Alert on cultured stem cells, a stem cell-based product can be regulated as a drug and/or a biological product. Under the PHSA, a "biological product" is defined as 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 humans.[2]

Unlike other drug products, biologics are subject to regulation by FDA under both the PHSA, an act that is predicated on the commerce clause of the U.S. Constitution, and the FDCA. Biologics are therefore subject to the FDCA's investigational new drug ("IND") and current good manufacturing practices ("cGMP") requirements and cannot be lawfully marketed in interstate commerce without an approved Biological License Application ("BLA") under the PHSA. Because a "biologic" is also a "drug" under the FDCA, a biologic product that fails to conform to the FDCA's applicable standards can be subject to regulatory action as a "misbranded" and/or "adulterated" drug product.

The Regenexx Case and the Court's Decision

As noted in our prior Alert on cultured stem cells, the fundamental question raised by the Regenexx case is whether a procedure that involves the non-surgical harvesting of a patient's MSC from his/her own bone marrow for reinjection into the patient for the treatment of moderate to severe joint, muscle,

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

[2] 42 U.S.C. § 262(i).

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and bone pain constitutes the practice of medicine or the manufacturing of a drug or biological product.[3]

Regenerative has consistently taken the position that the Regenexx procedure is the practice of medicine and thereby outside FDA's jurisdiction. It also takes the position that the manipulation of the stem cells occurs in the normal course of medical practice, which is regulated by Colorado, the state where the company is located. Since Regenerative contends the Regenexx procedure takes place completely within Colorado, the company takes the position that there is no interstate commerce and, therefore, the procedure is not subject to FDA's authority.

In contrast, FDA has argued that the Regenexx procedure involves growth factors, reagents and drug products that cross state lines, thereby placing the product in interstate commerce. The FDA has also taken the position that the product is more than "minimally manipulated" and, consequently, does not meet the conditions listed in 21 C.F.R. Part 1271 that exempts HCT/Ps from being regulated as drugs, devices, and/or biological products. As a result, FDA contends that Regenerative is shipping a non-licensed (unapproved) new drug or biologic product in interstate commerce in violation of the FDCA and PHSA.

In *United States v. Regenerative Sciences, LLC* (Civil Action No. 10-1327 (RMC) (U.S.D.C. July 23, 2012)), U.S. District Judge Rosemary M. Collyer found that the Regenexx procedure constituted the production of both a drug and a biologic under the relevant federal statutes. In considering whether the MSC were only "minimally manipulated" such that they should only be regulated under FDA regulations for HCT/Ps, which would not require FDA approval, the court found that the procedure exceeds mere "processing" of cells in that the procedure changed their relevant biological and physiological characteristics.

While the court recognized that the assessment of whether the MSC underwent more than minimal manipulation is a fact-specific finding, the court found that FDA is entitled to broad deference in its determination that the Regenexx procedure exceeded permissible regulatory limits on use of human tissues in medical procedures. The court also rejected Regenexx's argument that the procedure constituted the practice of medicine because the procedure involved the addition of an antibiotic, doxycycline, into the isolated MSC. Because the antibiotic had been shipped in interstate commerce before being reinjected into the patient, the court found the entire product was sufficiently linked to interstate commerce to be subject to regulation by FDA under the FDCA and the PHSA.

Based on these findings, the court ruled that the Regenexx procedure is an adulterated and misbranded drug and granted FDA's motion for summary judgment and a permanent injunction. The court found the Regenexx procedure to be "adulterated" because it was not manufactured in conformance with cGMP requirements and "misbranded" because the information on the syringe label that contained the processed stem cells did not include the required statutory or regulatory language. Finally, the court ruled that FDA is not interfering with the practice of medicine since the agency is not preventing doctors from using their medical judgment as to the treatment of a patient, but is exerting its jurisdiction to prevent the interstate distribution of a misbranded and adulterated drug product.

[3] For more background on the case, see *United States v. Regenerative Sciences, Inc*. briefing documents; FDA "Untitled Letter" to Regenerative (July 25, 2008); FDA News Release, "FDA Seeks Injunction Against Colorado Manufacturer of Cultured Cell Product," dated August 6, 2010; and prior case history, *Regenerative Sciences, Inc. v. United States Food and Drug Administration*, Civil Action No. 1:10-cv-01055-RMC (D.C. Dist. 2010).

Conclusion

As it currently stands, the opinion in the case reaffirms traditional deference to FDA's assertion of jurisdiction over biological products and indicates an unwillingness to permit local production and processing of biological products without a BLA. While a single district court case does not represent mandatory precedent for federal courts, the *Regenexx* decision may be a bellwether for future opinions that seek to define the contours of federal regulatory jurisdiction over stem cell procedures and commercialization. To date, Regenerative has not filed an appeal; however, we believe an appeal to be likely.

We would be pleased to provide additional details on this case and its potential implications upon request.

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