

IN THE SPOTLIGHT



Our Patient's Autologous Stem Cells are Drugs: The FDA Moving Down a Dangerous Slippery Slope

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Adult autologous stem cells (A-ASC's) show great promise in research and early pre-clinical/clinical use. These cells have the potential to revolutionize medicine by repairing tissues directly or assisting in tissue healing.¹ What you may not realize is that a herculean power struggle going on behind the scenes where the Food and Drug Administration (FDA) is now claiming, through the "canary in the coal mine" of the new field of cell therapy, to have authority over the stem cells in your body. If left unchecked, the next logical step in this regulatory pathway appears to be dividing certain common medical procedures into those that require federal regulation and those that do not.

Cellular therapy is the next logical step in regenerative medicine. The world's first regenerative medicine procedure in widespread use was Prolotherapy. This procedure simply spurred the body to repair itself through creating small injuries in need of healing. The next step beyond Prolotherapy is using the patient's own cells to act as stimulants for healing or the building blocks for new tissue. Platelet rich plasma (PRP) is a new technique that uses blood platelets (which contain healing growth factors) to help heal tissue. The next logical step in regenerative medicine beyond PRP is stem cell therapy. This procedure uses the patient's own stem cells to act as building blocks for new tissue. However, the FDA's new regulatory posture would seem to place both PRP and stem cell therapy at risk of being regulated into oblivion.

The problem began in 2005, when the FDA dramatically, and quietly, changed its regulatory approach with potential to upset the "great wall" between medical practice and mass drug production. Historically, the FDA has never had the power to control any aspect of the relationship between a doctor and a patient. In 2005, the agency made changes to the 361 Public Health Service (PHS) act to classify certain A-ASC's as biologic

drugs requiring pre-market, federal approval before sale in interstate commerce.² Before 2005, the FDA only had authority over tissue transplants, for example, where one patient's organ was transplanted to another person. This made sense, as nobody wants to get a diseased organ from someone else. Prior to 2005, the agency also had the power to declare certain transplanted cells as drugs, for example someone else's cells that were mass produced in vials for mass distribution. However, after 2005, this same rule was applied to **all human** tissue. For the first time, this gave the agency authority over the tissues in your body used to treat your disease as part of a surgical procedure. The agency now purports that it gave itself the ability to declare certain types of your tissues, processed in certain ways, to be drugs. For example, if PRP is activated in a certain way by your doctor, it's a drug. Again, stem cells processed in certain ways are also drugs.

The agency has traditionally gone to great lengths to differentiate *one on one* medical care risks (over which it has no authority) from *one on many* drug and device production risks (it's congressional mandate). *One on one* risks are the things you get exposed to everyday when you have a surgery. One patient, one doctor, one risk of the surgery. *One on many* risks are different, as their impacts are magnified. Imagine if one bad batch of drugs was contaminated and those drugs were shipped all over the country—one bad drug batch gets distributed to many patients or *one on many*. However, after this subtle change in its regulations, the agency drew a regulatory, public health risk line **through** a *one on one* medical procedure risk for the first time. For example, instead of only claiming authority over mass produced donor cells in a vial, the agency asserted authority over the re-implantation of the patient's own tissue. This change, may sound esoteric at first, yet by this regulatory sleight of hand, the agency gave itself the authority to regulate medical practice.

This wall between the agency and the practice of medicine has been defined by many court cases, but the case the agency brought against an Alabama physician (*United States v. Evers*) is illustrative. In this case, Dr. Evers was prosecuted by the government for using prescription drugs off label. The judge sided with Dr. Evers and explained why the FDA should not interfere with the practice of medicine. For example, the Court noted that a drug's package insert is not the most up-to-date information on the drug's uses. New uses are often discovered, reported through medical journals or seminars, and may become widely used in the medical profession; however, the drug manufacturer may not have sufficient financial or other interests to pursue FDA approval for the new uses. Further, if a doctor must prescribe and treat only within "federally sanctioned" methods, this would result in medical stagnation at the best, as physicians await drug manufacturers' initiative and FDA approval.³ The court reasoned, "***A free, progressive society has an enormous stake in recognizing and protecting this right of the physician.***"

The best everyday example of the line FDA has drawn between *one on one* medical care risks and *one on many* public health risks, is how it currently handles compounded pharmaceuticals.⁴ Compounding is a practice whereby a doctor writes a prescription for a non-FDA approved drug or formulation to treat one patient. After initially trying to assert regulatory control over pharmacy compounding and place it in the same category as drug mass production (something it is not), the FDA had to back off after it lost several key lawsuits brought by pharmacists. To clarify the issue and fill the regulatory gap left by these suits, the FDA issued a "Compliance Policy Guideline" (CPG) for compounding pharmacies. In this document, the agency states that since it doesn't regulate the practice of medicine or pharmacy, that it will only attempt to interfere in this relationship if a pharmacy is compounding drugs in advance of receiving a prescription, manufacturing on a commercial scale, or compounding drugs for resellers or for wholesale use. In essence, the FDA will only intervene if the pharmacy crosses the line and departs from filing a single patient's prescription and starts mass manufacturing of lots of drugs. However, the agency **has not** shown the same digression in its regulatory framework for autologous cell therapy and this marks a stark change in agency policy toward physicians and patients. Since A-ASC's can only represent a *one on one* medical care risk because they are derived from the same patient in which they will be

re-implanted, the FDA has now arbitrarily drawn the risk line through this *one on one* medical care risk and assigned it a mass production, public health risk status.

Are body parts drugs? In the same way that the agency in *Evers* (above) declared it had authority over how drugs should be prescribed, it has now declared authority over what constitutes a drug in the first place. This problem with this stance is further illustrated by a recent U.S. district court decision which stated that genes (and by extension stem cells) are laws of nature and therefore cannot be patented.⁵ This patent case creates clear precedence that the cells or genes in our bodies are not property of the biotech industry (devices or drugs) to be registered in the federal patent office, but body parts no different than a knee or an elbow. Nobody invented autologous stem cells, nor genes, nor knees or elbows, hence they are not biotechnology property to be regulated as drugs, but merely parts to be used in surgery.

A recent publication on stem cell treatment used to help patients avoid the need for a knee replacement shows this procedure was safer than the bigger orthopedic surgeries it helped many patients avoid.⁶ Even if for other types of therapies the risk of the stem cells is more than reported in this study, how does any aspect of an autologous *one on one* medical care risk transform that risk into a *one on many* batch drug production risk? Stated another way, can a medical procedure, no matter how unfamiliar, ever have the same widespread public health impact as drug production? As an example, we would all agree that a bad batch of mass produced drugs or devices would have serious and far reaching public health implications. A single bad batch of drugs may make many patients ill in all 50 states (a *one on many* risk, hence the reason we have an FDA in the first place). However, no aspect of a single medical care procedure, can be morphed into this kind of magnified public health impact. The surgery a patient chooses to undergo, the IVF fertility treatment, the testosterone use from a compounded prescription, or the Prolotherapy are all *one on one* medical care risks, which the doctor and patient discuss, and the patient either chooses to accept or avoid. They are not, by their *one on one* nature, national public health epidemics to be regulated at a federal level. Some *one on one* medical care risks are quite serious and some are miniscule; for example certain types of cardiac surgery have high morbidity or mortality rates while other types of cardiac procedures such as an EKG, have negligible risks. The medical care system goes

to great lengths everyday to mitigate these risks. However, drawing an arbitrary risk line through these procedures (or others in the future), allows the FDA to divide medical care into a type that requires federal regulation and a type that does not. If this is allowed, since all *one on one* procedures by their definition are medical practice, the FDA is by default regulating the practice of medicine.

To illustrate the problems with drawing the risk line through a medical procedure, consider a recent publication showing that a routine MRI magnetic field changes the biologic characteristics of stem cells.⁷ Before the publication of this MRI paper, the agency defined a biologic drug by cell processing that changed the biologic characteristics of the cells, however, this research confirms that a routine MRI changes the biologic characteristics of the cells. Do the stem cells injected into the patient as body parts become federally regulated drugs after a routine MRI?

In summary, the assertion by FDA that certain processing steps for autologous stem cells turns those cells into a drug production is not supported by any common sense argument. Furthermore, the agency's decision to insert itself into the practice of medicine by drawing a line through one procedure, sets a **dangerous** precedent. Where does this line get moved to in the future? Do certain compounded drugs get assigned a drug manufacture risk?

Certain fertility procedures? Certain high risk surgeries? Certain high risk surgeries involving cells? Prolotherapy? Congress has prohibited the agency from having any authority over the practice of medicine and as discussed, **there is great societal benefit in keeping it that way.**

If you have an interest in supporting safe A-ASC use, sign up at <http://www.cellmedicinesociety.org/>. ■

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