

Legislation for today's cell and tissue based therapies

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In a 2014 article, Caplan and West (Caplan AI, West MD. Progressive approval: a proposal for a new regulatory pathway for regenerative medicine. *Stem Cells Trans Med* 2014; 3(5): 560-563) highlighted the growing perception in the regenerative medicine community that 20th century drug regulations are not well suited for 21st century human cell- and tissue-based products. The recently introduced federal legislation offers an important stepping-stone to rectify this anomaly and improve access to safe regenerative medical treatments. REGROW — the Reliable and Effective Growth for Regenerative Health Options that Improve Wellness Act of 2016 (S. 2689/H.R. 4762) — seeks to modernize and tailor the FDA's current statutory framework to address cell therapies, while protecting current approval pathways under existing law.

Cell-based therapies offer a new frontier of medical science that can potentially cure or halt the progression of disease or stimulate regeneration/repair of tissue using the body's own building blocks. Age-related degenerative diseases involving cells and tissues are the single largest driver of the nearly \$3 trillion in annual health care costs in the United States.

We know, for example, that mesenchymal stem cells (MSCs) can secrete particular molecules at sites of injury that target opioid receptors and decrease pain. Treating a patient's osteoarthritis knee pain with therapeutic cells instead of oxycodone can be revolutionary. At the same time that the cells may safely reduce pain, they may also molecularly instruct inflamed or damaged cartilage cells to regrow.

Cellular therapies are moving very slowly into practice considering that the first patents were written in 1990. The U.S. lags behind other industrialized nations such as Japan and England, due in part

to the lack of a modern regulatory pathway in the USA. Currently, the FDA regulates cell-based therapies under essentially the same framework used for chemical drugs, vaccines and biologics. The process is a poor fit, at best, and often prevents patients from receiving beneficial treatment in a timely manner. It is essential that we modernize policies and streamline processes to keep pace with science and best practices, and, incidentally, to “stem” the tide of patients seeking treatment overseas.

In December 2015, the Bipartisan Policy Center released a report titled *Advancing Regenerative Cellular Therapy*, produced by an expert panel on which Caplan served. The report's recommendations formed the basis for the REGROW Act, designed to reduce barriers to progress by creating a new regulatory pathway that:

- Allows the FDA to grant a time-limited, conditional approval for “Phase 3-ready” therapeutic cells based on preliminary though rigorously-obtained and well-controlled clinical evidence of safety and efficacy;
- Provides patients who now have limited access to these therapeutic agents, a path to obtain conditionally-approved therapies much earlier that have well controlled monitoring and reporting requirements to the FDA;
- Requires the sponsor to submit a biologics license application (BLA) using the accrued data within five years of receiving conditional approval;
- May permit reimbursement during the conditional approval period; and
- Creates a simplified and expedited linked approval pathway for devices used in conjunction with cell therapies.

This pathway will enable the FDA to lead American medicine into the new era of cell-based therapies while ensuring and monitoring safety and

efficacy. The REGROW Act gives the FDA considerable latitude for accomplishing this important objective, including specific safety measures:

- During the conditional approval period, the sponsor is required to submit adverse event reports and annual patient outcome reports to the FDA;
- Each patient seeking a conditionally approved cell therapy product must have access based on agreed upon inclusion criteria and the understanding that the FDA will likely require long-term follow-up studies; and
- The FDA has the sole discretion to determine that a cell product is unsafe or does not work, and prohibit its use.

Scientists, practitioners, patients, sponsors and regulators could also benefit from dynamic, real-time assessment to support continued improvements in the science and practice. For example, a single registry for real-time data acquisition and monitoring could be created to view compliance with patient selection, treatment parameters, and detection of unexpected patient outcomes. Data could be aggregated and disseminated by the sponsor to regulatory authorities and participating physicians, as well as to patients and the general public with appropriate methods to protect patient privacy.

Moving new treatments into practice has often been a slow and prohibitively expensive process. The evolution of insulin is a perfect example. The gradual shift from treating patients with the extract of ground-up animal pancreases to recombinant human insulin was lengthy and slow, not just because careful scientific inquiry takes time. The evolution was also delayed because of resistance from the medical establishment and society at large.

Today, regenerative cell therapy is an explosive area of new knowledge, with more than 580 clinical trials registered by the end of 2015. It is both a scientific and a moral imperative that we responsibly reduce the regulatory hurdles to pave the way for use of effective therapies to safely treat the millions of U.S. patients with chronic degenerative diseases.

The practice of medicine relies on knowledge, skill and judgment. This legislation does not jeopardize these elements. Rather, it opens doors for the development of new and powerful tools that will help practitioners, with the assistance of industry, to cure and restore their patients' lives in ways they could only have dreamed about a few short years ago. Since many of these cell-therapy products were developed here in the USA, this legislation will allow us to once again take a leadership role in translating our science into breakthrough and curative health care.