

Editorial

Improving the regulatory framework for cell therapy does not equate to deregulation

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The introduction of the *Reliable and Effective Growth for Regenerative Health Options that Improve Wellness*, or REGROW Act¹, has already yielded a significant benefit: it has fostered a healthy dialogue about the right path forward. How will we regulate cell and other regenerative therapies in the future?

Detractors of REGROW claim that a conditional pathway for lower risk cell therapies will significantly weaken oversight. Supporters claim that a narrow set of lower risk cell therapies – such as autologous or immunologically compatible donor cells that are more than minimally manipulated for homologous use, or minimally manipulated for non-homologous use – should be regulated using a framework that recognizes the unique attributes of human cells, as opposed to one that is similar to that used for drugs.

Under current law, some cell therapies – a small minority – are regarded as the practice of medicine, and therefore are not subject to pre-market review by the Food and Drug Administration (FDA). The vast majority of the remaining therapies are regarded as drugs, and are regulated under Section 351 of the Public Health Service Act. Even though they are not drugs – in fact, some cell therapies involve using the patient's own cells – they are subjected to the same process used to evaluate new medications, a process that takes an average of 10 years and up to \$2 billion.

Living human cells used in cell therapies differ in important ways from inanimate, chemical drugs. First and foremost, their very purposes are distinct. Drugs are primarily designed to control symptoms and treat disease. Regenerative cell therapies are curative, and aimed at addressing a disease's root cause.

Used safely and effectively for more than 50 years, cell therapy has been shown to improve healthy function in tissues for osteoarthritis, bone and cartilage repair, and trauma-related injuries including burns and wounds. Today, cell therapies represent the next generation of groundbreaking treatments, showing enormous promise in the areas of cardiology, neurology, oncology, and ophthalmology. Hundreds of clinical trials are currently underway to address diseases for which there is currently no cure, including Alzheimer's, multiple sclerosis, and Parkinson's disease, as well as diabetes, heart disease, and stroke. About half of the 5,372 clinical trials involving stem cell therapy in clinicaltrials.gov are focused on curing and treating cancer. And 644 of all stem cell clinical trials involve the use of mesenchymal stem cells. The safety record of cell-therapy trials is notable: over the past five years, only two percent of all peer-reviewed articles that included safety assessments of clinical trials for autologous and allogenic cell therapies identified a safety issue.

The science behind cell therapy had progressed considerably since 2001, when the FDA first created a regulatory structure for human cells, tissues and cellular and tissue-based products. Unfortunately, the current regulatory approach has not kept pace with the rapidly evolving science.

Investigators that are doing rigorous clinical studies that demonstrate safety and efficacy – and the organizations that sponsor them – should be invited to submit to a new, improved review and oversight process at the FDA's sole discretion, to

bring curative and life-saving cell therapies more quickly and at a lower cost to patients in need.

Current policy proposals under review, including the REGROW Act, offer new tools for FDA regulation that recognize the unique attributes of cellular and other regenerative therapies^{2,3}.

New regulatory approaches need not take any regulatory powers away from the FDA. Legislative proposals in fact make it very clear that the new language shall NOT be applied or interpreted as restricting or otherwise modifying any pathway to market that is promulgated by the FDA, including those under sections 351 and 361 of the Public Health Service Act.

Rather, FDA will benefit from additional authorities granted by Congress to improve flexibility and explore new regulatory approaches. These approaches can leverage existing expedited programs that the FDA already uses for drugs, such as accelerated approval, break-through therapy, fast track, or priority review, or can create new pathways – such as conditional approval – that have been used successfully in Europe and Japan.

Stem cell clinics that are currently operating lawfully under the designation of “practice of medicine” would not be subject to the new regulatory pathway. FDA currently allows limited use of autologous, homologous, minimally manipulated cells if donor consent and good tissue practices are observed. New legislative proposals offer the opportunity for improved oversight over stem cell clinics operating outside the practice of medicine.

New regulatory approaches can and should involve close monitoring, providing FDA with the data necessary to assess long-term safety and efficacy in this rapidly emerging field. All individuals and organizations that deliver cell therapies, including those that fall both within and outside of the practice of medicine, should participate in reporting to a new, publicly accessible registry^{2,3}. Information reported should include the conditions for which the patient is being treated, the method of delivery (including source, number, and mode), and outcomes data, including long-term outcomes.

The public registry would offer clinicians and patients useful safety and outcomes data to support clinical decision-making. Payers could use the data to support reimbursement decisions. And regulators – including the FDA – could use the information to support regulatory decision-making. Such a registry could significantly bolster FDA’s current

mechanisms for monitoring clinics operating within and outside of section 361 of the Public Health Service Act.

New legislation introduced in Congress, combined with a September 2016 hearing scheduled by the FDA, will no doubt continue to stimulate dialogue, and this is both necessary and timely. But at some point, dialogue must give way to action.

One thing is clear: The current regulatory approach for cell therapy can be improved. Promising new approaches supported by rigorous clinical trials are not getting to patients because of a regulatory framework that treats human cells like drugs. On the other hand, there are some cell clinics offering services outside of the practice of medicine that are operating free of FDA regulation.

Both scenarios are damaging and unsustainable. We need a better way, and we could start by focusing on the 80 percent of the challenges and potential solutions we agree upon and share, while avoiding polarizing statements and positions that misleadingly label as “deregulation”, any proposal for collaborative work towards an improved regulatory framework. The second major misconception is that if there is a proposal put forward to streamline or improve the regulatory process, there must be some obscure for-profit agenda behind it. It is actually the status quo that feeds the \$3 trillion in national health care expenditures which now represent 17.5 percent of the GDP, and of course, there are for-profit entities that operate in the health-care space and contribute to these expenditures. However, public-private partnerships should be supported when the goal is to promote the delivery of new safe and cost-effective therapeutic options that could save hundreds of billions to taxpayers.

Working to reduce the time and costs associated with the safe delivery of novel therapies, while imposing mandatory reporting and monitoring of ALL clinical trials and outcomes in ALL subjects treated, could greatly benefit the patients we serve. We should all share the same goal: to deliver therapeutic options safely, but also in the fastest, most efficient and affordable way possible.

REFERENCES

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