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Is Your Regenerative Medicine Product Strategy Ready for May 2021?

What Manufacturers Need to Know about Upcoming Regulation Changes

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Development and growth of regenerative medicine products—including human cells, tissues, and cellular and tissue-based products (HCT/Ps), gene-based therapies, and tissue-engineered constructs—are forecast to expand considerably in the next five years. Since 2005, the U.S. Food & Drug Administration (FDA) has applied a tiered, risk-based approach to regulatory enforcement that accounts for how certain regenerative medicine products are administered and the conditions they treat. Building on this approach, in 2017 the FDA published a comprehensive regenerative medicine policy framework to spur innovation and efficient access to safe and effective regenerative medicine products. At the same time, the FDA also announced its intent to exercise enforcement discretion of these policies for certain products to give manufacturers time to determine what requirements apply and engage with the agency. This period of enforcement discretion is scheduled to end—and the next phase of more stringent regulation is set to begin—in May of 2021.

It is important for manufacturers who have already launched regenerative medicine products, as well as those planning future launches, to understand how their products will be classified as of next spring. By engaging with the FDA early and often, manufacturers can tailor their go-to-market strategies to stricter Agency requirements, protect the continuity of existing operations, and help support the timely approval of newly developed products.

Guidance Documents for the New Regulatory Framework

The FDA has developed four guidance documents addressing certain aspects of 21 CFR 1271 that form a framework for regulating the safety and effectiveness of regenerative medicine products. These documents can be thought of as a decision tree to assist manufacturers in understanding how their product should be classified (Figure 1). Using this approach, manufacturers can determine whether their products qualify for exception from the rule, can be regulated under HCT/P-specific rules, are eligible for Expedited Programs, or must be assessed under the general regulations for these products.

Same Surgical Procedure Exception: Questions and Answers Regarding the Scope of the Exception

The first step a manufacturer or health care provider may take is to assess the current biologics and medical device regulations and determine whether the product qualifies for an exception under this guidance.

The guidance for the same surgical procedure exception is intended to help establishments understand whether or not a regenerative medicine product qualifies for an exception from the requirements under Part 1271 by meeting the exception in 21 CFR 1271.15(b).

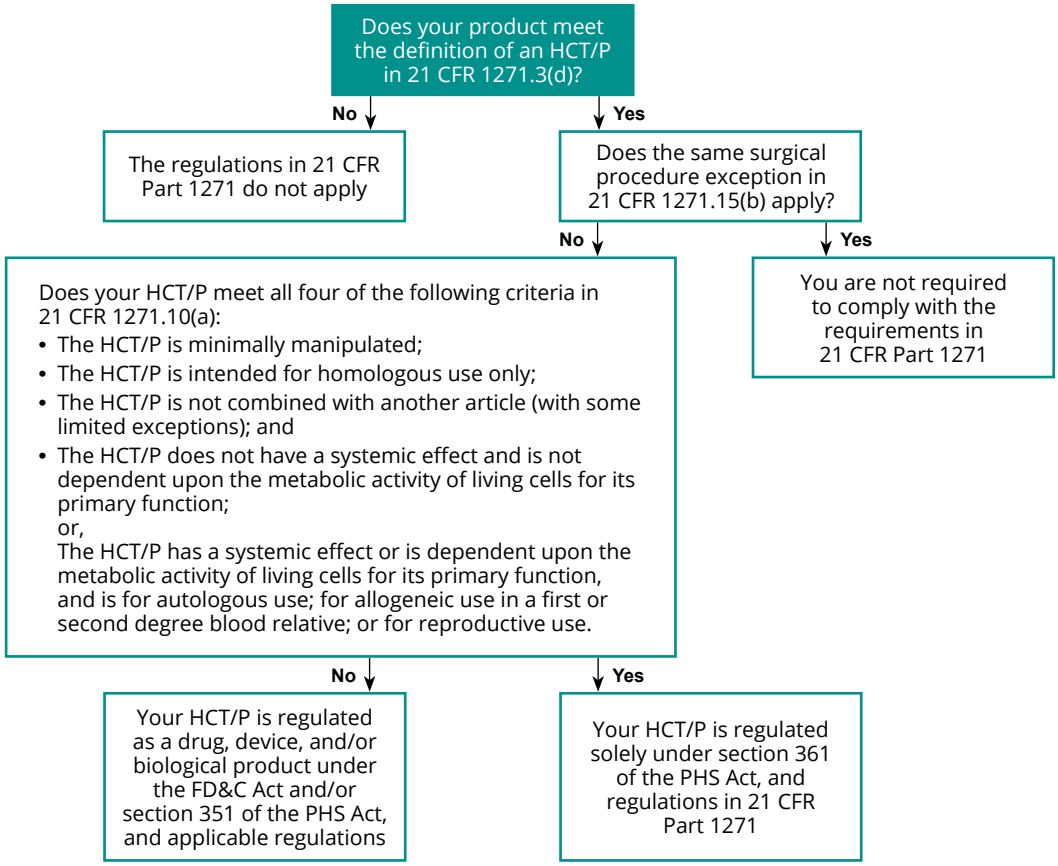

Figure 1. How to apply the criteria in 21 CFR 1271 from FDA's "Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use"

For example, removing a piece of skin for use as a skin graft elsewhere on the same person's body, all during the same procedure, likely would be an exception as identified in 21 CFR 1271.15(b). In contrast, processing or manipulating that same piece of skin, such as decellularizing the graft or combining it with a scaffold or drug, would not be an exception, even if it were still intended for grafting on the same person during the same procedure.

Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use

If the product does not qualify for an exception, the next step is to understand whether it can be considered an HCT/P rather than a broader regenerative medicine therapy using this guidance. Products qualifying as an HCT/P are regulated only under rules outlined by 21 CFR 1271.10 and Section 361 of the Public Health Service Act (PHS Act), which are focused on the reduced risk profile associated with HCT/Ps compared to other regenerative medicine therapies.

The guidance on minimal manipulation and homologous use is intended to provide clarity in determining whether HCT/Ps are subject to the FDA's premarket review requirements. If a cellular or tissue product is both minimally manipulated and intended for homologous use, it qualifies as an HCT/P and does not have to adhere to the requirements for medical devices, biologics, and drugs regulated under Section 351 of the PHS Act.

In the event that a manufacturer's or health care provider's product does not qualify as an HCT/P, additional mechanical, chemical, and human factors testing may be required to support a standard regulatory submission.

Expedited Programs for Regenerative Medicine Therapies for Serious Conditions

If the product does not qualify for an exception and cannot be classified as an HCT/P, the next step is to define a regulatory strategy that supports an efficient go-to-market strategy and provides evidence of safety and efficacy.

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The guidance on Expedited Programs describes several programs, such as the Fast Track and Breakthrough Therapy designations, that are available to sponsors of regenerative medicine therapies. It also provides information about the requirements for, and benefits of, the new Regenerative Medicine Advanced Therapies (RMAT) designation program created by the 21st Century Cures Act. While these designations can be attractive pathways for manufacturers because they are intended to shorten time to market, use of the correct designation is important to avoid potentially costly delays to regulatory approval.

Evaluation of Devices Used with Regenerative Medicine Advanced Therapies

The device guidance provides the FDA's current thinking about concepts related to the evaluation of devices used in the recovery, isolation, and delivery of RMATs. For example, a manufacturer may take a predicate device from manipulated cell type A and use it for cell type B if it can provide "valid scientific evidence" that the recovery, isolation, and delivery of the new cell type does not change the clinical outcome of the regenerative medicine product.

If the product does not meet the requirements of these guidance documents, it must be assessed under the general regulations for drugs, devices, and/or biological products. This generally includes establishing a classification and regulatory strategy, which can be enhanced by better understanding important aspects of FDA's evaluation of the product during regulatory approval.

Preparing for Successful FDA Engagement:

While the FDA intended its initial discretionary period to foster manufacturer/Agency engagement, the limited company engagement suggests that some companies are unaware of the May 2021 deadline and that others may not fully appreciate how the guidance applies to their products. In the remaining months, it will be important for companies to review the FDA's guidance documents and understand how their product(s) will be classified and regulated when the current enforcement discretion period ends. In our experience, proactive interaction with the FDA is a foundation for streamlined regulatory review and a beneficial strategy for efficiently bringing products to market.

How Exponent Can Help

Exponent's multi-disciplinary team of biomedical engineers, health scientists, and regulatory consultants can help health care providers and manufacturers of regenerative medicine products understand the nuances of the FDA's new regulatory framework and guide their products through the next phase of regulation, including managing the effects of the expiring enforcement discretionary period. Our experts have deep knowledge of FDA regulations including mechanical, chemical, and human factors testing to support a standard regulatory submission, regenerative medicine products, development of unique testing parameters for those products, and product life cycle risk management. Additionally, we work with the Standards Coordinating Body, ASTM, ASME, and ISO to create standard test methods for regenerative medicine products. We can help clients understand how their regenerative medicine products will be classified, what scientific evidence will be required, and how they can navigate the right regulatory pathway in the most efficient manner possible.

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