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FDA Finalizes Two Guidance Documents Regarding Regenerative Medicine Therapies

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On February 15, 2019, the U.S. Food and Drug Administration ("FDA") finalized two guidance documents regarding regenerative medicine therapies (see FDA's announcement here). This development comes nearly 14 months after FDA issued both guidance documents in draft form, which also coincided with FDA's announcement of a new comprehensive regenerative medicine policy framework intended to spur innovation and efficient access to new regenerative medicine products.

FDA Commissioner Scott Gottlieb remarked that the finalization of regenerative therapy guidance documents "demonstrate[s] [FDA's] continued commitment" to fulfilling the promise of providing a clear and predictable pathway to approval. Moreover, he noted that these guidance documents help stakeholders to "understand our regulatory framework" and, in turn, "may help to more efficiently advance access to safe and effective regenerative medicine therapies." These guidance documents, which are discussed in further detail below, provide information to product developers about FDA's current thinking with respect to evaluating devices used with regenerative medicine advanced therapies and provide information on the expedited development programs that may be available.

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Guidance for Industry: Evaluation of Devices Used with Regenerative Medicine

The final guidance entitled "Evaluation of Devices Used with Regenerative Medicine Advanced Therapies" (available here) clarifies how FDA will evaluate devices used in the recovery, isolation, or delivery of regenerative medicine advanced therapies (RMATs). This guidance finalizes FDA's current thinking on how the agency will streamline and simplify its application of regulatory requirements for combination device and cell or tissue products.

In this guidance document, FDA acknowledges that a wide range of devices may be used in conjunction with an RMAT, ranging from simple, low-risk devices to complex, higher risk devices to devices that are constituent parts of an RMAT that is classified as a combination product. FDA reiterates that the primary factor in determining the availability of premarket pathways for a device is the device's classification (i.e., Class I, Class II, or Class III), followed by the risks associated with the device type and the level of regulatory controls necessary to provide a reasonable assurance of safety and effectiveness.

In addition, FDA discusses the factors it will consider when determining whether a device may be labeled for use with a specific RMAT or class of RMATs. When determining which devices may be suitable for use with a specified RMAT or type of RMAT, FDA will consider the distinct biological and physical characteristics of RMATs, intended use, and conditions for use. With respect to cellular products that are RMATs, FDA intends to review the cellular products' characteristics, their interaction with different devices, as well as any impact on cell viability, differentiation potential, activation state and ability to respond to stimuli after administration and other similar factors.

Substantively, there were no major or unexpected changes between the draft guidance and the final guidance issued by FDA.

Guidance for Industry: Expedited Programs for Regenerative Medicine Therapies for Serious Conditions

The second final guidance, "Expedited Programs for Regenerative Medicine Therapies for Serious Conditions" (available here), provides information regarding the use of accelerated approval pathways for regenerative medicine therapies that have been granted designation as an RMAT, as well as considerations in the clinical development of regenerative medicine therapies and opportunities for sponsors of such products.

This guidance makes clear that the following therapies could qualify for an RMAT designation: cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products, except those regulated solely under section 361 of the Public Health Service Act (42 U.S.C. 264) and 21 C.F.R. Part 1271. Notably, the final version of this guidance clarifies that "cell therapies" includes both allogeneic and autologous cell therapies, as well as xenogenic cell products. Products that qualify for an RMAT designation receive all of the benefits of the fast track and breakthrough therapy designation programs, including early interactions with FDA. Although sponsors may apply for and receive both breakthrough and RMAT designation for a product, FDA advised that each designation requires a separate application.

Factors that FDA may consider when determining whether the preliminary clinical evidence is sufficient to support RMAT designation include, but are not limited to, the rigor of data collection; the consistency and persuasiveness of outcomes; the number of subjects and sites contributing to the data; and the severity, rarity, or prevalence of the condition. Unlike the breakthrough therapy designation, RMAT designation does not require a sponsor to produce evidence indicating that the drug offers a substantial improvement over available therapies.

To apply for RMAT designation, a sponsor should submit either a new investigational new drug application ("IND") or an IND amendment, along with a concise summary of information in support of the RMAT designation. The application should include a description of the investigational product; rationale for the investigational new drug meeting the definition of an RMAT; a discussion to support that the disease or condition the product is intended to treat is serious; and preliminary clinical evidence that the product has the potential to address the specified unmet medical need for the serious condition. The requirement to provide a description of the product is new to the final guidance. No later than 60 calendar days after receipt of the designation request, FDA will notify the sponsor as to whether the regenerative medicine therapy has received the RMAT designation.

Finally, this guidance provides recommendations for clinical trial design. FDA states that it will consider clinical trials in support of a Biologics License Application ("BLA") that "incorporate adaptive designs, enrichment strategies, or novel endpoints." This final guidance provides new language indicating that historical controls and natural history data (the course a disease takes from its onset, through presymptomatic and clinical stages, to a final outcome in the absence of treatment) may be considered, if appropriate. Natural history data, however, may only provide the basis of a historical control if the "control and treatment populations are adequately matched, in terms of demographics, concurrent treatment, disease state, and other relevant factors."

FDA's continued focus on developing and finalizing guidance in the regenerative medicine space suggests that FDA is serious about helping industry to both navigate the application process in an effort to streamline the premarket approval process and to better understand and address identified regulatory pain points. For these reasons, sponsors of investigational regenerative therapies should pay close attention to and take into consideration the recommendations set forth in these final guidance documents.

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