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FDA Cites Genetech, Inc. and Warns Other Stem Cell Firms Against Marketing Dangerous Unapproved Stem Cell Products

On Nov. 29, 2018, the U.S. Food and Drug Administration (FDA) issued a warning letter to Genetech, Inc., a manufacturer of umbilical-cord blood-sourced stem cells, based in San Diego, California. The warning letter detailed significant violations of current Good Manufacturing Practices (cGMP) and current Good Tissue Practices (cGTP) for manufacturing human cells, tissues, and cellular and tissue-based products (HCT/Ps). It was issued after patients in Florida, Texas, and Arizona became seriously ill from injections of umbilical cord blood sourced stem cells contaminated with E-coli, Enterococcus faecalis, and Proteus mirabilis. Notably, the FDA has also sent letters to 20 stem cell treatment firms, reminding them of the agency's current enforcement discretion period and encouraging them to determine their regulatory obligations before the end of the discretion period.

FDA generally regulates stem cell products as HCT/Ps under the Public Health Service Act (PHS Act). HCT/Ps may also be regulated under the Federal Food, Drug, and Cosmetic Act (FD&C Act) as biological products, drugs, and/or devices that require pre-market approval. If stem cell products are regulated as biological products under the FD&C Act, the products must be studied in human subjects under an investigational new drug (IND) application and subsequently an approved Biologics Licensing Application (BLA). In November 2017, however, FDA announced significant updates to its policies regarding HCT/Ps to deliver on certain provisions of the 21st Century Cures Act, including establishing a legal threshold for when a product is subject to FDA premarket approval. As part of the announcement, the FDA informed

stem cell firms and providers of its intent to exercise enforcement discretion until November 2020 to allow stem cell treatment providers and manufacturers time to comply with the new premarket approval policies. Products that raise safety concerns will still trigger FDA action, however.

The experience of Genetech is an example of how FDA is currently exercising its enforcement discretion. The San Diego-based company processed human umbilical cord blood and offered the resulting biological products through its distributor, Liveyon, for administration by intra-articular injection, intravenous injection, or application directly to affected tissue to treat a variety of orthopedic conditions. FDA found that the marketing of these products required a BLA – which Genetech did not have. Additionally, an inspection of Genetech facilities revealed significant deviations from current good tissue practice and current good manufacturing practice requirements, raising potentially significant safety concerns. FDA's warning letter cited 19 such violations, including deficient donor-eligibility practices; unvalidated manufacturing processes; uncontrolled environment; lack of control over the components used in production; lack of defined areas or a control system to prevent contamination and mix-ups; and failure to establish and implement quality control systems and processes. Genetech's stem cell products were voluntarily recalled in September 2017, and all product shipments were suspended pending resolution of the FDA investigation. Due to reported safety issues and potential significant safety concerns, FDA warned Genetech that failure to correct its deficiencies could result in regulatory action, including seizure and/or injunction.

In December 2018, FDA issued letters to other manufacturers and treatment providers who may be offering stem cell products or treatments and who may, therefore, be subject to the PHS Act and the FD&C Act. The letters reiterated the agency's current policy and encouraged affected parties to reach out to FDA "well in advance of November 2020 to determine whether their products are subject to the agency's premarket approval requirements."

Authors

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