



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2003-D-0370]

Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products--Submitting New Drug Applications; Withdrawal of Guidance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; withdrawal.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the withdrawal of a guidance for industry entitled “Exocrine Pancreatic Insufficiency Drug Products--Submitting NDAs,” which was issued in 2006. The guidance set forth the Agency’s thinking on data and information that may support a new drug application (NDA) for a proposed pancreatic enzyme product (PEP) that contains pancreatin or pancrelipase and is intended for the treatment of exocrine pancreatic insufficiency (EPI). FDA is withdrawing the guidance because an NDA for such a product may not be submitted after March 23, 2020. Sponsors interested in submitting a biologics license application (BLA) for a proposed PEP should contact the Agency with any questions.

DATES: The withdrawal is effective March 23, 2020.

FOR FURTHER INFORMATION CONTACT: Kristiana Brugger, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6262, Silver Spring, MD 20993, 301-796-3600.

SUPPLEMENTARY INFORMATION: FDA is withdrawing the guidance for industry entitled “Exocrine Pancreatic Insufficiency Drug Products--Submitting NDAs,” which was issued in

2006 (see 71 FR 19524 (April 14, 2006)). The guidance described FDA's thinking regarding the data and information that may support submission of NDAs, including submission of NDAs pursuant to section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 355(b)(2)), for products that contain the ingredients pancreatin or pancrelipase and are used to treat EPI.

Pancreatic enzyme preparations of porcine or bovine origin that contain the ingredients pancreatin or pancrelipase have a long history of use for the treatment of EPI in children and adults with cystic fibrosis and chronic pancreatitis. These products have been available in the United States for decades, largely marketed as unapproved drugs. On April 28, 2004 (69 FR 23410), however, FDA announced that all orally administered PEPs are new drugs that must be approved via a marketing application for prescription use only, and explained the conditions for continued marketing of these drug products. The guidance explained FDA's thinking regarding ways in which sponsors of products containing pancreatin and pancrelipase could design drug development programs to demonstrate the safety and effectiveness of their products and satisfy the requirements for approval of an NDA, including an NDA submitted pursuant to section 505(b)(2) of the FD&C Act.

Although most therapeutic biological products have been licensed under section 351 of the Public Health Service Act (PHS) (42 U.S.C. 262), some protein products historically have been approved under section 505 of the FD&C Act (21 U.S.C. 355). On March 23, 2010, the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) was enacted as part of the Patient Protection and Affordable Care Act (Pub. L. 111-148). The BPCI Act clarified the statutory authority under which certain protein products will be regulated by amending the definition of a "biological product" in section 351(i) of the PHS Act to include a "protein (except

any chemically synthesized polypeptide),” and describing procedures for submission of a marketing application for certain biological products. The Further Consolidated Appropriations Act, 2020 (Pub. L. 116-94) further amended the definition of a “biological product” in section 351(i) of the PHS Act to remove the parenthetical exception for “any chemically synthesized polypeptide” from the statutory category of “protein” (see Division N, section 605, of the Further Consolidated Appropriations Act, 2020). Products containing pancreatin or pancrelipase fall within FDA’s interpretation of the term “protein” in the statutory definition of a biological product (for additional information, see the final rule entitled “Definition of the Term ‘Biological Product’ (85 FR 10057, February 21, 2020)

The BPCI Act requires that a marketing application for a “biological product” (that previously could have been submitted under section 505 of the FD&C Act) must be submitted under section 351 of the PHS Act; this requirement is subject to certain exceptions during a 10-year transition period ending on March 23, 2020 (see section 7002(e)(1) to (3) and (e)(5) of the BPCI Act). On March 23, 2020 (i.e., the transition date), an approved application for a biological product under section 505 of the FD&C Act shall be deemed to be a license for the biological product under section 351 of the PHS Act (see section 7002(e)(4)(A) of the BPCI Act; see also section 7002(e)(4)(B) of the BPCI Act). After March 23, 2020, all sponsors seeking approval of a biological product (that previously could have been submitted under section 505 of the FD&C Act) will need to submit a BLA under the PHS Act (see section 7002(e) of the BPCI Act). (For additional information, see FDA’s guidance for industry entitled “Interpretation of the ‘Deemed to be a License’ Provision of the Biologics Price Competition and Innovation Act of 2009” (December 2018), available at <https://www.fda.gov/media/119272/download>.)

FDA is withdrawing the guidance because a marketing application for a proposed PEP that contains the ingredients pancreatin or pancrelipase may not be submitted under section 505 of the FD&C Act after March 23, 2020. The guidance included a description of data and information that may support submission of NDAs, including 505(b)(2) applications, for these products. FDA anticipates that there will be different considerations that may inform development of proposed PEPs intended for submission in BLAs under section 351 of the PHS Act. FDA intends to issue guidance regarding how the concepts described in the withdrawn guidance would apply to proposed pancreatic enzyme products submitted under the PHS Act, including the extent of integration of various types of data and information about the use of PEPs into BLAs. In the interim, the Agency encourages sponsors interested in submitting a BLA for a PEP to contact the relevant review division in the Office of New Drugs in FDA's Center for Drug Evaluation and Research with any questions.

Dated: March 2, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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