Guidance for Industry

Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(3) without seeking prior comment because the agency has determined that prior public participation is not feasible or appropriate because the guidance deals with an urgent issue affecting patients with life-threatening infections with Clostridium difficile.

FDA invites comments on this guidance. Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*. FDA will review any comments we receive and revise the guidance when appropriate.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or e-mail ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or e-mail address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
July 2013

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

We, FDA, are informing members of the medical and scientific community, and other interested persons that we intend to exercise enforcement discretion regarding the investigational new drug (IND) requirements for the use of fecal microbiota for transplantation (FMT) to treat *Clostridium difficile* (*C. difficile)* infection not responding to standard therapies. FDA intends to exercise this discretion provided that the treating physician obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products. Informed consent should include, at a minimum, a statement that the use of FMT products to treat *C. difficile* is investigational and a discussion of its potential risks. FDA intends to exercise this discretion on an interim basis while the agency develops appropriate policies for the study and use of FMT products under IND.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. DISCUSSION

Fecal microbiota collected from healthy individuals are being investigated for use in the treatment of *C. difficile* infection. Published data suggest that the use of fecal microbiota to restore intestinal flora may be an effective therapy in the management of refractory *C. difficile* infection. However, the efficacy and safety profiles of this intervention have not yet been fully evaluated in controlled clinical trials.

In the Federal Register of February 25, 2013 (78 FR 12763), FDA announced a public workshop, entitled "Fecal Microbiota for Transplantation." The purpose of this workshop was to provide a forum for the exchange of information, knowledge, and experience among the medical and scientific community about the regulatory and scientific issues associated with FMT.

The workshop to discuss the regulatory and scientific issues associated with FMT was held on May 2-3, 2013. FDA noted that use of FMT and clinical studies to evaluate its safety and effectiveness are subject to regulation by FDA, and that the complex nature of FMT products presents specific scientific and regulatory challenges. During that workshop, and in subsequent communications, physicians and scientists expressed concern to FDA that FMT is not appropriate for study under the agency's IND regulations (21 CFR Part 312). Some health care providers stated that applying IND requirements will make FMT unavailable and suggested that an alternative regulatory approach is needed to ensure the widespread availability of FMT for individuals with *C. difficile* infection unresponsive to standard therapies. In the weeks since the workshop, FDA has received numerous inquiries about the application of the IND regulations to the administration of FMT products, and many expressed concern about the use of these products under IND.

FDA acknowledges these concerns and intends to exercise enforcement discretion regarding the IND requirements for the use of FMT to treat *C. difficile* infection not responding to standard therapies. FDA intends to exercise this discretion provided that the treating physician obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products. Informed consent should include, at a minimum, a statement that the use of FMT products to treat *C. difficile* is investigational and a discussion of its potential risks.

FDA intends to exercise this discretion while we further consider the matter. During this period of enforcement discretion, FDA will continue to work with any sponsors who wish to submit INDs for this use of FMT.

This enforcement discretion policy does not extend to other uses of FMT. Data related to the use and study of FMT to treat diseases or conditions other than *C. difficile* infection are limited, and study of FMT for these other uses is not included in this enforcement policy.