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

DRAFT GUIDANCE

This guidance document is for comment purposes only.

Submit one set of either electronic or written comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. 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*.

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 email 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 email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Contains Nonbinding Recommendations

Draft – Not for Implementation

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 or agency, 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: (1) the licensed health care provider treating the patient obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products; (2) the FMT product is obtained from a donor known to either the patient or to the licensed health care provider treating the patient; and (3) the stool donor and stool are qualified by screening and testing performed under the direction of the licensed health care provider for the purpose of providing the FMT product to treat his or her patient. Note that the 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. We do not intend to exercise enforcement discretion when the FMT product is manufactured from the stool of a donor who is not known by either the patient or the licensed health care provider treating the patient; or the donor and donor stool are not qualified under the direction of the licensed health care provider treating the patient.

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.

This guidance, when finalized, will supersede the guidance document entitled "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," dated July 2013 (July 2013 Guidance).

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," which was held on May 2-3, 2013. 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. 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 Title 21 of the Code of Federal Regulations Part 312 (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. After the workshop, FDA 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.

In the *Federal Register* of July 18, 2013 (78 FR 42965), we announced the availability of the July 2013 Guidance. We informed members of the medical and scientific community and other interested persons that we intend to exercise enforcement 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.

III. WHEN FDA INTENDS TO EXCERCISE ENFORCEMENT DISCRETION

After publication of the July 2013 Guidance, FDA has continued to review this area and is clarifying its enforcement policy. FDA intends to exercise this discretion on an interim basis, provided that:

1. The licensed health care provider treating the patient obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT

products. The 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.

2. The FMT product is obtained from a donor known to either the patient or the treating licensed health care provider.
3. The stool donor and stool are qualified by screening and testing performed under the direction of the licensed health care provider for the purpose of providing the FMT product to treat his or her patient.

FDA does not intend to exercise enforcement discretion for the use of an FMT product when the FMT product is manufactured from the stool of a donor who is not known by either the patient or the licensed health care provider treating the patient, or when the donor and donor stool are not qualified under the direction of the treating licensed health care provider.

FDA will continue to evaluate its enforcement policy.

Furthermore, during the period of enforcement discretion, FDA will continue to work with sponsors who intend to submit INDs for use of FMT to treat *C. difficile* infection not responding to standard therapies.

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 more limited, and study of FMT for these other uses is not included in this enforcement policy.