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Ms. Leslie Kux
Assistant Commission for Policy
Office of Communication, Outreach and Development (HFM-40)
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448

***Re: Docket No. FDA-2013-D-0811: Guidance for Industry: Enforcement of Policy Regarding Investigational New Drug Requirements for use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies***

Dear Ms. Kux:

The Association for Professionals in Infection Control and Epidemiology (APIC) wishes to thank the Food and Drug Administration (FDA) for the opportunity to provide input into its draft Guidance for Industry: Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation To Treat *Clostridium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. APIC is a nonprofit, multi-disciplinary organization representing over 15,000 infection preventionists, whose mission is to create a safer world through prevention of infection. Our comments primarily reflect the views of our members, whose responsibilities include prevention of healthcare-associated infections.

APIC advocates for patient and product safety and also recognizes the urgent need for therapies to treat patients suffering from *Clostridium difficile* infection (CDI) that is nonresponsive to standard therapies. We support the use of fecal microbiota transplantation (FMT) to treat recurrent CDI as it has been shown in numerous peer-reviewed studies to be the most effective treatment for recurrent CDI.[1] FMT has rapidly become a reliable, safe, and effective treatment for recurrent CDI, especially given the growing prevalence of CDI and antimicrobial resistance in the U.S.

APIC believes that classifying FMT as biologic and requiring submission of an investigational new drug (IND) application by each provider may limit access to this proven effective treatment. APIC supports FDA's oversight to ensure patient safety, and is encouraged that the FDA is allowing stool banks to be direct IND sponsors. We believe that this will facilitate better participation in IND processes and allow for more robust data gathering that will facilitate reclassification of FMT products. APIC urges the agency to reclassify FMT stool as a tissue product, or as its own category, so it can be appropriately regulated.

In addition, the FDA proposes enforcement discretion only if the FMT product is not obtained from a stool bank. APIC is concerned that this language disqualifies the use of banked stool from standard donors and community donors for generating FMT product when this may be the only option available to patients and could potentially limit access to definitive care, especially in cases of fulminant *C. difficile* that require emergent treatment where a donor cannot be immediately located. Outside of emergent

cases, there are many cases where a suitable donor may not be available. In both of these circumstances, the submission of an IND imposes an onerous process when banked stool may be the only option available. As such, we believe that continued enforcement discretion should be extended to the use of banked stool from unrelated anonymous donors for these limited purposes.

APIC is also concerned that limiting access to banked stool may drive the use of donor-directed therapy, which has not been demonstrated to be safer. Blood products provide the most well studied analogous system to inform expectations of risk in FMT. Directed blood donors are over three times more likely to carry serious infectious agents like HIV or hepatitis than universal donors, primarily because universal donors have often been previously screened and lack the emotional incentive to hide risky behavior.[2] Moreover, research has demonstrated that utilizing unrelated donors is effective in FMT treatment. Utilizing stool banks supports standardizing stool supply including medical screening of donors over time.[3]

APIC encourages the FDA to collaborate with the medical and scientific community to continue to gather data on the use of banked stool and to establish guidelines for donor screening to prevent the transmission of infectious diseases during FMT. We hope that further review will show that it is not appropriate for study under the agency's IND regulations. APIC encourages the FDA to consider adapting the regulatory guidance for FMT that is consistent with a donated product such as blood and tissue. Blood and tissue donations require oversight of a physician, specific screening protocols for both patient and donor, and handling requirements, all of which would be applicable to FMT.

**APIC recommendations**:

- APIC supports use of FMT to treat recurrent *Clostridium difficile* infection.
- APIC supports stool banks being direct IND sponsors, as this will facilitate better IND participation and data gathering.
- APIC supports reclassification of FMT products as a tissue, or its own category, once data is available to allow for reclassification.
- APIC encourages the FDA to allow for the use of enforcement discretion for treatment of recalcitrant CDI with banked stool for emergent cases and cases with no apparent donor.
- APIC encourages FDA to continue to collaborate with the medical and scientific community to establish guidelines for donor screening to prevent the transmission of infectious diseases during FMT.

APIC appreciates the opportunity to comment on FDA's draft guidance on FMT and we look forward to continuing to work with the agency as it carries out its mission to protect patients and promote the public health.

Sincerely,

Susan Dolan

Susan Dolan, RN, MS, CIC
2016 APIC President

[1] Rohlke F, Stollman N. Fecal microbiota transplantation in relapsing *Clostridium difficile* infection. Therap Adv Gastroenterol 2012;5(6):403-420.

[2] Dorsey KA1, Moritz ED, Steele WR, Eder AF, Stramer SL. A comparison of human immunodeficiency virus, hepatitis C virus, hepatitis B virus, and human T-lymphotropic virus marker rates for directed versus volunteer blood donations to the American Red Cross during 2005 to 2010. Transfusion. 2013;53(6):1250-6.

[3] Youngster, I, Sauk, J., Pindar, C., et al. Fecal microbiota transplant for relapsing *Clostridium difficile* infection using a frozen inoculum from unrelated donors: a randomized, open-label, controlled pilot study. Clin InfectDis. 2014;58(11):1515-22..