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May 26, 2016

Dr. Robert Califf, M.D., Commissioner  
Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

RE: "Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies." [FDA-2013-D-0811]

Dear Dr. Califf,

The Infectious Diseases Society of America (IDSAs) welcomes the opportunity to provide comment on the draft guidance for industry related to the "Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation (FMT) to Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies." IDSAs represents more than 10,000 infectious diseases physicians and scientists devoted to patient care, prevention, public health, education, and research in the area of infectious diseases (ID). The Society's members focus on the epidemiology, diagnosis, investigation, prevention and treatment of infectious diseases around the world.

IDSAs continues to support the FDA decision to employ enforcement discretion on the use of FMT in patients with recurrent *C. difficile* Infection (RCDI). In the most recent draft guidance, the FDA sets forth policy that allows for FMT as a treatment for RCDI without the need for an Investigational New Drug (IND) Application on file, provided the following conditions are met:

- 1) The licensed health care provider treating the patient obtains adequate consent from the patient or his or her legally authorized representative for the use of FMT products. The 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 reasonably foreseeable risks;
- 2) the FMT product is not obtained from a stool bank; 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 for treatment of the patient.

Clinical research has shown that FMT has an efficacy rate of up to 95 percent when used to treat RCDI (van Nood); this has resulted in increasing levels of acceptance on the part of both practicing physicians and the affected patient population. FMT has now become the standard of care for recurrent CDI unresponsive to standard therapies. Given the rising incidence of CDI, we expect the demand for FMT to continue to increase.

While the FDA pursues a comprehensive approach for the study and use of FMT products under IND, it has set forth this draft guidance “to assure that patients with *C. difficile* infection not responding to standard therapies may have access to this treatment, while addressing and controlling the risks that centralized manufacturing in stool banks presents to subjects.”

IDSA understands that the FDA defines a stool bank as “an establishment that collects, prepares, and stores FMT product for distribution to other establishments, health care providers, or other entities for use in patient therapy or clinical research,” and that an establishment that “collects or prepares FMT products solely under the direction of licensed health care providers for the purpose of treating their patients (*e.g.*, a hospital laboratory) is not considered to be a stool bank,” under the FDA guidance. Furthermore, IDSA understands that a stool bank sponsor may request a waiver of certain IND regulations and, in response to the FDA’s request for feedback as to which IND regulations are appropriate to waive, we submit the following comments.

Despite efforts to facilitate the use of FMT to treat RCDI, anecdotal reports from our members maintain that the process to treat patients suffering from RCDI with FMT is still cumbersome as the time needed to screen a potential donor imposes an additional delay to treatment for the patient suffering from RCDI. Many facilities are able to store samples provided from commercial stool banks to have on hand in order to treat cases of RCDI in a timelier manner. The IDSA therefore urges the FDA to apply appropriate oversight of stool banking practices by the suppliers, without undue burdens imposed on the individual physicians and healthcare facilities that plan to treat their own patients who suffer from RCDI with these products. At the time of this writing, more than 11,300 patients have already been treated successfully and safely with commercial stool carefully screened and provided by one of the largest commercial FMT enterprises in the US.<sup>1</sup>

IDSA appreciates the FDA’s efforts to balance patient safety and unencumbered access to FMT for recurrent CDI. Indeed, IDSA has long advocated for measures that facilitate the treatment of recurrent CDI with FMT in a manner that prioritizes patient safety. However, requiring an individual physician provider to be subject to IRB review and a valid IND for the use of FMT samples derived from commercial stool banks to treat RCDI will prove burdensome and will likely result in an unacceptable delay in effective treatment for a potentially fatal infectious illness. The IDSA encourages the FDA to work with stool bank sponsors to establish parameters around the need for an IND to cover FMT for the treatment of RCDI, adherence to which will help to ensure that the stool donor and stool are appropriately qualified by screening and testing and that centralized processing of FMT adheres to appropriate current good manufacturing conditions. The IDSA believes that all IND regulations for healthcare providers

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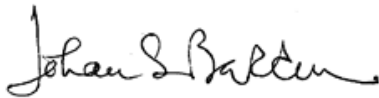
<sup>1</sup> Mark Smith, OpenBiome, Personal communication April, 2016

using FMT product from registered stool banks (i.e., sub-investigators) for the purpose of treating RCDI should be waived with the exception of IND safety reporting of serious and unexpected suspected adverse reactions (21 CFR 312.32). Specifically, sub-investigators using FMT product from registered stool banks for purposes of treating RCDI should only be required to report reactions directly to the IND sponsor through a platform administered by the sponsor. Most FMT patients are elderly and have significant and frequent comorbidities; as a result, reporting adverse events (many of which will be unrelated to FMT) could be burdensome for sub-investigators.

Finally, IDSA believes that a national FMT registry should be established in order to track adverse events and long-term safety of FMT.

We appreciate the FDA's decision to release new draft guidance that will hopefully address some of these issues. We look forward to assisting the FDA further as it develops finalized policy. Please feel free to contact Andrés Rodríguez, IDSA's Director of Practice & Payment Policy at [arodriguez@idsociety.org](mailto:arodriguez@idsociety.org) or 703-299-5146.

Sincerely,

A handwritten signature in black ink that reads "Johan S. Bakken". The signature is written in a cursive, flowing style.

Johan S. Bakken, MD, PhD., FIDSA  
President