

FDA Regulation of Fecal Microbiota for Transplantation

SUMMARY

- Prevailing FDA guidance allows physicians to perform FMT using OpenBiome material to treat *C. difficile* infection not responsive to standard therapy without filing an IND
- Physicians who intend to use FMT to treat *C. difficile* infection not responsive to standard therapy must obtain adequate informed consent from the patient or a power of attorney for the use of FMT products.
- FDA does not require donors to be “known” to either the patient or physician
- FDA does not restrict the use of FMT to any particular route of administration (e.g., colonoscopy, naso-enteric delivery, oral capsule).
- Treatment of indications other than *C. difficile* infection not responsive to standard therapy must be done as part of an IND application to the FDA

As a therapy at the forefront of a cutting-edge field, fecal microbiota transplantation (FMT) follows a unique model of federal oversight. At OpenBiome, we are committed to working with the U.S. FDA to provide safe access to FMT for patients suffering from *C. difficile* infection not responsive to standard therapy, and to support ongoing research into new microbiome-based therapies. Below are answers to common questions about FDA guidelines on the use of fecal microbiota for transplantation.

1. How does the FDA classify fecal microbiota for transplantation?

The FDA considers fecal microbiota for FMT an investigational drug, a classification that typically requires physicians and scientists to file an Investigational New Drug (IND) application if they intend to use the treatment for clinical practice or research.

2. If fecal microbiota is an investigational drug, can physicians perform FMTs without filing an IND?

Yes, for the treatment of *C. difficile* not responsive to standard therapy. When the FDA announced in May 2013 that it would regulate fecal microbiota as an investigational drug, medical professional societies, physicians, and patients reacted with concern over how the policy would limit access to a therapy with 80-90% efficacy rates for this illness and no known short-term safety risks ([Kassam et al., 2013](#)). Responding to these concerns, FDA issued guidance in July 2013 stating that it would exercise “[enforcement discretion](#)” – that is, it would allow doctors to provide FMT for patients with *C. difficile* infections not responding to standard therapies without filing an IND application. Enforcement discretion requires that physicians obtain adequate informed consent from the patient or a legal representative that includes, at minimum, a statement that the use of FMT products to treat CDI is investigational, and a discussion of the therapy's

potential risks and alternative options. Physicians must file an IND if they wish to use FMT products for any other indication.

3. Can physicians perform FMT for diseases other than *C. difficile*?

Yes, but they must file an Investigational New Drug (IND) application with the FDA. We can assist these investigations (see Question 6, below). Please reach out to our research team at science@openbiome.org to learn more about how we can help support your clinical trials.

4. Can physicians use encapsulated fecal microbiota for FMT outside of a clinical trial?

Yes, capsules may be used to treat CDI not responsive to standard therapy without IND.

5. Does the FDA require donors to be “known” to the physician or patient? How does this affect my collaboration with OpenBiome?

No: under the prevailing guidance the FDA does not require donors to be “known” to either the physician or patient.

In March 2014, the FDA released [draft guidance](#) for public feedback only, concerning two proposed changes to the current policy: (1) that the donor be “known” to the patient or physician and (2) that all donor and stool screening be conducted under the supervision of the physician performing the FMT. Medical professional societies raised significant concerns about the proposal's potential to compromise access and safety.

In March 2016, FDA [revised the draft guidance](#) to propose that enforcement discretion be narrowed so that physicians who obtain material from stool banks to treat CDI that is not responsive to standard therapy do so under IND. In their draft, FDA has requested feedback on how to implement this proposal so that it does not create undue burdens for physicians. The proposal was open to public comment through May 31, 2016, and you can review OpenBiome's comment [here](#).

OpenBiome's stool banking model of screening and testing universal donors' material complies with the agency's prevailing enforcement discretion policy.

6. What regulations govern stool banking?

Current guidance on FMT does not specify methods governing donor screening and material screening, preparation and storage. Given this regulatory environment, we're committed to maintaining a very rigorous set of community-enforced standards. Our [Quality and Safety Program](#), overseen by an independent Clinical Advisory Board, comprised of 12 leading physicians and clinical researchers, governs our protocols for donor management, production controls, data collection, and risk mitigation. The

Clinical Advisory Board meets quarterly with our Chief Medical Officer to review the program and make adjustments.

OpenBiome has also worked closely with federal regulators. OpenBiome's Biologics Master File (BB-MF 15543), registered with the FDA, provides regulators with comprehensive insight into OpenBiome's processes. Physicians who wish to conduct FMT under IND may also reference the OpenBiome BB-MF. By doing so, physicians may use our robust quality and manufacturing protocols rather than needing to develop these components internally to support their IND applications.

FMT practitioners should closely evaluate the set of safety and quality controls used in donor and material screening, material processing, and storage and shipping. At OpenBiome, we are committed to ensuring rigorous standards for the safety and quality of our fecal microbiota samples, and to continue working closely with the FDA to expand safe access to FMT for our patients.

7. I am a physician outside of the U.S. who wishes to offer FMT to my patients. What are the regulations for FMT in my country? What are the regulations governing the importation of OpenBiome material?

OpenBiome has some insight into the landscape of FMT regulations in countries outside the U.S., but it is the responsibility of any clinical partner we serve to know and comply with all applicable regulation. Effective May 25, 2018, we are not able to ship treatments to the European Union due to the General Data Protection Regulation. If you are a physician outside of the U.S. interested in working with us, and would like to discuss the regulatory landscape as it applies to your context, please reach out to info@openbiome.org.

8. What recommendations have medical societies issued regarding the use of FMT for recurrent *C. difficile*?

The Infectious Diseases Society of America (IDSA) released guidelines in February 2018 recommending FMT for patients with two or more recurrences of *C. difficile* that has not responded to antibiotic treatment ([McDonald et al., 2018](#)). The American College of Gastroenterology (ACG) recommends that physicians consider the use of FMT for recurrent *C. difficile* after three recurrences ([Surawicz et al. 2013](#)). The American Gastroenterology Association (AGA) refers physicians to working group guidelines that also recommend consideration of FMT following three failed rounds of antibiotics ([Kelly et al. 2015](#)). Additionally, the AGA has recently partnered with OpenBiome and the American Gut Project, as well as the National Institutes of Health, to establish the [AGA FMT Registry](#), which will explore the long-term safety profile of FMT.



See also: Correspondence record between OpenBiome and FDA – written confirmation from FDA that the use of OpenBiome material falls under enforcement discretion.