

Reporting Adverse Events

As with any medical intervention, investigational fecal microbiota transplantation (FMT) carries risks. These include possible transmission of infectious pathogens, multi-drug resistant organisms (MDRO), and microbiome-mediated diseases. Additionally, the administration of investigational FMT poses risks that vary by delivery modality (e.g., colonoscopy, upper endoscopy). Risks associated with investigational FMT should be clearly communicated to your patient during the informed consent process prior to the investigational FMT procedure.

Purpose of reporting adverse events

Clinicians should report adverse events suspected to be related to investigational FMT material within 24 hours of knowledge so that OpenBiome and our manufacturing partner, the University of Minnesota (UMN) can respond expeditiously for the protection of all patients being treated in the OpenBiome network.

Because OpenBiome distributes investigational FMT preparations that are not FDA-approved, our clinical partners are required to report any related serious adverse events. The adverse events contact(s) for your FMT program should be familiar with the risks posed by investigational FMT as well as the Adverse Event reporting protocols. This contact(s) is responsible for communicating reporting protocols to participating physicians before investigational FMT is performed.

What is an Adverse Event (AE)?

An adverse event is defined as *any untoward medical occurrence* in a patient or a clinical trial subject who is administered a drug/product which does not necessarily have a causal relationship with the product. An AE can be an unfavorable sign or unintended sign, a symptom, or a disease temporally associated with the use of a product, whether or not considered related to the product. An AE can arise from the use of the drug (or in combination with another product) and from any route of administration, formulation, or dose including an overdose. An AE also includes, but is not limited to, any clinically significant worsening of a pre-existing condition.

Examples include:

- Any sign (e.g., elevated temperature or blood pressure), Symptoms (e.g., headache, infection), or physical finding (e.g., rash, tender abdomen)
- Laboratory results (e.g., elevated glucose, elevated liver function tests), including those that have worsened in nature, severity or frequency compared to baseline
- Concurrent illness that was not present or worsened in nature (e.g., recurrence of cancer), severity, or frequency compared to baseline
- Injury or accident (i.e., fall)
- Exacerbation or worsening of a pre-existing condition (e.g., worsening of pre-existing hypertension)
- Drug interactions
- Congenital anomalies
- Adverse events associated with Product Quality Complaints
- Unexplained fatal outcome
- AEs documented in literature reports
- Suspected transmission of any infectious agent, which will be classified as an [Adverse Event of Special Interest](#)

What is a Serious Adverse Event (SAE)?

An SAE is any adverse event that results in any of the following:

- Death
- Hospitalization, or prolongation of hospitalization
- A life-threatening event
- A persistent or incapacitating disability
- A congenital anomaly or birth defect
- An important medical event (i.e. the event may not result in death, be life-threatening or require hospitalization but may be considered a serious event based on upon medical judgement. It may jeopardize the patient and may require medical attention or surgical intervention to avoid one of the outcomes listed above)

What is an Adverse Event of Special Interest (AESI)?

AESIs are adverse events that we are particularly interested in to ensure that they are promptly reported to OpenBiome. Any of the below AESIs suspected to be related to FMT material should be reported within 24 hours of knowledge:

- **Suspected Transmission of an Infectious Agent:** Any adverse event where transmission of an infectious organism via the FMT may have occurred.
- **Suspected Transmission of a Multi-Drug Resistant Organism:** Any adverse event where transmission of a multi-drug resistant organism via the FMT may have occurred.

How are AEs, SAEs, or AESIs reported?

If the treating physician or a member of the FMT program staff become aware of an **AE, SAE or AESI that occurs following treatment with an investigational FMT preparation provided by OpenBiome**, please follow these steps:

- 1. Report to OpenBiome within 24 hours:** An adverse event contact or the treating physician must inform OpenBiome using our online reporting tool at <http://www.openbiome.org/report-an-adverse-event>. Consult the checklist on the next page for the information needed to submit this report.
- 2. Follow local procedures:** Your institution may have further measures and reporting requirements in the case of an adverse event. Please consult your local guidelines.
- 3. Investigation:** Upon receipt of an adverse event report, an OpenBiome drug safety professional may reach out to the reporting individual to gather more information on the case and determine next steps. The information gathered during the investigation will be provided to the University of Minnesota, (the manufacturer of the investigational FMT preparation)
- 4. FDA reporting:** The University of Minnesota will use the details of your report and any ensuing investigation to determine if there are any additional reporting requirements, which may include submission of the event to the Food and Drug Administration via [Form FDA 3500A](#).

If you have any questions regarding an adverse event please contact our Clinical Safety team at safety@openbiome.org or call (617) 575-2201, option 1.

Clinician Checklist for Reporting Adverse Events to OpenBiome

To report an adverse event to OpenBiome, please collect the following information, and submit your report through the online form at <https://openbiome.org/fmt-access/report-an-adverse-event/>

Case Information

Patient demographics: Initials, DOB sex, weight, race, and ethnicity

Preexisting medical condition(s)/History

Medication(s) taken prior to investigational FMT and any known allergies

Comprehensive *Clostridioides difficile* infection (CDI) history

- Initial diagnosis technique (e.g. toxin EIA, qPCR, anaerobic culture)
- Modified Horn Index
- Recurrent or refractory disease
- Number of recurrences
- Anti-CDI therapy
- Previous FMT history

Information about the FMT procedure including the following **key pieces of information:**

- The **Unit ID(s)** of the OpenBiome treatment(s) used
- Route of administration
- Pre-procedural preparation by the patient
- Site of material delivery and how verified, if applicable (e.g., fluoroscopic verification of nasogastric tube placement)
- Any documented difficulty during the procedure
- Any significant findings documented during the procedure
- Current patient disposition and discharge date, if applicable

Detailed description of adverse event, including tests performed (with both dates and results), new medical conditions, new medications, etc.