



QUALITY & SAFETY PROGRAM

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Quality & Safety Program

Donors



OpenBiome



Partner Clinicians & Hospitals



Patients

Donor Assessment

Clinical Assessment

Prospective candidates undergo a 200-question clinical evaluation that includes medical histories, behavioral risks, and current health status.

Laboratory Screening

Prospective candidates are screened for over 30 stool and serological tests. Less than 3% qualify to become donors.

High-throughput Sequencing

We perform high-throughput 16S rRNA sequence characterization on stool samples from each of our donors.

Stool Collection & Production Controls

Standardized Stool Examination

Lab technicians evaluate every stool sample based on Bristol type and stool pathology.

Processing Controls

All stool processing occurs under a Class II BSC that is UV-sterilized and cleaned with a sporicidal agent. All equipment is sterilized and/or disposable.

Storage & Shipping Controls

All samples are stored in a glycerol buffer at -80° C, sealed with tamper-evident bands, and transported on dry ice with temperature verification.

Quality Assurance

Continuous Donor Re-qualification

Our donors are under medical monitoring throughout the entire donation and fully rescreened every 60 days.

Quarantine Procedure

Prior to release, donated material is quarantined for 60 days in between two full panel screens at a CLA-certified laboratory.

Safety Aliquots

Multiple samples of all material are preserved at our biomanufacturing site for a minimum of 24 months, enabling retesting as needed.

Monitoring & Traceability

Material Tracking

Clinical partners complete Material Tracking Logs to evaluate unit-specific inventory regularly, enabling response coordination and proactive system-wide recalls if necessary.

Efficacy Monitoring

Partners complete FMT Follow-Up Forms for each patient treated with OpenBiome material, reporting de-identified patient outcome data.

Adverse Event Reporting

All adverse events are reported to OpenBiome and evaluated using a standardized consensus-based decision-making algorithm.

To enable patient access to rigorously screened, high-quality, traceable FMT.

OpenBiome Quality Metrics

Donor Assessment | Stool Collection & Production Controls | Quality Assurance

Purpose

This section summarizes the assays and process controls that OpenBiome has developed to ensure consistent quality and minimize the risk of adverse events.

Documentation

Copies of relevant de-identified screening reports are included in each shipment for all donors that have contributed material to the units being shipped. This documentation is provided to enable OpenBiome's clinical partners to review and interpret these results directly and make their own informed medical decision about the suitability of this material for use in their medical practice.

Disclaimer

Although OpenBiome has designed a rigorous screening regimen, there are risks associated with the use of these materials, including, but not limited to the potential for the presence of infectious agents, risk factors for non-infectious diseases, or pathogens that were not detected by the assays employed. The treating physician should weigh the risks and benefits for each patient to determine the suitability of fecal microbiota transplantation (FMT), and all patients must provide adequate informed consent prior to the procedure.

A. Clinical Assessment

Prior to enrollment, donors (age 18-50), provide informed consent using a Stool Donation Agreement with oversight from FDA. Donors are assessed by a registered nurse and/or supervising clinician with final review by an internal medicine specialist to determine if they meet the following exclusion criteria:

1. Infectious risk factors:

- a. Known HIV or viral hepatitis exposures
- b. High risk sexual behaviors
- c. Use of illicit drugs
- d. Tattoo or body piercing within previous 6 months
- e. Incarceration or history of incarceration
- f. Known history of tropical infection or current communicable diseases
- g. Other personal infectious disease risk factors including Creutzfeldt-Jakob disease (CJD)
- h. Travel history to endemic regions with a high risk acquiring infectious pathogens

- i. Risk factors for multi-drug resistant organisms (MDROs) including work in clinical environment or long-term care facility; persons who have recently been hospitalized or discharged from long term care facilities; persons who regularly attend outpatient medical or surgical clinics; persons who have recently engaged in medical tourism

2. Potentially microbiome-mediated conditions:

- a. Gastrointestinal conditions (e.g., history of IBD, IBS, chronic constipation, chronic diarrhea, Celiac disease)
- b. Atopic conditions (e.g., asthma, atopic dermatitis, eosinophilic disorders of the gastrointestinal tract)
- c. Autoimmune conditions
- d. Chronic pain syndromes
- e. Metabolic conditions (i.e. clinician assessment of BMI and waist circumference)
- f. Neurological conditions
- g. Psychiatric conditions
- h. Malignancy history
- i. Surgeries / Other medical history
- j. Current symptoms
- k. Medications including antibiotics, antifungals, antivirals, and immunosuppressants
- l. Diet
- m. Family history (e.g., family history of IBD, colon cancer)

B. Laboratory Screening

Prospective donors that do not meet any of the exclusion criteria outlined above are then subjected to a battery of serological, stool-based, and nasal swab assays to determine whether infectious pathogens are present. All tests are outsourced to third-party Clinical Laboratory Improvement Amendments (CLIA) certified testing facilities. In some cases, a screening test may be performed by a research lab until a CLIA certified option is available. Abnormal infectious pathogen tests are treated as exclusion criteria for all materials:

1. Serologic testing:

- a. Complete blood count with differential
- b. Hepatic function panel (AST, ALT, ALP, bilirubin, albumin)
- c. HIV-1/2 antigen and antibodies, Fourth Generation
- d. Hepatitis A (IgM)
- e. Hepatitis B panel, (IgM anti-HBc, anti-HBc; HBsAg)
- f. Hepatitis C (HCV antibody)

- g. Hepatitis E (IgM)
- h. *Treponema pallidum* (Cascade with reflex to RPR)
- i. *Strongyloides* IgG, antibody

2. Stool testing:

- a. *Clostridium difficile* toxin A/B, PCR
- b. *Campylobacter* (*jejuni*, *coli*, and *upsaliensis*), PCR
- c. *E. coli* O157, PCR
- d. *Salmonella* spp, PCR
- e. *Shigella* spp, PCR
- f. *Vibrio* (*parahaemolyticus*, *vulnificus*, and *cholerae*), PCR
- g. Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*, PCR
- h. Enteropathogenic *E. coli* (EPEC), PCR
- i. Enteraggregative *E. coli* (EAEC), PCR
- j. Enterotoxigenic *E. coli* (ETEC) *lt/st*, PCR
- k. Enteroinvasive *E. coli* (EIEC), PCR
- l. Vancomycin-resistant *Enterococcus* (VRE), culture-based assay
- m. Extended spectrum beta-lactamase (ESBL), culture-based assay
- n. Carbapenemase-producing gram-negative rods (CRE), culture-based assay
- o. *Yersinia enterocolitica*, PCR
- p. *Plesiomonas shigelloides*, PCR
- q. *Helicobacter pylori*, EIA
- r. Ova and parasites, Microscopic exam
- s. *Giardia lamblia*, PCR
- t. *Cryptosporidium* spp, PCR
- u. *Cyclospora cayetanensis*, PCR
- v. *Entamoeba histolytica*, PCR
- w. *Isospora*, Microscopic exam
- x. Microsporidia, PCR
- y. Rotavirus, PCR
- z. Norovirus, PCR
- aa. Adenovirus, PCR
- bb. Sapovirus, PCR
- cc. Astrovirus, PCR

3. Nasal Swab Culture:

- a. Methicillin-resistant *Staphylococcus aureus* (MRSA), culture based assay

4. SARS-CoV-2

To All material collected from donors since December 1, 2019 will be qualified using a new direct test for the presence of SARS-CoV-2, the virus that causes COVID-19.

The test was developed by CosmosID, a microbiome bioinformatics company, and is being implemented following review and acceptance by the FDA in January. CosmosID is directly testing each stool donation that was processed into FMT preparations. The test uses RT-PCR, the same molecular technique used in nasopharyngeal swab testing, to check for the presence of SARS-CoV-2 genetic material in donor stool.

In addition to testing stool directly for SARS-CoV-2, OpenBiome has implemented the following donor health surveillance measures:

- a. **Donors are subject to regular COVID-19 screening by nasopharyngeal swab.**
 - o Beginning in March 2020, when testing by nasopharyngeal swab for asymptomatic individuals became available locally, OpenBiome began screening donors at a minimum of every 28 days, and in June 2020, began screening donors at a minimum of every 14 days.
 - o Any donors testing positive will have their material destroyed from the 28 days prior to any positive test and will be placed on hold and excluded from providing donations for a minimum of 8 weeks. Donors must fully requalify for the stool donation program in order to return from hold.
- b. **At each stool donation the donor's temperature is taken and donors are evaluated for travel, recent COVID-19 screening outside of OpenBiome, exposure to known or possible COVID-19 cases, and symptoms associated with COVID-19.**
 - o Travel deferral:
 - Donors traveling internationally are deferred from donating for 28 days upon return before undergoing COVID-19 screening by nasopharyngeal swab. Donors traveling domestically are assessed on a case-by-case basis for high-risk activities such as travel by plane, exposure to large groups (>10 people), or travel to states considered high-risk by the Massachusetts Department of Health. In high-risk

cases, donors are deferred from donating for 14 days upon return before undergoing COVID-19 screening by nasopharyngeal swab.

- Exposure:
 - Donors with exposure to known or suspected cases of COVID-19 within the past 28 days will have material from the 28 days prior to exposure destroyed and will be placed on hold for a minimum of 8 additional weeks.
- Symptoms:
 - Donors are screened for symptoms of fever, cough, shortness of breath, sore throat, headache, myalgia, severe fatigue, new loss of smell or taste, nausea, vomiting, or diarrhea.
 - A body temperature of greater than 100.4 °F will result in clinical evaluation to determine if symptoms are compatible with possible COVID-19 or other illness.
 - Material collected in the 28 days prior to any onset of symptoms associated with COVID-19 is destroyed. Donors reporting any symptoms are placed on hold for a minimum of 8 additional weeks.

- c. **All material remains quarantined until we can confirm it meets our safety and quality standards, including those for COVID-19.** Following guidance from the FDA, all FMT units manufactured after December 1, 2019 will be screened for SARS-CoV-2, the virus that causes COVID-19, using a stool-based RT-PCR assay on each raw material lot (every stool sample).

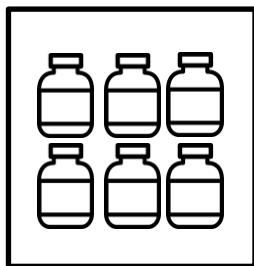
C. Continuous Requalification System

Prospective donors that meet the clinical and laboratory inclusion criteria described above are enrolled as active donors. Once enrolled, donors are carefully assessed for changes in health status. Our continuous requalification system ensures that material is not released for clinical use until donors have passed our rigorous battery of clinical and laboratory evaluations both before and after the material was produced. Our continuous requalification system includes the following features:

- 1. Collection period:** Qualified Donors that meet the above criteria are enrolled to provide material for FMT. Donor material is collected for up to 60 days following the initial screening. During this collection period donors must not violate any of the risk factors identified in Part A.
- 2. Quarantine and dual testing:** All material collected in the collection period is placed in quarantine until the donor has passed a second battery of clinical, serological and stool assessments, as described in Part A and B. Material is only released for clinical use after the donor has successfully passed dual testing, specifically two complete clinical assessments and two full sets of the assays described above both before and after the collection period. Dual testing helps mitigate the risk of false negative intrinsic to some laboratory tests and ensures that the health status of a donor hasn't changed after initial testing.



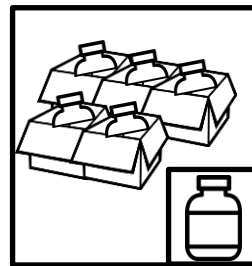
1. Qualified donor passes clinical, serological & stool assessment



2. Stool is collected over 60 days & quarantined



3. Donor re-qualifies by passing clinical, stool & serological assessment



4. Quarantined stool released for clinical use. Stool collected <21 days prior to donor's re-qualification stays in quarantine.

- 3. Seroconversion window:** Testing of individual samples also carries with it the possibility of false negatives from recent infection falling within an infective seroconversion window. Accordingly, a 21-day seroconversion delay is employed before release of any material. Consequently, material in the final 21 days of a collection window is not released until a third screening is performed outside the 21-day seroconversion window.
- 4. Safety aliquot:** Multiple samples of all material are preserved for at least 24 months. If there is a suspected adverse event, the exact material that was used in the recipient may be assessed for pathology.
- 5. Quality Assurance Monitoring:** In contrast to directed donor approaches, de-

identified quality assurance data on efficacy and safety is collected from other patients treated with each donor. As a result, in addition to the intensive laboratory and clinical assessments described above, donors that have previously provided material that has already been safely and effectively used in dozens, or even hundreds of patients, accumulate a track record that mitigates the risk of future FMTs from these experienced donors.

D. Continuous Donor Health Monitoring

In between screens conducted in our continuous requalification system, donors are under active medical supervision as described below:

1. Quality controls at the time of collection for each donation:

- a. Trained technician performs in-person, general health inspection upon sample check-in. If there are any concerns or signs of illness, the material is destroyed and the donor is suspended with a comprehensive supervising clinician's clinical assessment to determine donor eligibility.
- b. Donors are required to complete health status update outlining any behavioral changes, illness or exclusion criteria risk factors during sample check-in process. Any clinical concern triggers a comprehensive by a supervising clinician's clinical assessment to determine donor eligibility.
- c. The sample is assessed by a trained technician for:
 - i. Stool Pathology (melena, hematochezia, mucus). Any sample with concerns for pathology is documented and discarded, triggering a comprehensive clinician-led clinical assessment to determine donor eligibility.
 - ii. Stool Quality (Bristol Stool Score 3-5). All Bristol Stool Score 1-2 samples (constipation) and Bristol Stool Score 6-7 (diarrhea) are documented and discarded, triggering a comprehensive clinician-led clinical assessment to determine donor eligibility.

2. Periodic Quality Assurance Assessment:

- a. Donor Health Check: All donors undergo periodic health checks by a registered nurse and/or clinical assistant supervised by an internal medicine specialist. During the health check, a clinician performs a brief clinical assessment and measures vital signs including BMI, waist circumference, blood pressure, and temperature.

3. Clinical Monitoring:

- a. 24/7 On-Call Access: All donors have on-call access to a registered nurse or physician in the event of a health concern or question.
- b. Defined Illness Protocols: In the event that the donor experiences any abnormal symptoms, including fever or a change in bowel habit, donors are instructed to notify OpenBiome immediately. Donors discuss their symptoms with a clinician and are directed to their primary care provider

(PCP), if needed. If the clinician determines that the donor's symptoms could impact the health of a recipient, the donor is temporarily suspended from participation awaiting examination of the underlying symptoms by clinical assessment and/or diagnostic tests. In the event that a relevant diagnosis is confirmed, the donor is retired from the program at the discretion of OpenBiome's supervising clinician. All material collected from an excluded donor in the preceding collection period is destroyed. In the event of transient or non-concerning symptom, donors will be re-enrolled when symptoms are resolved and at the discretion of the OpenBiome's supervising clinician.

4. Incidental Findings:

- a. In the event of minor, non-contributory, incidental finding (e.g., CBC, liver function panel), a focused clinical assessment will occur. OpenBiome's supervising clinician will determine ongoing eligibility, and provide a summary and rationale in the documentation sent to health care institutions to help a patient's primary physician evaluate clinical suitability.

E. Production and Process Controls

Within OpenBiome's processing facility, technicians follow a carefully validated set of standard operating procedures to ensure consistent quality production. Below we have summarized the basic workflow that is used to register, process and track samples during production:

- 1.** The donor deposits stool in a commode, seals the lid, and places the collection container in one re-sealable LDPE plastic bag (Ri-Pac 2GN or similar) as secondary containment. Donors receive training to prevent contamination during collection.
- 2.** The sealed sample collection container is transferred from the donor to a qualified technician.
- 3.** The mass of the sample is measured, subtracting the tare weight of the collection container.
- 4.** Samples are transferred to a UV-sterilized biosafety cabinet cleaned with a sporicidal agent dedicated for sample processing and isolated from any other processes or materials within OpenBiome's facility.
- 5.** Within the biosafety cabinet, the stool is transferred to a sterile, disposable filter bag. The filter bag fits around the collection commode entirely, so there is no risk of material escaping during this transfer process. All stool material will be added to the same side of the membrane in the filter bag.
- 6.** Sterile dilutant consisting of 12.5% glycerol and a normal saline buffer (0.90% w/v NaCl in water) is added to the filter bag. The volume of buffer added is normalized to the mass of the sample.
- 7.** The sample solution sealed inside the filter bag is then introduced to a homogenizer blender for 120 seconds to suspend the bacterial communities in the aqueous phase buffer. Fibrous material is contained on one side of the bag, while a liquid suspension of the bacterial community is collected on the other side of the 330-micron filter.
- 8.** Samples are then aliquoted into sterile bottles using sterile, disposable serological pipettes.
- 9.** The bottles are capped and frozen immediately at -80°C . Caps are sealed with tamper-evident, perforated PVC shrink bands to ensure samples have an additional level of containment and are not contaminated or tampered with during storage and distribution.
- 10.** Samples are delivered to clinicians on dry ice, in double-containment vessels, with temperature indicators to ensure that samples have not thawed during transportation.
- 11.** Each sample is labeled with a unique barcode enabling full batch traceability.

Monitoring and Traceability

[Material Tracking](#) | [Efficacy Monitoring](#) | [Adverse Event Reporting](#)

The OpenBiome Quality & Safety Program governs our operations from donor assessment through stool processing, monitoring controls, and continuous improvement. In this section, we introduce the roles and responsibilities of clinical sites using OpenBiome material to record and report safety and efficacy data. Your participation helps to ensure that this lifesaving therapy continues to be available for patients nationwide.

Regulatory Context

The U.S. Food & Drug Administration (FDA) regulates fecal microbiota transplantation (FMT) as an investigational drug. Typically, a clinician needs to file an investigational new drug application (IND) to provide an investigational therapy to a patient. However, given published data suggesting that FMT may be an effective therapy for management of recurrent *Clostridioides difficile* infections (rCDI) not responsive to standard therapy, the FDA allows clinicians to provide the therapy to rCDI patients without an IND. We aggregate and share your submissions to our safety data collection program with FDA and across our clinical network.

Your Contribution

We depend on the participation of our clinical partners in the continuous assessment of our material, which is central to our mission of enabling safe, accountable, high-quality access to FMT.

This program requires your participation in three parts:

- 1. Material Tracking Logs** – to be submitted with every order, or as completed, whichever is first
- 2. FMT Follow-Up Forms** – to be submitted 8 weeks after FMT procedure for every patient treated
- 3. Adverse Event Reporting** – to be submitted within 24 hours of an adverse event

These three touchpoints with our clinical network are instrumental to patient safety, and to compliance with FDA reporting requirements. They are also a mandatory component of your partnership with OpenBiome. For clinical programs that are noncompliant with our reporting requirements, we will not ship to the noncompliant program until outstanding data are submitted.

Points of Contact

At registration, OpenBiome asks for important points of contact from the registering site, including:

- One person who will manage the submission of Material Tracking Logs and the distribution of Follow-Up Forms
- One person who will manage the reporting of any suspected adverse events following administration of FMT
- Any physician planning to administer OpenBiome FMT at your facility

This guide explains how these forms should be maintained and submitted, and the rationale behind each requirement. Please review it before selecting the points of contact for your program.

Questions or Comments: You may contact our Clinical Outreach Team at info@openbiome.org, or call 617-575-2201, option 3.

Material Tracking Logs

A Material Tracking Log will be included in every shipment you receive from OpenBiome. We use this log to facilitate inventory tracking across our network. The person in charge of Material Tracking Logs at your facility will also receive a digital copy attached to an email when we ship your order.

The Material Tracking Log will list the Unit ID for every treatment included in your shipment, and any treatments not marked used or destroyed that are still in your inventory. As you receive, store, and use the units in your order, we ask that you record the information shown in Table 1.

Table 1: Sample row from an OpenBiome Material Tracking Log, with columns labeled A through H.

A	B	C	D	E	F	G	H
Item	Unit ID	Expiration Date	Date Shipped	Frozen on Receipt	Unit Status	Physician Initials	Follow-Up Form Sent to Physician
FMP250	0001-0001-01	2/16/20	8/16/19	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Used <input type="checkbox"/> Destroyed		<input type="checkbox"/> Yes <input type="checkbox"/> No

Automatically-generated columns (A-D):

Column A: Item

This column will be automatically generated. This represents the type of product.

Column B: Unit ID

This column will be automatically generated. This represents the unique unit ID of the product.

Column C: Expiration Date

This column will be automatically generated. This represents the last date you can use the material if you store it in a -20 degrees Celsius freezer. The expiration date is 6 months after the ship date.

If you are storing your unit at -80 degrees Celsius, the expiration date is 1 year after the date shipped. This date will not be reflected on the material tracking log.

Column D: Date Shipped

This column will be automatically generated. This is the date OpenBiome shipped the material.

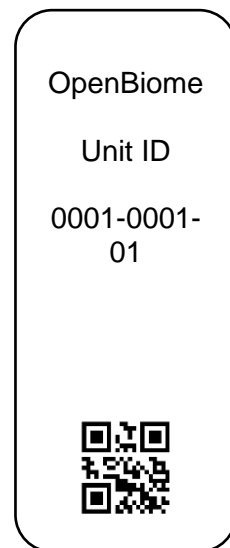


Figure 2: Example of Unit ID sticker affixed to every treatment.

Columns to be completed by the facility (E-H):

Completion of the following columns is mandatory. The MTL contact is responsible for completing these columns as treatments are received, stored, and used.

Column E: Frozen on Receipt

Confirm that the units in your order are frozen at arrival. You may use the temperature indicator affixed to the lid of the shipping cooler or visually inspect that each treatment is frozen solid. We ask you to validate that the cold chain was maintained from our facility to yours to help ensure the treatments' viability.

Column F: Unit Status

Mark the unit "used" once it is administered to a patient. Mark the unit "destroyed" if it is discarded (e.g. upon expiration or after being thawed without use). Do not mark this column if the unit is still in your freezer.

Column G: Physician Initials

For every treatment unit marked "used" on the Material Tracking Log, OpenBiome requires a record of the authorized physician who used that unit. **All physicians**

authorized to provide OpenBiome FMT at your facility must be registered with OpenBiome with current contact information prior to administering OpenBiome FMT, and will appear in a legend on your Material Tracking Log. To add a new authorized physician, please visit www.openbiome.org/add-physician. This record supports the traceability of treatment units throughout our network and allows us to conduct appropriate follow-up regarding adverse events and safety data reporting.

Column H: Follow-Up Form Sent to Physician

Provide an FMT Follow-Up Form (see below) to the administering physician or his or her staff at the time of the procedure. Make sure the proper Unit ID is legibly recorded on the form. Mark "Yes" in this column once the appropriate staff member has received this form.

Which sections need to be complete to avoid a hold on my order?

Orders will be put on hold for the following reasons:

- Frozen upon receipt column not completed
- Usage status is not provided for previously received material
- Physician initials are not complete or are from an unregistered physician

FMT Follow-Up Form

An FMT Follow-Up Form must be completed for each patient that receives an OpenBiome FMT. It asks for de-identified case specifics, including delivery modality, disease phenotype, treatment outcome, and incidence of any adverse events. The form should be provided to the administering physician or his or her staff and returned to OpenBiome after an 8-week post FMT follow-up with the patient.

When we ship an order, the Material Tracking Log contact at your facility will receive an email with the Material Tracking Log and FMT Follow-Up Forms, each pre-populated with a Unit ID that corresponds to a treatment in your shipment. Your shipment will also include a blank paper copy of the FMT Follow-Up Form that you may duplicate and use as needed.

When a treatment is used in a procedure, the Material Tracking Log contact should provide the FMT Follow-Up Form with the matching Unit ID to the administering physician or their staff. Be sure to record this transaction on the Material Tracking Log. Either the digital or paper version of the form may be used, but it is crucial that the Unit ID on the form matches the Unit ID of the treatment being used.

The administering physician should schedule a phone call or office visit with the patient to assess for clinical cure 8 weeks after the FMT procedure, following standard of care. Clinical guidelines define clinical cure of CDI as the absence of diarrhea. Although there is no test of cure, patients with active diarrhea should be evaluated for *C. difficile* recurrence as well as alternative diagnoses (e.g. post-infectious irritable bowel syndrome).

This form allows us to proactively monitor the efficacy of our treatments network-wide and on a per-donor basis. We are committed to tracking outcomes in case a discrepancy should arise.

Additionally, because our partners are treating patients with a novel intervention that is considered investigational, we feel it is our collective duty to the medical community and the patients we serve to collect, evaluate, and share safety and efficacy data on this therapy.

Reporting Adverse Events

As with any medical intervention, Fecal Microbiota Transplantation (FMT) carries certain risks. Risks include possible transmission of infectious pathogens, including multi-drug resistant organisms (MDRO), and a potential risk of causing microbiome-mediated diseases. The procedure of FMT administration (e.g., colonoscopy, upper endoscopy) poses risks that vary by delivery modality. These risks should be clearly communicated to your patient during the informed consent process prior to the FMT procedure.

Purpose of reporting adverse events

Clinicians should notify us of serious adverse events suspected to be related to FMT material within 24 hours of knowledge so we can effectively respond in a timely manner for the protection of all patients being treated in the OpenBiome network.

Because the FDA regulates the stool used in FMT as an investigational new drug, our clinical partners are required to report any related serious adverse events to OpenBiome. The adverse events contacts for your FMT program should be familiar with these risks, and should communicate the following Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs) reporting protocol to all physicians before performing FMT at your institution.

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, 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), physical finding (e.g., rash, tender abdomen)
- Laboratory result (e.g., elevated glucose, elevated liver function tests), including those that has 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 SAEs or AESIs reported?

If the treating physician or a member of the FMT program staff become aware of an **SAE or AESI that occurs following treatment with OpenBiome FMT treatment**, 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 www.openbiome.org/adverse-events. 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.
- 4. FDA reporting:** An OpenBiome medical professional 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 3500](#).

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 www.openbiome.org/adverse-events.

Case Information	
<input type="checkbox"/>	Patient demographics: Initials, DOB sex, weight, race, and ethnicity
<input type="checkbox"/>	Preexisting medical condition(s)/History
<input type="checkbox"/>	Medication(s) taken prior to FMT and any known allergies
<input type="checkbox"/>	Comprehensive <i>Clostridioides difficile</i> infection (CDI) history <ul style="list-style-type: none"> • 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
<input type="checkbox"/>	Information about the FMT procedure including the following key pieces of information: <ul style="list-style-type: none"> • 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
<input type="checkbox"/>	Detailed description of adverse event, including tests performed (with both dates and results), new medical conditions, new medications, etc.

Clinical Advisory Board

Roles and Responsibilities | Principles and Guidelines

As an organization dedicated to enabling safe access to FMT for CDI patients and for catalyzing research of the microbiome, OpenBiome maintains an independent Clinical Advisory Board (CAB) to provide medical advice that will drive safety and best practice in FMT. Members of OpenBiome's CAB have the opportunity to shape the emerging field of FMT across our clinical network. The CAB provides unbiased input that adds to the decision-making capacity of the OpenBiome clinical team. The members of the CAB include world leaders in gastroenterology, infectious diseases and microbiology who bring combined expertise to enhancing safe access to FMT.