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 \textit{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.

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item</td>
<td>Unit ID</td>
<td>Expiration Date</td>
<td>Date Shipped</td>
<td>Frozen on Receipt</td>
<td>Unit Status</td>
<td>Physician Initials</td>
<td>Follow-Up Form Sent to Physician</td>
</tr>
<tr>
<td>FMP250</td>
<td>0001-0001-01</td>
<td>2/16/20</td>
<td>8/16/19</td>
<td>yes</td>
<td>Used</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no</td>
<td>Destroyed</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td> </td>
<td>Yes</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td> </td>
<td>No</td>
<td> </td>
<td> </td>
</tr>
</tbody>
</table>
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.

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 temporarily 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.
Clinicin 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

- Patient demographics: Initials, DOB sex, weight, race, and ethnicity
- Preexisting medical condition(s)/History
- Medication(s) taken prior to 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.