Monitoring & 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 guide, 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

Figure 1 shows which data to collect and submit on each form. 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 Appendix 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>Yes</td>
<td>No</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.

**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.
Material Tracking Logs (continued)

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
- More than 5 units not marked used/destroyed
- Physician initials not complete or incorrect for a unit marked used

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 (Appendix 1) and FMT Follow-Up Forms (Appendix 2), 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.
FMT Follow-Up Form (continued)

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 tested for *C. difficile*. Patients that are negative for *C. difficile* and have ongoing diarrhea likely have an alternative etiology (e.g. post-infectious IBS) and can be deemed a clinical cure for CDI.

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 the largest cohort of FMT patients in the history of this emerging medical practice, 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, FMT carries certain risks. In addition to the possible transmission of infectious pathogens, including multi-drug resistant organisms, and a theoretical risk of causing microbiome-mediated diseases, the procedure itself poses risks that will vary by delivery modality. The risk of such events should be clearly discussed with your patient during the informed consent process prior to the FMT procedure.

The adverse events contact for your FMT program should be familiar with these risks, and should communicate the following Serious Adverse Event (SAE) reporting protocol to all physicians performing FMT at your institution.

*Purpose of reporting adverse events:* We ask that clinicians notify us of SAEs as soon as possible so that we can effectively respond in a timely manner for the protection of all patients being treated in the OpenBiome network. In the case of a serious adverse event suspected to be related to FMT material, timely reporting could be critical in protecting other would-be recipients.

Because the FDA regulates the stool used in FMT as an investigational new drug, our clinical partners are required to report any related adverse events to OpenBiome, and in some circumstances, to the FDA.

*Reporting suspected adverse events:* If the treating physician or a member of the FMT program staff become aware of a serious adverse event that could be related to an 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](http://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.
Reporting Adverse Events (continued)

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 [Form FDA 3500](#).

If you have any questions regarding a suspected adverse event please contact our Clinical Safety team at safety@openbiome.org or call (617) 575-2201, option 9.

**Questions?**

If you have questions, comments, or concerns, please reach out to the Clinical Outreach team at info@openbiome.org, or 617-575-2201. We are here to assist!
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.

<table>
<thead>
<tr>
<th>Case Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient demographics: age, sex, weight, race, and ethnicity</td>
</tr>
<tr>
<td>Preexisting medical condition(s)</td>
</tr>
<tr>
<td>Medication(s) taken prior to FMT and any known allergies</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Information about the FMT procedure including the following <strong>key pieces of information:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The <strong>Unit ID(s)</strong> of the OpenBiome treatment(s) used</td>
</tr>
<tr>
<td>Route of administration</td>
</tr>
<tr>
<td>Pre-procedural preparation by the patient</td>
</tr>
<tr>
<td>Site of material delivery and how verified, if applicable (e.g., fluoroscopic verification of nasogastric tube placement)</td>
</tr>
<tr>
<td>Any documented difficulty during the procedure</td>
</tr>
<tr>
<td>Any significant findings documented during the procedure</td>
</tr>
<tr>
<td>Current patient disposition and discharge date, if applicable</td>
</tr>
</tbody>
</table>

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