# Quality & Safety Program

<table>
<thead>
<tr>
<th>Donor Assessment</th>
<th>Stool Collection &amp; Production Controls</th>
<th>Quality Assurance</th>
<th>Monitoring &amp; Traceability</th>
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<tbody>
<tr>
<td><strong>Clinical Assessment</strong> Prospective candidates undergo a 200-question clinical evaluation that includes medical histories, behavioral risks, and current health status.</td>
<td><strong>Standardized Stool Examination</strong> Lab technicians evaluate every stool sample based on Bristol type and stool pathology. <strong>Processing Controls</strong> All stool processing occurs under a Class II BSC that is UV-sterilized and cleaned with a sporicial agent. All equipment is sterilized and/or disposable.</td>
<td><strong>Continuous Donor Re-qualification</strong> Our donors are under medical monitoring throughout the entire donation and fully rescreened every 60 days.</td>
<td><strong>Material Tracking</strong> Clinical partners complete Material Tracking Logs to evaluate unit-specific inventory regularly, enabling response coordination and proactive system-wide recalls if necessary.</td>
</tr>
<tr>
<td><strong>Laboratory Screening</strong> Prospective candidates are screened for over 30 stool and serological tests. Less than 3% qualify to become donors.</td>
<td><strong>Storage &amp; Shipping Controls</strong> All samples are stored in a glycerol buffer at 80°C, sealed with tamper-evident bands, and transported on dry ice with temperature verification.</td>
<td><strong>Quarantine Procedure</strong> Prior to release, donated material is quarantined for 60 days in between two full panel screens at a CLA-certified laboratory.</td>
<td><strong>Efficacy Monitoring</strong> Partners complete FMT Follow-Up Forms for each patient treated with OpenBiome material, reporting de-identified patient outcome data.</td>
</tr>
<tr>
<td><strong>High-throughput Sequencing</strong> We perform high-throughput 16S rRNA sequence characterization on stool samples from each of our donors.</td>
<td></td>
<td><strong>Safety Aliquots</strong> Multiple samples of all material are preserved at our biomanufacturing site for a minimum of 24 months, enabling retesting as needed.</td>
<td><strong>Adverse Event Reporting</strong> All adverse events are reported to Finch Therapeutics and evaluated using a standardized consensus-based decision-making algorithm.</td>
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</tbody>
</table>

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).

Finch Therapeutics
As of March 1, 2017, OpenBiome licenses Finch Therapeutics to carry out biomanufacturing of FMT preparations. As the manufacturer, Finch Therapeutics is responsible for implementing certain aspects of OpenBiome’s Quality & Safety Program.

A. Clinical Assessment
Prior to enrollment, donors (age 18-50), receive informed consent with oversight from the New England Institutional Review Board (IRB). Donors are assessed by a registered nurse and/or physician 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

2. Potentially microbiome-mediated conditions:

j. Gastrointestinal conditions (e.g., history of IBD, IBS, chronic constipation, chronic diarrhea, Celiac disease)

k. Atopic conditions (e.g., asthma, atopic dermatitis, eosinophilic disorders of the gastrointestinal tract)

l. Autoimmune conditions

m. Chronic pain syndromes

n. Metabolic conditions (i.e. clinician assessment of BMI and waist circumference)

o. Neurological conditions

p. Psychiatric conditions

q. Malignancy history

r. Surgeries / Other medical history

s. Current symptoms

t. Medications including antibiotics, antifungals, antivirals, and immunosuppressants

u. Diet

v. 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. As a condition for participation in this program, donors are required to submit written authorization for the disclosure of the results of these tests to Finch Therapeutics, in compliance with the Health Insurance Portability and Accountability Act (HIPAA). Finch redacts all personal identifying information from each report and shares copies of de-identified diagnostic reports with OpenBiome’s clinical partners. Documentation is provided for the battery of tests prior to enrollment of a donor and for tests performed at the end of the collection period. 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. *Treponema pallidum* (Cascade with reflex to RPR)
h. HTLV I and II, antibody
i. Strongyloides IgG, antibody

2. **Stool testing:**
   a. *Clostridium difficile* toxin B, PCR
   b. Culture-based assays for common enteric pathogens (including *Salmonella, Shigella, Campylobacter, Vibrio*)
   c. Shiga toxin EIA with reflex to E.coli 0157 culture
d. *Helicobacter pylori*, EIA
e. Ova and parasites
f. *Giardia lamblia*, EIA
g. *Cryptosporidium*, EIA
h. *Cyclospora and Isospora*, Microscopic exam
i. *Microsporidia*, Microscopic exam
j. Rotavirus, EIA
k. Norovirus, Real-time PCR
l. Adenovirus, EIA
m. Vancomycin-Resistant Enterooccus (VRE), culture-based assay
n. Extended spectrum beta-lactamase (ESBL), culture based assay
o. Carbapenemase producing gram-negative rods (CRE), culture based assay

3. **Nasal Swab Culture:**
   a. Methicillin-resistant Staphylococcus aureus (MRSA), culture based assay

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.

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, many of our donors have previously provided material that has already been safely and effectively used in dozens, or even hundreds of other patients. This direct clinical-track record 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. Physician-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 physician-led 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 physician-led clinical assessment to determine donor eligibility.

c. The sample is assessed by a physician-trained technician for 2 factors:
   i. Stool Pathology (melena, hematochezia, mucus). Any sample with concerns for pathology is documented and discarded, triggering a comprehensive physician-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 physician-led clinical assessment to determine donor eligibility.

2. Randomized Quality Assurance Assessment
   a. Donor Health Check: All donors undergo periodic, random health checks by a registered nurse and/or physician 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 Finch Therapeutics 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 the Finch Chief Medical Officer and/or Finch Therapeutics’ Clinical Advisory Board (CAB), which includes thought leaders in infectious diseases, medical microbiology and gastroenterology. 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 Finch Chief Medical Officer and/or the Finch CAB.

4. Incidental Findings:
   a. In the event of minor, non-contributory, incidental finding (e.g. CBC, liver function panel), a physician-led focused clinical
assessment will occur. The physician 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 Finch’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 Finch’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 diluant 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

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 life-saving 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 the therapy to a patient. Given the efficacy of FMT for treatment of recurrent Clostridium difficile infections (rCDI), 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 constituent 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 what data to collect and submit on each form. These touch points with our clinical network are instrumental to patient safety and complying 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 issue three warning notices. After the third notice, we will not ship to the noncompliant program until pending data are submitted.

Points of Contact
At registration, OpenBiome asks for three important points of contact from the registering site:
- One person who will be managing the submission of Material Tracking Logs and the distribution of FMT Follow-Up Forms
- Two people who will be managing the reporting of any adverse events related to FMT

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.

Further Questions or Comments
You may reach 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 (see Figure 2) for every treatment included in your shipment, and any treatments 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. See a sample log on p. 7.

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

<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>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Item</td>
<td>Unit ID</td>
<td>Expiration Date</td>
<td>Ship Date</td>
<td>Date Received</td>
<td>Frozen on Receipt</td>
<td>Unit Status</td>
<td>Administering Physician</td>
</tr>
<tr>
<td>FMP250</td>
<td>0001-0001-01</td>
<td>2/16/15</td>
<td>8/16/14</td>
<td>☑ Yes ☑ No</td>
<td>☑ Used ☑ Destroyed</td>
<td>☑ Yes ☑ No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Columns A through D: OpenBiome will complete Columns A – D when we ship an order to you. Each Unit ID in Column B is a unique identifier that corresponds to a matching Unit ID label on a treatment included in your shipment. The expiration date in Column C can be found on both the box and bottle of our 250 mL Lower Delivery preparation and FMT Capsule G3, and just on the box of our 30 mL Upper Delivery preparation.

Columns E through I: You are responsible for completing these columns as treatments are received, stored, and used.

Column E: Record the date that your facility received the treatment unit(s).

Column F: 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.

Purpose of Columns E and F: We ask you to validate that the cold chain was maintained from our facility to yours to help ensure the treatments’ viability.

Column G: 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). Treatments may be discarded following your internal protocols for handling human waste.

Purpose of Column G: Should there be recall of OpenBiome treatments, it might only apply to specific treatment units (e.g. units associated with a particular donor). It is critical that your facility maintain unit-specific inventory records (and note Unit IDs in patients’ records) to facilitate an appropriate response.

Column H: Once a treatment is prepped for use in a procedure, record the name of the administering physician.
Material Tracking Logs (continued)

**Column I:** 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.

_Purpose of Columns H and I:_ We will use this information to monitor your program’s compliance with the FMT Follow-Up Form requirement on a per-physician basis.

**Progress Report:** Appended to each digital copy of the Material Tracking Log, we list a) the Unit IDs for which we received FMT Follow-Up Forms since your last order, and b) the Unit IDs and administering physician associated with pending FMT Follow-Up Forms. We provide this summary as a tool, but it is your responsibility to ensure that all reporting requirements are met. See sample on p. 9.

**FMT Procedure Tracker:** We provide this form as an _optional_ tool to help you trace treatment units internally. It is intended only to facilitate your own recordkeeping. You should not return it to us. See sample on p. 11.

**FMT Follow-Up Form**

An FMT Follow-Up Form must be completed for each patient that receives an FMT from OpenBiome. 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 the patient’s 8-week follow-up.

When we ship an order, the Material Tracking Log contact at your facility will receive an email with the Material Tracking Log (see above) 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. See sample form on p. 8.

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 (Column I, see above). 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 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.

_Purpose of the FMT Follow-Up Form:_ 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 such a discrepancy should arise.

Additionally, because our partners are effectively 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.

* (*>=3 stools in 24 or fewer consecutive hours, Bristol Stool Score >=6*)
Reporting Adverse Events

As with any medical intervention, FMT carries certain risks. In addition to the possible transmission of infectious pathogens 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 contacts for your FMT program should be familiar with these risks, and should communicate the following SUSAR (Suspected Unexpected Serious Adverse Reaction) reporting protocol to all physicians performing FMT at your institution.

Purpose of reporting adverse events: We ask that clinicians notify us of SUSARs 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 an adverse event related to FMT material, timely reporting could be critical in protecting other would-be recipients.

As well, 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. We will assist you with this process.

Reporting suspected adverse events: If the treating physician or a member of the FMT program staff become aware of a SUSAR 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. Consult the checklist on the next page for the information needed to submit this report. This report will be passed on to Finch Therapeutics, OpenBiome’s licensed manufacturer.

2. Triage call: Upon receipt of an adverse event report, a Finch medical professional will reach out to the report’s author to triage the case according to FDA guidelines* and determine next steps in the investigation.

3. FDA reporting: A Finch medical professional will use the details of your report and any ensuing investigation to advise you and your program of any additional reporting requirements, which may include submission of Form FDA 3500. Please consult with us before filing Form FDA 3500, as over-reporting can create inefficient delays.

If you have any questions regarding an adverse event please contact us 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. This report will be passed on to Finch Therapeutics, OpenBiome’s licensed manufacturer. A member of the safety team from Finch will contact you.

<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>
<tr>
<td>❑ Comprehensive <em>Clostridium difficile</em> infection (CDI) history</td>
</tr>
<tr>
<td>❑ Initial diagnosis technique (e.g. toxin EIA, qPCR, anaerobic culture)</td>
</tr>
<tr>
<td>❑ Modified Horn Index</td>
</tr>
<tr>
<td>❑ Recurrent or refractory disease</td>
</tr>
<tr>
<td>❑ Number of recurrences</td>
</tr>
<tr>
<td>❑ Anti-CDI therapy</td>
</tr>
<tr>
<td>❑ Previous FMT history</td>
</tr>
<tr>
<td>❑ Information about the FMT procedure including the following key pieces of information:</td>
</tr>
<tr>
<td>❑ The Unit ID(s) 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>
<tr>
<td>❑ Detailed description of adverse event, including tests performed (with both dates and results), new medical conditions, new medications, etc.</td>
</tr>
</tbody>
</table>

*A Finch clinician will assist you in determining if the adverse event meets the criteria for reporting to the FDA. Adverse events should only be reported to the FDA if it meets ALL three of the following criteria as outlined in 21 CFR 312.32(c)(1)(i)):*

1. **Suspected:** Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the FMT material caused the adverse event. For the purposes of FDA safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between FMT and the adverse event.

2. **Unexpected:** An adverse event or suspected adverse reaction is considered “unexpected” if it is not consistent with the risk information described in the FMT inserts.

3. **Serious:** An adverse event or suspected adverse reaction is considered “serious” if it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or
significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect.
Adverse Event Decision Algorithm Overview

As part of our commitment to enabling safe, accountable, high-quality treatments for FMT patients, OpenBiome requires all of its partners to report adverse events to the FDA and to OpenBiome. OpenBiome will pass this report on to Finch Therapeutics, OpenBiome’s licensed manufacturer of FMT preparations. A Finch medical professional will reach out to the report's author to triage the case according to FDA guidelines and determine next steps in the investigation. We have established a series of actions that are triggered upon an adverse event report. This algorithm allows OpenBiome, its partners, and Finch Therapeutics to coordinate responses in a timely and comprehensive manner.
Figure 1. Adverse events decision algorithm
Adverse Event Decision Algorithm Steps

1.A. Suspected adverse event occurs
[Actors: Clinician, Patient]
Fecal microbiota transplantation (FMT) remains an investigational therapy and OpenBiome expects clinicians to perform a follow-up assessment with patients up to eight weeks after FMT to determine whether the patient has experienced a recurrence or whether any short-term adverse events have occurred as a result of the FMT. Long-term adverse events, if suspected, should also follow the same adverse event decision pathway.

Adverse event is defined as any untoward medical occurrence associated with the use of FMT and does not imply judgment about causality.

As soon as the clinician is made aware of an adverse event (AE) then proceed to Step 1.B.

1.B. Follow institutional adverse event policies
[Actor: Clinician]
The clinician should follow local adverse event policies and protocols that have been established at the clinician’s institution.
Proceed to Step 1.C.

1.C. Determine if the adverse event requires reporting to OpenBiome
[Actor: Clinician]
Partners should determine whether the AE requires reporting to OpenBiome. Four questions should be answered in order to determine whether reporting OpenBiome is necessary:

1. Determine the relatedness of the AE to the FMT material or procedure
2. Determine if the AE is expected or unexpected
3. Determine the severity of the AE
4. Determine if the AE requires reporting to OpenBiome

The decision tree below summarizes how clinicians should determine when to report an AE to OpenBiome:
**Figure 2.** Decision tree to determine when clinicians should report an AE to OpenBiome

1.C.1. Determine the relatedness of the AE to the FMT material or procedure

The AE must, in the opinion of the most responsible physician, be possibly related or definitely related on the initial assessment to be reported to OpenBiome. A modified Naranjo scale is used (NIH, 2011):

<table>
<thead>
<tr>
<th>Determination</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td><strong>Definitely Related</strong></td>
</tr>
<tr>
<td></td>
<td>The adverse event is clearly related to the FMT material – i.e. an event that follows a reasonable temporal sequence from administration of the FMT material, follows a known or expected response pattern to the FMT material, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the patient’s clinical state.</td>
</tr>
</tbody>
</table>
Possibly Related
An adverse event that follows a reasonable temporal sequence from administration of the FMT material follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.

Not related:
The adverse event is clearly not related to the FMT material, i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or causal relationship is considered biologically impossible.

1.C.2. Determine if the AE is expected or unexpected
Based on the peer review literature, potential expected adverse events are highlighted below:

<table>
<thead>
<tr>
<th>Determination</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ 1. Common, mild adverse reactions:</td>
<td>Transient diarrhea (70%), Transient abdominal cramps/discomfort (20%) and nausea (&lt;5%) in 24 hours post-FMT. Fever, bloating, belching, vomiting, borborygmus has also been reported. Constipation (20%) and excess flatulence (25%) has been reported in follow-up. There is also a theoretical risk of small intestinal bacterial overgrowth.</td>
</tr>
</tbody>
</table>
| ☐ 2. Rare, serious adverse events: | There have not been any definitely related serious adverse events attributable to FMT material. However, the following risks should be considered:  
  - Infection: Although this material has been screened for bacteria, viruses, fungi and parasites there is a risk of transmission of known and unknown infectious organisms contained in the donor stool. Post-FMT bacteremia (e.g. E. coli), sepsis and fatal events may rarely occur;  
  - Inflammatory bowel disease (IBD) flare in those with underlying IBD;  
  - Allergy/Anaphylaxis to antigens in donor stool;  
  - Non-infectious disease transmission: There is a theoretical risk of developing disease that may be related to donor gut microbiota. These include obesity, metabolic syndrome, cardiovascular disease, autoimmune conditions, allergic/atopic disorders, neurologic disorders, psychiatric conditions and malignancy. Persons with these known
conditions are excluded from donating stool.

3. **Unexpected adverse events:**
   Any adverse event that is not listed above.

1.C.3. **Determine the severity of the AE**
Using the NIH Severity Scale determine the severity of the AE:

<table>
<thead>
<tr>
<th>Determination</th>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>1</td>
<td>Mild: Symptoms causing no or minimal interference with usual social and functional activities</td>
</tr>
<tr>
<td>☐</td>
<td>2</td>
<td>Moderate: Symptoms causing greater than minimal interference with usual social and functional activities</td>
</tr>
<tr>
<td>☐</td>
<td>3</td>
<td>Severe: symptoms causing inability to perform usual social and functional activities</td>
</tr>
<tr>
<td>☐</td>
<td>4</td>
<td>Potentially life-threatening: Symptoms causing inability to perform basic self-care functions OR Medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death</td>
</tr>
<tr>
<td>☐</td>
<td>5</td>
<td>Death: Fatal event related to adverse event</td>
</tr>
</tbody>
</table>

1.C.4. **Determine if the AE requires reporting to OpenBiome**
Based on response to these three questions, only if the AE fulfills the following criteria should it be reported to OpenBiome:

<table>
<thead>
<tr>
<th>Criteria 1</th>
<th>Criteria 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely or possibly related AND one of the following:</td>
<td>Common, mild adverse events AND Grade 4 or higher.</td>
</tr>
<tr>
<td></td>
<td>Rare, serious adverse events AND Grade 3 or higher.</td>
</tr>
<tr>
<td></td>
<td>Unexpected adverse events AND Grade 3 or higher.</td>
</tr>
</tbody>
</table>

If on the initial assessment by the most responsible physician, the AE fulfills all of the above criteria for reporting then proceed to **Step 1.D.**

If on the initial assessment by the most responsible physician, the AE does not fulfill the above criteria for reporting then the AE does not need to be reported to OpenBiome or the FDA.

Clinicians may contact our Clinical Safety team to discuss immediate questions at safety@openbiome.org or call (617) 575-2201, option 1.
1.D. Report the adverse event to OpenBiome within 24 hours
[Actor: Clinician, OpenBiome]
The clinician must report the suspected adverse event to OpenBiome within 24 hours through the online AE reporting form at www.openbiome.org/adverse-events.

Clinicians may also contact our Clinical Safety team to discuss immediate questions at safety@openbiome.org or call (617) 575-2201, option 1.

On the AE reporting form the clinician must provide de-identified case information on the following:

| □ | Patient Demographics: Age, sex, weight, race, and ethnicity |
| □ | Preexisting medical condition(s) |
| □ | Medication(s) taken prior to FMT and any known allergies |
| □ | Comprehensive Clostridium 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: |
| | • Unit ID(s) of the OpenBiome treatment(s) used |
| | • Route of administration |
| | • Pre-procedure patient preparation |
| | • Site of instillation of material |
| | • 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. |

All adverse events reported to OpenBiome are logged in both electronic and paper form.
Information gathered through the online reporting form will be directly relayed to the Finch Therapeutics Safety Team. A Finch Therapeutics clinical safety professional will manage the case from this point onwards.

Proceed to Step 1.E.

1.E. Triage call
[Actor: Clinician, Finch Therapeutics]
On reporting the suspected adverse event to Finch Therapeutics through the online reporting form, an Finch Therapeutics clinician will schedule a call with the reporting team to discuss the case. Prior to the call, Finch Therapeutics will collate the following information:

<table>
<thead>
<tr>
<th>Information</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor related documents</td>
<td>Including all donor screens performed on the relevant donor by a CLIA-certified laboratory, all accompanying donor medical history, screens, and health status held at Finch</td>
</tr>
<tr>
<td>Manufacturing related documents</td>
<td>OpenBiome Material Tracking Logs with information on the relevant material and units</td>
</tr>
<tr>
<td>Available safety and efficacy information for donor material</td>
<td>OpenBiome FMT Follow-Up Forms returned from partners who utilized donor material</td>
</tr>
<tr>
<td>Details on specimen</td>
<td>Any currently known information on the affected donor’s specimen relevant to the investigation</td>
</tr>
</tbody>
</table>

During the call the case is discussed in-depth with the reporting clinician. The aim of the call is to assess three areas that will determine the investigation and reporting pathway for the case:

1. If the AE is a Serious Unexpected Suspected Adverse Reaction (SUSAR) and requires reporting to the FDA or if it is suspected to be related to FMT material but does not fulfill the criteria for SUSAR (i.e. non-SUSAR).
2. If the AE is an infectious or non-infectious disease diagnosis
3. If the AE is FMT procedure related

The method for evaluating these three is as are as follows:

1.E.1. SUSAR and FDA reporting
During the call, Finch Therapeutics will assist the reporting physician to determine whether, on initial assessment, the suspected adverse event meets any of the following outlined in 21 CFR 312.32(c)(1)(i):
Determination | Definition
--- | ---
☐ **Serious:**
An adverse event is considered “serious” if, in the view of either the clinician or OpenBiome, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

☐ **Unexpected:**
An adverse event is considered “unexpected” if it is not listed as an expected adverse event or is not listed at the specificity or severity that has been observed. Expected AE’s are outlined in Step 1.C..

☐ **Suspected:**
Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the FMT material caused the adverse event. For the purposes of safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the FMT material and the adverse event.

Should an adverse event meet all three of the criteria above, it is determined to be a Suspected Unexpected Serious Adverse Reaction (SUSAR).

If the adverse event is only suspected then it is classified as a Suspected Non-SUSAR.

1.E.2. Infectious or non-infectious disease diagnosis
The adverse event must be classified as either infectious or non-infectious disease.

<table>
<thead>
<tr>
<th>AE Diagnosis</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious Disease</td>
<td>Diagnosis involves a disease caused by known agents, such as bacteria, viruses, fungi or parasites, and is known to be passed from person-to-person</td>
<td>e.g. HIV, viral hepatitis, Giardia, Salmonella bacteremia</td>
</tr>
<tr>
<td>Non-communicable</td>
<td>Diagnosis involves a non-</td>
<td>e.g. Inflammatory bowel</td>
</tr>
</tbody>
</table>
Disease | communicable disease, such as a medical condition that is non-infectious and not believed to be directly transmissible among people | disease, Diabetes, Sjogren’s syndrome, Anaphylaxis, Mood disorders

1.E.3. FMT procedure related
If the adverse event is determined to be unrelated to FMT material then there should be an assessment made to evaluate whether it is FMT procedure related.

<table>
<thead>
<tr>
<th>AE Diagnosis</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMT Procedure</td>
<td>It is possible or definite that the adverse event is attributable to the FMT administration procedure or delivery modality</td>
<td>e.g. Perforation during colonoscopy</td>
</tr>
</tbody>
</table>

Following this initial triage call the AE is categorized in collaboration with the reporting clinician and a report card is completed by the Finch Therapeutics clinician:
- Suspected AE (SUSAR or Suspected non-SUSAR): Proceed to 2.A
- Non-suspected AE: If not FMT procedure or FMT material related proceed to Endpoint A
- FMT procedure related: Proceed to Endpoint B
- Disagreement or uncertain attribution: Proceed to 3.A

2.A. Stop shipping all donor material
[Actor: Finch Therapeutics]
Finch Therapeutics will halt shipments of and physically quarantine all material made from the donor whose stool was used in the reported adverse event. This quarantine will continue until the investigation has been completed and one of the endpoints is reached.
- If the AE is defined as a SUSAR in Step 1.E (Triage call) proceed to Step 2.B.
- If the AE is defined as a Suspected non-SUSAR and infectious disease in Step 1.E (Triage call) proceed to Step 2.C.
- If the AE is defined as a Suspected non-SUSAR and non-infectious disease in Step 1.E (Triage call) proceed to Step 2.D.

2b. SUSAR: Submit FDA MedWatch Form 3500 and 3500A to the FDA
[Actor: Clinician, Finch Therapeutics]
If the AE is defined as a SUSAR in Step 1.E (Triage call) then an FDA MedWatch Form 3500 must be submitted to the FDA. Instructions for completing FDA MedWatch Form 3500 can be found on the FDA website.¹

Once the adverse event is considered to be a SUSAR the F3500 form must be submitted to the FDA by fax at 800-FDA-0178 or by standard mail to:

The FDA Safety Information and Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787.

The completed F3500 form must also be forwarded to Finch Therapeutics.

Finch Therapeutics will submit an F3500A form in response to the FDA within 7 calendar days for a fatal SUSAR or within 15 calendar days for a non-fatal SUSAR.

Should any new information emerge during the investigation a second F3500A form will be submitted by Finch Therapeutics updating the FDA.

If the AE is defined as a SUSAR and infectious disease in Step 1.E (Triage call) proceed to Step 2.C.

If the AE is defined as a SUSAR and non-infectious disease in Step 1.E (Triage call) proceed to Step 3.B.

2.C. Rescreen safety aliquot and/or donor for presence of infectious disease
[Actor: Finch Therapeutics]
Finch Therapeutics stores safety aliquots of every fecal microbiota preparation for at least 24 months for any retesting or clinical follow-up. These safety aliquots, as with all of Finch Therapeutics' material, are stored at -80°C in an ultra-low temperature freezer equipped with a remote alarm triggered by any abnormal temperature fluctuations and a temperature chart recorder to ensure temperatures have remained at levels appropriate for cryo-preservation.

Finch Therapeutics will retest the safety aliquot of the donor material under investigation for the existence of the infectious disease. Only pathogens screened for in the Finch Therapeutics CLIA certified panel will be performed. If the pathogen is not performed in the Finch Therapeutics CLIA certified panel the AE will be taken to the CAB.

¹ Available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf
Proceed to **Step 3.A.**

**3.A. Risk assessment**  
*[Actor: Clinician, Finch Therapeutics]*

Following the investigation, Finch Therapeutics and the reporting clinician must determine whether the diagnosed AE is a patient-specific or universal threat as follows:

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient dependent</td>
<td>Based on the qualified medical opinion mutually held between Finch Therapeutics and the clinician, it is determined that the AE is most likely due to current or historical health factors and/or patient-specific variables that are predominantly unique to the patient experiencing the AE, and does not pose a broader possible threat.</td>
</tr>
<tr>
<td>Donor dependent</td>
<td>Based on the qualified medical opinion mutually held between Finch Therapeutics and the clinician, it is determined that the AE is most likely due to factors related to the donor used in the AE, irrespective of patient factors, and could pose a broader possible threat. Any adverse event where there is a positive safety aliquot result is categorized as “donor dependent”.</td>
</tr>
</tbody>
</table>

The AE should also be reassessed for relatedness following the investigation as per the definitions in Step 1.E using the modified Naranjo scale is used (NIH, 2011):

<table>
<thead>
<tr>
<th>Determination</th>
<th>Definition</th>
</tr>
</thead>
</table>
| ☑             | **Definitely Related**  
The adverse event is clearly related to the FMT material – i.e. an event that follows a reasonable temporal sequence from administration of the FMT material, follows a known or expected response pattern to the FMT material, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the patient’s clinical state. |
| ☐             | **Possibly Related**  
An adverse event that follows a reasonable temporal sequence from administration of the FMT material follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors. |
| ☐             | **Not related:**  
The adverse event is clearly not related to the FMT material, i.e.
another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or causal relationship is considered biologically impossible.

If the threat type of the AE is uncertain, Finch Therapeutics and the clinician cannot reach a consensus on the threat type or the AE is classified as possibly related, proceed to **Step 3.B.**

Otherwise proceed to **Step 4.A.**

**3.B. Clinical Advisory Board gives external counsel**

**[Actor: Clinical Advisory Board, Finch Therapeutics]**

As part of Finch Therapeutics' commitment to enabling safe, accountable, high-quality treatment for FMT patients, Finch Therapeutics maintains an objective and independent Clinical Advisory Board (CAB) to provide qualified medical advice. The CAB provides unbiased input that adds to the decision-making capacity of Finch Therapeutics staff, as Finch Therapeutics strives to improve the standard of care for FMT.

The Clinical Advisory Board consists of an odd number of qualified medical professionals who meet to review any operations at Finch Therapeutics that would benefit from the input of a broader group of clinicians. The CAB meets biannually, and can also be convened at the request of Finch Therapeutics’ Board of Directors or Management Team. Specifically, member(s) of the CAB with case-appropriate expertise would be convened to provide objective and independent expertise on the type of threat and classification of the suspected AE.

If the AE is “possibly related” after the collaborative investigation, the CAB will determine the threat type and advise on the action steps. After considering the opinion of the CAB return to the previous step.

**4.A. Closing report and submission of an updated F3500A**

**[Actor: Finch Therapeutics]**

A closing report will be completed by the Finch Therapeutics clinician and physician for internal documentation. The report will provide an in-depth review of the adverse event including:

- Unit ID(s)
- Patient clinical course
- Patient lab results
- Donor efficacy and safety record
- Joint investigation by reporting clinician and Finch Therapeutics
- CAB review (if necessary)
- Consensus-based final determination of:
  - NIH severity grade
  - NIH relatedness grade
  - Threat level
  - AE protocol endpoint

Following submission of the 7-day or 15-day preliminary F3500A form Finch Therapeutics will submit an updated F3500A referencing the original submission with new information (e.g., identification of an infectious disease pathogen in the safety aliquot).

Finch Therapeutics will maintain records of the closing report and share in a de-identified format any lessons learned from the case. All closing reports will be reviewed by the CAB on a quarterly basis.

Following investigation:
- If the AE is no longer suspected to be related to FMT material return to Step 1.E
- If the AE remains suspected to be FMT related and is donor dependent in Step 4.A, proceed to Endpoint C
- If the AE remains suspected to be FMT related and is patient dependent, in Step 4.A, proceed to Endpoint D
Adverse Event Decision Algorithm Endpoints

Endpoint A
[Actor: Finch Therapeutics]
1. **No further action required:** Finch Therapeutics and/or the partner has determined that it is definite that the complication is not attributable to the FMT procedure or the FMT material. No further action is required on the part of OpenBiome or Finch Therapeutics.
2. **Donor material shipping:** Donor material can be taken out of quarantine and shipped for routine clinical use.

[Actor: Partners]
1. **Complete any institutional adverse event protocols if needed:** Partners should complete any applicable adverse event protocols that are required by the FDA or their institution due to the complication.

Endpoint B
[Actor: OpenBiome]
1. **Include in Quality & Safety Program Biannual Report:** OpenBiome will aggregate all reports of AEs within its partner network in OpenBiome’s Quality & Safety Program (Q&SP) Biannual Report. All AE reporting will be blinded and conveyed in aggregate statistics within OpenBiome’s Q&SP Reports, except in severe cases (determined mutually) where particular details materially help OpenBiome and its partners reduce the risk of adverse events in the future. OpenBiome upholds the privacy and integrity of its partner institutions in all of its external reporting.
2. **OpenBiome clinical safety consultation:** At the discretion of the Clinical Program Director or Chief Medical Officer, OpenBiome may contact or visit the clinical site and discuss patient safety and quality improvement methods to mitigate risk to patients (e.g., in the case of aspiration secondary to use of FMP250 by naso-enteric delivery).

[Actor: Finch Therapeutics]
1. **Donor material shipping:** Donor material can be taken out of quarantine and shipped for routine clinical use.

[Actor: Partners]
1. **Complete any institutional adverse event protocols:** Partners should complete any outstanding adverse event protocols that are required by the FDA or their institution.

Endpoint C
[Actor: OpenBiome]
1. **Immediately report AE to all partners:** OpenBiome will notify all partner hospitals and clinicians that have received any material made from the same donor under investigation. This notification will be distributed via email to the Adverse Event (AE) contact provided as part of provider registration. This notification will include details on the AE, the donor and associated units under investigation, and any additional follow-up tasks that are required. In the notification, OpenBiome will require that these partners halt the use of FMT material made from the same donor under investigation.

2. **Include in Q&SP Biannual Report:** OpenBiome will aggregate and include all reports of AEs from across its partner network in OpenBiome’s Biannual Safety & Quality Program Report. All AE reporting will be blinded and conveyed in aggregate statistics within OpenBiome’s Q&SP Reports, except in severe cases (determined mutually) where particular details materially help OpenBiome and its partners reduce the risk of adverse events in the future. OpenBiome upholds the privacy and integrity of its partners in all of its external reporting.

[Actor: Finch Therapeutics]

1. **Destroy all donor material and permanently exclude donor:** Finch Therapeutics will immediately destroy all material associated with the donor related to the investigation. Finch Therapeutics will also permanently exclude the donor from providing any material.

2. **Update panel to include the diagnosis if a screen exists:** If there is a CLIA-certified test available for the infectious disease, Finch Therapeutics will update its Clinical Screening Panel to test for the concern during new donor enrollment and at every 60-day rescreening window. If a CLIA-certified test does not exist, feasible and reasonable precautions and alternatives will be implemented to minimize the risk of the AE in the future. Specifically, Finch Therapeutics will consult its Clinical Advisory Board to brief the situation and receive external guidance on appropriate prevention and response mechanisms.

3. **Inform the FDA & CDC:** Finch Therapeutics will proactively follow up with the Food & Drug Administration and other regulatory stakeholders to brief the situation, receive guidance on appropriate prevention and response mechanisms, and ensure compliance with any applicable regulatory requirements as a result of the AE.

[Actor: Partners]

1. **Destroy all donor material:** Partners must immediately destroy all material associated with the donor under investigation. Finch Therapeutics manufactured FMT material contains human fecal material, and so
standard protocols for handling biohazardous material should be followed at all times.

2. Assess all patients treated with donor material for any signs of the same adverse event: Partners should perform proactive follow up assessments with all patients treated with material made from the donor under investigation to ensure there are no unreported adverse events that require escalation or signals of an adverse event that may require attention. Follow up assessments should be conducted within two weeks following this endpoint.

Endpoint D

[Actor: Finch Therapeutics]
1. Donor material shipping: Donor material can be taken out of quarantine and shipped for routine clinical use.

[Actor: OpenBiome]
1. Include in Q&SP Biannual Report: OpenBiome will aggregate all reports of AEs from across its partner network in OpenBiome’s Safety & Quality Program Report. All AE reporting will be blinded and conveyed in aggregate statistics within OpenBiome’s Q&SP Reports, except in severe cases (determined mutually) where particular details materially help OpenBiome and its partners reduce the risk of adverse events in the future. OpenBiome upholds the privacy and integrity of its partners in all of its external reporting.

[Actor: Partners]
1. Review and implement updated Quality & Safety Program (e.g. new eligibility criteria for patients seeking an FMT to account for patient-specific risks): Partners should factor in the patient’s risk of experiencing an adverse event. An email will be sent to all AE contacts to inform them of any new updates to the Quality and Safety Program. All documentation sent to partners will also include necessary updates.
Clinical Advisory Boards

As organizations dedicated to enabling safe access to FMT for CDI patients and for catalyzing research of the microbiome, both OpenBiome and Finch Therapeutics maintain separate, independent Clinical Advisory Boards (CABs) to provide medical advice that will drive safety and best practice in FMT. Members of OpenBiome and Finch CABs have the opportunity to shape the emerging field of FMT across our clinical network. The CABs provide unbiased input that adds to the decision-making capacity of the OpenBiome and Finch clinical teams. The members of the each CAB include world leaders in gastroenterology, infectious diseases and microbiology who bring combined expertise to enhancing safe access to FMT.

Roles and Responsibilities

Both OpenBiome and Finch CABs consist of odd numbers of qualified medical professionals that meet to review the clinical operations at OpenBiome and Finch. The CAB formally meets biannually to review safety data and update our screening and processing protocols based on the latest scientific evidence. Additionally the CABs can be convened at the request of either organizations’ Board of Directors or management team. Members of the CAB are invited for a term of one year, renewable upon the completion of each term.

Each organization’s CAB provides objective and independent expertise in the following domains:

1. **Finch Therapeutics Clinical Advisory Board**
   a. Adverse Events: Although AEs associated with FMTs have been infrequently reported, we continue to monitor and evaluate these events vigilantly. The Finch CAB provides external consultation in evaluating suspected adverse events. Finch engages the CAB as needed to protect patient care in the short term and disseminate safety data and lessons learnt ensure continued improvement both in OpenBiome’s network and beyond.
   b. Donor Screening: The Finch CAB provides immediate support to Finch’s Clinical Assessment and Safety Team regarding donor exclusion criteria. Finch’s CAB, in collaboration with OpenBiome’s CAB, also conducts an annual review of proposed modifications to the donor screening criteria.
   c. Quality Assurance: To ensure FMT care continues to improve in safety, accessibility and ease-of-use, the CAB reviews Finch’s biomanufacturing protocols, methodologies, policies and operations.

2. **OpenBiome Clinical Advisory Board:**
a. Clinical Education: The CAB reviews OpenBiome’s clinical education material to ensure that such education reflects the latest clinical evidence.
b. Donor Screening: The OpenBiome CAB, in collaboration with Finch’s CAB, conducts an annual review of proposed updates to the donor screening criteria.
c. Research Methodology: OpenBiome supports, and in some cases, sponsors trials into new indications of FMT in an effort to help advance the field. The CAB provides feedback on OpenBiome’s clinical trials and academic research efforts by providing expert opinion on protocols, methodology, and data collection efforts.
d. Quality Assurance: To ensure FMT care continues to improve in safety, accessibility and ease-of-use, the CAB reviews OpenBiome’s clinical protocols, methodologies, policies and operations.

Principles and Guidelines

1. **OpenBiome Clinical Advisory Board**:
   a. The OpenBiome CAB provides objective and independent clinical advice and counsel as a representative link between OpenBiome and the broader clinical community that we serve. This voluntary advisory role does not hold formal managerial authority or associated medical liability. The following principles and guidelines define the interactions between OpenBiome and the CAB:
      i. OpenBiome bears responsibility for decisions made, with or without the CAB’s input
      ii. OpenBiome will take inputs from the CAB under advisement, but is not required to follow the CAB’s endorsed position
      iii. All CAB members are subject to the same Conflict of Interest guidelines followed by OpenBiome’s Board of Directors (i.e., all research funding and commercial partnerships must be publicly disclosed)
      iv. Both to protect the integrity of the board and because OpenBiome is a modest non-profit, active members of the CAB cannot be compensated by OpenBiome for their service

2. **Finch Therapeutics Clinical Advisory Board**
   a. The Finch CAB provides objective and independent clinical advice and counsel as a representative link between Finch Therapeutics and the broader clinical community that we serve. This voluntary advisory role does not hold formal managerial authority or associated medical liability. The following principles and guidelines define the interactions between Finch Therapeutics and the CAB:
i. Finch bears responsibility for decisions made, with or without the CAB's input

ii. Finch will take inputs from the CAB under advisement, but is not required to follow the CAB's endorsed position

iii. All Finch members are subject to the same Conflict of Interest guidelines followed by OpenBiome’s Board of Directors (i.e., all research funding and commercial partnerships must be publicly disclosed)