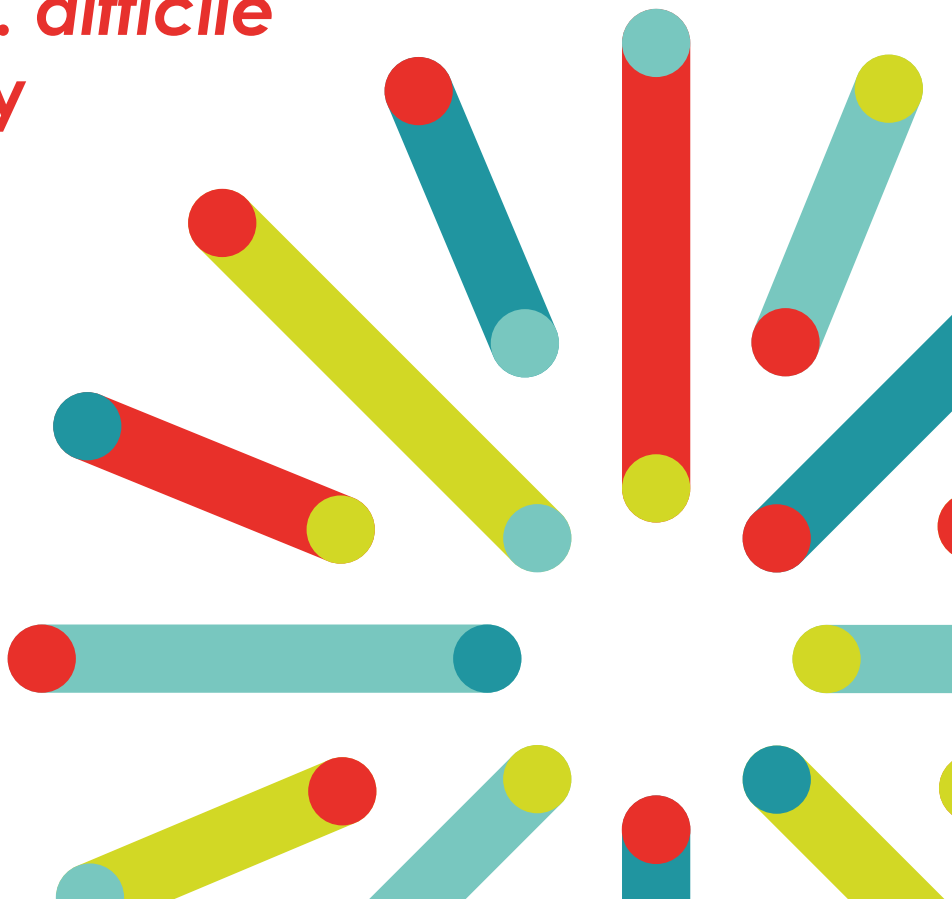
OPENBIOME

MTP-101LF

Fecal Microbiota Preparation
For Treatment of Fulminant *C. difficile*
Administer via Lower Delivery



Clinician's Checklist

Version: July 11, 2023

Clinician's checklist for the infusion of MTP-101LF for fulminant *C. difficile*

Note: For recurrent, non-fulminant *C. difficile* infection (CDI), patients should be treated with MTP-101LR. (MTP-101LF is a more highly concentrated investigational FMT preparation specifically for fulminant CDI.)

Important Reminders

- MTP-101LF is limited by Federal (or United States) law to investigational use. **Immediately report any adverse events to https://www.openbiome.org/adverse-events.**
- MTP-101LF must be stored in a medical-grade freezer at -20°C or colder at all times, and should never be refrozen.
- After it has been thawed, MTP-101LF material should be administered within 6 hours. Thawed material should not be refrozen.
- Immediately dispose of unused material as biohazardous waste.

Ingredients

Frozen human microbiota (≥2.5 x 10^{12} bacteria) suspended in normal saline with 10% glycerol.

Table of Contents

General Patient Preparation

1. Review Indications & Contraindications

☐ Confirm that the indication to be treated by investigational Fecal Microbiota Transplantation (FMT) is **fulminant *C. difficile* infection (CDI)** that is not responsive to standard therapy, and rule out alternative diagnoses (e.g., post-infection IBS, inflammatory bowel disease, celiac disease).

• Current evidence suggests that the treatment of fulminant CDI by investigational FMT may require different protocols than those outlined in this document. This may include potential retreatment. We suggest reviewing the protocol outlined in the Investigator's Brochure for MTP-101LF which can be found at https://www.openbiome.org/umn-fmt.

General Patient Preparation (continued)

- ☐ Review contraindications specific to lower delivery (i.e., colonoscopy, sigmoidoscopy, enema).
- ☐ Review contraindications for investigational FMT material, including but not limited to:
  - Severe food allergy (e.g. anaphylaxis or anaphylactoid reaction).
  - Severe adverse event attributable to a previous FMT.
  - Patients with allergies to sodium chloride or glycerol, both ingredients Generally Recognized As Safe (GRAS).
  - Ongoing antibiotic use for *C. difficile* infection or non-*C. difficile* indication.
  - Any condition for which the treating physician thinks the treatment may pose a serious health risk (e.g., severely immunocompromised with neutropenia).

2. Obtain Informed Consent

- ☐ Inform patients of the potential risks and benefits associated with investigational FMT and treatment alternatives for CDI.
- ☐ Inform patients that the use of investigational FMT to treat fulminant *C. difficile* infection (CDI) is not FDA-approved.

General Patient Preparation (continued)

3. Review Medications

☐ Discontinue anti-rCDI antibiotics (e.g., vancomycin, fidaxomicin) **48 hours** prior to FMT. Concomitant use of other antibiotics could reduce the procedure's efficacy.

4. Patient Preparation

☐ **For colonoscopy/sigmoidoscopy**, use a standard bowel preparation for lower gastrointestinal delivery.

Note: Do not administer MTP-101LF via upper delivery (nasogastric, esophagogastroduodenoscopy (EGD), push enteroscopy).

Warnings and Caution

- May contain food allergens, including nuts. Contraindications include known anaphylactic food allergies and pregnancy. Investigational FMT carries the risk of known and unknown infectious disease transmission and potentially microbiome-mediated disease.

- Interactions with other drugs have not been systematically investigated. Consider closely monitoring medication levels for medications potentially impacted by microbiota-mediated drug metabolism by gut microbiota (e.g., warfarin, anti-rejection medications).

- **New Drug**—Limited by Federal (or United States) law to investigational use. **Immediately report any adverse events to https://www.openbiome.org/adverse-events.**

Material Handling and Thawing

- ☐ Store immediately at -20°C or -80°C in freezers **without** an auto defrost function. Use before applicable expiration date indicated on product label.
- ☐ Remove MTP-101LF cryobag from the freezer and check to make sure that formulation is not expired.
- ☐ Thaw before use by placing cryobag into a wet ice bath for at least 30 minutes until preparation becomes a liquid. No additional blending, mixing, or other preparation is required.
- ☐ After thawing, samples must be administered within 6 hours of thawing. Discard MTP-101LF after six hours thawed.
  Note: Once thawed, MTP-101LF cannot be refrozen and remain active.

Instructions for Lower Delivery

Materials: You will need the following supplies

- Normal saline
- 30 or 60 ml slip tip syringes
- BD Interlink™ blunt tip plastic cannula: Item number 303345
- A graduated beaker

The blunt cannula will be mounted on the slip tip syringe and used to access the cryobag through one of the two ports. Do not use metal needles to access the cryobag – these do not maintain a seal following puncture of the port and may result in leakage.

- ☐ Follow routine pre-procedure preparation for colonoscopy/sigmoidoscopy (e.g. diet/bowel preparation instructions).
- ☐ Mount the blunt tip cannula onto the slip tip syringe.
- ☐ Draw out the contents of the cryobag, which comprise 35mL of material (a single 60 mL syringe is sufficient, or you can use two 30 mL syringes. The blunt cannula remains in the port; only the syringes need to be switched).

Instructions for Lower Delivery (Continued)

- ☐ Once cryobag is empty, you can inject 30 mL of normal saline into the cryobag and draw out the residual microbiota.
- ☐ Fill an additional syringe with normal saline only.
- ☐ Inject the microbiota through the biopsy channel of the colonoscope once you're in the desired position (e.g., cecum).
- ☐ Flush the biopsy channel with normal saline into the colon.
- ☐ Avoid aspiration during scope withdrawal.

Note: The dose is defined as the number of bacteria rather than volume administered or grams of raw stool that went into the manufacturing. **We recommend the total volume administered into the cecum or terminal ileum to be 60 – 180 mL.**

Post Administration

For Lower Delivery

- ☐ Observe standard best practices for post-colonoscopy, sigmoidoscopy or retention enema care.

Adverse Reactions

This is a summary of adverse reactions reported in peer-reviewed literature; however, it may not be not be a comprehensive list. Please consult the primary sources listed in the references section of the OpenBiome Clinical Primer for more detailed information. A review of procedure-related adverse events (e.g. perforation, aspiration) are beyond the scope of this document.

☐ Common, mild adverse events that occur in the first weeks after FMT include:

- Transient diarrhea (70%)
- Transient abdominal cramps/discomfort (20%)
- Nausea (<5%) in 24 hours post-FMT.
- Transient fever, bloating, belching, vomiting, and borborygmus
- Constipation (20%)
- Excess flatulence (25%)

Sustained diarrhea, especially with fecal urgency and night symptoms should prompt evaluation for recurrence of *C. difficile* infection.

Adverse Reactions (continued)

☐ Rare, serious adverse events: The following risks should be considered:

- **Infection:** Although this material has been screened for microbial pathogens, there is a risk of transmission of known and unknown infectious organisms contained in the donor stool.
- **Multi-drug resistant organisms (MDROs):** Although this material tested negative for common MDROs, including ESBL, MRSA, VRE, and CRE, there remains a possibility of a systemic infection with an MDRO.
- **Inflammatory bowel disease (IBD) flare** in those with underlying IBD.
- **Allergy/Anaphylaxis** to antigens in donor stool.
- **Non-infectious disease transmission:** Although all donors participating in the University of Minnesota's stool donor program meet strict criteria and are healthy, metabolically fit, and take no prescription medications, there remains 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.

Mandatory Clinical Follow-Up

- ☐ Complete the mandatory paper-based Material Tracking Log to report use of material.
- ☐ Assess patients around 1-2 months after investigational FMT administration (phone/clinic visit) for clinical cure (e.g., resolution of diarrhea) and occurrence of adverse events.
- ☐ **Clinicians must report patient outcomes via the online registry at www.openbiome.org/outcomes**
- ☐ Send Material Tracking Log by email to safety@openbiome.org or by fax to (617) 575-2201.

This quality assurance data is critical to our efforts to guard against potential threats to the safety and efficacy of investigational FMT.

Your participation in reporting Material Tracking Log and clinical outcomes via the online registry is a strict condition for receiving future preparations.

Post-FMT Patient Counseling

Advise patient to thoroughly clean their home to avoid reinfection after investigational FMT. When cleaning, the patient should:

- ☐ Use an Environmental Protection Agency (EPA)-registered disinfectant with a *C. difficile*-sporicidal label claim, such as household bleach
- ☐ Scrub high-touch surface areas such as toilets, faucets, and showers
- ☐ Wear disposable gloves when cleaning; wash hands with soap and water thoroughly afterwards
- ☐ Consult OpenBiome's Patient Education materials: www.openbiome.org/patient-support

Frequently Asked Questions (FAQ)

Visit openbiome.org/umn-fmt for more clinical guidance and answers to frequently asked questions

OPENBIOME

Contact Information

Safety & Adverse Events
safety@openbiome.org
(617) 575-2201 x9

General
info@openbiome.org
(617) 575-2201