

PROTOCOL CREATION GUIDE

A suggested Pre-treatment plan consists of:

- Gut Prep with antibiotics (and antifungals and antiparasitic if indicated) for 2 weeks pre-FMT (stopping 48 hours before FMT)
- Bowel cleanse (day before FMT)
- Fasting (done the day before starting FMT and on the first day of FMT, this is optional)

FMT treatment is divided into a loading and maintenance dose.

Loading Dose: takes place the day following a bowel cleanse. Loading doses are bolus FMT doses (over 1-2 days) designed to rapidly establish the new gut microbiome to allow for engraftment by providing a sufficient concentration of transplanted microbiota.

Maintenance Dose: Extended smaller additional dosing for FMT over a period of weeks/months. The goal is to improve and sustain therapeutic effects by reinforcing microbiota engraftment by promoting colonization and stability of the microbiome transplant. Extended treatment allows patients to make lifestyle changes (i.e. diet expansion) and allows systems impacted by the gut microbiome (i.e. immune, inflammatory, and axis like the gut-brain and gut-liver) to re-regulate after chronic deregulation.

EXAMPLE PROTOCOL OUTLINE

OPTION 1: SMALL LOADING DOSE

Pretreatment and informed consent

- Pre-Treatment stop 48 hours before FMT
- Bowel Cleanse 24 hours before FMT

Loading dose: Day 1 and 2 of FMT

- 15 capsules per day for 2 days (1 bottle of 30 caps split over 2 days)

Maintenance dose: Day 3 to Day 30

- 1 cap/day for 30 days (1 bottle per month)

FMT evaluations

- Monthly touchpoint to evaluate FMT effectiveness
- Determine if additional maintenance would be beneficial: Are benefits being seen but not plateaued ? Is patient still making diet and lifestyle modifications?

Repeat until improvements plateau

OPTION 2: EXTENDED LOADING DOSE

Pretreatment and informed consent

- Pre-Treatment stop 48 hours before FMT
- Bowel Cleanse 24 hours before FMT

Loading dose: Day 1 and 2 of FMT

- 30 capsules per day for 2 days (2 bottles of 30 caps)

Maintenance dose: Day 3 to Day 30

- 1 cap/day for 30 days (1 bottle per month)

FMT evaluations

- Monthly touchpoint to evaluate FMT effectiveness
- Determine if additional maintenance would be beneficial: Are benefits being seen but not plateaued ? Is patient still making diet and lifestyle modifications?

Repeat until improvements plateau

OPTION 3: ENEMA OPTION

Pretreatment and informed consent

- Pre-Treatment stop 48 hours before FMT
- Bowel Cleanse 24 hours before FMT

Loading dose: Day 1 and 2 of FMT

- 1 enema per day for 2 days (2 enemas)
- Or 1 enema and start maintenance on day 2

Maintenance dose: Day 3 to Day 30

- 1 cap/day for 30 days
- 1 powdered vial in liquid per day (for those who cannot swallow caps)

FMT evaluations

- Monthly touchpoint to evaluate FMT effectiveness
- Determine if additional maintenance would be beneficial: Are benefits being seen but not plateaued ? Is patient still making diet and lifestyle modifications?

Repeat until improvements plateau

Example maintenance length: Acute Cases: 1-2 Months, Moderate Cases: 2-3 Months, Chronic cases: 4+ months

TRACKING IMPROVEMENTS

Using validated measures to track improvements helps to interpret FMT impacts and ensure sustained improvements.

Examples of validated measures (there are measure for specific conditions as well, below are general measures):

Gastrointestinal: Gastrointestinal Symptom Rating Scale (GSRS) and Bristol Stool Scale (BSS)

Quality of Life: 36-item Short Form Survey (SF-36), Health Related Quality of Life (HRQOL) and (EQ-5D)

Symptoms Improvements: 36-item Short Form Survey (SF-36), PROMIS (Patient-Reported Outcomes Measurement Information System)

Diet expansion and lifestyle changes: Asking patients about how their diet is changing and other standard lifestyle metrics of health and wellbeing as good measures of improvements

Disclaimer: Novel Biome is a contract manufacturer of FMT products, providing high-quality FMT products to physicians. The information provided in this document should not be considered medical advice and is based on Novel Biome's understanding of their FMT products and past experience treating patients with FMT. Our hope is that this information helps as a starting point for physicians. If you have more questions, comments or concerns with these instructions, please email us at support@novelbiome.com.

Pre-FMT Protocol Creation Guide

WHAT IS PRE-TREATMENT

Pre-treatment, also known as microbiome prep, prepares the gut by reducing species richness and adjusting dominant microbiota prior to FMT, allowing for better engraftment of the donor microbiome and, therefore, better outcomes post-FMT. At Novel Biome, we have extensive knowledge of FMT treatment and can offer support through consultation with our medical team to help create pre-treatment protocols.

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- Bowel cleanse (day before FMT)
- Fasting (done the day before starting FMT and on the first day of FMT, this is optional)

GUT PREP

Antibiotics: Studies have shown that pre-treatment with antibiotics may impact the magnitude and duration of improvements after FMT, indicating that a recipient's microbiome before FMT may play a primary role in the outcomes of FMT (Schmidt, T. S. et al. 2022, Kang, D.W. et al. 2017, Li, N. et al. 2021). One suggested antibiotic is **Vancomycin** for 2 weeks, starting treatment 16 days before FMT (40mg/kg divided in 3 doses/day with a max of 2g/day) . Important to stop any antibiotics (antifungals and antiparasitic if indicated) 48 hours (2 days) before the start of FMT.

BOWEL CLEANSE

We believe it is important to do a bowel cleanse prior to starting FMT. Our reasoning behind this is that clearing out as much fecal matter as well as "washing out" as much antibiotic or antimicrobial that may still be in the system should help to enhance engraftment and FMT success. We believe the use of a bowel cleanse is more important for patients who are suffering from constipation. Some examples of bowel cleanse are Magnesium Citrate, Magnesium Oxide, MoviPrep, etc. Goal is to initiate soft/loose stool movement before FMT.

FASTING

On the day of the bowel cleanse and during the first day of FMT treatment, we suggest patients go on a water fast if possible. This should hopefully reduce the amount of food/stool in the digestive system and provide an enhanced environment for FMT engraftment. If fasting is too challenging, a light diet of juice, smoothies, soups, broths, etc., is recommended. Fasting is an optional step and only used if a patient can tolerate it.

OTHER CONSIDERATIONS

- If the oral powder is used for treatment (i.e. can't swallow capsules), it is important to have them on an acid-lowering medication to allow more bacteria to survive and colonize their gut; one example is Prilosec, starting a week before FMT and continuing throughout treatment.
- If there is a history of elevated yeast (candida) and/or a past stool test that shows elevated yeast, consider a 7-10 day course of Nystatin, stopping 48 hours before FMT.
- Liver Support: Supporting the liver once FMT has begun can be very helpful. When introducing large amounts of bacteria into the gut, it can lead to die-off reactions in some patients.

SUPPLEMENTS WITH FMT

It is important that these contain NO antimicrobial ingredients, as these can kill off transplanted bacteria. Any supplement with antimicrobial ingredients should be stopped 48 hours before starting FMT. Reviewing a patient's supplements before starting FMT can help increase FMT success. Here are supplements to avoid. This list is NOT exhaustive but are supplements commonly taken which can affect FMT engraftment. It may be worth suggesting at a patient attempts to reduce supplements to 5-10 core supplements while doing FMT.

- Probiotics
- Single-ingredient prebiotics
- Binding agents of any kind (i.e. activated charcoal, clays)
- Any supplement that contains herbs with antimicrobial activity, such as:
 - Berberis Aquifolium/vulgaris (Oregon Grape / Barberry)
 - Origanum Vulgare (Oregano)
 - Curcuma Longa (Turmeric/Curcumin)
 - Allium sativum (Garlic)
 - Thymus vulgaris (Thyme)
 - Baptisia tinctoria (Wild Indigo)
 - Hydrastis canadensis (Goldenseal)
 - Ligusticum porteri (Osha)
 - Lomatium dissectum (Lomatium)
 - Echinacea angustifolia (Echinacea)
 - Commiphora molmol (Myrrh)

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