

OPENBIOME

Research Collaboration Guide

For Non-Clinical Researchers

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Introduction: The OpenBiome Dual Mission

Safe Access | Catalyzing Research

Since its founding in 2012, OpenBiome has reached significant milestones in our commitment to expand safe access to fecal microbiota transplantation (FMT) and has provided fecal microbiota preparations for more than 55,000 *C. difficile* treatments with over 1,200 clinical partners in 50 states and 7 countries.

In addition to our commitment to provide safe access to FMT, we are here to partner with investigators to uncover the role of the gut microbiome in health and discover how engineering the microbiome might drive better health outcomes. OpenBiome seeks to catalyze academic and commercial microbiome research with our expertise in the microbiome and by providing access to standardized microbiota research materials.

Fecal Microbiota Preparation Biospecimen (FMP-Bio) Packs: FMP-Bio packs contain a customizable number of stool aliquots prepared in four different formulations. The aliquots, sourced from rigorously screened stool donors, are designed to support non-clinical science researchers that are interested in harnessing the microbiome to develop biological tools, including humanized animal models and biomarker screening methods.

In the sections below, you can learn more about the resources we can bring to your research program, and the process for working with us. To begin a conversation about how we may work together, please complete our short [Non-Clinical Research Request Form](#) and submit it to science@openbiome.org.

If you have any further questions, please feel free to contact our research team at science@openbiome.org.

FMT Microbiota Preparation Biospecimen (FMP-Bio)

Quality & Safety | In Vivo/Vitro

For researchers looking for standard methods to humanize animal models, develop diagnostics, or harness universal biological standards for microbiome analysis, we have designed the Fecal Microbiota Preparation Biospecimen (FMP-Bio) pack.

Each FMP-Bio pack contain a customizable number of stool aliquots prepared in four different formulations listed below. These samples can be used for *in-vitro* assays and *in-vivo* applications (i.e. humanization, colonization, and competition experiments) in pre-clinical animal models.

FMP-Bio Formulations:

Raw, flash-frozen donor stool

1. Sample contains approximately 0.7 grams of stool per aliquot.

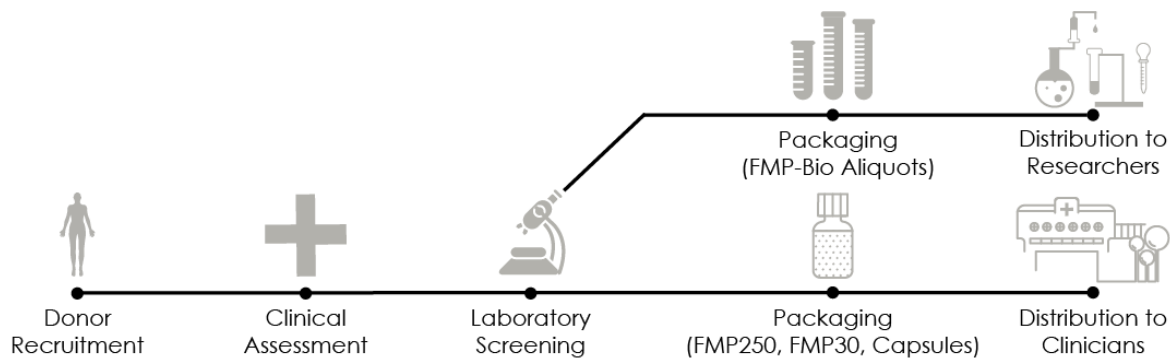
Donor stool that has been suspended in a glycerol/saline buffer via the same process used to create OpenBiome FMT preparations for clinical use

2. Sample prepared at a concentration of 0.1 grams of stool in 1.5 milliliters of buffer
3. Sample prepared at a concentration of 0.4 grams of stool in 1.5 milliliters of buffer
4. Sample prepared at a concentration of 0.7 grams of stool in 1.5 milliliters of buffer

Please refer to the product specifications below and to our [Quality Metrics](#) reference at www.openbiome.org/safety for a description of our donor screening and quality procedures.

FMP-Bio Specifications

Material Support | Analysis | Quality & Safety



FMP-Bio aliquots are sourced from rigorously screened stool donors and follow the same Quality and Safety program—including clinical assessment and laboratory screening—as material processed for clinical use. After receiving your research request, our research team will contact you to affirm your study requirements and material need. We tailor our involvement in investigations on an individual basis, usually providing the tools and services listed below.



IRB-supervised Donor Recruitment: We have recruited a registry of over 8,000 prospective donors to enter our screening and collection program and have screened over 1,300 candidates under IRB supervision. This large pool of prospective donors is a critical resource that enables exceptional selectivity as we seek to identify healthy participants



Clinical Assessment: Each donor undergoes a 200-point clinical assessment for a wide range of risk factors for chronic and infectious diseases ranging from behavioral traits like travel and sexual health histories to a careful review of medical history and direct measurement of BMI and vital signs



Laboratory Screening: Donors that pass the clinical assessment provide blood and stool samples that are evaluated for a broad range of over 30 viral, bacterial and parasitic infectious agents, including multi-drug resistant organisms, using FDA-cleared laboratory tests conducted at a CLIA-certified testing facility. Less than 3% of prospective donors pass both the clinical and laboratory assessments and enter our program as qualified donors



Material Processing and Monitoring: Material is processed in a sterile 12.5% glycerol and 0.9% saline buffer at 2.5 ml of buffer per gram of stool. This buffer acts as a cryo-protectant for long-term storage. Each sample is passed through a 330 µm filter to remove large particulate matter and facilitate liquid handling for gavage and molecular analysis. We deliver material by overnight courier on dry ice with temperature monitoring and verification

To speak with a member of our team about our resources and how we may support your research, please email us at science@openbiome.org.

Purchase of FMP-Bio Packs for Non-Clinical Research

[Material Details](#) | [Non-Clinical Research Request Form](#) | [Material Transfer Agreement](#)

To submit a request for FMP-Bio Packs for research usage, please fill out our short [Non-Clinical Research Request Form](#) and submit it to science@openbiome.org. OpenBiome's Research Review Panel reviews requests on a quarterly basis.

If your proposed study is (1) funded or sponsored by commercial entities or (2) investigating Inflammatory Bowel Disease (IBD) or *C. difficile* Infection (CDI), there will be an additional review process. We have a collaboration with Finch Therapeutics, who holds intellectual property on some of the material that we provide ([learn more here](#)). Due to the terms of our agreement, research that meets the above criteria will need to be reviewed by Finch prior to our engagement with you. We are happy to answer any questions you may have about this process – please do not hesitate to reach out to us at science@openbiome.org.

All investigators' institutions must execute a material transfer agreement with OpenBiome prior to shipment of FMP-Bio packs to sites.

Item	Description	Price
FMP-Bio	Custom number of aliquots	\$150 per aliquot Bulk order discount: \$100 per aliquot for orders of 25 aliquots or more

Delivery

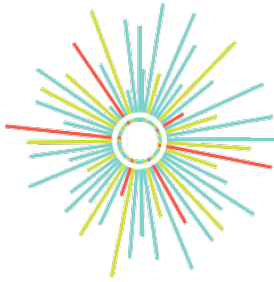
Material will be delivered on dry ice via overnight courier with temperature verification.

Handling Precautions

When handling fecal microbiota preparation (FMP-Bio) packaging and the aliquots contained within, always wear appropriate personal protective equipment. Researchers should work with FMP-Bio Pack materials only in a certified biosafety cabinet within a BL2-rated facility. Upon delivery, always examine packaging integrity and shipping temperature indicator. Contact OpenBiome immediately if package or product integrity has been compromised.

Animal Use

All users who indicate that will be using FMP-Bio Pack materials in mouse models or other animal testing must provide OpenBiome with a current approval from their Institutional Animal Care and Use Committee (IACUC) approval for the proposed research prior to shipment.



APPENDIX

8		Frequently Asked Questions
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Frequently Asked Questions

- 1. How are laboratory assays of donor health and product safety performed?** Our [Quality Metrics](#) guide contains a full description of our donor screening and quality procedures.
- 2. How do I confirm that the samples have been tested for pathogens of interest?** Donors undergo a series of stool-based and serological assays by a third-party Clinical Laboratory Improvement Amendments (CLIA) certified testing facilities to assess for infectious pathogens, including multi-drug resistant organisms, and general health metrics. For stool preparations, we currently use a combination of microbiological culturing, enzyme immunoassays and PCR technologies to detect potential infectious agents in a CLIA-certified laboratory. These diagnostics were developed through the review of best clinical practices published in the literature^{1,2,3} coupled with the consensus guidance from our clinical advisory board.
- 3. Do I have to work with FMP material in any particular setting?**
Yes. Researchers should work with FMP-Bio Pack materials only in a certified biosafety cabinet within a BL2-rated facility.
- 4. How much do these research products cost?**
The price for an FMP-Bio Pack starts at \$150 per sample. For bulk orders we offer a discounted price of \$100 per aliquot for orders of 25 or more samples.
- 5. What is OpenBiome's relationship with Finch Therapeutics Group?**
OpenBiome collaborated with Finch to develop CP101, a freeze-dried oral FMT capsule, for treatment of recurrent *C. difficile*. Finch is running a clinical trial to test CP101, and trial sites around the U.S. and Canada are now enrolling patients. You can read more about the relationship between OpenBiome and Finch, and our commitment to integrity, [here](#).
- 6. Was OpenBiome impacted by the safety alert from FDA in June 2019? Does OpenBiome screen for multi-drug resistant organisms (MDROs) and meet the updated screening guidelines from FDA?**
OpenBiome material was not involved with, nor impacted by, FDA's safety alert from June 2019. We have been screening for MDROs, including Extended-Spectrum Beta Lactamase (ESBL) since 2016, and meet all updated guidelines from FDA. Trials using OpenBiome material were not halted, and OpenBiome material may continue to be used under FDA's latest guidance.

7. Does OpenBiome screen FMT preparation for SARS-CoV-2?

Yes, we have implemented [new screening protocols](#) to mitigate the risk of transmitting SARS-CoV-2 through FMT material.

Every stool sample provided by donors since December 1, 2019 has been directly tested for SARS-CoV-2 using a new direct test for the presence of SARS-CoV-2, the virus that causes COVID-19.

The test, which was developed by [CosmosID](#), uses RT-PCR, the same molecular technique used in COVID-19 diagnostic testing such as nasopharyngeal swab testing, to check for the presence of SARS-CoV-2 genetic material in donor stool. Every stool donation that was processed into FMT preparations is being directly tested.

In addition to testing stool directly for SARS-CoV-2, OpenBiome has implemented the following donor health surveillance measures:

- **Stool donors are subject to regular COVID-19 screening by nasopharyngeal swab.**
 - Beginning in March 2020, when testing by nasopharyngeal swab for asymptomatic individuals became available locally, OpenBiome began screening donors at a minimum of every 28 days, and in June 2020, began screening donors at a minimum of every 14 days.
 - Any donors testing positive will have their material destroyed from the 28 days prior to any positive test and will be placed on hold and excluded from providing donations for a minimum of 8 weeks. Donors must fully requalify for the stool donation program in order to return from hold.
- **At each stool donation the donor's temperature is taken and donors are evaluated for travel, recent COVID-19 screening outside of OpenBiome, exposure to known or possible COVID-19 cases, and symptoms associated with COVID-19.**
 - Travel deferral:
 - Donors traveling internationally are deferred from donating for 28 days upon return before undergoing COVID-19 screening by nasopharyngeal swab. Donors traveling domestically are assessed on a case-by-case basis for high-risk activities such as travel by plane, exposure to large groups (>10 people), or travel to states considered high-risk by the Massachusetts Department of Health. In high-risk cases, donors are deferred from donating for 14 days upon return before undergoing COVID-19 screening by nasopharyngeal swab.
 - Exposure:
 - Donors with exposure to known or suspected cases of COVID-19 within the past 28 days will have material from the 28 days prior to exposure destroyed and will be placed on hold for a minimum of 8 additional weeks.

- Symptoms:
 - Donors are screened for symptoms of fever, cough, shortness of breath, sore throat, headache, myalgia, severe fatigue, new loss of smell or taste, nausea, vomiting, or diarrhea.
 - A body temperature of greater than 100.4 °F will result in clinical evaluation to determine if symptoms are compatible with possible COVID-19 or other illness.
 - Material collected in the 28 days prior to any onset of symptoms associated with COVID-19 is destroyed. Donors reporting any symptoms are placed on hold for a minimum of 8 additional weeks.
- **All material remains quarantined until we can confirm it meets our safety and quality standards, including those for COVID-19.** Following guidance from the FDA, all FMT units manufactured after December 1, 2019 have been screened for SARS-CoV-2, the virus that causes COVID-19, using a stool-based RT-PCR assay on each raw material lot (every stool sample).
- No donors who provided stool donations that were processed into FMT material had received the COVID-19 vaccine at the time of sample donation. We stopped collecting stool samples from donors on February 13, 2021. Therefore, questions regarding the implications of COVID-19 vaccination, asymptomatic carriage of SARS-CoV-2 and stool shedding are not relevant for the FMT treatments that will be provided by OpenBiome.

References

1. Kassam, Z., Lee, C. H., Yuan, Y. & Hunt, R. H. Fecal microbiota transplantation for *Clostridium difficile* infection: systematic review and meta-analysis. *Am. J. Gastroenterol.* **108**, 500–508 (2013).
2. Bakken, J. S. *et al.* Treating *Clostridium difficile* Infection With Fecal Microbiota Transplantation. *Clin. Gastroenterol. Hepatol.* **9**, 1044–1049 (2011).
3. Hamilton, M. J., Weingarden, A. R., Sadowsky, M. J. & Khoruts, A. Standardized Frozen Preparation for Transplantation of Fecal Microbiota for Recurrent *Clostridium difficile* Infection. *Am. J. Gastroenterol.* **107**, 761–767 (2012)