It’s time for FDA approval: An open letter to the clinicians and researchers we serve

Just last month, we processed our millionth gram of stool since opening our doors in late 2012. This stool has been screened, homogenized, frozen, heaped in dry ice, and sent to your hospitals and clinics for the treatment of intractable C. difficile infections, or for clinical trials aiming to broaden and deepen our understanding of how gut bacteria can affect our health.

Together, we have provided more than 21,000 treatments across 800 medical centers in every U.S. state. Before your work, very ill patients often traveled long distances to one of the few physicians performing fecal microbiota transplants (FMTs), or resorted to self-treatment at home. Today, 97% of the U.S. population lives within a two-hour drive of one of your facilities. At a pace of nearly 1,000 treatments per month, you are supporting FMTs for about 20% of all recurrent C. difficile infections in the country. Our work together also includes 22 active clinical trials that encompass 75% of all the diseases for which FMT is under investigation, and half of all of the FMT trials in the country. In three years, you’ve enabled ready access to this life-saving therapy and worked to expand its reach. We want to ensure that we can keep building on the strong foundation that we have built together.

A temporary FDA policy enabled this impact
As many of you know, underpinning all of this progress is the U.S. Food and Drug Administration (FDA)’s flexible policy towards fecal microbiota for transplantation. FMT is not FDA-approved. Instead, the agency has allowed physicians to perform FMT for patients whose C. difficile infection does not respond to antibiotics. The policy has allowed us to fill an important unmet need together, changing the standard of care while building a platform for research.

However, the FDA has indicated that its policy towards FMT is temporary. We have assumed that once a commercial product gained FDA approval, the nature of enforcement discretion might change. A few companies are pursuing FDA approval for FMT products to treat recurrent C. difficile infection. Their success will mean that patients will have access to a therapy that will have demonstrated safety and efficacy to the FDA’s very high standards and these treatments will likely be well-covered by insurers.

KEY POINTS
• We are partnering with Finch Therapeutics to enable FDA approval of an FMT product for recurrent C. difficile infection (rCDI)
• We will continue to provide treatment under FDA’s current policy for rCDI and for research
• Let us know if you are interested in helping to enroll or refer patients in the clinical trials for this product by completing this brief survey.

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As a result, although we have long advocated for an alternative regulatory paradigm for FMT that would treat stool more like a tissue product than a traditional drug, we have also acknowledged that commercial producers would provide a long-term solution to the problem we have been addressing under enforcement discretion.

The latest evaluations of these commercial products were discouraging, though. Meanwhile, the outcomes you reported for 2,050 patients show a cure rate of 84%, suggesting that when the entire microbial community is delivered appropriately it retains the remarkable efficacy that has been observed across the multiple randomized trials that have evaluated the use of whole stool transplants for recurrent C. difficile patients.

An FDA-approved, whole-community microbiome therapy

In light of the conflicting results between generic FMT and these commercial variants, we feel that it is all the more important to demonstrate the safety and efficacy of FMT in adequate, well-controlled studies. It should be shown that the intervention works consistently and can gain the regulatory approvals required to ensure a long-term supply for patients. We also want to be sure that the treatment we rely on today is not replaced by a less effective variant.

The challenge is that it takes tens of millions of dollars, invested in new manufacturing systems and robust clinical trials, to gain FDA approval. After an extensive evaluation, we have concluded that as a nonprofit, we cannot access the significant risk capital needed to successfully do so on our own.

Instead we’re partnering with Finch Therapeutics, a mission-driven biopharmaceutical company founded by a group of MIT and OpenBiome scientists, to pursue FDA approval for FIN-403, an orally delivered FMT product for recurrent C. difficile infections. Unlike other commercial products, this approach will deliver microbial communities comparable to those in traditional FMT and release them at the site of the infection. With these distinctions, and the 88% efficacy demonstrated in Finch’s initial dose-finding work, we see a path forward towards an FDA-approved product that has the efficacy we have come to expect from FMT.

Through the collaboration, OpenBiome will license its donor screening and material processing quality systems to Finch. Finch will build additional quality and safety controls to support FDA approval, and will

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1 Seres Therapeutics reported interim results from a trial of their product, an oral administration of bacterial spores: 56% of patients who received the drug achieved a clinical cure, vs. 47% of patients who received placebo, a difference that was not statistically significant. Rebiotix reported a combined cure rate of 64% from the treatment arms in a trial of their FMT enema product, vs. 45.5% of patients who received placebo, a statistically significant difference (p=0.045).
provide material produced in this improved quality environment back to OpenBiome for provision to its clinical and research partners. OpenBiome will also receive upfront, milestone and royalty payments that will support our mission of enabling patient access and clinical research.

Beyond its work on an FMT product for recurrent C. difficile, Finch is also working on discovering new treatments composed of specific strains of bacteria isolated from the gut and grown in pure cultures. You can read more about the collaboration [here](#). In the future:

- **Validation of FMT:** The FDA approval process will allow Finch to validate the safety and efficacy of a manufacturing process and delivery mechanism for FMT in recurrent C. difficile infection. If this effort succeeds, more patients will be able to access FMT because reimbursement will improve and institutional barriers to adoption will decline. We hope this will ensure long-term access to an effective, affordable treatment for the patients we serve.

- **Endowed platform for microbiome research:** OpenBiome will receive milestone payments and royalties that we will use to support early-stage, high-risk, and long-term microbiome research programs that might not be able to secure traditional funding. With this endowed, independent research program, we hope to advance public knowledge of how gut bacteria can be

**HELP SUPPORT FDA APPROVAL**

We are collecting contact information from clinical sites that may be interested in participating in the clinical evaluation of Finch’s FMT product. Please complete this brief survey if you are interested in learning more.

What this means for you and your patients

OpenBiome will continue to provide all of its current products and services, but now with improvements and additional resources:

- **Upgraded quality systems and material:** Over the coming months, Finch will introduce screening and manufacturing upgrades across the board and provide treatments manufactured under this improved system to OpenBiome. OpenBiome will continue to distribute these FMT preparations to its clinical network for use in the treatment of recurrent C. difficile infection and for clinical investigations of FMT. Finch is separately fundraising to introduce the quality upgrades necessary for FDA approval.

- **New resources for clinical research:** In addition to developing an FMT product for C. difficile, Finch has significant expertise in bioinformatics, microbiology, molecular biology and drug delivery and may be able to provide financial and scientific support for your clinical research. More information can be found [here](#).
engineered to help cure or even prevent disease.

The way forward

This collaboration with Finch will allow OpenBiome to execute our mission at a level we could not have imagined before. We will provide safe access to fecal transplantation for patients with recurrent C. difficile today, and help Finch pursue FDA approval so that patients have access to FMT in perpetuity. OpenBiome will continue to catalyze research in the microbiome by providing clinical investigators with logistical and material support and by facilitating standardization and knowledge transfer across this field.

In an op-ed today, we reflected with the Fecal Transplant Foundation on the impact this may have on patients. In the past few years, we’ve seen the emergence of FMT as a standard of care treatment for intractable C. difficile infection. The scientific community has begun to demonstrate that the bacteria in our guts play a wide-ranging role in our health. We have seen mounting evidence that the gut microbiome can be linked to chronic autoimmune conditions, metabolic diseases, and antibiotic-resistant infections. We’ve seen hints that even in oncology, malnutrition, and mental health, microbiota may have a role to play.

As we begin to understand these relationships, we will also learn how to harness these bacterial communities to protect and advance our health. We are thrilled to continue onto the next phase of this journey with all of you.

James Burgess
Executive Director
OpenBiome

THE RISE OF A NEW PUBLIC HEALTH CHALLENGE

The hygiene hypothesis posits that the rise in autoimmune conditions in industrialized countries may be related to modern hygiene practices and use of antibiotics. Given compelling evidence that microbes play a role in training and regulating our immune systems, we intend to investigate how engineering the human gut microbiome can help to tackle this public health crisis. We aim to find new therapies that will change the epidemiology of autoimmune and inflammatory diseases so Panel B mirrors the success with infectious diseases shown in Panel A.