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Canadian Agency for Drugs and Technologies in Health
865 Carling Ave., Suite 600
Ottawa, ON K1S 5S8
Submitted electronically via CADTH website

**Re: Stakeholder Feedback Submission – Draft Environmental Scan – ES0341**

Dear members of the advisory committee,

Thank you for the opportunity to provide input regarding CADTH's Draft Environmental Scan Report on Fecal Microbiota Therapy in Canada: Barriers and Facilitators to Access. The Gastrointestinal Society, along with our partner charity, the Canadian Society of Intestinal Research, are committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, and promoting gastrointestinal and liver health. Since 1976, we have been advocating for patients with digestive and liver diseases and disorders (everything from gum to bum). This includes, among a host of other conditions, as many as 6 million Canadians with irritable bowel syndrome (IBS), more than 9 million with functional dyspepsia, as many as 8 million with chronic acid reflux (GERD), and an additional 270,000 suffering from inflammatory bowel diseases (IBD) including Crohn's disease and ulcerative colitis.

Below, we provide our feedback to the following questions.

1. **Please look at Table 3, on page 30, Location of FMT Programs in Canada, and let us know if you are aware of any other FMT programs that are missing here.**

OpenBiome is a non-profit stool bank that provides safe access to fecal transplants and also collects stool donations.[1] All of their materials are compliant with the US Food and Drug Administration and they have developed oral capsules for administering FMT primarily for *Clostridioides difficile* Infection (CDI), formerly known as *Clostridium difficile* infection. They allow use of their products for other indications, such as Crohn's disease and irritable bowel syndrome, only if it is in a clinical trial setting. As a result, OpenBiome is used in clinical trials in the US and various international locations, including Canada. However, most of them have been paused due to the novel coronavirus (COVID-19) pandemic.

While OpenBiome is in the US, under Health Canada's personal use regulations, Canadian physicians can help patients legally obtain a three-month supply of OpenBiome's fecal transplant material. The treatment is costly to patients (USD $1,695 to $2,050 per 6-month dose), but OpenBiome has a Patient Assistance Program to help patients gain access to these important therapies. OpenBiome is a safe and convenient alternative for physicians to finding and screening appropriate donors.

2. **Are you aware of any provincial or regional stool bank programs that are in development?**

No.

3. **Do you have any comments on standards or guidance, or other measures needed to facilitate access to this therapy?**

At this time, we support the position of the Canadian Gastroenterology Association to limit fecal microbiota transplant therapy to CDI at this time.[2] The use of FMT for other indications, such as IBD, multiple sclerosis, and obesity (to name a few), should move forward only on a therapeutic class basis, directly linked to clinical studies for those indications, as evidence on safety and effectiveness are still emerging and/or are in their infancy.

We encourage research and development since evidence is showing promising results for FMT in treating other gastrointestinal conditions. Guidance on treatment should also look at assessing the potential use of FMT in standard of care for severe or fulminant CDI and in early intervention, particularly nine days following diagnosis.

Research has found that it may decrease mortality rates by 77% and more with early intervention.[3] Currently, the Association of Medical Microbiology and Infectious Disease Canada do not have any recommendations for the use of FMT in severe CDI, even though there have been case uses reported.[4] Assessing this implementation contributes to the need for a standardized protocol regarding FMT (line 572).

It is worth mentioning, and perhaps including in the report, that the Gastrointestinal Society conducted the first survey of patient perspectives and experiences of Canadians living with CDI.[5] This initiative received the support of our medical advisory council and internal medicine physicians across Canada, who helped craft the survey questions and disseminate the survey to patients. The study used a mixed method approach (qualitative and quantitative) to gather input. We reported that FMT is used as second line therapy after antibiotics and is a safe and effective alternative to treatment. However, its use is still lagging. We found that 1 out of 167 participants received FMT for their first occurrence of CDI, while a few more participants received it for subsequent CDI (5 out of 67). Again, we found its use to be much less than expected. Despite this, patients who received FMT acknowledged it as the cure for their CDI and responses indicate that a majority of patients treated with standard of care (antibiotics) are turning to probiotics for recurrent infections.

In both our 2017 Canadian-wide survey[6] of patients with CDI and our 2020 study on patient experiences mentioned above, an estimated 60-80% of respondents lived with at least one additional gastrointestinal condition prior to contracting CDI. Most of these individuals have IBS, IBD, and/or GERD. Other reported conditions were diverticular disease and celiac disease. However, these concurrent diseases and disorders present symptoms that may exclude patients from receiving FMT, providing further explanation to its lower utilization rates in Canada. From our patient-focused study and analysis, our findings support the need for further standardization and control practices across Canada. In fact, several patients reported that they received misdiagnoses of CDI, increasing anxiety during their visits to the emergency room, which adds to the delays patients experience in receiving proper care.[5] Our research also found that there are no publicly available data on recent incidence rates of CDI in Canada. This needs to be addressed to improve reporting on patient outcomes, understand demand for FMT therapy, and whether the needs of patients are being met. Accurate and timely monitoring will ultimately benefit patients and supplement research efforts in evaluating the effectiveness of treatments for CDI/rCDI.

The importance of patient and physician education and public awareness to eliminate stigma surrounding FMT (the 'ick' factor) cannot be underplayed. Qualitative data we gathered from our research also found poor, and sometimes degrading, attitudes of hospital staff related to patients' bowel issues. We found that 2% of respondents wanted to see alternative providers to improve their care experience.[5] This signals a need for improved patient-staff communication and training for healthcare professionals on appropriate behaviors and attitudes to patients with CDI.

**4. Is the information contained within the document complete? Are there any inaccuracies in the report, or is any relevant information missing?**

We believe that it is important to discuss the regulatory process for FMT products entering the Canadian market and how it contributes to barriers to access. Currently, Health Canada has labelled FMT as an investigational new biologic drug and has implemented an interim risk-based approach.[7] However, the report mentions that there is ongoing debate surrounding FMT's appropriate classification (line 630). Furthermore, the Guidance Document created by Health Canada limits the use of FMT for the treatment of CDI. Due to lack of evidence, FMT can only be used for other indications in a clinical trial setting. While Health Canada recognizes the need for allowing greater access to this treatment, we encourage discussions regarding other policy options, to help eliminate the access barriers identified in this report. For example, a microbiota-based product administered as an enema, RBX2660, is currently under clinical trial studies across the US and Canada for the indication of recurrent CDI.[8] We do not know how Health Canada will classify this drug in its regulatory framework.

On the other hand, a potential solution to some of the challenges brought forward in the report regarding stool banks is to promote research into finding alternatives to FMT, such as artificial stool (line 551).[9] One study assessed the effectiveness of using a stool substitute transplant for CDI and its results were promising. However, we do not know whether further studies were undertaken to move the results forward.

The report also needs to disclose specifically which search terms and keywords were used in conducting their literature search, since this is not only standard practice in literature reviews but it also helps us and other stakeholders understand if different terminologies are used and whether these may contribute to

misunderstandings, stigma, and barriers to access (lines 165-169). For instance, we know that some centres process their stool donations via the hospital's multi-organ donor programs whereas some may have designated supply instructions.

Lastly, with the wide distribution of false information online it is important to discuss how these practices portray fecal microbiota transplant and further signal the need for evidence-based public awareness and outreach. The environmental scan briefly mentions the extensive coverage of FMT by Canadian media (line 615). However, more discussion is warranted on the spread of false information regarding FMT, since this may be more pervasive. It only takes a google search to find various websites and videos on do-it-yourself FMT, which may be a reflection of patients' frustration in accessing treatment. These practices also pose a real danger to the health and safety of Canadians that needs to be addressed.

**5. How can the wording of the document be improved?**
We do not have any comments to provide on this.

**6. Do you foresee the document being useful for your work and your organization? If so, how?**
Yes. CADTH's environmental scan on the availability of programs across Canada and existing barriers for FMT supports us in our initiatives to spread awareness and evidence-based information. The research findings legitimize our concerns and further help us understand the gaps in care and public education, especially with the prevalence of stigma in both physician and patient communities. We may reference this report in our programs such as our patient information pamphlets, which cover information on more than 30 gastrointestinal conditions, and in our *Inside Tract*® newsletter, when appropriate. We will also use the environmental scan to promote further research on the efficacy of FMT for CDI and a growing number of other potential indications.

**7. Please provide any additional comments you may have about this report.**
We have no further comments.
Thank you for the opportunity to provide feedback on this important issue. We believe that there are several challenges that urgently need to be addressed in facilitating access for FMT therapy and we are eager to support and grow our initiatives to tackle these. We welcome further discussions and opportunities for collaboration on ways to improve access via public education and awareness for fecal microbiota transplant.

Yours sincerely,

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