Quality & Safety Program
QUARTERLY REPORT
Q1 | 2015 | JAN - MAR
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Dear Partners,

The first quarter of 2015 was another exciting step forward for our organization as we added 78 new hospitals to our network and delivered 1,205 treatments to 185 partners in 41 states. Today, 94% of the US population lies within 150 miles of one of our clinical partners, ensuring nearly universal safe access to FMT for recurrent C. difficile patients. Beyond these immediate efforts to address the C. difficile epidemic, we continue to work with many of you to develop bench-to-bedside research collaborations aimed at elucidating the role of microbial engineering in a range of microbiome-associated diseases.

We were also pleased to announce the availability of OpenBiome’s Capsule G3, an encapsulated microbiota preparation for oral administration, currently available under our Compassionate Care program while we conclude dose-finding studies, and which will be fully available in Fall 2015. We have also introduced new material release criteria based on 16S rRNA sequencing of our donors’ stool—a first for the field. Stay tuned as well for updates to the names and packaging of the treatment types that we offer to make their respective applications more distinct.

We would like to remind you that you are required to report all FMT-related adverse events both to OpenBiome and directly to the FDA. It is critical for us to learn about any potential adverse events quickly so that we may mount an appropriate response to ensure patient safety across our network. Similarly, we would like to remind you to continue submitting Material Tracking Logs (MTLs). The MTL system forms the backbone of our quality assurance program and enables us to detect donor or batch-related outcome inconsistencies. Your small time contribution has a powerful impact on all of our partners and their patients. We thank you for your continued dedication to this program.

In May, OpenBiome participated at Digestive Diseases Week in Washington, DC. We were thrilled to meet many of you at our oral plenary and our booth on Foundation Row. Your thoughtful feedback and support was an uplifting reminder of the community of outstanding practitioners that we serve. As one tangible outcome from DDW, you can look forward to the development of new educational programming as we aim to synthesize and promote best practices among our clinical partners.

Thank you very much for your continued partnership and support as we move this field forward together.

Sincerely,

James Burgess
Executive Director
Fellow Physicians,

Thank you for another wonderful quarter of partnership. Recently, I've had the privilege of sharing some of our safety research both at Digestive Disease Week and Canadian Digestive Diseases Week. These opportunities sparked inspiring safety discussion with many of you – long-time, new and future partners. In particular, we were thrilled to present results from our Donor Screening Program in the Clinical Practice Distinguished Abstract Plenary Session. Among a cohort of 459 prospective donors, conservatively only 8.5% of potential donors were able to qualify. The burden of asymptomatic rotavirus was particularly striking despite an absence of risk factors. As rotavirus is not routinely assessed in most FMT programs, this is a meaningful reminder that together we must strive towards consensus guidelines for FMT donor screening.

Additionally, it's pivotal we continue to catalyze research in FMT safety, trials such as OpenBiome's STOOL study, which began enrolling this quarter, aims to capture the long-term safety profile of FMT. We encourage any sites interested in joining this study to contact us at science@openbiome.org to learn more. Armed with this data from studies like these, clinicians and scientists can drive towards evidence-based guidelines to ensure the best care for our patients in this emerging field.

From an adverse events perspective, I'm happy to report there are no adverse events attributable to FMT reported across our network this quarter. This said there is an important public health lessons regarding animal exposures in hospitals linked to a Pasteurella multocida infection that we describe in this report. As physicians we must be thoughtful about the principles of public health that underpin the fabric of illness.

I'm also excited to introduce Dr Majdi Osman MD MPH this quarter as our Clinical Program Director. Trained at Harvard, University College London and the London School of Hygiene and Tropical Medicine, Majdi will take a leading role in OpenBiome's mission to increase safe access to FMT, and growing our FMT Education Program. We are thrilled to bring his complementary clinical insights and deep public health knowledge as we continue to improve the standard of care in this emerging field.

Together, we are entering a new an exciting frontier of microbiota-based therapy, and we are thrilled to have the opportunity to share this journey with each of you.

Sincerely,

Zain Kassam, MD, MPH, FRCPC  
Chief Medical Officer
• **There was 1 suspected adverse event reported** in our network this quarter. An adverse event debrief is found in this report. All identifying patient information has been removed.
  
  o The reported AE was a case of *Pasteurella multocida* infection.
  
  o **FMT attribution: Unlikely source**

• Questions are always welcome by reaching out to OpenBiome at 617-575-2201 ext. 1 (for Safety) or safety@openbiome.org
• No updates were made to the Q&SP this quarter.
There was a suspected adverse event that was flagged and escalated for an in-depth review by the Chief Medical Officer and independent consultation by two Clinical Advisory Board physicians in keeping with the OpenBiome Adverse Event Decision Algorithm.

**Figure 1: Path 1c excerpt from the OpenBiome Adverse Event Decision Algorithm**

![Figure 1](Source: http://www.openbiome.org/safety)

Ultimately, to help debrief the lessons and key takeaways from these experiences, this suspected adverse events is summarily debriefed in the following section.
Date of Suspected AE
March 2, 2015

Unit ID
7-34-B

ID
An 81 year old severely immunocompromised vasculitis patient was diagnosed with severe-complicated, NAP-1 positive C. difficile infection with Pasteurella multocida infection status-post FMT.

Past Medical History
1. ANCA positive vasculitis treated with Rituximab and Prednisone
2. Hemodialysis-dependent ESRD due to vasculitis associated rapidly progressive GN
3. Type 2 DM
4. Recent healthcare associated pneumonia with hospital discharge January 10, 2015 following standard HAP antimicrobial therapy course

Clinical Course
Briefly, the severely immunocompromised patient was diagnosed with severe-complicated, NAP-1 C. difficile infection. He was treated with oral vancomycin and IV metronidazole; however, given ongoing deterioration, vancomycin enemas were added without clinical improvement. On February 26, 2015, a FMT by colonoscopy was performed and diffuse, moderate-severe pseudomembranes were detected throughout the colon on endoscopic assessment. Fecal material was delivered in the cecum and throughout the colon, and post-procedure day #1 there was some clinical improvement.

Unfortunately, clinical diarrhea recurred on post-procedure day #2, although interestingly C. difficile testing was negative. On post-procedure day #3 the patient experienced clinical deterioration of uncertain etiology with respiratory failure and hypotension. Diagnostic work-up revealed an AXR with ongoing dilated loops but no overt perforation although visibility was limited. No CT was conducted. Subsequent, blood cultures revealed 2/2 Pasteurella multocida; however, the patient experienced rapid hemodynamic deterioration and expired.

Assessment
An initial consultation by the Chief Medical Officer on March 4th triggered a detailed collaborative investigation conducted in keeping with the OpenBiome SAFE protocol and included strict donor material quarantining during the investigation as well as consultation with two independent Clinical Advisory Board members. Specifically, physicians with special skills for this case were selected: an infectious diseases specialist and a gastroenterologist, the latter with extensive expertise in FMT for severe-complicated CDI.
As a background, *P. multocida* is typically associated with canine or feline exposures leading to a localized cellulitis or occasionally respiratory tract and regional lymph node involvement, however; bacteremia is rare. In a large case series, 13 patients with *P. multocida* bacteremia in 12 years were reported in France, all were immunocompromised by either chemotherapy, like the patient in question, or cirrhosis (Raffi F et al 1987).

Upon detailed infection control review, there were a number of therapy dogs on the hospital ward during the patient’s admission although the patient himself did not have any pets or animal contacts prior to his admission.

On further examination of FMT as a potential source, a clinical interview of the donor suggested an absence of *P. multocida* risk factors including pet or animal exposures. Additionally, quality assurance data suggested successful FMT in 38 patients without any reported adverse events using the donor’s fecal material. As *P. multocida* is an oral/respiratory microorganism, despite significant exploration, no CLIA-certified, validated stool test was identified to assess the stool safety sample or the patient’s pre-FMT stool. Also, assessment of the literature highlighted no cases of *P. multocida* bacteremia for patients undergoing FMT for severe-complicated disease (Fischer M et al 2014) or those with underlying immunosuppression (Kelly C et al 2014).

After a comprehensive investigation, the local hospital infectious disease specialist and infection control team, OpenBiome Chief Medical Officer, and both Clinical Advisory Board member all independently concluded that the *P. multocida* sepsis was not related to the FMT.

Upon deep assessment, given the characteristics of the microorganism and the clinical context, the body of evidence suggested the underlying source of the *P. multocida* sepsis was most likely linked to the in-hospital canine exposure in the context of an immunocompromised patient.

**Best-Practices Learned**

1. Public health and hospital stakeholders must ensure that immunocompromised patients are not exposed to canines and other animals that may confer disease and put patient care at risk. Visitors, healthcare workers and patients should be counseled on the health risks of a subpopulation of vulnerable patients when exposed to animals.

2. Although there is emerging, promising data for using FMT to treat severe-complicated CDI not responsive to standard therapy, clinicians should comprehensively review the risks, benefits and alternatives during the FMT informed consent process. Additionally, given the success of more distal delivery of fecal material, clinicians may reconsider the utility of depositing fecal material into the cecum in the context of extensive pseudomembranes, which may increase the risk of perforation.
3. Clinicians must be particularly cautious performing FMT on immunocompromised patients who may be at higher risk for adverse events. A detailed dialogue must occur and be documented regarding the risks, benefits and alternatives of FMT for this patient population.
There were no changes to the OpenBiome Adverse Event Watch List this past quarter. For reference, an image capture of the AE Watch List is included here. This document will be updated and circulated to all partners in the event of an AE attributable to OpenBiome material.

<table>
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<th>Date Added</th>
<th>Adverse Event Diagnosis</th>
<th>Threat Type</th>
<th>Donor</th>
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<th>Notes</th>
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**TEMPORARY WATCH LIST**

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|            |                         |             |       |                             |       |

**PERMANENT WATCH LIST**

|            |                         |             |       |                             |       |
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|            |                         |             |       |                             |       |
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