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Dear Partners,

I am proud to share an update on the accomplishments of this network in the last quarter of 2015. Across more than 300 healthcare facilities, you delivered over 2,100 treatments to patients suffering from recurrent *C. difficile*. 87 new healthcare facilities joined the OpenBiome network, helping us collectively reach another significant milestone: there is now an OpenBiome-supported FMT program in every U.S. state. To support your continued efforts to reach patients in need of FMT, we also introduced the following:

**FMT capsules now available:** At the beginning of 2015, we announced that FMT Capsule G3, OpenBiome’s formulation of encapsulated stool, was available under our Compassionate Care program. This fall, we completed a dose-finding study to evaluate optimal dosage levels and conducted follow-up validation studies. With this work complete, we made FMT capsules available to our entire clinical network. You can find more information about FMT Capsule G3, the results of our dose-finding study, and how to order at [www.openbiome.org/fmtcapsules](http://www.openbiome.org/fmtcapsules).

**Clearer packaging and guides for clinicians:** We made several improvements to the packaging of our three treatment formats to enhance patient safety. We updated the information on our packaging boxes, and introduced a clinical checklist insert with each shipment to help guide FMT administration. Furthermore, the previous plastic-sealed caps on our treatment bottles have been replaced with tamper-resistant caps, making it easier for you to identify if an FMT bottle has been tampered with.

**Safety tracking and clinical support:** At OpenBiome, patient safety is our primary concern. We would like to remind you that the outcome data you are required to submit through Material Tracking Logs (MTLs) is crucial to our quality assurance efforts and to the protection of patients throughout our network. This information allows us to monitor the efficacy of our material, and proactively respond to any network-wide patterns that could be linked to one of our stool donors. It is also critical that you review and follow OpenBiome’s [guide](http://www.openbiome.org/guide) to responding to adverse events and continue to submit any adverse events to OpenBiome. This quarter, OpenBiome expanded its Clinical Assessment & Safety team.
to be able to better support our clinical partners and respond effectively to any potential adverse events or patient safety concerns.

In October, OpenBiome participated at Infectious Disease Week in San Diego and the American College of Gastroenterologist’s Annual Scientific meeting in Honolulu, where we were grateful to meet many of you in person. Your thoughtful feedback will help shape many of our next steps as we strive to make improvements that will promote patient safety and best practices in the field.

Thank you very much for your continued partnership and support.

Sincerely,

James Burgess
Executive Director
Fellow Physicians,

Thank you for another wonderful quarter of partnership. I was delighted to meet many of you at this year’s American College of Gastroenterology meeting in October, where we presented our Quality and Safety Program (Q&SP) including our adverse events reporting algorithm. I had the opportunity to engage in inspiring discussion with many of you at the conference and look forward to getting to know many more of you over the coming months.

From an adverse events perspective, I’m happy to report there were no adverse events attributable to FMT reported across our network this quarter. However, adverse events reported to us provide important lessons on how we can enhance safety for patients receiving FMT. We have re-structured the Q&SP report to summarize salient, best practice lessons from each case at the front of the report (page 7).

We are grateful to all those partners who contacted us this last quarter to discuss suspected adverse events. We would like to advise partners to report adverse events first to OpenBiome via the online reporting form openbiome.org/adverse-events. Using this information, an OpenBiome clinician will contact you and assist you in determining whether the adverse event requires reporting to the FDA.

I would like to reiterate the importance of MTLs to our collective mission of improving access to safe FMT. Our first priority at OpenBiome is safety and the information you provide is the single most important thing. If you have feedback on how we can make MTLs easier to complete please do let us know.

Together, we are entering a new and exciting frontier of microbiota-based therapy, and we are thrilled to have the opportunity to continue pursuing the highest standards of safety in this field.

Sincerely,

Majdi Osman, MD, MPH, MRCP, DTM&H
Clinical Program Director
• **Material Tracking Log submissions are mandatory** to place an order for new OpenBiome material
  - MTLs provide critical (non-patient identifying) data on delivery modalities, follow-ups being performed, and patterns of non-responses and adverse events tied to any specific donors for quality assurance
  - MTL submission is critical to enabling the full transparency of best-practices and flagging of safety patterns afforded in our universal donor model

• Our Clinical Safety team is available to answer any questions about an adverse event. As an investigational drug, reporting adverse events to OpenBiome and the FDA, in cases of a Severe Unexpected Suspected Adverse Reaction (SUSAR), is mandatory and helps assess the safety of FMT material.
  - Please report adverse events first to OpenBiome via openbiome.org/adverse-events. Information gathered in this form will be used to assess whether the adverse event requires reporting to the FDA.
  - Partners with questions about adverse events are welcome to reach out to OpenBiome at:
    - 617-575-2201, ext. 1 (for Safety)
    - safety@openbiome.org

• 14 adverse events were reported to OpenBiome this quarter.

• **No reported adverse events were determined to be definitely related to FMT material** in our network this quarter.
No updates were made to the Q&SP this quarter.
• **Reducing the risk of infectious gastroenteritis post-FMT**

We report a case of a patient who experienced gastroenteritis (norovirus and *E. coli*) after eating several meals from fast food outlets immediately post-FMT. Patient education is crucial before and following FMT. Patients should be counseled on healthy eating, hand washing and ensuring that food is prepared in hygienic conditions to mitigate the risk of food-borne illnesses as well as *C. difficile* reinfection.

• **Patients with recurrent infections, sepsis, or asymptomatic colonization with multi-drug resistant organisms (MDROs)**

In this Q&SP report we present cases of sepsis during hospital admissions in patients with known risk factors including MDRO colonization, indwelling lines and recurrent bacterial infections. Where sepsis occurs in a patient post-FMT, routine sepsis screen should be performed to exclude all potential sources of infection. In complex cases, such as those outlined in this Q&SP report, hospital infection control teams can also offer further support in evaluating adverse events where an infectious etiology is suspected.

• **Upper delivery FMT in patients with ongoing or recent bowel obstruction**

Ongoing or recent intestinal bowel obstruction is a contraindication to upper delivery due to the increased risk of aspiration (Baxter et al 2015). The most responsible physician should assess the patient for risk of aspiration and consideration other treatment options if there is any increased risk of aspiration.

• **Immunocompromised patients**

There is limited data for FMT in recurrent CDI among immunocompromised patients. The most robust data come from a multi-center retrospective review of 80 (75 adult and 5 pediatric) immunocompromised patients with CDI, predominantly outpatient, undergoing FMT (Kelly et al 2014). The reason for immunosuppression included: HIV/AIDS (3), solid organ transplant (19), oncologic condition (7), immunosuppressive therapy for inflammatory bowel disease (IBD; 36), and other conditions/medications (15). The cure rate after a single FMT was 78% and the overall cure rate was 80%. Overall, 15% of patients had a serious adverse event within 12-weeks post-FMT, of which 10 were admitted to hospital. Two deaths occurred: a sedation-associated aspiration during FMT by colonoscopy; and the other unrelated to FMT. No patients developed infections definitely related to FMT; however 2 patients developed unrelated infections and 5 had self-limited diarrheal illness in which no causal organism was identified.
One patient had a superficial mucosal tear at the time of colonoscopy. Broadly speaking, immunocompromised patients appear to have approximately the same rates of clinical cure; however, serious adverse events must be monitored for closely, and more data is needed given the limitations of retrospective case series data.

The risks, benefits and alternatives should be discussed in detail with the patient and other approaches including antibiotic therapy or a directed donor approach could be considered.

- **Use of FMT to treat severe-complicated *C. difficile* infections**

Severe and severe/complicated *Clostridium difficile* infection (CDI) can result in ICU admission, sepsis, toxic megacolon and death. In this setting, colectomy is the standard of care but it is associated with a 50% mortality.

The Fischer protocol provides an alternative approach to managing severe-complicated disease (Fischer et al., 2015). Treatment consisted of sequential FMTs via colonoscopy with the need for repeat FMT and continued vancomycin guided by clinical response and pseudomembranes at colonoscopy. The authors observed an 89% (17/19) treatment response in severe-complicated disease. Although this was a small study, it provides potential options for the management of patients with severe-complicated disease with the aim of preventing further progression of CDI.
There were 9 suspected adverse events that were flagged and escalated to OpenBiome in Q4 2015 (MedWatch 3500 reporting) in accordance with our Adverse Event Decision Algorithm. All such cases entered the “1c - Consult OpenBiome” pathway of the Decision Algorithm.

*Figure 1: Path 1c excerpt from the OpenBiome Adverse Event Decision Algorithm (Source: http://www.openbiome.org/safety)*

All reported adverse events were reviewed in-depth by our Clinical Program Director and Chief Medical Officer. Upon immediate contact with the reporting institution, all cases were classified using the following NIH Relatedness definitions.

- **Definitely Related**: The adverse event is clearly related to the investigational agent/procedure – i.e. an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject’s clinical state.

- **Possibly Related**: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern
to the suspected intervention, but that could readily have been produced by a number of other factors.

- **Not Related:** The adverse event is clearly not related to the investigational agent/procedure. - i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

There were no cases that were definitely related to FMT material. All 9 adverse events are reported below.
Date of Suspected AE
10/3/2015

Unit ID
65-004-D

Summary
An 87-year old male with significant cardiovascular comorbidities received a Fecal Microbiota Transplant (FMT) for recurrent NAP-1 severe-complicated *Clostridium difficile* infection (CDI) presented with *Escherichia coli* bacteremia two weeks post-FMT.

Past Medical History
1. Ventricular arrhythmias
2. Implanted cardioverter-defibrillator with pacemaker
3. Myocardia infarction
4. Coronary artery bypass x 4
5. Hypertension
6. Benign prostatic hyperplasia (BPH)
7. NAP-1 recurrent *Clostridium difficile*

Clinical Course
Briefly, an 87-year-old male inpatient with a background history significant for cardiovascular comorbidities and importantly benign prostatic hyperplasia (BPH) on Proscar was admitted for NAP-1 *Clostridium difficile* infection (CDI) confirmed by qPCR (Modified Horn Index 3). CDI was not responsive to standard therapy including multiple courses of oral vancomycin and metronidazole. The patient’s clinical picture was consistent with severe-complicated CDI.

Oral vancomycin antibiotics were discontinued 3 days prior to the FMT procedure. PEG bowel prep in keeping with Van Nood et al. (2013) and PPI therapy were appropriately initiated. A total of 30ml of fecal microbiota material (Unit# 65-004-D) was infused by EGD (van Nood, Dijkgraaf, & Keller, 2013). It was unclear in what segment of the upper GI tract the material was infused (pre- or post-pylorus). Post-FMT the patient had a decrease in stools and was discharged to a rehab facility.

On day 15 post-FMT, the patient presented to the emergency department obtunded with diarrhea and abdominal pain. The patient showed continuing clinical decline and blood cultures were drawn from a peripheral line. Initial fast read, and subsequent cultures, returned a positive result for *Escherichia coli* sensitive to cephalosporins. Urine culture was negative and no other source of *Escherichia coli* was found. No imaging (X-rays, CAT scans etc.) was
performed during the patient’s admission due to their unstable condition and at the patient’s request for conservative management.

Subsequently, the patient was commenced on Cefepime Hydrochloride, USP, a broad spectrum cephalosporin antibiotic, due to unknown antibiotic sensitivities. Metronidazole was initiated for anaerobic cover as there was a concern for an intra-abdominal source. Upon starting the antibiotics, the patient experienced an increase in stool frequency and a positive *Clostridium difficile* PCR stool culture was noted consistent with re-infection given initiation of broad-spectrum antibiotics.

The patient began to clinically decompensate and there appeared to be an elevated lactic acid. Blood gases and pro-BNP were sent for a suspected myocardial infarction. Unfortunately, the patient continued to decline rapidly and became hypotensive, went into respiratory failure, and expired.

**Assessment**

At OpenBiome we were informed of the adverse event and in keeping with our SAFE protocol, immediately placed donor 65 on shipping hold. An in depth investigation was commenced with our reporting clinical partner.

The source of the *Escherichia coli* bacteremia is unclear, and the impact of FMT on the course of the patient’s deterioration is unclear. One urine culture was done on the patient which was negative but a urinary source, particularly given the patients enlarged prostate, cannot be ruled out. It is unclear if the patient had a catheter and whether that was cultured. Overall, the source of the *E. coli* bacteremia was unknown.

Following an in-depth investigation of the case in collaboration with the reporting team, the diagnosis is sepsis of unknown origin though the patient’s serious cardiovascular history accompanied by suspicion of myocardial infarction immediately prior to expiring cannot be ruled out.

Upon receipt of this information, data from Donor 65 was evaluated and there were no reported adverse events among material used across the network (n=50). As a precautionary measure, the safety sample for unit 65-004-D was sent to Quest lab for testing of Shiga toxins, EIA with reflex to *E. coli* O157 culture, Campylobacter, Salmonella and Shigella cultures. Results of the safety screen returned negative. It is unclear if the fecal material may have been a source, but this appears less likely given the demonstrated safety profile among 50 other patients treated with the material, negative safety testing, and given the bacteremia occurred over 2 weeks post-FMT.
In summary, an 87-year-old male with NAP-1 positive *Clostridium difficile* underwent an upper delivery FMT and subsequently developed *Escherichia coli* bacteremia 2 weeks post-FMT. Although the etiology is unclear, given the temporality and the negative safety aliquot testing, it was determined that the bacteremia was not related to the FMT material.

**Adverse event classification:**

- **NIH Severity Grade:** Grade 5 (fatal)
- **Relatedness:** Not related to FMT

**References**

Date of Suspected AE
10/6/2015

Unit ID
26-041-I

Summary
An 89-year-old female with significant cardiovascular disease received a second fecal microbiota transplant (FMT) for recurrent *Clostridium difficile* infection (CDI) and expired five days post-FMT due to suspected cardiac event and arrhythmias.

Past Medical History
1. Atrial fibrillation
2. Coronary artery disease
3. Aortic stenosis
4. Hypertension
5. Peripheral venous insufficiency
6. History of DVT and pulmonary embolism
7. Hyperlipidemia
8. Osteoporosis
9. Alzheimer Disease
10. Refractory *Clostridium difficile* infection

Clinical Course
Briefly, an 89-year-old patient with a significant background history of cardiovascular disease and refractory *Clostridium difficile* infection (CDI), Modified Horn Index 4, underwent fecal microbiota transplantation (FMT) after failing several courses of fidaxomicin and metronidazole with no response. A total of 30ml of FMT material was delivered via upper endoscopy without complication. The patient did well post-FMT with a decrease in diarrhea and CDI symptoms and was subsequently discharged.

On day 21 post-FMT, the patient was readmitted with recurrence of diarrhea and a second FMT was performed. A total of 30ml of FMT material (Unit# 26-041-I) was delivered via upper endoscopy without complication. The patient remained well post-FMT with resolution of CDI symptoms and return of normal bowel movements. Of note, approximately 48 hours prior to the second FMT, the patient had undergone a DC cardioversion for atrial fibrillation.

On day 5 post-FMT, the patient developed cardiac arrhythmias including supraventricular tachycardia and non-sustained ventricular tachycardia. Serological results demonstrated an
elevated Troponin and BNP of >1000 suggesting an underlying cardiac event. Cardiovascular consult was requested and conservative treatment in view of her advanced age and likelihood of poor clinical outcome was recommended. The patient was also reviewed by neurology who felt there was no evidence of stroke.

The patient decompensated with ongoing sustained ventricular tachyarrhythmia despite conservative management and remained sleepy and lethargic with poor oral intake throughout admission. Her condition continued to deteriorate and the patient expired peacefully day 5 post-FMT.

**Assessment**

At OpenBiome we were informed of the adverse event on 11/9/15 and immediately placed Donor 26 on hold. An in depth investigation was commenced with our reporting clinical partner.

The patient received two FMTs to treat recurrent CDI, both of which were initially successful post-procedure. Unfortunately, on a background of significant cardiovascular disease and cardiac arrhythmia, the patient developed a supra-ventricular tachycardia post- second FMT and expired on day 5 post-FMT. Given the patient's history of significant cardiac disease, raised troponin and BNP and documented arrhythmias throughout admission our collaborative review of the case with the reporting team indicates this fatal adverse event was not related to FMT.

Donor 26's fecal microbiota preparation (FMP) has a reported efficacy rate of 85% (n=137). Two other reported adverse events have involved use of Donor 26 FMP. In one adverse event, the patient experienced a progression of severe-complicated CDI and subsequently expired. This adverse event was determined not to be related to FMT material. In the other adverse event the patient experienced aspiration and respiratory distress post-FMT. This adverse event was determined not to be related to FMT material. Donor 26’s material has passed all safety screens.

In summary, this fatal adverse event occurred in an 89-year-old female patient who developed arrhythmias and possible cardiac event 5 days post upper delivery FMT. This adverse event has been determined to be NIH severity grade 5 and “not related” to the FMT material given the patient’s significant pre-existing cardiac comorbidities.

**Adverse event classification:**

- **NIH Severity Grade:** Grade 5 (fatal)
- **Relatedness:** Not related to FMT
Date of Suspected AE
10/9/2015

Unit ID
0065-0062-04

Summary
A 26-year-old female patient with significant gastrointestinal comorbidities received a fecal microbiota transplant (FMT) for recurrent *Clostridium difficile* infection (CDI) not responsive to standard therapy. The patient developed norovirus positive diarrhea post-FMT.

Past Medical History
1. MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes)
2. Intestinal pseudo-obstruction
3. Colectomy with ileostomy and ileorectal anastamosis
4. Chronic pancreatitis
5. Total pancreatectomy
6. Failed B-islet cell transplant
7. Asthma
8. Multiple drug allergies: lidocaine, sertraline, nitazoxanide, bactroban, misoprostol, methadone, morphine, pantoprazole, trazodone
9. Recurrent *Clostridium difficile* infection

Clinical Course
Briefly, a 26-year-old patient with a significant background history of MELAS (Modified Horn Index 3) and refractory *Clostridium difficile* infection (CDI), Modified Horn Index IV, unresponsive to multiple rounds of standard antibiotic therapy underwent fecal microbiota transplantation (FMT). The patient had previously failed several courses of oral fidaxomicin, metronidazole, and vancomycin. Prior to FMT, the patient was tested for Hepatitis B, Hepatitis C, HIV, and CMV which all returned negative.

A total of 250 ml of FMP material (Unit # 0065-0062-04) was delivered via colonoscopy without complication. The patient did well post-FMT with a decrease in CDI symptoms and normally formed bowel movements over 48 hours. The patient was subsequently discharged home 2 days post-FMT.

Shortly after discharge, the patient developed flu-like symptoms including malaise, chills, self-reported fever, and muscle pain, which lasted until day 5 post-FMT and resolved spontaneously without any intervention. The patient was not examined by a physician for these symptoms.
During this time, the patient’s bowel movements remained unchanged with normally formed stool. No changes were made to the patient’s medications nor were any antibiotics or antivirals prescribed.

On day 27 post-FMT, the patient presented with diarrhea (15 stools per day), nausea, and vomiting. A stool sample was sent for testing which returned positive for norovirus (Norwalk-Like AG). Stool sample test results were negative for microsporidium, ova and parasites, cryptosporidium, isospora, and cyclospora. A stool PCR for *Clostridium difficile* was not repeated at this time. However, diarrheal symptoms continued and a stool sample was sent for *Clostridium difficile* PCR which returned positive. The patient was subsequently commenced on oral vacomycin 500mg QID. Repeat Norwalk-Like AG stool testing returned negative for norovirus and the patient was discharged home.

On day 65 post-FMT, the patient was re-admitted to the hospital with frequent diarrhea and CDI symptoms to receive IVIG 1400mg every 6 hours x 4 via doiboff tube. Serological testing returned sodium (Na) 144, chloride (Cl) 117, carbon dioxide (CO$_2$) 18, and anion gap of 9. The patient was diagnosed with hyperchlorine metabolic acidosis and prescribed vancomycin taper, Kefir, nitazoxanide, and rifaximin during the admission. Although the patient remained stable throughout admission, the diarrhea continued. On day 69 post-FMT, the patient experienced a transient improvement in symptoms with nitazoxanide and was discharged home.

**Assessment**

At OpenBiome we were informed of the adverse event on 11/18/15 and immediately placed donor 65 on hold. An in depth investigation was commenced with our reporting clinical partner including discussions with the reporting pharmacist and Infectious Disease expert.

Upon notification of the adverse event, the safety sample for unit 0065-0062-04 was sent for norovirus RNA testing which returned negative. Given the patient’s norovirus symptoms occurred almost 1 month post-FMT the collaborative review of the case along with the reporting team is that the patient contracted norovirus post-FMT. This would be in keeping with the incubation period of norovirus which is approximately 36 hours post exposure. The patient presented almost 4 weeks post-FMT suggesting that norovirus is unlikely to have been contracted at the time of FMT. As such this NIH severity grade 4 adverse event was deemed “not related” to FMT.

Donor 65’s FMP has a reported efficacy rate of 84% (n=37). Donor 65 material has been associated with one prior adverse events in an 87-year-old male who experienced intra-abdominal sepsis due to progression of severe-complicated CDI and toxic megacolon.
In summary, this adverse event occurred in a 26-year-old female patient who acquired norovirus post-FMT. This adverse event has been determined to be NIH severity grade 3 and “not related” to the FMT material given the temporality of the symptoms which occurred outside the average 36-hour incubation period and negative results of the safety sample testing.

**Adverse event classification:**

- **NIH Severity Grade**: Grade 4 (Life-threatening)
- **Relatedness**: Not related to FMT
**Date of Suspected AE**
11/24/15

**Unit ID**
0074-0019-01

**Summary**
A 52-year-old female patient in a long-term care facility with locked-in syndrome and recurrent sepsis received a fecal microbiota transplant (FMT) for recurrent *Clostridium difficile* infection (CDI) and subsequently developed fever and leukocytosis post-FMT.

**Past Medical History**
1. Locked-in syndrome (LIS)
2. Recurrent sepsis
3. Recurrent urinary tract infections
4. Tracheostomy
5. Cerebral vascular disease
6. Myocardial infarction
7. Recent acute respiratory distress syndrome (ARDS)
8. Recurrent *Clostridium difficile* infection

**Clinical Course**
Briefly, this adverse event occurred in a 52-year-old female patient in a long-term care facility with multiple significant comorbidities including locked-in syndrome requiring a tracheostomy and long-term indwelling urinary catheter upon a background of recurrent episodes of sepsis, acute respiratory distress syndrome (ARDS), and urinary tract infections. Most recently the patient was on Cefapime for catheter related chronic urinary tract infection (*Proteus mirabilis* and pan-resistant *Acinetobacter*) and recurrent pneumonia and chronic colonization with *Pseudomonas* diagnosed by positive sputum culture.

The patient was diagnosed with hospital acquired recurrent *Clostridium difficile* infection (CDI) by EIA, which was not responsive to standard antibiotic therapy (Modified Horn Index 4). Given the patient’s health and CDI status, a fecal microbiota transplant (FMT) was recommended.

Antibiotics were stopped 4 days prior to FMT. The patient underwent a FMT via nasogastric tube with 30mls of donor fecal material (Unit # 0074-0019-01) instilled at approximately 1PM. No complications were noted during and immediately after the procedure. There was no emesis during the procedure and the patient tolerated the FMT well.
Shortly after, at 11PM on the same day of the procedure, the patient spiked a temperature of 101 degrees Fahrenheit. A blood draw revealed WBC 31,000, Absolute neutrophils 27 and lactate 2.2. Blood cultures taken x2 at this time returned negative with no positive growth after 48 hours. The patient was immediately started on Cefapime and Tobramycin.

The symptoms responded well to antibiotics and fluid therapy and the fever settled, promptly returning back to within normal limits. The patient had normally formed bowel movements following the FMT. At the time of this report the patient remained hospitalized inline with her previous disposition at her baseline clinical state.

**Assessment**

At OpenBiome we were informed of the adverse event on 11/25/15 and immediately placed donor 74 on hold. Following an initial triage conversation between the reporting pharmacist and OpenBiome’s Clinical Program Director, an in-depth review of the case was commenced and a detailed collaborative investigation was immediately conducted in keeping with OpenBiome’s SAFE protocol.

This adverse event occurred in a 52-year-old chronically ill and immobile female patient with significant comorbidities previously colonized by pathogenic bacteria upon a history of prior multiple infections. There was no evidence of infection transmitted by FMT however with no persistent fever or evidence of sepsis. Based on this investigation, the adverse event was determined to be “not related” to the FMT material.

Donor 74’s FMP has a reported efficacy rate of 87% (n=60). Donor 74 material has passed all safety screens and has not been associated with any prior adverse events at this time.

In summary, this adverse event occurred in a 52-year-old chronically ill female patient with Locked-in syndrome who developed fever and leukocytosis post-FMT. This adverse event has been determined to be NIH severity grade 4 and “not related” to the FMT material given the pre-existing comorbidities and transient nature of the patient’s symptoms with no further positive microbiology or evidence of infection.

**Adverse event classification:**

- **NIH Severity Grade:** 3 (Severe)
- **Relatedness:** Not related to FMT

**References**
Date of Suspected AE
11/30/15

Unit ID
0078-0015-01

Summary
A 59-year-old female patient with history of ovarian cancer and recurrent bowel obstruction on PEG tube feedings received a fecal microbiota transplant (FMT) for recurrent Clostridium difficile infection (CDI) and subsequently expired as a result of respiratory distress and sepsis secondary to aspiration.

Past Medical History
1. Recurrent bowel obstruction
2. PEG tube feeding
3. Peripheral vascular disease
4. Diabetes mellitus
5. Bilateral lower extremity amputations
6. Cerebral vascular disease
7. Ovarian cancer
8. Recurrent Clostridium difficile infection

Clinical Course
Briefly, 59-year-old female patient with background history of metastatic ovarian cancer on PEG feedings was diagnosed with hospital acquired recurrent Clostridium difficile infection (CDI) not responsive to standard therapy (Modified Horn Index 4).

The patient underwent a fecal microbiota transplant (FMT) delivered by upper endoscopy with 30mls of donor fecal material instilled (Unit # 0078-0015-01). No complications were noted during and immediately after the procedure. There was no emesis during the procedure and the patient tolerated the FMT well. The patient's diarrhea settled after 48 hours with normally formed bowel movements.

On day 18 post-FMT the patient developed constipation, abdominal distension and emesis. The patient was not tolerating PEG feeding and colonoscopy demonstrated no evidence of active CDI. A chest radiograph was ordered which demonstrated bilateral consolidation and signs of small bowel obstruction. Attempts to relieve the obstruction during colonoscopy were not successful. Subsequently, a rectal tube was sited for ileus.
Despite intervention, the patient’s ileus persisted and the patient developed signs of aspiration pneumonia with respiratory distress and secondary sepsis. The patient was transferred to the intensive care unit on day 23 post-FMT. In consultation with the family, comfort measures were taken given the patient’s age, co-morbidities and likelihood of recovery. No blood cultures, sputum cultures or stool cultures were sent and no further imaging was performed during the admission in line with the family’s requests. The patient expired due to aspiration pneumonia with sepsis on day 25 post-FMT.

**Assessment**

At OpenBiome we were informed of the adverse event on 12/04/15 and immediately placed donor 78 on hold. Following an initial triage conversation between the reporting pharmacist and OpenBiome’s Clinical Program Director, an in-depth review of the case was commenced and a detailed collaborative investigation was immediately conducted in keeping with OpenBiome’s SAFE protocol.

This adverse event occurred in a frail 56-year-old female with metastatic ovarian cancer and a notable history for prior bowel obstruction prior to the FMT. The presence of a PEG tube indicates the patient was already at a heightened risk for aspiration. A review of the FMT procedure demonstrated that the patient tolerated the upper endoscopy and FMT instillation well and without any complications. However, small bowel obstruction developed 18 days post-FMT. Despite this finding, the patient continued to receive PEG tube feedings which may have contributed to aspiration and subsequent pneumonia. The significant pre-existing comorbidities, advanced cancer, and low baseline health status placed this patient at heightened risk for sepsis and morbidity due to aspiration post-FMT. The presentation of aspiration pneumonia day 23 post-FMT suggests FMT is highly unlikely to be the cause of this patient’s aspiration pneumonia. Rather, the small bowel obstruction secondary to ileus that developed 5 days prior to onset of symptoms is more likely to be the causative event. Based on this investigation, the adverse event was determined to be “not related” to the FMT material.

Donor 78’s FMP has a reported efficacy rate of 80% (n=10). Donor 78 material has passed all safety screens and not been associated with any prior adverse events at this time.

All materials sent to partners include clear instructions that patients should be assessed for risk of aspiration when performing FMT by upper delivery including gastroparesis, recent history of intestinal obstruction or other potential risk factors.

In summary, this fatal adverse event occurred in a 56-year-old female patient who developed bowel obstruction precipitating emesis with subsequent aspiration pneumonia and sepsis post-FMT. This adverse event has been determined to be NIH severity grade 5 and “not related” to
the FMT material given the pre-existing comorbidities and time interval between FMT and the delayed presentation of aspiration pneumonia (18 days).

**Adverse event classification:**

- **NIH Severity Grade:** Grade 5 (fatal)
- **Relatedness:** Not related to FMT
Date of Suspected AE
December 9, 2015

Unit ID
62-0035-01
62-0034-12

Summary
A 75-year-old immunocompromised male patient with history of renal transplant and basal cell carcinoma underwent fecal microbiota transplant (FMT) for recurrent *Clostridium difficile* infection (CDI) and experienced transient Extended spectrum beta-lactamase (ESBL) *Escherichia coli* bacteremia post-FMT.

Past Medical History
1. Nephrectomy
2. Renal transplant recipient
3. Basal cell carcinoma
4. Hypertension
5. Joint replacement
6. Hernia repair
7. Recurrent *Clostridium difficile* infection

Clinical Course
Briefly, a 75-year-old male with multiple medical co-morbidities on daily oral cyclosporin and prednisone, presented to an infectious disease unit with fever and diarrhea. The patient had previously failed two courses of vancomycin and fidaxomicin for recurrent CDI (Modified Horn Index 3). Stool PCR for *Clostridium difficile* toxin returned positive. The patient was admitted to the hospital and received a fecal microbiota transplant (FMT) (Unit # 60-0004-02) with 30mls of donor material via nasogastric tube with no complications. The patient responded well and their symptoms gradually improved with normal bowel movements. The patient was discharged home following an uneventful recovery post-FMT #1.

On day 6 post-FMT #1, the patient reported an increase in frequency of loose stools accompanied with low-grade fever, chills, nausea and vomiting. Repeat stool PCR for *Clostridium difficile* toxin returned positive. The patient was admitted to the ICU and started on IV metronidazole and oral vancomycin. Blood cultures drawn (x2) from peripheral lines returned negative. No other cultures were drawn. The patient remained hemodynamically stable and gradually improved while on antibiotics and was discharged home on day 12 post-FMT #1.
On day 15 post-FMT #1, the patient contacted ID to report an increase in the frequency of loose stools accompanied by a low-grade fever, chills, nausea and vomiting, malaise, lethargy, and loss of appetite. The patient was readmitted to the ICU where blood cultures were drawn (x2) from peripheral lines which returned negative. Repeat stool PCR for CDI toxin also returned negative. No other cultures were drawn at that time. On day 18 post-FMT #1, a urine culture was drawn which returned positive for low colonies of *Psuedomonas spp.* The patient was subsequently placed on a 7-day course of IV Cefepine. Symptoms gradually improved and the patient was discharged on day 28 post-FMT #1 to a skilled nursing facility and then discharged home.

On day 43 post-FMT #1, the patient was readmitted to the ICU with diarrhea, fever, and nausea and vomiting. Blood cultures drawn (x2) from peripheral lines returned negative. On day 44 post-FMT #1, a urine culture was sent which returned positive for multiple gram negative organisms. Repeat stool PCR for *Clostridium difficile* toxin returned positive, Repeat urine returned positive for *Escherichia coli* (ESBL negative). The patient was restarted on oral vancomycin and IV fidaxomycin.

On day 47 post-FMT, ID inserted a nasogastric tube without complication in the post pyloric position with the tip pre-jejenum as confirmed by radiology. A total of 30ml of FMP (Unit # 62-0035-01) was infused. On day 2 post-FMT #2 (12/9/15), an additional 30ml of FMP (Unit # 62-0034-12) was infused through the same nasogastric tube without complication.

Approximately 12 hours post-FMT #3 the patient developed hypertension, chills, nausea and vomiting, and fever of up to 102.6 degrees Fahrenheit without any increase in stool frequency. Blood cultures were drawn (x2) from peripheral lines and returned positive for Extended spectrum beta-lactamase (ESBL) *Escherichia coli.* The patient was prescribed IV Zosyn and blood cultures (x2) from peripheral lines were immediately repeated. Prior to commencing the antibiotic, the blood cultures returned negative. The patient was stabilized and symptoms gradually improved accompanied by continued decrease in stool frequency and improved in consistency. The patient was subsequently discharged home on day 7 post-FMT #3.

Upon follow-up, the diarrhea has resolved and the patient remains stable without any issues.

**Assessment**

At OpenBiome we were informed of the adverse event on January 5, 2016 and immediately placed donor 62 on hold for shipment as per the SAFE protocol. An in depth investigation was commenced with our reporting clinical partner.
Given the clinical context, the most likely source of this patient’s *Escherichia coli* positive blood culture was a urinary source. On the day prior to FMT, the patient’s urine culture returned positive for *Escherichia coli*, a frequent site of *Escherichia coli* infection (Madappa, 2015). The lack of infectious diarrheal symptoms and improving stool consistency post-FMT reduce the likelihood of a gastrointestinal source of *Escherichia coli*. The reporting physician also expressed concern about poor patient hygiene as stool contamination was found under their long fingernails on admission. The likelihood of contamination of the blood culture from the peripheral IV site cannot be entirely ruled out given blood cultures drawn the following day returned negative prior to any medical or antibiotic intervention. In terms of the reporting clinician, she believes the *Escherichia coli* bacteremia was “not related” to the FMT and chose not to file a MedWatch 3500 form.

Donor 62’s FMP has a reported efficacy rate of 91% (n=68). Donor 62’s FMP has been associated with one other adverse event in the case of a 15-year-old female who experienced an IBD flare post-FMT. Following an in-depth investigation, it was determined that this adverse event was not related to FMT.

In terms of the safety sample testing, given that there was a clearly identifiable source, blood results spontaneously returned negative without intervention and the patient did not experience any infectious bowel symptoms, the safety sample was not assessed. The Donor material has passed all safety screening tests prior to this adverse event.

In summary, this adverse event occurred in a 75-year-old male who returned positive for *Escherichia coli* on blood culture testing on the evening of the 2\(^{nd}\) FMT which spontaneously resolved without medical or antibiotic intervention. This adverse event has been determined to be NIH severity grade 3 and “not related” to the FMT material.

**Adverse event classification:**

- **NIH Severity Grade:** 3 (Severe)
- **Relatedness:** Not related to FMT

**References**

Date of Suspected AE
12/18/15

Unit ID
0097-009-06
0102-0017-09

Summary
A 73-year-old immunocompromised female patient with multiple myeloma received a fecal microbiota transplant (FMT) for recurrent *Clostridium difficile* infection (CDI). Post-FMT the patient subsequently developed SIRS with urine culture positive for *Klebsiella, Escherchia coli*, and *Candida*.

Past Medical History
1. Multiple myeloma
2. Arthritis
3. Scoliosis
4. Chronic hypercalcemia
5. Hypothyroid
6. Right humerus open induction internal fixation
7. Tubal ligation
8. Recurrent *Clostridium difficile* infection

Clinical Course
Briefly, this adverse event occurred in a 73-year-old female inpatient from a long-term care facility with multiple myeloma being treated with chemotherapy who presented with recurrent *Clostridium difficile* infection (Modified Horn Index 3) not responsive to standard antibiotic therapy.

The patient underwent a fecal microbiota transplant (FMT) by colonoscopy with 250mls of donor fecal material (Unit# 0097-009-06) instilled in the cecum. The patient responded to this initial FMT with full resolution of diarrheal symptoms by day 4 days post-FMT.

Later that day the patient developed a single temperature spike with an elevated WBC and infectious disease consult was requested. Blood cultures x2 were drawn with no positive growth. Urine culture via Foley catheter specimen returned positive for *Klebsiella, Escherchia coli*, and *Candida*. The infectious disease team declined to commence antibiotics immediately given the patient remained apyrexial.
On day 5 post-FMT, a partial dose of Levofloxacin was commenced to cover for the organisms detected on urine culture. Subsequently, the patient experienced an increase in loose stools on day 6 post-FMT, 6 days post-FMT, with a spike in temperature. Additional blood cultures x2 were drawn with no positive growth.

On day 7 post-FMT, 7 following the initial FMT, the patient underwent a second FMT (Unit #0102-0017-09) by colonoscopy instilled at the terminal ileum with no apparent procedural complications. Findings on colonoscopy were diverticulosis, mucosal edema and spasms but no overt colitis.

Approximately 24 hours following the second FMT, the patient declined clinically, desaturating with respiratory distress and fever documented at 102 degrees Fahrenheit. Further blood cultures x2 were drawn with no growth. Urine specimen returned positive for Candida and multiple gram-positive cocci. Stool testing returned positive for Clostridium difficile (PCR) but no other organisms were identified by stool culture and microscopy. The patient was commenced on IV vancomycin and continued to experience fever, hypotension, elevated lactate and was transferred to ICU.

**Assessment**

At OpenBiome we were informed of the adverse event on 12/22/15 and immediately placed donor 102 on hold. Following an initial triage conversation between the reporting clinician and OpenBiome, an in-depth review of the case was commenced and a detailed collaborative investigation was immediately conducted in keeping with OpenBiome’s SAFE protocol.

This adverse event occurred in a 73-year-old immunocompromised female patient who is a long-term care resident with an indwelling catheter and significant comorbidities resulting from multiple myeloma. The patient had initially tolerated an FMT to treat her refractory and recurrent CDI demonstrating complete resolution of diarrhea by 4 days post-FMT. However, recovery was complicated by the development of a urinary tract infection (UTI) positive for Klebsiella, Eschericia coli, and Candida and for which the patient received a partial dose of antibiotics. A second FMT was subsequently warranted based on a return of CDI symptoms after antibiotic intervention for the UTI. The patient continued to be positive for UTI following a second FMT and experienced a desaturation due to an escalation in symptoms related to the UTI.

A clear source for this polymicrobial infection was found in the positive urine culture and based on a collaborative investigation with the reporting clinicians, the adverse event has been determined to be “not related” to the FMT material.
Donor 102's FMP has a reported efficacy rate of 100% (n=129). Donor 102 material has passed all safety screens and has not been associated with any prior adverse events at this time.

In summary, this adverse event occurred in a 73-year-old immunocompromised female patient with long-term indwelling Foley catheter who developed fever and sepsis post-FMT. This adverse event has been determined to be NIH severity grade 4 and “not likely related” to the FMT material given that blood and stool cultures returned negative and the patient was symptomatic for UTI both pre- and post-FMT.

**Adverse event classification:**

- **NIH Severity Grade**: Grade 4 (Life-threatening)
- **Relatedness**: Not related to FMT
Date of Suspected AE
12/20/15

Unit ID
102-0017-02

Summary
A 73-year-old female long-term care home resident with severe-complicated recurrent Clostridium difficile infection (CDI) received a fecal microbiota transplant (FMT) for and subsequently developed SIRS and CDI recurrence post-FMT.

Past Medical History
1. Coronary Artery Disease
2. Chronic kidney disease
3. Gastroperisis
4. Type 2 Diabetes Mellitus
5. Recurrent, severe-complicated Clostridium difficile infection

Clinical Course
Briefly, this adverse event occurred in a 73-year-old female long-term care home resident who presented with recurrent severe-complicated Clostridium difficile infection (CDI) (Modified Horn Index 4) not responsive to standard antibiotic therapy, including metronidazole and vancomycin. The patient’s severe CDI was confirmed by sigmoidoscopy which demonstrated pseudomembranes throughout.

The patient underwent fecal microbiota transplant (FMT) by colonoscopy and a total of 250mls of donor fecal material (Unit# 102-0017-02) was instilled at the caecum successfully with no complications. Significant psuedomembranes and colitis throughout were observed on colonoscopy. No complications were reported during the procedure or immediately post-procedure. Vancomycin and metronidazole were stopped 24 hours prior to the FMT. The patient was discharged to a long-term care facility the following day with resolution of CDI symptoms and clinically improved.

Three days post-FMT, the patient was readmitted with fever and diarrhea. A CAT scan demonstrated colitis throughout with no signs of perforation. Blood cultures were drawn x2 which returned negative. Urine culture returned positive for Klebsiella pneumonia. Stool cultures were not repeated at this time. Systemic inflammatory response syndrome (SIRS) and diarrheal symptoms continued, prompting commencement of antibiotics, IV metronidazole and oral vancomycin. The patient was admitted to ICU for treatment recurrence of severe CDI. A
gradual improvement was observed and the patient returned to the medical wards with ongoing antibiotic therapy.

**Assessment**

At OpenBiome we were informed of the adverse event on 12/23/15 and immediately placed donor 102 on hold. Following an initial triage conversation between the reporting clinician and OpenBiome, an in-depth review of the case was commenced and a detailed collaborative investigation was immediately conducted in keeping with OpenBiome’s SAFE protocol.

The likely differential in this case was a progression of severe-complicated CDI. Other possible causes for the observed colitis include inflammatory bowel disease or ischemic colitis as the patient does have some background history of risk factors for ischemic colitis. Although positive urine cultures were identified, the treating clinician did not suspect that this adverse event was due to a urinary tract infection but rather severe symptoms secondary to recurrence and progression of severe CDI with a known history of pseudomembranes.

Donor 102’s FMP has a reported efficacy rate of 100% (n=129). Donor 102 material has passed all safety screens and has not been associated with any prior adverse events at this time.

In summary, this adverse event occurred in a 73-year-old long-term care female patient with severe-complicated CDI not responsive to standard treatment who developed CDI recurrence and SIRS post-FMT. This adverse event has been determined to be NIH severity grade 4 and “not related” to the FMT material given symptoms of CDI recurrence and progression of disease.

**Adverse event classification:**

- **NIH Severity Grade:** Grade 4 (Life-threatening)
- **Relatedness:** Not related to FMT
**Date of Suspected AE**
12/30/2015

**Unit ID**
0052-0057-33

**Summary**
63-year-old male with Fournier's gangrene colonized with ESBL+ *Escherichia coli*, *Enterobacter cloasae*, and ESBL+ *Klebsiella pneumoniae* presented with recurrent *Clostridium difficile* infection (CDI), developed bacteremia and subsequent fatal clinical deterioration.

**Past Medical History**
1. Fournier’s gangrene
2. Previous colonization with ESBL+ *Escherichia coli* and ESBL+ *Klebsiella pneumoniae*
3. Chronic kidney disease with abdominal peritoneal dialysis
4. Diabetes mellitus
5. Coronary artery disease
6. Peripheral vascular disease
7. Glans penis removal
8. Below knee amputation
9. Recurrent *Clostridium difficile* infection

**Clinical Course**
Briefly, a 63-year-old male (Modified Horn Index 4) with multiple medical co-morbidities and being treated for scrotal burn status post glans penis removal, presented to Infectious Disease (ID) with left thigh swelling, abdominal pain and distention, and frequent diarrhea. Stool culture PCR returned positive for *Clostridium difficile* and the patient was started on a 10-day course of oral vancomycin per ACG guidelines. The patient underwent surgical wound debridement and swabs sent for testing returned positive for ESBL+ *Escherichia coli* and *Enterobacter cloasae*. Blood cultures drawn (x2) from peripheral lines returned negative. Clinical respiratory and urinary assessments were unremarkable with no overt signs of infection.

Three months following this initial presentation the patient was reassessed by ID for evaluation of impaired wound healing. Cultures of wound swabs returned positive for ESBL+ *Escherichia coli*, *Myroides* species, and ESBL+ *Klebsiella pneumoniae*. Stool culture PCR returned negative for *Clostridium difficile*.

A further three months following this presentation the patient developed signs of recurrent CDI, frequent watery diarrhea, abdominal cramping, bloating, and distention. Stool culture PCR
returned positive on for *Clostridium difficile*. The patient was admitted to the hospital and started on 2g IV vancomycin. On this admission the wound remained partially healed, suggesting potential residual infection, although there were no overt signs of gangrene or necrosis.

IV antibiotics were discontinued and the patient underwent a fecal microbiota transplant (FMT) by nasogastric tube with 30 mL of donor fecal material (Unit ID 0052-0057-33) instilled past the second portion of the duodenum. Placement was confirmed by radiograph. There were no complications during the procedure. CDI symptoms and diarrhea improved post-FMT and the patient was discharged home.

Two days post FMT, the patient was found at home unresponsive, exhibiting symptoms of septic shock and diarrhea. The patient was admitted to ICU and started on vasopressors. Blood cultures were drawn (x2) from peripheral lines which returned positive for ESBL+ *Klebsiella pneumoniae*. The patient was started on IV antibiotics Zosyn and Ertapenem. Upon examination, the scrotal area and wound remained partially healed although no abscess, discharge or necrosis was noted. Urine cultures returned negative. The patient underwent ultrasound to rule out cholecystitis which was unremarkable. Liver function tests were within normal limits. No other cultures were drawn including no sputum testing, skin swabs or stool testing for *Klebsiella pneumoniae*.

Repeat blood cultures (x2) were drawn from central femoral line and peripheral line returned negative though symptoms of sepsis persisted and patient remained in ICU. During admission the left thigh wound showed signs of worsening with Fournier’s gangrene. Repeat blood cultures (x2) were drawn and central line returned positive for *Candida spp*. The patient’s abdominal peritoneal dialysis insertion site was also swabbed and found to be positive for *Candida spp*. Peripheral line blood cultures were negative.

Despite antibiotics, antifungals and medical resuscitation the patient continued to decline with worsening sepsis secondary to Fournier’s gangrene and dialysis site infection. One week into their clinical course, repeat blood cultures (x2) returned positive for *Serratia spp* from both peripheral and central lines. Urine cultures also returned positive for multiple gram-negative rods. The patient continued to deteriorate and expired due to progressive sepsis secondary to Fournier’s gangrene and dialysis site infection.

**Assessment**

At OpenBiome we were informed of the adverse event on January 5, 2016 and immediately placed donor 52 on hold for shipment of this donor material as per the SAFE protocol. Donor 52
had been previously retired and was no longer donating. An in depth investigation was commenced with our reporting clinical partner.

The patient’s initial presentation with multiple medical comorbidities and treatment of recurrent CDI on the background of impaired wound healing previously cultured for multiple drug-resistant organisms including ESBL+ *Klebsiella pneumonia* and *E.coli* placed this patient at very high risk of sepsis and death in the context of *C. difficile* and immunosuppression. Although there was some clinical improvement in the patient’s wound healing and despite aggressive antibiotic and antifungal treatment, the patient unfortunately deteriorated due to sepsis secondary to Fournier’s gangrene and dialysis site infection.

Given the clinical context, the most likely differential diagnosis for the source of the ESBL+ *Klebsiella pneumoniae* bacteremia would be secondary to pre-existing wound colonization. The reporting clinician believed that the *Klebsiella pneumoniae* bacteremia is not related to the FMT, although we acknowledge that it cannot be fully ruled out given it occurred 2 days post-FMT.

Donor 52’s FMP has a reported efficacy rate of 80% (n=265). Donor 52 FMP has been associated with two other adverse events. Donor 52’s material was used in the case of an 86-year-old male who developed *Salmonella infantis* associated diarrhea without bacteremia post-FMT and in the case of a 74-year-old male who developed ischemic colitis post-FMT. In terms of the safety sample testing, there are no CLIA validated stool tests for *Klebsiella pneumoniae*, so this was not assessed. Following an in-depth collaborative investigation in both cases it was determined that these adverse events were not related to FMT.

In summary, this fatal adverse event occurred in a 63-year-old male who developed *Klebsiella pneumoniae* bacteremia 2 days post-FMT. This adverse event has been determined to be NIH severity grade 5 and “not related” to the FMT material given the patient’s previous colonization by ESBL+ *Klebsiella pneumoniae* and progressive clinical decline due to polymicrobial infections over 30 days post-FMT.

**Adverse event classification:**

**NIH Severity Grade:** Grade 5 (Fatal)

**Relatedness:** Not related to FMT
### Q4 2015 Summary of Not Suspected or Expected Serious Adverse Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Unit ID</th>
<th>Demographic Profile</th>
<th>FMT Indication</th>
<th>Suspected Adverse Event</th>
<th>Severity</th>
<th>Related to FMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/2/15</td>
<td>71-0009-07</td>
<td>Not available</td>
<td>Recurrent CDI</td>
<td>Heart failure</td>
<td>Grade 4</td>
<td>Not related, Non-SUSAR</td>
</tr>
<tr>
<td>11/2/15</td>
<td>72-0021-05</td>
<td>Not available</td>
<td>Recurrent CDI</td>
<td>Fever</td>
<td>Grade 2</td>
<td>Possibly related, Non-SUSAR</td>
</tr>
<tr>
<td>11/24/15</td>
<td>44-0076-02</td>
<td>20F, fistulizing Crohn’s, extensive allergies</td>
<td>Recurrent CDI</td>
<td>Anaphylaxis</td>
<td>Grade 4</td>
<td>Not related, Non-SUSAR</td>
</tr>
<tr>
<td>10/11/15</td>
<td>44-0041-04</td>
<td>61M, cirrhosis, hepatic encephalopathy diverticulitis, COPD</td>
<td>Recurrent CDI</td>
<td>Fever</td>
<td>Grade 2</td>
<td>Possibly related, Non-SUSAR</td>
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<tr>
<td>12/9/15</td>
<td>62-0034-12</td>
<td>75M, kidney transplant, immune-compromised</td>
<td>Recurrent CDI</td>
<td>ESBL - Escherichia coli transient bacteremia</td>
<td>Grade 4</td>
<td>Not related, Non-SUSAR</td>
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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>
<thead>
<tr>
<th>Date Added</th>
<th>Adverse Event Diagnosis</th>
<th>Threat Type</th>
<th>Donor</th>
<th>Hold All Units Starting From</th>
<th>Notes</th>
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- **TEMPORARY WATCH LIST**
- **PERMANENT WATCH LIST**