Assessing Infectious Threats in "Healthy" FMT Donors: Results of an Assessment Program to Support a Next-Generation Drug for Recurrent *Clostridium difficile* Infection

Courtney Jones, BS; Mary Kay Sobcinski, RN, MHA; Matt Adams MS; Rebiotix Inc, Roseville, MN

Corresponding Author
Courtney Jones
Rebiotix Inc.
Roseville, MN 551113
Tel: 651-705-8770
E-mail: cjones@rebiotix.com

Background

- Microbiota Restoration Therapy is the Rebiotix platform for delivering human-derived microbes into a sick patient's intestinal tract to treat disease.
- RBX2660 (microbiota suspension) is currently under investigation for recurrent *Clostridium difficile* infection (CDI).
- RBX2660 is sourced from human-derived microbes and manufactured using standardized, quality controlled processes.
- A donor program was implemented to provide a reliable source of raw material to supply Phase 2 studies.

Donor Recruitment and Screening

- Potential donors were recruited by word-of-mouth.
- Nearby universities were targeted as a source of young, healthy donors.
- A one-time recruitment bonus and nominal payments for accepted donations were offered.
- Potential donors underwent an initial screening process (Figure 1) for an extensive list of blood and stool pathogens prior to enrollment.
- Failures were permanently excluded.

Ongoing Donations

- If accepted into the program, donors agreed to make a minimum of 3 donations per week. A maximum of 10 donations per week was allowed (2 times daily, Monday through Friday). Each donation was tested for blood and stool pathogens.
- Daily health and diet questionnaires were completed with each donation to ensure there were no major changes in travel, medication, diet and health status (Figure 2).
- All donations were made on site and stored under controlled conditions.
- Donations were not pooled; aliquots from every donated stool were tested for pathogens using an extensive screen.
- At the end of each approximately 45-day donation cycle (Figure 3), donors underwent blood testing and donated aliquots underwent testing for pathogens.
- A positive result on any of the screens triggered destruction of all drug product associated with the donor during a cycle and exclusion of the donor from the program.

Figure 1. Initial Screening Process for Potential Donors

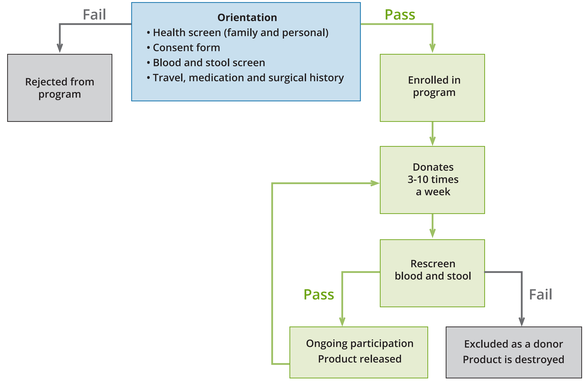


Figure 2. Screening Process for Enrolled Donors: Per Donation

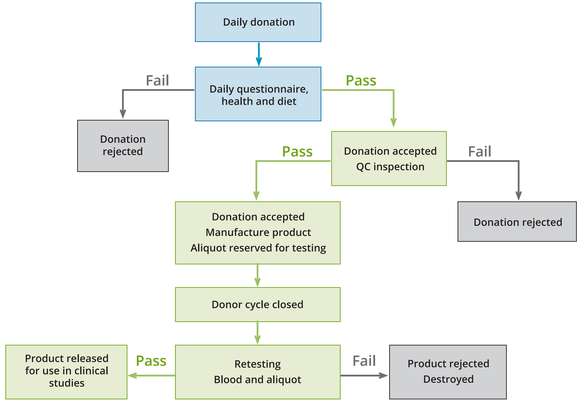
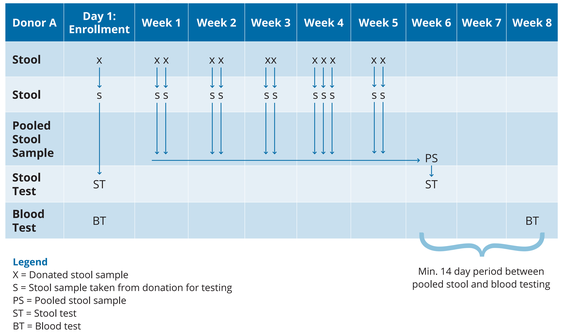


Figure 3. Donation Cycle



Results

- A total of 62 potential donors were recruited from July 15, 2013 through August 25, 2015.
- Of these, 11 (17.8%) failed the initial screening protocols.
- A total of 51 (82.2%) passed the screening protocols and made at least one donation.
- On subsequent retesting, a further 22 people (43% of the remaining donor pool) were excluded: 12 donors failed one or more of the blood and pathogen screens; 10 donors discontinued participation.

Donor Characteristics (N=62)

Parameter	Value
Mean, age, years	28 (19-59)
Gender, male	66%
Race, white	93.5%
Full or part-time student	53.2%

Initial Screen Failures (n=11)

Parameter	Value
Asymptomatic *E. Coli* strain #0157	1
Rheumatoid arthritis	1
Hepatitis C	1
Malaria (past infection)	1
Grave's disease	1
Antibiotic use within past 90 days	2
Incomplete screening	1
Psoriasis	1

Rescreen or Intra-Cycle Failures (n= 12)*

Parameter	Value
Asymptomatic norovirus	2
Asymptomatic rotavirus	2
Ova & parasites	3
Medications	1
Antibiotic use	3
Asymptomatic *Salmonella*	1
Vancomycin-resistant *Enteroccocus* (VRE)	1
Staphylococcus aureus	3

* A donor could be excluded for multiple reasons

Conclusions

- A substantial number of outwardly healthy donors used to source intestinal microbes for a drug under study for recurrent *Clostridium difficile* infection were found unsuitable due to underlying conditions.
- Reasons for rejection included asymptomatic carriage of an *E. coli* strain associated with hemorrhagic diarrhea and asymptomatic norovirus and rotavirus, which typically cause symptoms.
- Stringent screening of donors is required when sourcing live human-microbes used for treatment of disease.