positivity once all organisms are cleared, and finally a return to normal CSF biochemical parameters. Such studies might guide modifications in the approach to treatment of acute bacterial meningitis. In addition, although inflammatory responses in acute bacterial meningitis are mainly restricted to astrocytes and other glial cells, ascertainment of how much of these responses can be detected in the peripheral blood warrants examination. Identification of a surrogate marker of acute bacterial meningitis from blood (perhaps through transcriptomics) will be an invaluable diagnostic capability.

Stephen Obaro
Division of Pediatric Infectious Disease, University of Nebraska Medical Center Omaha, NE 68198, USA; International Foundation against Infectious Diseases in Nigeria, Abuja, Nigeria
stephen.obaro@unmc.edu

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A necessary discussion after transmission of multidrug-resistant organisms through faecal microbiota transplantations

On June 13, 2019, the US Food and Drug Administration (FDA)[1] issued a safety alert concerning the risk of serious adverse reactions due to transmission of multidrug-resistant organisms through faecal microbiota transplantations (FMTs). This alert was in response to transmission of an extended-spectrum β-lactamase-producing *Escherichia coli* strain from a faeces donor to two immunocompromised recipients. One of the individuals died, but the report does not provide information on the cause of death. For reasons not specified, the donor had not been screened for multidrug-resistant organisms. The FDA now requires inclusion of multidrug-resistant organism screening into all active and future FMT-based study protocols.

The use of FMT for the treatment of patients with recurrent *Clostridioides difficile* infections is recommended by clinical guidelines worldwide.[2,3] Experts in different countries have established stool banks that provide safe and effective FMT products for the treatment of these infections and for use in trials assessing other indications. All major stool banks have implemented screening protocols to detect multidrug-resistant organisms and exclude potential donors who test positive.[4-6] No serious adverse reactions due to transmission of multidrug-resistant organisms have been observed in more than 45 000 FMT treatments supported by OpenBiome, a non-profit stool bank, founded in 2012 in Cambridge, MA, USA, and in randomised controlled trials assessing other indications.[7] Transmission of multidrug-resistant organisms was also absent in a systematic review of 50 publications reporting 78 types of adverse events of FMT and in a retrospective analysis of FMT in 99 immunocompromised patients.[8,9] Adherence to standard screening protocols used by major stool banks worldwide is most likely to have prevented these incidents, even though this speculation is uncertain due to limited information available from the FDA alert.

These incidents, however, point to another important discussion in the field of FMT. Should donors whose faeces are to be used for the treatment of immunocompromised patients undergo more extensive screening for potential pathogens than individuals donating to immunocompetent patients? In this

context, it is important to acknowledge that the type and depth of a specific immunosuppression and the intestinal barrier status largely determines susceptibility to infections by different pathogens. To continue this discussion in a meaningful way, experts will have to agree on defined categories of immunosuppression. Furthermore, different quality control measures, mostly adapted from laws regulating blood transfusions and drugs can be applied. For quality control, not only donors, but also FMT products can be screened for transmissible pathogens. Alternatively, or in addition, many stool banks have chosen to put FMT products under quarantine until the donor testing has been found acceptable in a repeat screen. The use of a combined quarantine and quality control approach might be wise if the manufactured FMT products are intended for use in severely immunocompromised patients.

These issues are currently being discussed in two European consensus groups supported by United European Gastroenterology and the European Society for Clinical Microbiology and Infectious Diseases in which FMT specialists have united with the aim of developing uniform manufacturing and treatment standards.

Discussing safety inevitably leads to discussing regulation. Most stool banks have evolved from academia and their primary interests are not profit oriented. The role of pharmaceutical companies in the regulatory process should, however, not be underestimated. On the basis of the FDA announcement from 2013, physicians do not require an Investigational New Drug Application (IND), if they are treating patients with recurrent *C difficile* infections. For this aim, they might use FMT products from stool banks, provided the physician has obtained adequate informed consent from the patient. In 2016, the FDA issued a second draft guidance requesting an IND for any use of FMT products from stool banks. This document has been discussed controversially by the different interest groups involved, and its finalisation is still pending. Stool bank coordinators now fear that the recent incidents could be capitalised on by the pharmaceutical industry to call the safety of their products into question and limit future patient access. For the sake of our patients, we can only hope that further discussions will not be based on who produces and distributes the FMT, but on how it should be done.

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Department of Medical Microbiology, Center for Infectious Diseases (EJK), and National Donor Feces Bank (EJK, JK), Leiden University Medical Center, 2333 ZA Leiden, Netherlands; Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA (JRA); Institute of Microbiology and Infection, University of Birmingham, Birmingham, UK (PH); Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, Hôpital Saint Antoine, Service de Gastroenterologie, Paris, France (HS); French Group of Faecal Microbiota Transplantation, Paris, France (HS); Centre for Clinical Infection and Diagnostics Research, King's College London and Guy's and St Thomas' NHS Foundation Trust, London, UK (SG); Digestive Disease Center, Fondazione Policlinico Universitario A Gemelli, Università Cattolica del Sacro Cuore, Rome, Italy (GI, AG); Department of Internal Medicine, Division of Gastroenterology and Hepatology, Medical University Graz, Graz, Austria (PK); Department of Gastroenterology, Queen Elizabeth Hospital, Adelaide, SA, Australia (SPC); Department of Gastroenterology, Haaglanden Medical Center, Den Haag, Netherlands (JK); Department I of Internal Medicine, University of Cologne, Cologne, Germany (MJGTV); Center for Integrated Oncology Aachen-Bonn-Cologne-Duesseldorf, Cologne, Germany (MJGTV); German Centre for Infection Research, partner site Bonn-Cologne, Germany (MJGTV); and Department of Internal Medicine and Infectious Diseases, Goethe University Frankfurt, Frankfurt am Main, Germany (MJGTV)
ejkuijper@gmail.com

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