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Commentary

Faecal microbiota transplantation: A life-saving therapy challenged by commercial claims for exclusivity

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ABSTRACT

Faecal microbiota transplantation (FMT) is an innovative treatment which is challenged by a regulatory struggle in Europe. A recent publication in EClinicalMedicine describes the successful adaptation of FMT to a National drug legislation, but this approach fails to take into account the donor-related aspects. The European tissue and cells directive and affiliated technical guide provide extensive safety and quality standards which may readily be adopted in an FMT service to provide patients with this life-saving treatment embedded in a public blood centre.

Faecal microbiota transplantation (FMT) has revolutionised the management of patients with recurrent *Clostridioides (Clostridium) difficile* infection (rCDI) [1]. With resolution rates exceeding 90%, the use of FMT has surged in clinical practice. FMT is now a recommended treatment for rCDI and reduces mortality and hospital costs alike [2]. The application of viable intestinal microbiota obtained from healthy donors requires strict compliance with acknowledged safety standards to minimise risks. A technical guide issued by the European Council [3] and a recent international consensus conference describe in detail how safety and quality measures may be applied according to tissue and cells standards [4]. In a recent report, published in EClinicalMedicine, McCune and co-workers describe how a hospital-based stool bank using FMT to treat rCDI may be adapted to comply with national drug legislation [5]. The two competing approaches reveal a regulatory struggle challenging the development of FMT as an integral service in modern healthcare.

Classification of minimally manipulated donor faeces as a drug paves the way for an unethical commercialisation of human material. Donated material is in essence diverse, and the process of obtaining human material and the precautionary measures needed are not covered by current drug legislation. The English stool bank, embedded in the National Health Service, has eminently adapted to an unfit legislation model to provide the public with FMT free of charge for patients [5], but the push for classifying FMT as a drug is headed by the pharma industry aiming to gain market exclusivity. At a recent public hearing held by the Federal Drug Administration, industry leads argued in favour of regulating FMT entirely as a drug and restricting patients' access to FMT outside of drug company-sponsored trials [6]. In this manner, a selective regulation may impose serious and unjustified limitations on the research into and clinical use of FMT at the cost of ill patients.

A legal basis already exists for the activities needed to safely handle donor faeces. Specifically, regulation of donor faeces as a tissue provides indispensable standards for donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. Although the European Commission concluded that intestinal microbiota are not currently covered by the European Tissue and Cells Directive (EUTCD 2004/23/ec), the Commission defines donor faeces as a substance of human origin comparable to a tissue [7]. Regulating FMT as a tissue allows for both hospital-based and commercial production ensuring wide access to the treatment (Table 1). A hospital-based FMT service similar to the handling of blood and tissue donors is already in place.

During the past decade, FMT has transitioned from a low-tech procedure, sporadically used by clinicians who were committed to treating severely ill patients, to a safe and quality-audited routine treatment. This process mirrors the early phases of transfusion medicine when enthusiasts implemented small-scale donation and transfusion facilities. Important lessons may be learned from this. Early on, it was found that infectious diseases could be transmitted by blood transfusion, first documented in 1915 by the transmission of syphilis. The transmission of viral hepatitis failed to drop until non-remunerated volunteer donors were used instead of paid donors [8]. A similar recruitment of faeces donors along with adherence to minimum standards for the handling of donor material may be expected to increase the safety of FMT.

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Table 1
Hospital-based faecal microbiota transplantation (FMT) and industrial microbiota-based drugs differ in fundamental ways that must be mirrored in handling and regulation.

	Faecal microbiota transplantation (FMT)	Microbiota-based drugs
Facilitating institution	Mainly hospitals	Mainly industry
Donor recruitment and screening	Volunteer, pre-screened donors embedded in blood centres or similar institutions	Recruitment from the public with reimbursement
Constituents	Unprocessed and cryopreserved faeces from a thoroughly screened faeces donor	Standardised, specific, and industrially produced microbiota-based product
Application method	In liquid form through endoscopy or tube, or in capsules for oral ingestion	Mainly capsules
Potential European regulation	EU Tissue and Cells Directive (2004/23/EC)	EU directive relating to medicinal products for human use (2001/83/EC)
Traceability	30 years according to legislation	No formal requirements
Donor-specific legislation	Extensive	None
Regulating authority	Patient safety authority	Medicines authority

Like several other academic institutions, we have established an FMT service embedded in a hospital-based blood service and the department of gastroenterology [9]. We ask blood donors to help severely ill patients by donating intestinal microbiota. Our FMT service complies with the EUTCD. Donor recruitment amongst blood donors assures a high eligibility rate [10]. This setup allows for recruitment of enough healthy donors to meet the FMT donation requirements. Feedback from the clinic to the production facility ensures a dynamic development.

Research and development of FMT in clinical settings are crucial to assure the continued scrutiny of FMT procedures, effects and mechanisms of action. Anchoring the service in public blood banks provides a safety level and an infrastructure that have proven their worth for more than a century.

Authors' contributions

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Declaration of Competing Interest`

All authors declare no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2020.100436.

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