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Letter to the Editor

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Donated stool for faecal microbiota transplantation is not a drug, but guidance and regulation are needed

Josbert J Keller[1,2,3], Maria JGT Vehreschild[4,5,6], Christian L Hvas[7], Simon MD Jørgensen[7], Juozas Kupcinskas[8], Alexander Link[9], Chris JJ Mulder[10], Simon D Goldenberg[11], Ramesh Arasaradnam[12], Harry Sokol[13,14,15], Antonio Gasbarrini[16], Christoph Hoegenauer[17], Elizabeth M Terveer[3,18], Ed J Kuijper[3,19] and Perttu Arkkila[20]

We would like to thank Mikkelsen et al. for their response to our statement that stool for faecal microbiota transplantation (FMT) should be classified as transplantation product. Fortunately, we all agree that guidance and regulation is required for this rapidly emerging treatment, which makes the use of donated stool a substance of human origin (SoHO).

The European Union Tissue and Cell Directives (EUTCD) cover the processing, preservation, storage and distribution of transplantation products. As the authors state, stool for FMT does not currently fulfil the requirements for guidance by the EUTCD because the human cells in it are not the active component. Yet, in their evaluation of the blood, tissue and cell (BTC) legislation (including the EUTCD) of 10 October 2019, the European Commission indeed states that FMT falls outside the scope of the directive. This report also mentions that the reason is that FMT had not emerged as an accepted treatment strategy at the time of adoption of the BTC legislation, although it is a SoHO, and it implies similar risks to those regulated by the BTC legislation.[1] Given the similar risks and the fact that FMT products are made of donor stool, there is no doubt that the EUTCD is appropriate for guidance of FMT.

The European *Guide to the Quality and Safety of Tissues and Cells for Human Application*, published and updated by the Council of Europe, describes in detail how transplantation products, including stool, should be produced and handled.[2] This guide is also a reference tool for competent authorities to regulate stool banks and FMT treatment. In most European

[1]Department of Gastroenterology, Haaglanden Medical Centre, The Hague, The Netherlands
[2]Department of Gastroenterology, Leiden University Medical Centre, Leiden, The Netherlands
[3]Netherlands Donor Faeces Bank, Leiden University Medical Centre, Leiden, The Netherlands
[4]Department of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, University of Cologne, Cologne, Germany
[5]Department of Internal Medicine, Infectious Diseases, University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt am Main, Germany
[6]German Centre for Infection Research (DZIF), partner site Bonn-Cologne, Germany
[7]Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark
[8]Department of Gastroenterology and Institute for Digestive Research, Lithuanian University of Health Sciences, Kaunas, Lithuania
[9]Department of Gastroenterology, Hepatology and Infectious Diseases, Otto-von-Guericke University, Magdeburg, Germany
[10]Department of Gastroenterology, Amsterdam University Medical Centre, Amsterdam, The Netherlands
[11]Centre for Clinical Infection and Diagnostics Research (CIDR), King's College London and Guy's and St Thomas' NHS Foundation Trust, London, UK
[12]Warwick Medical School, University of Warwick, Coventry, UK
[13]Sorbonne Université, INSERM, Saint-Antoine Research Center (CRSA), Paris, France
[14]French Group of Faecal Microbiota Transplantation (GFTF), Paris, France
[15]INRA, UMR1319 Micalis, AgroParisTech, Jouy-en-Josas, France
[16]Gastroenterology Area, Fondazione Policlinico Universitario Gemelli, Università Cattolica del Sacro Cuore, Rome, Italy
[17]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[18]Department of Medical Microbiology and Netherlands Donor Faeces Bank, Leiden University Medical Centre, Leiden, The Netherlands
[19]Centre for Microbiota Analysis and Therapeutics, Department of Medical Microbiology, Leiden University Medical Centre, Leiden, The Netherlands
[20]Department of Gastroenterology, Helsinki University Hospital and Helsinki University, Helsinki, Finland

Corresponding author:
Josbert J Keller, Medisch Centrum Haaglanden Lijnbaan 32 Den Haag Den Haag, Zuid-Holland 2596SR Netherlands.
Email: j.keller@haaglandenmc.nl

countries, stool banks seek a dialogue with competent authorities, and both parts recognise that regulatory oversight is limited by the current lack of formal legislation. This does not mean that stool banks operate outside the view of competent authorities, as postulated by Mikkelsen et al. Stool banks are created to centralise the production of donor faeces–derived FMT products with the aim of increasing the safety of FMT and enabling quality assurance, auditing and biovigilance. These areas are specifically addressed in the European guide.[2] Importantly, the regulatory oversight that is needed should cover both donors and recipients.

It is of utmost importance that governments encourage the daily practice of stool banking and align the (European) legislation in accordance with the developing evidence-based practice. In order to protect and sustain donor recruitment and screening, human-derived donor material should be embedded in established tissue-banking environments rather than developing the use of voluntarily donated faeces into a commercial trade. Large-scale accredited production is performed in all blood and tissue centres and does not render the derived components drugs. The development of microbiota-based drug therapies consisting of, for example, standardised microbial mixtures could be feasible and possibly replace the use of FMT. Not until then will tissue become a drug.

ORCID iDs

Simon MD Jørgensen https://orcid.org/0000-0002-5135-7435
Ramesh Arasaradnam https://orcid.org/0000-0002-2231-3062

References

1. European Commission. Evaluation of the Union legislation on blood, tissues and cells. https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/swd_2019_376_en.pdf (2019, accessed 21 January 2020).
2. EDQM. *Guide to the quality and safety of tissues and cells for human application*, 4th ed. Strasbourg, France: EDQM, 2019.