

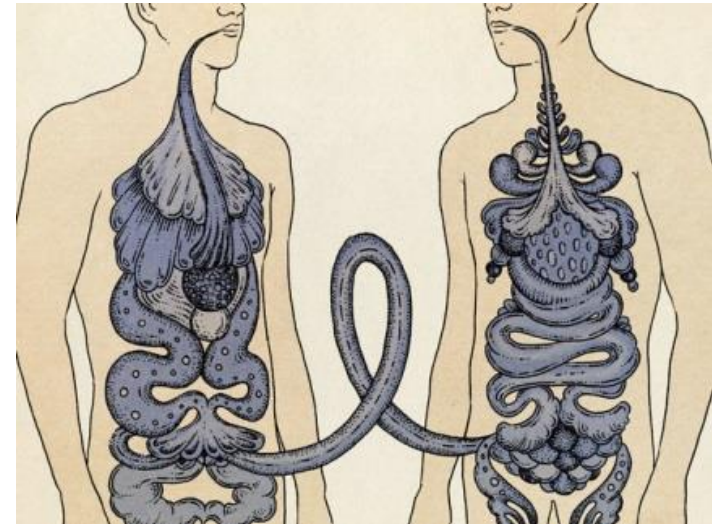
From Clinic to Regulation:

Fecal Microbiota Transplantation under the SoHO framework

Dr. E.M. (Liz) Terveer
Medical microbiologist, LUMC
Head Netherlands Donor Feces Bank

November 6th 2025

ANUAL MEETING BELGIAN ASSOCIATION FOR TISSUE
AND CELL BANKS



Topics covered – from clinic to regulation

Indication: fecal microbiota transplantation (FMT)

The organization: Netherlands Donor Feces Bank (NDFB)

The donor: selection & screening

The product: fecal suspension

The patient: success, safety & biovigilance

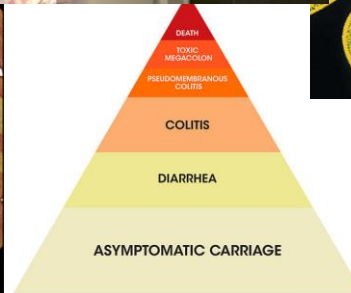
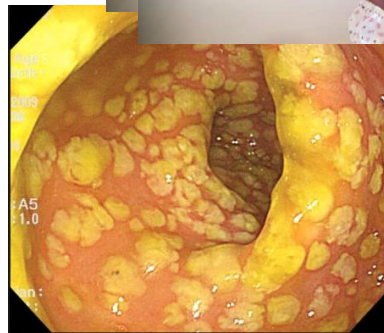
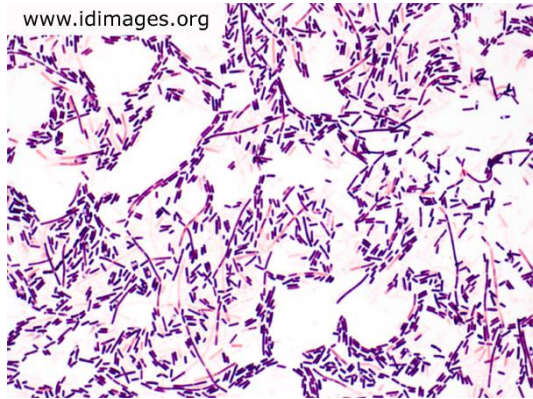
The regulation: from national framework to SoHO-Regulation



Disrupted microbial ecosystem

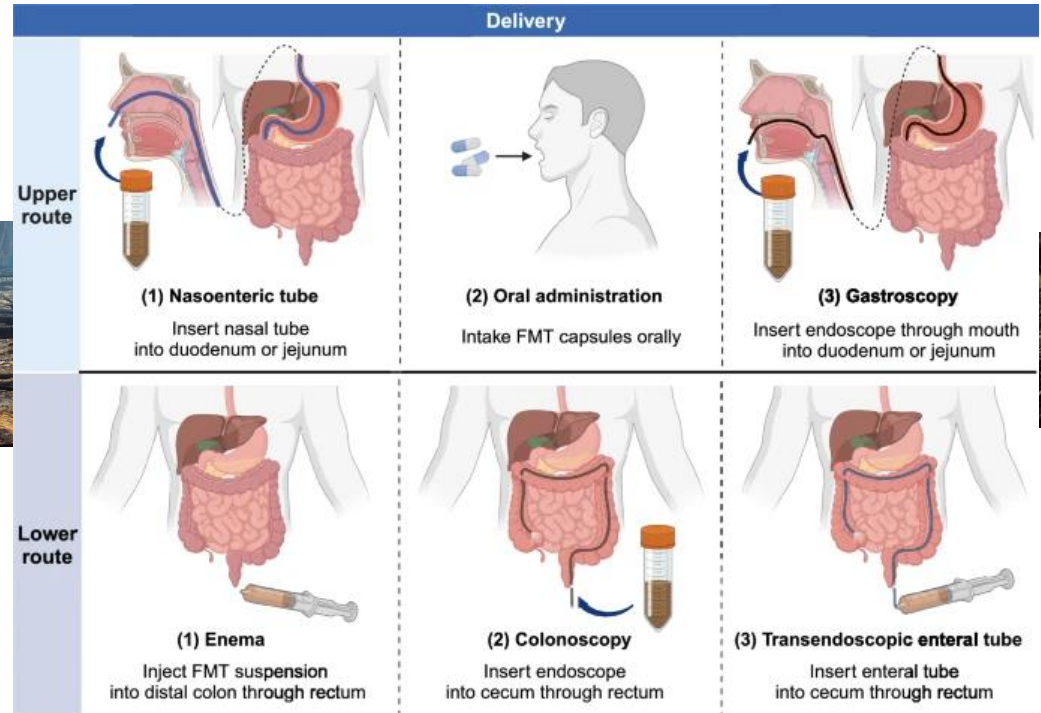
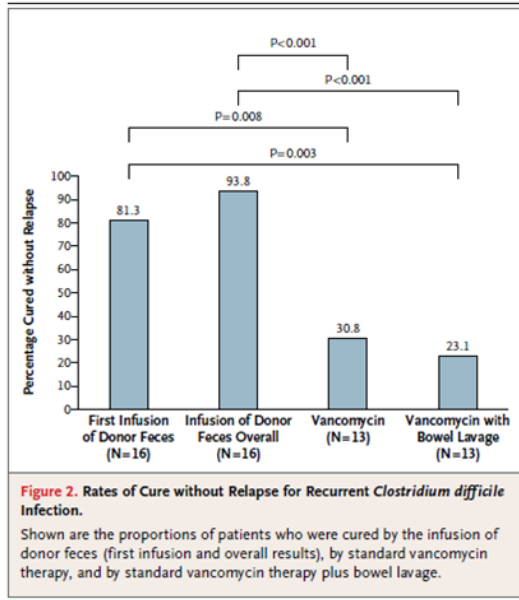


Recurrent *Clostridioides difficile* infection



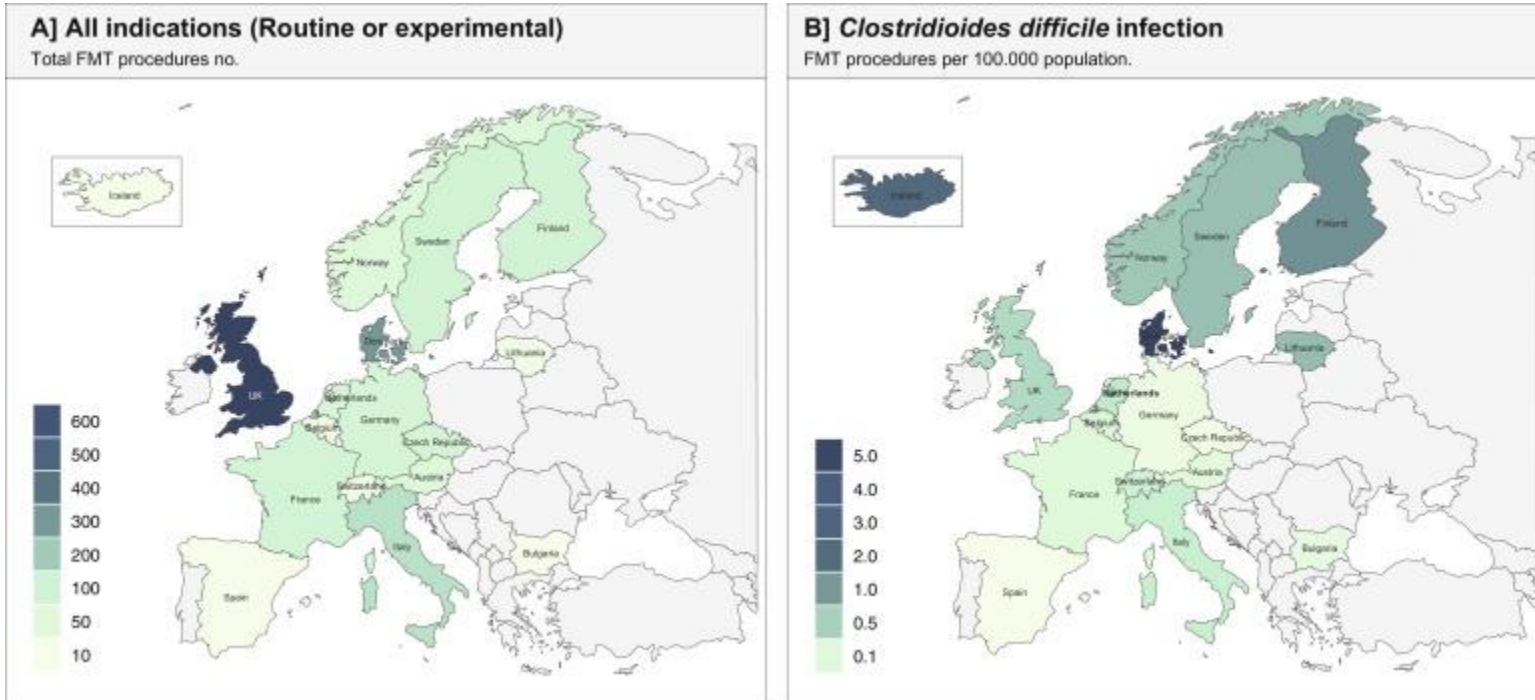
Fecal microbiota transplantation for rCDI

Highly effective in preventing further recurrences of *Clostridioides difficile* infectie (rCDI)



FMT in Europe

Also promising, and applied in other microbiota-related illnesses



Netherlands Donor Feces Bank (NDFB)

- Non-profit
- Provide ready-to-use donor fecal suspensions
 - Widely available, treatment in local hospital
- Guarantee safety and quality of FMT
 - Central donor pool of well screened donors
 - Uniform and standardized procedures
 - Storage of feces quality controls in case of adverse event
- Research & innovation



Feces



Production process

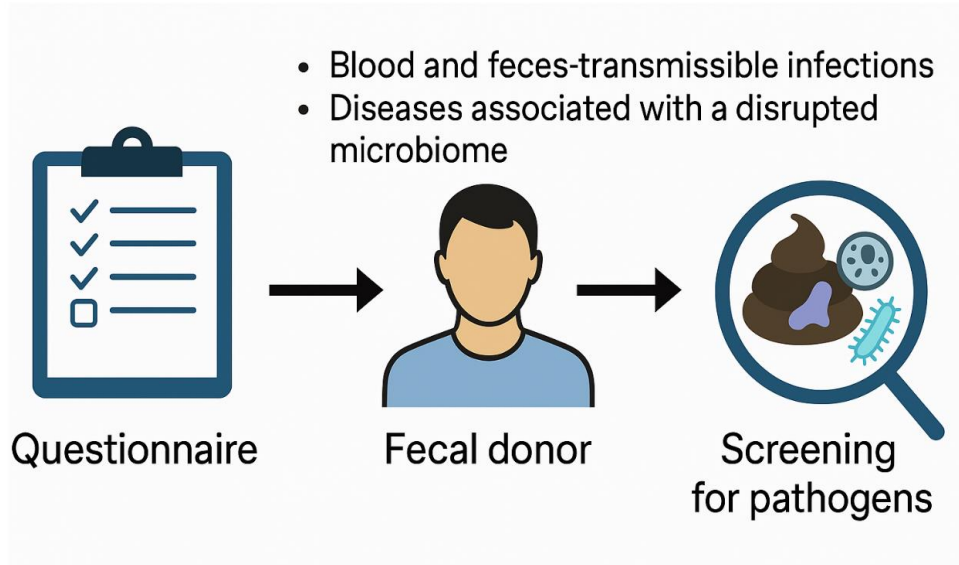


Ready-to-use fecal suspension



The donor: fecal donor screening

Purpose: Minimize the risk of transmission of infections OR microbiome-associated conditions through FMT (enhance effectivity?)



Assess recent exposures and health changes before donation

The product: Fecal suspension

- 60 gram donor feces < 2h after defecation
- Homogenized: Physiological saline + bagmixer
- + bag with integrated filter, pore $\leq 250 \mu\text{m}$
- 10% glycerol (cryoprotectant)
- 200 cc fecal suspension
- Stored at -80°C
 - Quality Control: suspension 2cc & donor feces
- Quarantined until re-screening
- Double-encapsulated capsules in testing phase



5501177 - 001

FMT Feces



NDFB
Nederlandse Donor Feces Bank

Nederlandse Donor Feces Bank

Fecessuspensie voor Feces Microbiota Transplantatie

Ingrediënten: Donorfeces gefilterd tot 300 micron, glycerol (10%) in NaCl (0.9%).

Bewaren bij -80°C !

Ontdooi advies voor gebruik:

- Ontdooi de donor fecessuspensie na aankomst overnacht bij 4°C (in koelkast) of 5 uur bij kamertemperatuur.
- Indien de donor fecessuspensie in de koelkast is ontdooid, laat de suspensie dan circa 1 uur op kamertemperatuur komen voorafgaand aan infusie.
- Op kamertemperatuur is de fecessuspensie maximaal 3 uur houdbaar (eventueel nog 6 uur op ijs/in de koelkast).
- De donor fecessuspensie kan niet opnieuw worden ingevroren.

Waarschuwing:

Dit product kan voedselallergenen bevatten.

Adverse event:

Direct melden aan info@NDFB.nl en/of een van de artsen van de Nederlandse Donor Feces Bank werkgroep (zie formulier Toediening Feces Microbiota Transplantatie).

Houdbaarheidsdatum:

xx-xx-xxxx (productiedatum +2 jaar).

FMT Feces suspensie

Donornr.: 5501177
Suspensienr.: 5501177-001A
Productiedatum: 08-03-2016
Houdbaarheidsdatum: 08-03-2018
Volume suspensie: 198 ml
Bewaren bij -80°C



5501177 - 001OCSA
08 - 03 - 2016

FMT QC



5501177 - 001OCFA
08 - 03 - 2016

Feces QC



The patient: multidisciplinary assessment FMT-request

Evaluation 241 FMT requests:

- 177 (73%) suitable for FMT
 - 64 (27%) not suitable
 - Mostly due underlying bowel disease + *C. difficile* carriage
- Limit unnecessary use
- Appropriate use of unstandardized therapy



NDFB results: Who receives an FMT?

May 2016 – Dec 2024:

- 376 FMTs in 336 patients with rCDI
 - + >250 FMTs for FMT trials & expanded access
- 66 different hospitals
- 22 donors

Patient characteristics:

- 1st episode – 9th recurrence
 - median 3 recurrences
- Mean age: 70 years

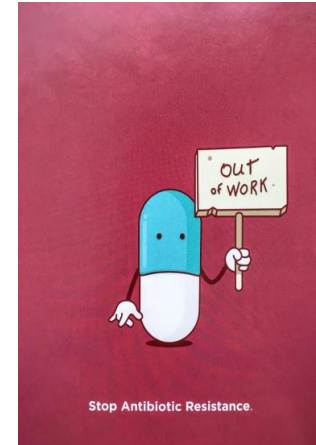
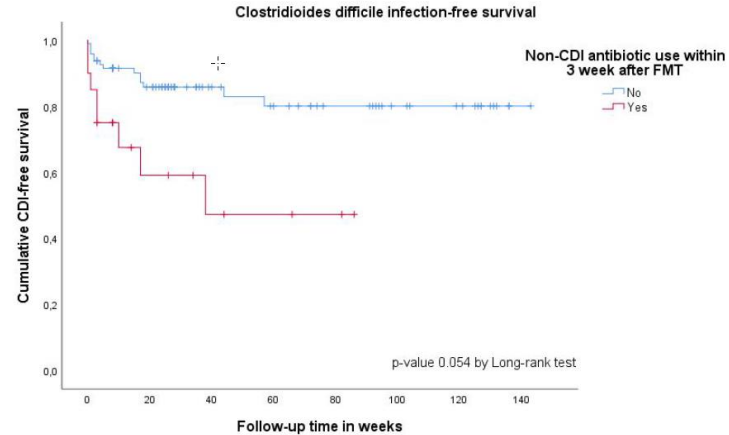
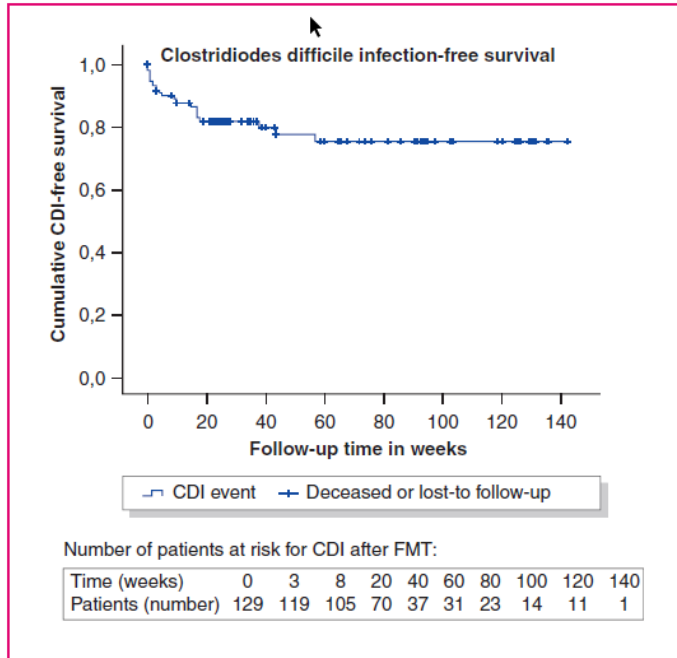


Monitoring of effectiveness, safety & quality

- Tissue Guide: “*Systematic monitoring of serious adverse reactions and events from donor selection to follow up of the recipient*”
- Sample storage: donor & patient samples (pre- & post-FMT)
- Evaluation of outcomes & (S)AR’s
 - At 3 weeks, 6 months, several years post-FMT
 - Patient questionnaire and contact with treating physician
- Assessment of suspected SARs
 - Working group evaluates infectious and newly developed conditions
 - Relation to SAE? Donor placed “on hold” → suspensions not used during investigation
 - Any other patients with similar AEs?
 - Microbiological analysis of donor and patient samples

NDFB results: Success percentage after FMT

- Cure rate 90% after 2 months (142/158)

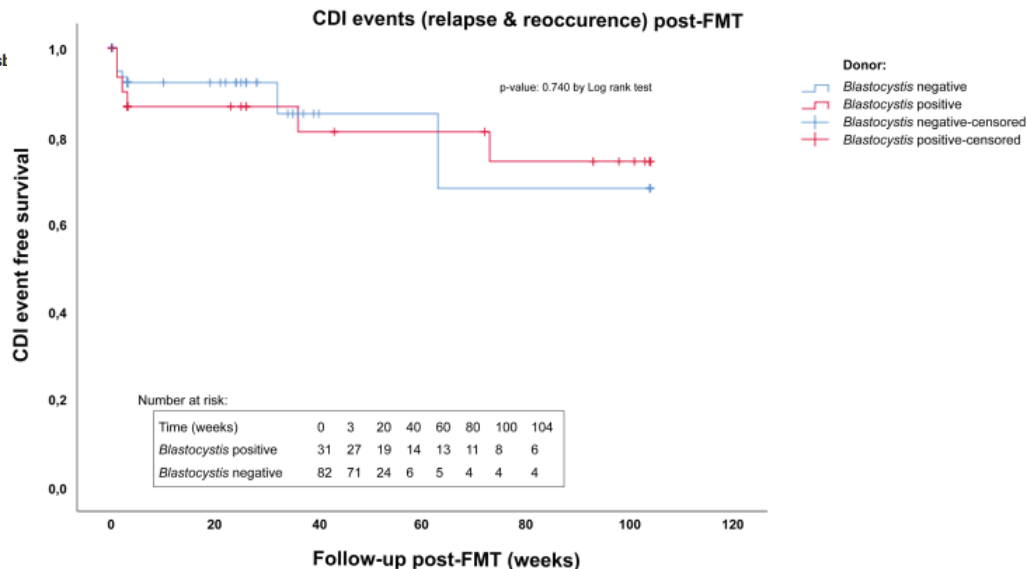
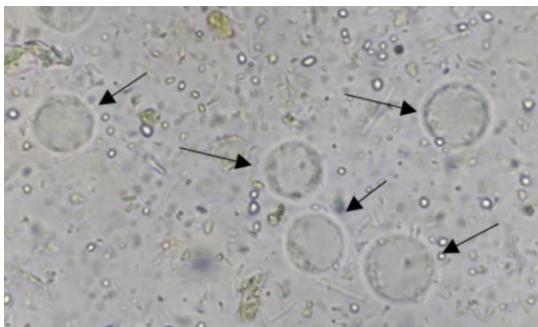


NDFB results: biovigilance pre-SoHO

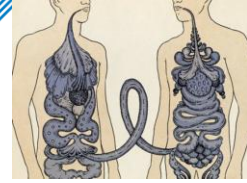
Description adverse event		Number of patients
Definitively or probably related to FMT		
SAE	None	0% (0/128)
AE	Procedure-related AEs	4% (5/128)
	– Regurgitation, no aspiration, patient successfully treated	– 4
	– Sore throat after placing duodenal tube	– 1
Possibly related to FMT		
SAE	Hospitalization within 3 weeks post-FMT due to:	8% (9/115)
	– Lower respiratory tract infection (causing pathogen unknown) ^a	– 5
	– Urinary tract infection (causing pathogen unknown) ^b	– 3
	– Diarrhoea (non-CDI)	– 1
AE	Gastro-intestinal (see Table 4)	11–52%
	Infections	– 5
	– Urinary tract infection (causing pathogen unknown) ^b	– 1
	– Urinary and lower respiratory tract infection ^a	– 1
	Other	– 1
	– Fever	
	– Possible flare IBD (ulcerative colitis), uncertain if it was pre-existent	

Human Transmission of *Blastocystis* by Fecal Microbiota Transplantation Without Development of Gastrointestinal Symptoms in Recipients

Elisabeth M. Terveer,^{1,2} Tom van Gool,³ Rogier E. Ooijevaar,^{2,4} Ingrid M. J. G. Sanders,¹ Eline Boeijs-Koppenol,^{1,2} Jost Ed J. Kuijper,^{1,2} for the Netherlands Donor Feces Bank (NDFB) Study Group

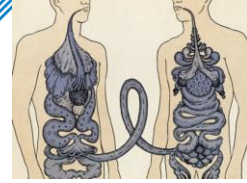


NDFB results: Evaluation imputability SAR



- 38-year-old patient with refractory GvHD
- Allo-SCT +117 days, FMT via expanded access
- GvHD complicated by HSV-esophagitis, pleural effusion & ascites (hypoalbuminemia)
- Treatment included ruxolitinib (+ 4 weeks), ketamine infusion
- Neutrophil normal
- + 6 days post-FMT: *E. coli* bacteremia
- No evidence of biliary, pulmonary or urinary tract infection
- Treating physician: “Not related to FMT” but is it?

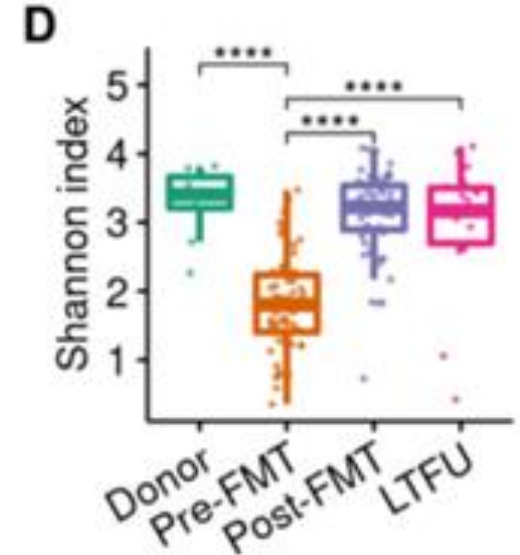
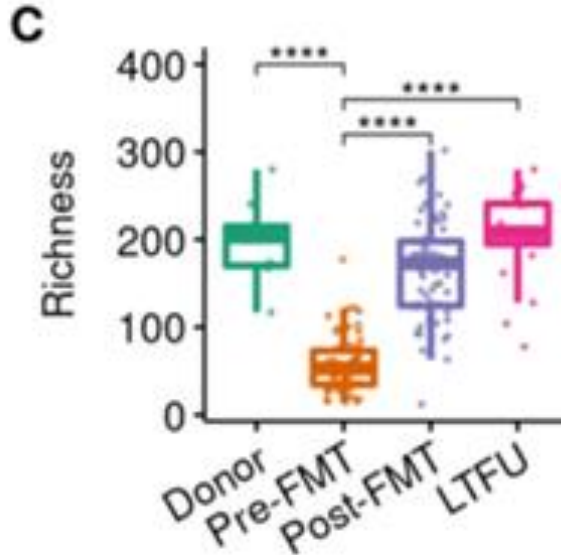
Microbiological investigation donor & patient sample



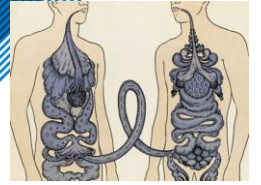
- Donor immediately placed “on hold”
- Collected: Patient data, isolate, donor & patient feces
- **Microbiological investigation**
- Pending further analysis;
- *E. coli* from blood and donor
- Whole Genome Sequencing

Sample	Sequence
<i>E. coli</i> patient (blood culture)	ST 357
<i>E. coli</i> donor (faeces)	ST 357

- No additional virulence factors



Translocation of donor-engrafted strains in GvHD



Diagnosis: translocation of donor-engrafted strains in a patient with a vulnerable intestinal barrier due to GvHD

Clinical improvement:

- Rising albumin levels, reduced ascites/pleural effusion, markedly less pain
- Diarrhea resolved within weeks, discharged after 2 weeks
- Case reviewed by multidisciplinary team + external experts:
- Conclusion: translocation related to underlying disease
- Decision: FMT-course* continued (2 additional FMTs) with good outcome
- Question: Is this a SAR?

Regulatory framework for FMT in Europe pre-SoHO

Table 2. Regulatory frameworks for FMT in European Countries and developments from 2019 to 2022.⁶⁷

Domain	HCT/P (clinical trial required)	Unlicensed Medicinal Product	Unlicensed/ Experimental Drug	None	Unclassified Treatment
2019	Belgium Italy	Denmark Norway UK Switzerland***	Finland France	Austria Estonia Germany* Ireland** Malta Portugal Slovenia Spain	The Netherlands
2022	Belgium Italy	Denmark**** Germany Ireland Norway UK Croatia Czechia Portugal Spain Sweden Switzerland*	Finland France	Austria Estonia Malta Slovenia	The Netherlands

*No federal level guidance; regulation at state level on case-by-case basis.

**Considered practice of medicine.

***Investigational Medicinal Product.

****EU Report states that in Denmark, classification of FMT as HCT/P considered on a case-by-case basis based on degree of manipulation and indication.

Consensus guidelines

Clinical Microbiology and Infection 23 (2017) 924–930

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com



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Review

How to: Establish and run a stool bank[☆]

E.M. Terveer^{1,*,12}, Y.H. van Beurden^{2,3}, A. Goorhuis⁴, J.F.M.L. Seegers, M.P. Bauer⁵,
E. van Nood⁶, M.G.W. Dijkgraaf⁷, C.J.J. Mulder³, C.M.J.E. Vandenbroucke-Grauls²,
H.W. Verspaget⁸, J.J. Keller^{9,10,*,*,11}, E.J. Kuijper^{1,11,12}

Guidelines



OPEN ACCESS

International consensus conference on stool banking for faecal microbiota transplantation in clinical practice

Giovanni Cammarota^{9,1}, Gianluca Ianiro,² Colleen R Kelly,³ Benjamin H Mullish^{9,4},
Jessica R Allegretti⁵, Zain Kassam,^{6,7} Lorenza Putignani,⁸ Monika Fischer,⁹
Josbert J Keller,^{10,11} Samuel Paul Costello,¹² Harry Sokol,^{13,14,15} Patrizia Kump,¹⁶
Reetta Satokari,¹⁷ Stacy A Kahn,¹⁸ Dina Kao,¹⁹ Perttu Arkkila,²⁰ Ed J Kuijper,²¹
Maria J GT Vehreschild,²² Cristina Pintus,²³ Loris Lopetuso,²⁴ Luca Masucci,²⁵
Franco Scaldaferri,²⁴ E M Terveer,^{11,21} Max Nieuwdorp,²⁶ Antonio López-Sanromán,²⁷
Juozas Kupcinskas,²⁸ Ailsa Hart,²⁹ Herbert Tilg,³⁰ Antonio Gasbarrini³¹

Original Article

A standardised model for stool banking for faecal microbiota transplantation: a consensus report from a multidisciplinary UEG working group

Josbert J Keller^{1,2,3}, Rogier E Ooijsaar^{3,4}, Christian L Hvas⁵,
Elisabeth M Terveer^{3,6}, Simone C Lieberknecht⁷,
Christoph Högenauer⁸, Perttu Arkkila⁹, Harry Sokol^{10,11,12},
Oleksiy Gridnyev¹³, Francis Mégraud¹⁴, Patrizia K Kump⁸,
Radislav Nakov¹⁵, Simon D Goldenberg¹⁶, Reetta Satokari¹⁷,
Sergiy Tkatch¹⁸, Maurizio Sanguinetti¹⁹, Giovanni Cammarota²⁰,
Andrey Dorofeev²¹, Olena Gubska²², Gianluca Ianiro²⁰,

Eero M
Ajit So
Simon
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Georg
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Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin



Guidelines

The use of faecal microbiota transplant as treatment for recurrent or refractory *Clostridioides difficile* infection and other potential indications: second edition of joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines[☆]

B.H. Mullish^{a,b,#}, B. Merrick^{c,#}, M.N. Quraishi^{d,e,f,#}, A. Bak^g, C.A. Green^{h,i},
D.J. Moore^j, R.J. Porter^k, N.T. Elumogo^{l,m}, J.P. Segal^{n,o}, N. Sharma^{d,e,f},
B. Marsh^p, G. Kontkowski^{p,q}, S.E. Manzoor^e, A.L. Hart^{a,r}, C. Settle^s,
J.J. Keller^{t,u}, P. Hawkey^{e,v}, T.H. Iqbal^{d,e,f}, S.D. Goldenberg^{c,w,†},
H.R.T. Williams^{a,b,w,†}

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0(0) 1–19

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2024/1938

17.7.2024

REGULATION (EU) 2024/1938 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 13 June 2024

on standards of quality and safety for substances of human origin intended for human application
and repealing Directives 2002/98/EC and 2004/23/EC

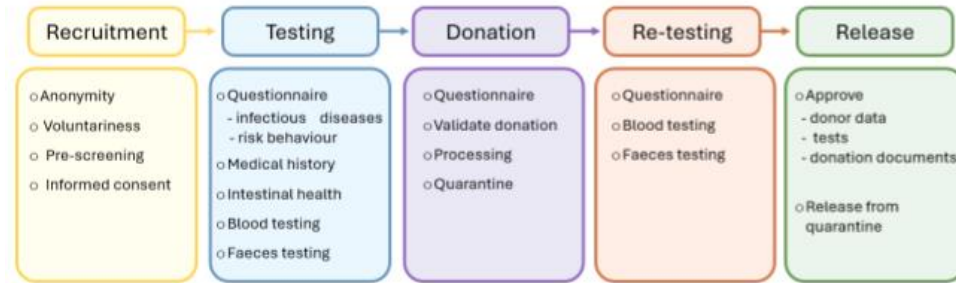
Most important changes

- **SoHO** introduced as a new overarching term (replacing separate directives)
- Inclusion of donor milk and intestinal microbiota
- **National legislation and inspection**, aligned closely with expert organizations
 - Reference to the **EDQM** technical guide
 - **ECDC** involved in quality and safety monitoring
- Outcome registration → need for an **EU registry**: EurFMT

EDQM guide – Chapter 32: Intestinal microbiota

Quality and safety framework for FMT

Part of the Tissue & Cells Guide of the EDQM (Eu Dir. Q. Med. & Healthcare)



Monographs:

- Cryopreserved donor fecal suspension
- Cryopreserved donor fecal capsules

Guide to the quality and safety of
TISSUES AND CELLS
for human application

www.edqm.eu
Facebook: [edqm](https://www.facebook.com/edqm)
Twitter: [edqm_euro](https://twitter.com/edqm_euro)
LinkedIn: [edqm_euro](https://www.linkedin.com/company/edqm)

EDQM
5th Edition
2022

Co-funded by the European Union

EUROPEAN UNION

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CONSEIL DE L'EUROPE

Co-funded and implemented by the Council of Europe

Towards a European framework for safe and effective FMT

European Fecal Microbiota Transplantation (EurFMT)

International collaboration of academic FMT centers

Objectives:

- Strengthen collaboration and communication among FMT experts across Europe
- Develop standardized procedures, guidelines and a EurFMT registry

EU Project: Harmonize

- Harmonization of expert groups, activities, and guidelines in line with new SoHO requirements
- Develop **technical guidelines** for donor screening and FMT-processing (WP NDFB)
- Develop of **oversight and quality assurance** guidelines (WP NDFB)
- Establishment of **training programs** and facilities
- Gap-analysis: including **audit** program and European **FMT-registry**



2023 EU4Health calls for action grants



Is the NDFB ready for the SoHO Regulation?

- NDFB = SoHO Establishment
- FMT treating centres (hospitals) = SoHO Entity
- **Current status:**
- Farmatec application not yet processed – still early in the implementation phase
- Informal and constructive visit from Dutch Inspectorate IGJ already took place
- Further clarification from the Ministry of Health (VWS) on SoHO framework implementation forthcoming
- Since this year, we report our SARs and SAEs to TRIP
- Start reporting in EurFMT registry (patients)
- November 2025: Audit by Aarhus



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 Bijlage 3.8_B_Mandaatregelin... 192 KB	 Bijlage 3.5_Accreditatiebewijs... 919 KB
 Bijlage 3.7_CV verantwoordel... 188 KB	 Bijlage 3.1_Uittreksel KvK_27... 412 KB
 Aanvraagformulier Farmatec ... 638 KB	 Bijlage 3.3_Omschrijving mat... 410 KB
 Bijlage 3.12_SOP Vrijgave FM... 149 KB	 Bijlage 3.9_A_Akte van aanste... 31 KB
 Bijlage 3.8_A_Nederlandse D... 203 KB	 Bijlage 3.9_B_Addendum bij a... 414 KB
 Bijlage 3.6_Organogram NDF... 294 KB	 Bijlage 3.11_Lijst essentiële m... 196 KB

Wat are your takeaways about FMT?

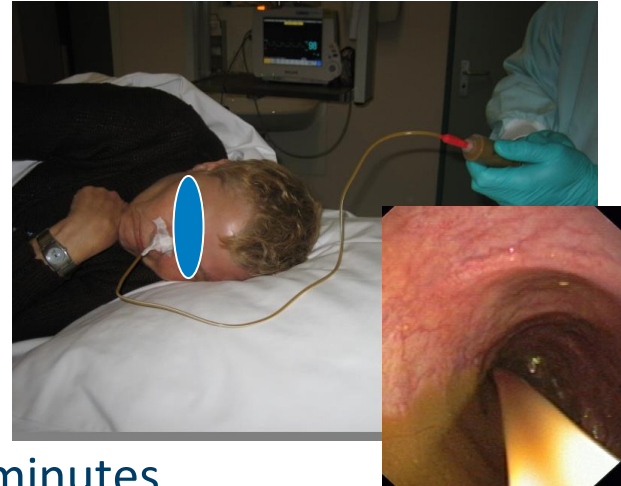
- **From clinic to framework:** FMT has evolved from experimental treatment to regulated medical application
- **Solid experience:** ± 400 FMTs, high success rates and manageable infection risks
- **Safety & transparency:** biovigilance performed, no serious adverse events in rCDI, trends monitored through the EurFMT registry
- **Learn from data:** Biovigilance can improve FMT care (e.g. remove *Blastocystis hominis* as donor exclusion criterion)
- **Looking ahead:** SoHO, EDQM, ECDC, (VWS, TRIP) and EurFMT together provide a clear European framework for safe and accessible FMT
- **Collaboration is key:** FMT-experts, clinicians, regulators and researchers work closely together in this field

Questions?



The patient: pretreatment and administration

- Anti-CDI antibioticsn pretreatment \geq 4 days, stop 1 day before FMT
- 2ltr Klean-prep (half bowel lavage)
- Nasoduodenal tube
- 200cc administered over 20 minutes



- Nasoduodenal tube removed after 30 minutes
- Monitor patient for 2 hours (p/RR/T)