Draft standards for faecal microbiota transplant (FMT) products

[REDACTED] RESPONSE

Overall, [REDACTED] welcome these TGA's efforts to improve the safety of faecal microbiota transplantation in Australia.

In our view these regulations should help to ensure consistency of practice, and promote appropriate levels of caution in the application of this therapy.

Document section	**Specific questions**	**Comments**
Commencement of draft Therapeutics foods order: standards for faecal microbiota transplant product Page 9	**Q1.** Is the application of *TGO 87* appropriate to FMT products?	**Q1.** Yes. This is an important and appropriate measure
	Q2. If changes to current FMT practice are required to comply with these requirements, what is the expected cost impact? Is a 12-month transition period sufficient to update current practice? Please provide enough information to allow us to understand any impact.	**Q2.** Changes will likely be required from healthcare services and laboratories to comply with these requirements, however these changes are appropriate and necessary to help ensure community safety. There will be a cost impact which will vary depending on what standards the practice is currently employing. It is important that all services offering this treatment are brought up to an equivalent standard to ensure quality and safety. In our view 12 months is an adequate time for hospitals and clinics to develop and implement new policies and procedures

		based on these requirements.
Appendix 1 Part 2 Subsection 1 and 2 Page 11- 14	**Q3.** For hospital-based providers of FMT products, do you envisage any problems with meeting these requirements outlined? Do you need further guidance from TGA? **Q4.** If changes to current FMT practice are required to comply with these requirements, what is the expected cost impact? Is a 12-month transition period sufficient to update current practice? Please provide enough information to allow us to understand any impact.	**Q3 & Q4.** The requirements seem reasonable. Some facilities will need to implement change to comply and there may be costs incurred but these are necessary to protect patient safety. 12 months does seem adequate to implement change. We note that there are no national cleaning guidelines. It would be recommended that the level of environmental cleaning be specified in line with a PC2 laboratory. There are currently two Australian Standards for reprocessing of reusable medical devices. One used within hospitals and one within office-based practices. Recommend listing both of these standards: AS/NZS 4187 AS/NZS 4815
Appendix 1 Part 3 Page 15 - 17	**Q5.** Are the timeframes proposed for the initial collection of donor medical and social history and for repeat donors appropriate? If not, then please provide justification for alternative requirements. **Q6.** If changes to current FMT practice are required to comply with these requirements, what is the expected cost impact? Is a 12-month transition period sufficient to update current practice? Please provide enough information to allow us to understand any impact.	**Q5.** The timeframes seem appropriate. Re-screening repeat donors every 3 months is reasonable to identify any new issues. **Q6.** We expect that this will require changes to practice in some sites who are not currently re-evaluating and rescreening donors, and this will have cost implications,

		but this is appropriate to ensure patient safety. 12 months seems sufficient for sites to review their current procedures and implement changes.
Appendix 1 Part 3 Subsection 3 ineligibility criteria Page 17 - 33	**Q7.** Is infection with HTLV-1 / HTLV-2 considered relevant to screening of stool donors? The faecal route is not a known mode for transmission, and the level of evidence to support screening is low.	**Q7.** In our view, a cautious approach should be taken with regard to donor screening. It would be prudent to test for HTLV 1 and 2, even if the likelihood of transmission is very low.
	Q8. Is the risk of FMT recipients being exposed to xenogenic infections as a result of receiving viable, non-human cells or tissue sufficiently low in Australia at this time? Should this donor requirement be retained or removed?	**Q8** In our view xenotransplantation is not a common issue in Australia and thus this requirement does not seem necessary.
	Q9. Is the risk of prion transmission from donors that have received human derived pituitary hormone sufficiently negligible in Australia at this time? Should this donor requirement be retained or removed?	**Q9.** Although there is no known risk of transmission of CJD from faeces, studies are limited. We would recommend a cautious approach and suggest that the same risk assessment and exclusion criteria regarding CJD used by the Australian Red Cross Blood Bank for blood donations be implemented for faecal microbiota transplants. As such, we recommend that section (g) be removed in its entirety as recipients of human pituitary derived hormone should be included as part of the general assessment for having a risk of prion disease as outlined

		in section (c). Under the guidance information in section (c), information regarding recipients of human pituitary derived hormone (as well as recipients of dura mater homografts) should be included as an iatrogenic means of transmission. The National CJD Infection Control Guidelines can also be referenced to help make this assessment. https://www1.health.gov.au/internet/main/publishing.nsf/content/icg-guidelines-index.htm
	Q10. Is the risk of donor being exposed to xenogenic infections as a result of working closely with animals sufficiently low in Australia at this time? Should this donor requirement be retained or removed?	**Q10.** This seems an extremely unlikely risk and it may be difficult to define levels of animal contact that warrant exclusion. Does this relate to livestock or exotic animals or domestic animals? At this point we don't see it as being a major issue but suggest that more specific advice be sought from veterinary microbiologists.
	Q11. Should any of the donor screening ineligibility criteria listed above under 'other criteria', or any others, be included in the draft TGO? If yes, please outline your evidence-based reasoning.	**Q 11.** None to add
Subsection 4 autologous use Page 33	**Q12.** How common are autologous FMT transplants in Australia, and is the drafted concession appropriate?	**Q12.** To our knowledge they are still rare in Australia but there is increasing interest in the haematology/oncology population so it may become

		relevant later. Screening of autologous stool would be relevant to ensure patient safety in the event of samples being confused/mislabelled in the laboratory and administered to incorrect patients (rare but can happen). It would be useful to know that the stool has been screened and is negative for pathogens or to know what the positive pathogens are in order to treat the recipient.
Appendix 1 Part 3 Subsection 6 exemptions of donor criteria Page 34 - 35	**Q13.** Is the obligation of providers to determine a list of diseases or conditions that could impact the quality, safety or efficacy of the product reasonable and understood? Does this requirement reflect current practice? **Q14.** If changes to current FMT practice are required to comply with these requirements, what is the expected cost impact? Is a 12-month transition period sufficient to update current practice? Please provide enough information to allow us to understand any impact.	**Q13.** The provision of this information seems reasonable. However, it does not reflect current practice to our knowledge. **Q14**.This would require changes in practice, which would vary across facilities depending on their current practice. The changes should be possible within 12 months
Appendix 1 Part 3 Section 9 donor and blood and stool testing Page 36 - 40	**Q15.** Are the proposed timeframes for the initial collection of blood and stool samples for testing, and the frequency of repeat collections and testing for repeat donors, appropriate? If not, then please provide justification for alternative requirements. **Q16.** If changes to current FMT practice are required to comply with these requirements, what is the expected cost impact? Is a 12-month transition period sufficient to update current practice? Please provide enough information to allow us to understand any impact.	**Q15.** Yes, they are reasonable timeframes **Q 16.** Changes will be required to current practice and there will be cost implication, but these are justifiable to ensure patient safety.
Appendix 1	**Q17.** A definitive solution is not provided here as to the appropriate validation of test methods used on stool	**Q 17.** Ongoing engagement with the sector would be

Part 3 Section 9 Subsection 5 test kits / methodologies Page 40 -	samples for FMT products, but is the proposed pathway for continued engagement with the sector appropriate?	important. This is a complex area and evidence is likely to change over time.
Appendix 1 Part 3 Section 9 Subsection 6 service agreements with testing labs Page 42	**Q18.** Is the requirement for testing to occur under contracted arrangements currently occurring? If not, then are there any problems or anticipated costs associated with establishing this arrangement?	**Q18.** It is our understanding that this is not always happening. We believe it would be useful for pathology services and FMT providers to have a clear understanding of what they are being asked to deliver and what the strengths and limitations of the tests being used are. If tests are changed, providers should be informed and understand the impact of different test strategies. There may be costs incurred to establish contracted arrangements, but these explicit arrangements would help provide clarity on testing procedures and improve safety.
Appendix 1 Part 3 Section 9 Subsection 9 blood (serum/plasma) and stool archiving Page 43 - 44	**Q19.** Is archiving of blood and stool samples currently being undertaken? If not, are there any problems or anticipated costs associated with establishing this arrangement?	**Q19**. Archiving of donor blood and stool is currently not being routinely done in Victoria, and it will incur a cost. However, we believe this is important to establish. If a recipient has an adverse outcome after FMT there should be capacity to re test the archived donor stool and any screening samples from the donor.

Appendix 1 Part 3 Section 10 Subsection 4 donor blood sample testing Page 44 - 48	**Q20.** Is testing for HTLV-1 / HTLV-2 considered relevant to screening of stool donors? The faecal route is not a known mode for transmission, but the level of evidence is low. **Q21.** *Strongyloides stercoralis* transmission has been demonstrated in organ donation and is likely to be transmissible via stool transplants. However, it is possible to pre-treat susceptible patients (e.g. with low T cell counts), which may be more appropriate than the testing of donors. In addition, the current blood test has a relatively low sensitivity (70-95%). Do you support the requirement for testing and deferral of donors that test positive for this helminth? If not, then please provide your justification. **Q22.** Is the requirement for repeat serology to be performed in the absence of NAT likely to have a significant impact on facilities manufacturing FMT products from fresh donors? Does your facility, or those you are aware of perform NAT, or will repeat serology need to be completed before a donor can be accepted? If NAT is not being performed, what are the process and cost implications of this requirement? **Q23.** Should any of the blood tests listed above under 'other criteria', or any others which are relevant, be included in the draft TGO? If yes, please outline your evidence-based reasoning.	**Q20**. Yes, we would advise a cautious approach be taken and testing of donors for HTLV 1 and 2 should occur. **Q21.** Yes, we would advise a cautious approach be taken and testing of donors for *Strongyloides* should occur. **Q22.** Clinicians should be able to select either strategy based on the time available to them. NAT may be required in a more urgent situation where a recipient cannot wait 3 months for the donor stool. Serology would likely be more useful for repeat donors. **Q23.** Nil to add
Appendix 1 Part 3 Section 10 Subsection 8 Microorganisms in stool Page 49 - 53	**Q24.** Is there a need to test for Norovirus and Rotavirus? If there is a very limited window where an infected individual would present asymptomatic, then testing may not be necessary. Please comment. **Q25.** The prevalence of *Entamoeba histolytica* in Australia is unknown and likely to be rare, although it is known to be present in specific groups of individuals. The Australian CWG chose detection of this organism in stool (microscopy or ELISA for antigen), presumably because it	**Q24.** Yes, this should be tested for. Recipients may be heavily immunocompromised people and infection with these viruses could have a major clinical impact **Q25** Yes this should be tested for. Recipients may be heavily immunocompromised people and infection with these

	is more relevant than the blood test for antibodies to the organism which cannot distinguish current from previous exposure. Is this considered appropriate?	viruses could have a major clinical impact
	Q26. Shiga toxin-producing types of *E. coli* is a common cause of acquired gastroenteritis in Australia. Despite this organism not being listed in the Australian CWG, it is recommended in all other consensus statements and the prevalence in Australia does not seem to justify varying from the international position. Is this considered appropriate?	**Q26** Yes this should be tested for. Recipients may be heavily immunocompromised people and infection with these viruses could have a major clinical impact
	Q27. Testing for enteroviruses was listed in the Australian CWG statement so has been listed in the draft TGO at this time but is not recommended in most consensus documents. Are there any factors that make explicit testing of potential donors for enteroviruses relevant in the Australian context?	**Q27** Yes this should be tested for. Recipients may be heavily immunocompromised people and infection with these viruses could have a major clinical impact
	Q28. Should any of the stool tests listed above under 'other criteria', or any others which are relevant, be included in the draft TGO? If yes, please outline your evidence-based reasoning.	**Q28** Yes MDR Gram negatives should be tested for. This includes ESBL and MDR Gram negatives Serious adverse events have already been reported in the literature for patients acquiring these through FMT. Parasites should also be tested for (microsporidia, cryptosporidia, cyclospora). The recipients may be heavily immunocompromised.
Other comments	Regarding section (f) subsection (e): We recommend stating "acupuncture or dry needling, unless performed using sterile, single use needles" Acupuncture is a protected term for use only by traditional Chinese medicine practitioners.	

	Dry needling is the term used for other practitioners such as physiotherapists.	