[redacted]

[redacted]

12 March 2019

Biological Science Section
Therapeutic Goods Administration
PO Box 100 WODEN ACT 2606
Email: bloodandtissues@health.gov.au

To Whom It May Concern

Re: Feedback from [redacted] in response to the Therapeutic Goods Administration's Public Consultation on FMT, January 2019

[redacted] would like to express its strong support of the aims of the Therapeutic Goods Administration's (TGA) Consultation paper on the "Options for the regulation of Faecal Microbiota Transplantation (FMT) materials" and thank the TGA for the opportunity to feedback. At this point in time, access to safe and screened FMT in Australia is inequitable in terms of actual access and cost, not always evidence-based and '*ad hoc*'.

Key points [redacted] to convey to the TGA are:

1. There is clear evidence that FMT successfully treats recurrent Clostridium difficile infection (CDI); in this context, the current evidence is that FMT is safe and cost effective, moreover FMT in the setting of recurrent CDI, is more efficacious and less costly than further antibiotic therapy.
2. There is emerging evidence (Phase II level data and a meta-analysis) that FMT induces remission in active ulcerative colitis (UC). Meta-analysis of 4 randomised controlled trials demonstrates an odds ratio of 3.7 (1.8-7.4) favouring donor FMT over placebo (N=140 donor FMT exposed patients vs 137 controls).
3. There is no high quality evidence to support FMT for the maintenance of remission in UC at this time. Clinical trials in this setting are required – and access to safe, reliable FMT is important to support these.
4. FMT as a therapy should not be held to a different standard from other drugs.
5. [redacted] notes and is cognizant of the potential risks of FMT as listed on page 11-12 of the document.
6. Frozen stool banking provides timely 'on demand' therapy for patients with recurrent CDI, allowing pre-screening and re-screening of donors.
7. [redacted] supports the use of frozen stool banking and recommends that consideration is given to this being coordinated and regulated at a national level.
8. Rigorous and preferably standardised protocols for donor stool screening and processing should be developed and TGA endorsed.
9. Standardised stool banking and processing protocols will enhance the safety and quality of donor stool as well as facilitate safe and reliable research in FMT.
10. The governance of standardized stool banking should allow the TGA to identify and recall all affected patients were a safety issue raised requiring open disclosure and reassessment.
11. [redacted] strongly advocates for the establishment of a National Stool Bank and propose that a bespoke regulatory standard be applied by the TGA.

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12. [redacted] supports the establishment of a registry for all FMT conducted in Australia, including FMT indication, aliquot used (for traceability) and outcomes (to inform future practice).

[redacted] *response to the specific question raised by the TGA Consultation re: support for the proposal to consider all FMT material that has been originally sourced from human donors as biologicals:*

[redacted] prefers a *hybrid* model where FMT and direct stool derivatives that contain human cells are considered biologicals but defined microbial therapeutics that do not contain human cells are regulated as drugs. Note that a *defined microbial therapeutic* need not come from stool (but rather its composition may have been informed by FMT research) and thus referring to it as "Faecal" is inaccurate. [redacted] recommends that very precise language and definitions are used to distinguish between these products as they emerge.

Defined microbial therapeutics may consist of bacteria that are the progeny of organisms derived from human faeces and these should not be considered biologicals. These products, unlike whole FMT may be able to be produced to ensure a more consistent content, not contain human material and therefore would be analogous to traditional drugs. However, under the current wording of the legislation, they could potentially be considered to be "derived" from human tissue and thus this distinction should be clearly delineated.

Option 1 (pg 32 – 33 of Consultation paper, version 1.0, January 2019) is our professional society's preferred option. We believe that this would provide the safest and most reliable long-term model. It would be important that stool banks had at least 12 months to reach a GMP standard before enforcement of the code was implemented.

Our major concern with options 2 and 3 is that hospitals are not the ideal sites to prepare biological materials because the risk of contamination would be higher than in dedicated laboratory facilities. Hospital environments have high levels of multi-resistant organisms and encouraging the siting a stool bank within a hospital, and requiring a lesser degree of manufacturing standard within that environment, is not ideal. Option 4 could be the optimal model, but this would depend on the details of the standard. Although we do favour a bespoke approach to regulating FMT, there is insufficient detail here to support option 4 at this time.

[redacted] will continue to engage and work collaboratively with the TGA during this process in order to ensure that all the objectives of the Consultation are met and realised with outcomes mutually benefitting all Australians.

Yours sincerely,

[redacted]

[redacted]