Fiona Stanley Hospital Clinicians Response to TGA Consultation Paper:
Options for the Regulation of Faecal Microbiota Transplantation (FMT) materials Version 1.0, January 2019-03-01

Who we are:
Fiona Stanley Hospital (FSH) is an 800 bed tertiary hospital in Western Australia. It is the only centre in Western Australia that performs FMT and we take referrals from around the state. Epidemiological and hospital morbidity data suggests there is a huge unmet need for FMT. The service is run by two gastroenterologists (Drs Oliver Waters and Jesica Makanyanga), and an infectious diseases physician (A/Prof Laurens Manning). To date, we have treated 40 patients with recurrent/relapsing *Clostridium difficile* infection (rCDI), with a success rate of 90%. Our FMT service is run as an observational study with frozen stool from healthy donors, processed in a lab at the research institute adjacent to the main hospital. The HREC at FSH approved the study, which allows it an exemption from the TGA regulatory framework.

Input relating to specific questions in the document:

1. We do not think it is logical to regulate stool as a biological (regardless of whether processing removes the human cells present) for the following reasons:
    a. Nearly all regulatory agencies (FDA, EMA, Health Canada, UK HTA) consider FMT to be a 'drug', 'medicinal product' or 'drug that cannot be standardised'; presumably there is some legal consistency across these jurisdictions to determine this.
    b. Our digestive tracts are exposed to external human cells during normal everyday activities (e.g. sex, kissing, eating restaurant food etc.). By contrast, incidental exposure to other tissues (e.g. stem cells or renal tissue) does not occur in the same way.
    c. The human gut is also adapted to deal with foreign material, including viable cellular material from both humans and animals; this means that FMT is very different to other recipient tissues.
2. We believe there are substantial logistical and cost barriers to establishing a functional, safe FMT service at any site. This is particularly relevant for practitioners considering infrequent FMT procedures.
    a. Our experience is that finding a space for processing and handling that is isolated from both other products (e.g. medicines in a pharmacy or infectious material in a pathology laboratory) is very difficult and will require investment in specific infrastructure at each site.
    b. There is still an 'ick' factor when processing the product.
    c. These features have been associated with a huge unmet need for providing routine FMT in Australian health care facilities.

Our vision for FMT in Australia:
To ensure access for all Australians with rCDI and to promote FMT research for other conditions we strongly believe that a single, or few processing centres could supply high quality product to most hospitals in Australia. When established, ideally as a not-for-profit organisation, this would still require a cost-recovery model to ensure

sustainability. In this situation, a third party provider of FMT samples to a hospital, or other facility, should adhere to GMP standards. For individual clinicians performing infrequent FMT, agreed minimal standards of FMT manufacturing could be adhered to by any hospital for treatment of its patients without necessarily having to conform to GMP standards.

One of the cornerstones of quality and safety would be to implement a ***national registry*** of donors and recipients of FMT (similar to the AOA national joint registry) that would allow long-term tracking of patients and safety issues. Like many other situations, a registry should be an integral part of a post-marketing surveillance as part of a risk management plan with a poorly characterised product with unknown long term effects and a situation where traditional passive surveillance will not be adequate.

We believe the regulatory framework should only apply for recognised indications for FMT such as rCDI and perhaps inflammatory bowel disease. Use outside these indications should be only be in the setting of a clinical trial. However, donor screening and processing should be to the same standard as for rCDI.

How does our vision for FMT align with the options proposed in the consultation paper?

As noted above, we do not think it logical for FMT to be considered a biological, or regulated as such. But if this were to remain the case, Options 3 and 4 potentially provide a workable regulatory environment for practitioners. If centralised processing centres were established, we believe the logistical challenges for individual clinicians performing infrequent FMT would be too great when compared with obtaining high quality reliable product for elsewhere with a short turn-around time.

Signed

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