29-01-2020

[REDACTED] Response to the TGA's draft standards for faecal microbiota transplant (FMT) products

As researchers, infectious diseases physicians and microbiologists we have concerns that the TGA's plans to regulate some FMT products as Class 2 biologicals and impose the requirement that all screening tests used on donors be validated for screening purposes will ultimately result in reducing the safety and availability of FMT in Australia.

Although validation of pathology tests for screening purposes might be ideal, such validated tests for use in stool products are currently not available and there are very significant logistical and financial obstacles to such validation ever occurring. The concern is that this requirement would encourage the manufacturers of FMT products to argue for the minimum possible screening on their products. Stool is a vastly complex substance whose content, beyond digested food, is almost entirely microbial, and even with modern technology is still not entirely defined. As such, the list of pathogens, pathobionts, diseases states and resistance determinants that should be screened for in FMT donors or products is constantly evolving. To enhance the safety of FMT, we should be encouraging expanded pathogen testing and be able to rapidly adapt to changing infection and resistance epidemiology. By necessity this will involve the use of tests validated primarily for diagnostic purposes not screening purposes. In practice many laboratory tests used by diagnostic laboratories are already used in patients with very low pre-test probability of having the disease, effectively as screening tests.

Clearly tests that are already validated in donor populations, such as those currently used in blood donor screening, should be used for FMT donor screening. However, where such tests do not yet exist, the screening test used should be validated for diagnostic use and be performed in a NATA accredited laboratory. While the further validation of stool screening tests is awaited, both donors and recipients of FMT should be made aware of the limitations of using screening tests not validated for this purpose through an informed consent process.

A second concern is that these regulatory burdens fall disproportionately on stool banks. Stool banks are the best regulated, and arguably the safest environment in which to produce FMT. If regulation is too burdensome, the stool bank model will cease to be viable. Unlike in tissue transplantation settings, the technology to produce and administer FMT is extremely simple and available to the public. The regulations currently proposed could encourage the manufacture of FMT in much less well-regulated settings or in completely un-regulated settings such as in the recipient's own home. To prevent this occurring, all FMT products should be regulated as Class 1 biologicals.

It is essential that FMT remain easy to access for use in proven clinical indications such as for the treatment of *C. difficile* colitis. It is equally important that regulation not impede

research into FMT. Microbiome science is rapidly evolving field and we are increasingly aware of the essential role of human gut microbiota in health and disease.

Intervention to alter the gut microbiome has enormous therapeutic potential which is only just beginning to be investigated. Safer, microbially defined therapies are the ultimate goal of microbiome interventions; however, in the interim FMT is the best existing intervention to alter the human gut microbiota. Adverse events, such as the transmission of antibiotic-resistant *E. coli* through capsule FMT occurred in the context of a clinical trial and resulted in widespread disruption to clinical trials in the USA. As such, it is also in the interest of the research community to have FMT produced in well-regulated environments with safety as a primary consideration.

Sincerely yours,

[REDACTED]