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## **Position Statement On Faecal Microbiota Transplant (FMT)**

**GESA is committed to the best practice and service delivery for optimum patient care. With this in mind, GESA council have considered the role of faecal microbiota transplant (FMT) in current clinical practice.**

FMT involves delivering the faecal microbiota from one individual to another individual for therapeutic benefit. FMT is currently the most efficacious treatment for recurrent or refractory *C. difficile* infection (rCDI) and is an important medical advance in this setting as the rate of first relapse following antibiotic therapy for CDI is 25-30%. Moreover, in those patients who do relapse, further antibiotic treatment gives diminishing rates of cure, such that, after a second recurrence, the chance of further recurrence increases to 60%, and is even greater for subsequent recurrences(1, 2). In contrast to traditional antibiotic therapy alone, FMT has a primary cure rate for rCDI of 81 - 94%(3-9). Additionally, FMT is supported for this indication by randomised clinical trial evidence(7, 9).

### **Recommendation 1**

**GESA therefore recommends that FMT should be made available as a treatment option for all patients in the Australian healthcare system with recurrent or refractory CDI.**

**This requires that FMT services be developed in at least one public hospital in each state or territory.**

In establishing each FMT service, GESA recommends the development of a stool bank of pre-screened frozen faecal aliquots from healthy volunteer donors. This standardised approach offers many benefits over the use of patient- directed donors or ad hoc arrangements(8). These benefits include avoiding possible coercion of donors known to a recipient and also ethical and confidentiality concerns regarding screening known donors in the event that disease subsequently arises in a donor or is transmitted to a recipient. There is also evidence from blood transfusion safety analyses that recipient-directed donors are more likely to test positive for infectious disease(s) than unrelated healthy volunteer donors(10). In addition, stringent exclusion criteria can be more easily applied to volunteer donors from the community than to recipient-directed donors. Using pre-screened, stored volunteer donor stool also saves time, as fresh stool requires a donor to be identified and screening tests to be undertaken which may take more than 1 week to complete. If abnormalities are detected in the screening, another donor must be found. Lastly, donor recruitment and testing is time-intensive and costly. By using a frozen stool bank with anonymous donors, the process becomes more economical(11).

FMT has a favourable short-term risk profile. However, the long-term risks are unknown at this time. The potential for, as yet unknown, long-term risk must be factored into screening protocols and conveyed to patients during consent for the procedure. There are a number of screening protocols that have been developed for FMT donors(12, 13). These should be adapted in consultation with local infectious disease experts, to reflect the risk of disease relevant to the local population and

thus may vary depending on the geographical location of the service. There is evidence that an obesogenic phenotype may be transmitted via FMT in animal studies(14) and therefore potential donors with any element of the metabolic syndrome should be excluded. A history of active gastrointestinal illness, malignancy, autoimmune or atopic disease, chronic pain syndromes, neurological or developmental disorders or antibiotic use in the preceding 3 months also should be exclusion criteria.

Internationally, there has been difficulty classifying FMT as to whether it is a therapeutic “drug”, biologic product or tissue(15). Despite randomized control trial efficacy data for FMT to treat rCDI, the United States Food and Drug Administration (FDA) have labelled FMT as investigational and implemented a policy of “enforcement discretion” after initially imposing a moratorium on the procedure. GESA believes that faeces for FMT would be better classified as a bodily tissue donation in a similar way that blood and blood donation is regarded. Stool is derived from human donors, and is therefore not a “standard” defined product like manufactured drugs.

Whilst FMT’s therapeutic efficacy is proven for rCDI, there is currently insufficient evidence to recommend FMT as a treatment for any other indication. There are a number of clinical trials recently reported(16, 17) and currently underway in Australia (ACTRN12613000236796, NCT01896635) and around the world assessing the therapeutic potential of FMT in a number of gastrointestinal and other diseases. The results of these should be awaited prior to any more general adoption of this therapy, given the lack of longer-term safety data and the possibility that FMT may transmit unintended disease.

## **Recommendation 2**

**GESA therefore recommends that, at this time, FMT for indications other than for CDI should be carried out only in the clinical trial setting and with careful evaluation and transparent reporting of efficacy and safety.**

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## **References**

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