30 January 2020

Dear TGA,

We are based in Perth and are planning to be a major centre for faecal microbiota transplantation in alliance with the Australian Red Cross Blood Service. Our chief feedback on the "Draft standards for faecal microbiota transplant (FMT) products, Version 1.0, November 2019" relates to question 17 and the stipulation of Class 4 IVD level validation of assays. You've suggested that all microbial screening donor tests are validated to the level of a Class 4 in-vitro diagnostic device. For the serology and NAT tests for HIV, HCV, HBV this is not a problem as there are existing assays. For the stool microbial assays, there are none which are validated to this level. However is this even possible? As no one tests asymptomatic patients for stool pathogens, what gold standard would we use as a comparison for the assay sensitivity in detecting microbes in asymptomatic individuals? Surely studies of spiked samples would not be acceptable. We don't have the equivalent data for blood borne virus assays from blood donors, or performance of tests in the seroconverting individual. Given the veracity required for a Class 4 IVD listing, we figure we would need to test all the components of assay validity for each of the individual microbes, using reference material across genotypes. This is a mammoth undertaking. No commercial test provider will undertake this work for the small number of stool donor tests from which they could recoup costs, and no laboratory will have the resources to do it either. Similar issues apply to strongyloides serology which has terrible performance. Is the transmission of these microbes of the same clinical significance as HIV, HBV, HCV? Most of the bacterial and parasite pathogens are treatable, and the viral pathogens generally resolve by themselves without significant morbidity. If Class 4 IVD standard is stipulated, this will stop FMT going ahead. We do not think "authorised prescriber" status, or FMT as a "clinical trial" are acceptable avenues to get around the Class 4 IVD requirement.

We advocate that tests for microbes, other than HIV, HBV, HCV should not require validation to a Class 4 IVD standard. We believe the approach should be that "the best available tests are utilised", wording applied in other parts of the standards. As an analogy, I (Peter Boan) was involved in the update of chapter 2 solid organ donor infection screening in "Clinical Guidelines for Organ Transplantation from Deceased Donors, Version 1.3-May 2019" for the Transplantation Society of Australia and New Zealand. We have advocated testing of all donors with tests which do not have Class 4 IVD listing (I may be incorrect here but I don't think HTLV, Toxoplasma IgG, CMV IgG or EBV IgG commercial tests have such listing). Additionally we have advocated tests in certain donors which certainly don't have Class 4 IVD listing (Urine microscopy and culture, Blood culture, Respiratory culture, testing for HHV8, Influenza, West Nile virus, Zika virus, Tuberculosis, Malaria, Strongyloides, Trypanosomiasis). There is a pragmatic acceptance that these tests will never be validated to Class 4 IVD standard, but that we ought to use the best available tests to hand even though their validation has been for purposes other than organ donation. We think you should take a similar pragmatic approach for testing FMT donors.

Regards,

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