EXPLANATORY STATEMENT

Therapeutic Goods Act 1989

Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020

The *Therapeutic Goods Act 1989* ("the Act") provides for the establishment and maintenance of a national system of controls for the quality, safety, efficacy and timely availability of therapeutic goods that are used in or exported from Australia. The Act is administered by the Therapeutic Goods Administration ("the TGA") within the Department of Health.

Subsection 10(1) of the Act provides that the Minister may, by legislative instrument, make an order determining that matters specified in the order constitute a standard for therapeutic goods or a class of therapeutic goods identified in the order. Subsection 10(2) provides that an order establishing a standard for therapeutic goods may be specified by reference to the quality of the goods, or the procedures to be carried out in the manufacture of the goods, among other matters. An order may also require that a matter relating to the standard be determined in accordance with a particular test.

Importantly, a person who imports, exports or supplies therapeutic goods that do not conform to an applicable standard may be subject to offence and civil penalty provisions in sections 14 and 14A of the Act. The Secretary may, however, consent in writing to the importation, exportation or supply of therapeutic goods that do not conform to an applicable standard, in accordance with those sections.

The *Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020* ("the Order") is made under section 10 of the Act. The purpose of the Order is to establish a ministerial standard for therapeutic goods that are faecal microbiota transplant products ("FMT products"). The Order specifies the minimum requirements for the quality and safety of FMT products, principally by reference to procedures that must be carried out in the manufacture of those products.

Background

The Australian Government is responsible for regulating the quality, safety and efficacy of therapeutic goods. This is achieved in part by specifying ministerial standards under section 10 of the Act by reference to a range of matters including the manufacture of therapeutic goods, and by otherwise applying default standards that are constituted by statements in three international pharmacopoeias defined in the Act.

FMT products are therapeutic goods that comprise, contain, or are derived from human stool and that are for introduction into a person for therapeutic use. Faecal microbiota transplantation describes the process of collecting stool from an acceptable donor, using that stool in the manufacture of an FMT product, and administering or applying the FMT product in the treatment of a person, including by means of rectal enema, sigmoidoscopy, colonoscopy, nasogastric or nasoduodenal tube, or oral ingestion. At present, the therapeutic uses of FMT products include treatment of recurrent *Clostridium difficile* infection (an often serious bacterial infection of the gut).

As FMT products are an emerging spectrum of therapeutic goods, those products have not until recently been subject to the regulatory scheme established under the Act. Since 2019, a number of legislative measures have been introduced to support the regulation of FMT products in Australia.

The *Therapeutic Goods (Things that are Biologicals) Specification 2019* was made under subsection 32A(2) of the Act with the principal purpose of clarifying that FMT products are indeed biologicals. The *Therapeutic Goods Legislation Amendment (2019 Measures No.1) Regulations 2019* ("the 2019 Amendment Regulations") introduced a tailored regulatory framework for FMT products, in order to ensure the safety, quality and efficacy of those products for Australian patients. Under the 2019

Amendment Regulations, FMT products were categorised as Class 1 or 2 biologicals, depending whether the products are principally manufactured, tested and provided to a patient in a hospital setting under the supervision or direction of a medical practitioner or not.

The 2019 Amendment Regulations provided FMT products with an exemption until 1 January 2021 from both the requirement to be included in the Australian Register of Therapeutic Goods ("the Register") under Part 3-2A of the Act, and the requirement to be covered by a manufacturing licence issued under Part 3-3. The exemption was provided to allow manufacturers of FMT products to prepare for regulation under the regulatory scheme.

The *Therapeutic Goods Legislation Amendment (2020 Measures No.1) Regulations 2020* were made to extend the exemption until 1 July 2021, in recognition of the delays and impacts on manufacturers of FMT products as a result of the ongoing public health emergency caused by the outbreak of the coronavirus disease (COVID-19). Consequently, from that date, all FMT products will be required to comply with the requirements under Part 3-2A of the Act.

The Order is similarly intended to support the regulation of FMT products in Australia by specifying a range of matters that broadly relate to requirements that must be met, and procedures that must be implemented, in the manufacture of FMT products. The requirements and procedures are designed to ensure that the quality and safety of stool used in the manufacture of FMT products, and ultimately the quality and safety of FMT products manufactured from stool, is acceptable. Most notably, procedures must be implemented relating to:

- screening and selection of donors, including conducting interviews to obtain a medical and social history, conducting physical assessments, taking blood, stool and other samples, testing those samples for unacceptable microorganisms and diseases, and applying any relevant periods of ineligibility as specified in the Order; and
- microbial control of stool and FMT products, including in relation to processing, storage and transportation.

Importantly, FMT products can only be manufactured using stool collected from a donor who has satisfied the screening procedures in relation to a 'proposed donor' specified in Division 2 of the Order, and who has been determined eligible to donate stool for that purpose (" an accepted donor").

A person ceases to be an accepted donor if the person subsequently fails to satisfy any of the screening procedures applicable to an accepted donor specified in the Order. Accordingly, if such a person proposed to again donate stool for use in the manufacture of FMT products, the person would first need to repeat the applicable screening procedures in Division 2 in order to be determined eligible.

The development of the Order reflects the unique nature and challenges presented by FMT products. FMT products are sufficiently different from other therapeutic goods of human origin, principally blood, cells, tissues and organs. As such, a specific standard is needed to establish minimum quality and safety thresholds for the safe use and manufacture of these products.

Finally, it should be noted that the existing Therapeutic Goods Order No. 87 *General requirements for the labelling of biologicals* will apply in relation to FMT products to specify minimum requirements for labelling.

Incorporation by reference

The Order incorporates by reference the *Therapeutic Goods Order No.88 Standards for donor selection, testing, and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products* ("TGO 88"). TGO 88 is a legislative instrument, which similarly constitutes a standard for the purposes of

section 10 of the Act and applies to human blood and blood components, human tissues (such as skin and ocular tissue) and human cellular therapy products (including haematopoietic progenitor cells), collected from living and deceased human donors.

TGO 88 is incorporated as in force from time to time, in accordance with paragraph 14(1)(a) of the *Legislation Act 2003*. TGO 88 is available for free from the Federal Register of Legislation and may be accessed on the internet at www.legislation.gov.au.

Consultation

The Office of Best Practice Regulation ("OBPR") advised that a regulation impact statement was not required in relation to the making of the Order (OBRP ID 25297).

However, extensive consultation was conducted in relation to the development of the Order. Between 15 November 2019 and 31 January 2020, the TGA publicly released an early draft version of the Order and associated guidance document and sought submissions from interested parties.

The TGA received 19 responses to the public consultation, including from all major industry stakeholders. There was widespread support for the contents of the Order, with detailed feedback on many requirements being incorporated where appropriate and grounded in evidence-based practice.

Following public consultation, the TGA conducted further targeted consultation with the three major Australian providers of FMT products (BiomeBank, Centre for Digestive Diseases, and Australian Red Cross Lifeblood). This included provision of a further revised version of the Order for supplementary comment by these providers. Comments were received on numerous aspects, including timeframes for repeat stool screening, microorganism testing, blood tests, and overall readability. These comments were incorporated as appropriate into the final version.

The Advisory Committee on Biologicals was also consulted on a draft version of the Order, and provided advice in September 2019, February 2020, and May 2020.

Details of the Order are set out in **Attachment A**.

The Order is compatible with the human rights and freedoms recognised or declared under section 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*. A full statement of compatibility is set out in **Attachment B**.

The Order is a disallowable legislative instrument and commences on 1 July 2021.

Attachment A

Details of the *Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020*

Part 1 – Preliminary

This Part provides for the name of the *Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order* 2020 ("the Order"), its commencement, authority and application, and a small number of other matters including, for example, setting out definitions for key terms used in the Order.

Section 1 – Name

This section provides that the name of the instrument is the *Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020*, and that the instrument may also be cited as TGO 105.

Section 2 – Commencement

This section provides that the Order commences on 1 July 2021. The commencement date provides sufficient time for manufacturers to comply with requirements and implement procedures.

Section 3 – Authority

This section provides that the legislative authority for making the Order is section 10 of the *Therapeutic Goods Act 1989* ("the Act").

Section 4 – Definitions

This section provides the definition of terms used in the Order, including 'accepted donor', 'proposed donor', 'allogeneic use', 'autologous use', 'collection period', 'FMT products', and 'fresh FMT products'. This section also notes that some expressions used in the Order, for example 'container', 'health practitioner', 'manufacture' and 'Register', are defined in the Act, and therefore have the same meaning as in the Act.

Section 5 – Standard

This section provides that the matters specified in the Order constitute a standard for FMT products.

Section 6 – Application

This section provides that the Order applies to FMT products.

Part 2 – Requirements for FMT products

This Part provides for general requirements that must be complied with, and procedures relating to screening of donors and microbial control that must be implemented, in the manufacture of FMT product.

Division 1 – General requirements

Section 7 – What this Division is about

This section explains that Division 1 specifies the general requirements that must be met in the manufacture of FMT products.

Section 8 – General requirements

This section provides the general requirements that must be met in the manufacture of FMT products. These include that the procedures and controls used in the manufacture of FMT products must be clearly defined and documented, ensure FMT products are manufactured consistently and comply with specifications, and ensure the traceability of stool used in the manufacture of FMT products from the collection of the stool to the supply of the FMT products.

Division 2 – Requirements relating to screening

Section 9 – What this Division is about

This section explains that Division 2 specifies procedures relating to screening that must be implemented in the manufacture of FMT products.

Section 10 – Proposed donors and accepted donors

This section provides the meaning of two key expressions used throughout the Order, namely, 'proposed donor' and 'accepted donor'. A proposed donor is a person, other than an accepted donor, from whom stool is proposed to be collected for use in the manufacture of FMT products.

An accepted donor is a person who has undertaken the screening procedures applicable to proposed donors specified in Division 2 and who, following those procedures, has been determined to be eligible to donate stool for use in the manufacture of FMT products in accordance with Division 2. A person ceases to be an accepted donor if the person fails to satisfy any applicable screening procedures in Division 2.

The effect of these provisions is to ensure the ongoing screening of stool donors to determine that those persons remain eligible to donate stool for use in the manufacture of FMT products. Where a person fails to satisfy any of the applicable screening procedures and ceases to be an accepted donor, that person must repeat the screening procedures in relation to a proposed donor in order to once again be determined eligible to donate stool.

Section 11 – General screening procedures

This section provides that screening procedures must be implemented in relation to both proposed donors and accepted donors, to ensure that the quality, safety and efficacy of FMT products is acceptable. Those procedures must include the procedures specified in sections 12 to 15 of the Order.

Section 12 – Medical and social history

This section provides requirements relating to the review of the medical and social history of proposed donors and accepted donors. A complete medical and social history, covering the ineligibility criteria for donor selection specified in Schedule 1 and any other relevant matters, must be obtained by interview, and reviewed for the purposes of screening. The complete medical and social history must be repeated on an ongoing basis within 90 days of the last complete medical and social history. In addition, an abridged medical and social history must also be obtained at each collection of stool.

Other requirements specified in this section include periods of ineligibility that must be applied depending on whether an FMT product is intended for allogeneic use or autologous use, requirements

relating to stool proposed to be collected outside Australia, and upper and lower age limits that must be applied in relation to a donor.

Section 13 – Blood, stool and other samples—taking

This section provides a number of requirements relating to the taking of blood, stool and other samples from proposed donors and accepted donors. The requirements for blood and stool samples vary depending on whether stool is to be collected for use in fresh FMT products or other FMT products. However, some of the requirements are consistent. For example, blood and stool samples must be taken from a proposed donor not more than 30 days before the first collection of stool for use in the manufacture of FMT products, regardless of whether the stool is to be collected for use in fresh or other FMT products. This section also provides requirements in relation to the taking of blood and stool samples from an accepted donor on an ongoing basis.

Section 14 – Blood, stool and other samples—testing

This section provides a number of requirements relating to the testing of blood, stool and other samples taken in accordance with section 13. The general requirements specified in this section include that samples must be tested as soon as practicable after collection, and within the claimed sample stability timeframe specified by the manufacturer of the in vitro diagnostic ("IVD") medical device or in-house IVD medical device to be used for the testing.

This section also specifies the particular tests that must be conducted in relation to blood samples and the microorganisms that must be tested for in relation to stool samples. The blood tests that must be conducted depend on the specific provisions in section 13 under which blood samples are taken.

Section 15 – Physical assessment

This section provides that a physical assessment must be conducted in relation to a donor not more than 30 days before the first collection of stool for use in the manufacture of FMT products, and subsequently, on an ongoing basis within 90 days of the last physical assessment.

Division 3 – Requirements following collection

Section 16 – What this Division is about

This section explains that Division 3 specifies procedures relating to microbial control that must be implemented in the manufacture of FMT products.

Section 17 – Microbial control procedures

This section provides requirements relating to microbial control procedures that must be implemented in the manufacture of FMT products. These procedures are intended to minimise the proliferation of intrinsic microbial contamination and prevent extrinsic microbial contamination of stool during the manufacture of FMT products.

This section also specifies processing, storage and transportation requirements in relation to FMT products and stool used in the manufacture of both fresh and other FMT products. These requirements similarly ensure the microbial control of the stool and the FMT product.

Schedule 1 – Ineligibility criteria for donor selection

This Schedule specifies the ineligibility criteria for donor selection and minimum periods of ineligibility for the purposes of section 12.

Attachment B

Statement of Compatibility with Human Rights

Prepared in accordance with Part 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*.

Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020

This disallowable legislative instrument is compatible with the human rights and freedoms recognised or declared in the international instruments listed in section 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*.

Overview of the legislative instrument

The *Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020* ("the instrument") is made under section 10 of the Act. The purpose of the instrument is to establish a ministerial standard for therapeutic goods that are faecal microbiota transplant products ("FMT products"). The instrument specifies the minimum requirements for the quality and safety of FMT products, principally by reference to procedures that must be carried out in the manufacture of those products.

The instrument is intended to support the regulation of FMT products in Australia by specifying a range of matters that broadly relate to requirements that must be complied with, and procedures that must be implemented, in the manufacture of FMT products. The requirements and procedures are designed to ensure that the quality and safety of stool used in the manufacture of FMT products, and ultimately the quality and safety of FMT products manufactured from stool, is acceptable. Most notably, procedures must be implemented relating to:

- screening and selection of donors, including conducting interviews to obtain a medical and social history, conducting physical assessments, taking blood, stool and other samples, testing those samples for unacceptable microorganisms and diseases, and applying any relevant periods of ineligibility as specified in the instrument; and
- microbial control of stool and FMT products, including in relation to processing, storage and transportation of stool and FMT products.

Importantly, FMT products can only be manufactured using stool collected from a donor who has satisfied the screening procedures specified in the instrument.

The development of the instrument reflects the unique nature and challenges presented by FMT products. FMT products are sufficiently different from other therapeutic goods of human origin (principally blood, cells, tissues and organs). As such, a specific standard is needed to establish minimum quality and safety thresholds for the safe use and manufacture of those products.

The instrument is a disallowable legislative instrument and commences on 1 July 2021.

Human rights implications

The instrument engages the right to health in Article 12 of the International Covenant on Economic, Social and Cultural Rights ("the ICESCR"). Article 12 of the ICESCR promotes the right of all individuals to enjoy the highest attainable standard of physical and mental health, and includes an obligation to take reasonable measures within available resources to progressively secure broader enjoyment of the right.

In *General Comment No. 14: The Right to the Highest Attainable Standard of Health (Art. 12)* (2000), the United Nations Committee on Economic, Social and Cultural Rights states that health is a 'fundamental human right indispensable for the exercise of other human rights', and that the right to health is not to be understood as the right to be healthy, but includes the right to a system of health protection which provides equal opportunity for people to enjoy the highest attainable level of health.

The instrument takes positive steps to promote the right to health by helping to ensure the safety, quality and efficacy of therapeutic goods that are FMT products. The instrument establishes a ministerial standard for FMT products and specifies the minimum requirements that must be implemented in the manufacture of these products.

These requirements are generally aimed at controlling the risk of transmission of communicable diseases that may be associated with faecal microbiota transplantation. As such, the Order addresses aspects of the right to health that relate to preventing and controlling the spread of diseases and creating conditions that improve medical service and medical attention in the event of sickness.

The requirements of the instrument are further bolstered in this regard by the criminal, civil and regulatory sanctions that may apply under the Act for persons who import, supply or export therapeutic goods that do not comply with applicable standards.

Conclusion

This instrument is compatible with human rights because it promotes the right to health in Article 12 of the ICESCR and otherwise does not raise any other human rights issues.