

EXPLANATORY STATEMENT

Therapeutic Goods Act 1989

Therapeutic Goods (Manufacturing Principles) Determination 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 36(1) of the Act provides that the Minister may, from time to time, determine written principles to be observed in the manufacture of therapeutic goods for use in humans. Subsection 36(4) of the Act provides that such manufacturing principles are legislative instruments.

Under subsection 36(2) of the Act, manufacturing principles may relate to any of the matters specified in paragraphs 36(2)(a) to (e), including the standards to be maintained and the equipment to be used at manufacturing premises, procedures for quality assurance and quality control and the manufacturing practices to be employed in the manufacturing of therapeutic goods.

The *Therapeutic Goods (Manufacturing Principles) Determination 2020* (“the Determination”) is an instrument made by a delegate of the Minister under subsection 36(1) of the Act for the purpose of determining written principles to be observed in the manufacture of therapeutic goods.

The Determination repeals and replaces the Therapeutic Goods (Manufacturing Principles) Determination 2018 (“the former Determination”) and makes a small number of changes to the principles determined under the former Determination. These changes are primarily:

- to incorporate the most recent version of the *Guide to Good Manufacturing Practice for Medicinal Products* (PE 009-14) (“PIC/S Guide to Good Manufacturing Practice”) published by the Pharmaceutical Inspection Co-operation Scheme (“PIC/S”) in July 2018; and
- to remove the provisions relating to therapeutic devices, as this category of therapeutic goods is now superseded (goods formerly included in this category are now regulated as other therapeutic goods or medical devices, following the introduction of a specific regulatory regime by the *Therapeutic Goods Amendment (Medical Devices) Act 2002* and the conclusion of the transitional arrangements under that Act in 2007).

Background

Part 3-3 of the Act sets out requirements relating to the manufacture of therapeutic goods other than medical devices, Class 1 biologicals, or goods or persons exempt from the operation of that Part by regulations made for the purposes of section 34 of the Act.

Part 3-3 contains criminal offences and civil penalty provisions that apply where a person carries out, at premises in Australia, a step in the manufacture of therapeutic goods and the person does not have a licence issued under Part 3-3 (or the person, or the goods involved, are not exempt from the operation of that Part under section 34 of the Act).

It is a condition of each manufacturing licence that a manufacturer of therapeutic goods complies with the manufacturing principles (subparagraph 40(4)(a)(ii) of the Act refers). If the holder of a manufacturing licence breaches this or any other condition of the licence, the Secretary may suspend or revoke the licence (subparagraph 41(1)(a)(viii) of the Act refers). The Secretary can

also refuse to grant a manufacturing licence if satisfied that the applicant for the licence will be unable to comply with the manufacturing principles (paragraph 38(1)(e) of the Act refers).

The manufacturing principles set out the minimum requirements that are to be observed in the manufacture of therapeutic goods (other than medical devices), to ensure that therapeutic goods are produced to a high quality. The Determination separately specifies the principles to be observed in relation to the manufacture of the following therapeutic goods:

- registered and listed therapeutic goods (principally, these are medicines, active pharmaceutical ingredients and sunscreens), and biologicals that comprise or contain live animal cells, tissues or organs;
- blood, blood components, haematopoietic progenitor cells and biologicals (other than biologicals that comprise or contain live animal cells, tissues or organs).

The Determination also reflects contemporary drafting standards and practices on matters relating to style and form, such as the use of plain English and compliance with the Office of Parliamentary Counsel's Drafting Directions. As such, the Determination improves readability, accessibility and presentation for stakeholders, without making any other substantive changes to the manufacturing principles that are the subject of the former Determination.

The TGA uses internationally harmonised manufacturing standards to allow manufacturers to operate in an international environment. The TGA maintains Good Manufacturing Practice ("GMP") requirements in line with updates issued through PIC/S. Updates are necessary in order to maintain mutual confidence with regulators overseas, and to promote quality assurance of inspections and the harmonisation of technical standards and procedures with international inspection standards for the production and testing of medicinal products.

PIC/S is a non-binding, informal co-operative arrangement between regulatory authorities in the field of GMP of medicinal products for human or veterinary use. PIC/S leads the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates. The PIC/S Guide to Good Manufacturing Practice (PE 009-14) introduces a number of new measures as compared to the version published on 1 January 2017 (PE009-13), including:

- new guidance in relation to the assessment and control of contamination and cross-contamination risks;
- greater oversight and management of the suppliers of raw materials (active ingredients and excipients) that may impact on the quality of products manufactured;
- additional guidance in relation to the management and investigation of product complaints and product recalls; and
- additional guidance and requirements in relation to the application of real-time-release-testing and parametric release of medicinal products.

The incorporation of the most recent version of the PIC/S Guide to Good Manufacturing Practice in the Determination ensures that an appropriate level of GMP applies to the manufacture of therapeutic goods in Australia. These changes reflect the need to provide guidance on the management of new technologies, to address gaps in existing requirements, to manage risks identified through inspections of manufacturing premises and to ensure continuous improvements in the way goods are manufactured.

Australian manufacturers benefit from reduced regulatory burden where the TGA is able to adopt harmonised international standards and establish mutual recognition agreements and cooperation arrangements with comparable overseas regulatory authorities.

Incorporation by reference

The Determination incorporates the following documents by reference:

- *Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products* (Version 1.0, April 2013), which sets out manufacturing practices that manufacturers of blood, tissue and cellular therapy products must comply with as a condition of their manufacturing licence under the Act. This document is available for free from the TGA website (www.tga.gov.au). The same version of this document was incorporated by reference in the former Determination;
- *Guide to Good Manufacturing Practice for Medicinal Products* (PE 009-14, 1 July 2018), which sets out standards that apply to the manufacture of medicines and similar products intended for human use. This document is available for free from the PIC/S website (<https://picscheme.org>) and is reproduced on the TGA website (www.tga.gov.au). As above, the incorporation of this document is updated to reflect the most recent version available at the time of the commencement of the Determination;
- *Guideline on the Scientific Data Requirements for a Plasma Master File (PMF)* Revision 1 (2006) (Doc. Ref. EMEA/CHMP/BWP/3794/03 Rev.1), which provides guidance on the structure and requirements for presentation of data on starting material in a plasma master file. This document is available for free from the European Medicines Agency website (www.ema.europa.eu). The same version of this document was incorporated by reference in the former Determination;
- *Guideline for the Preparation of Technical Master Files for Blood, Blood Components and Haematopoietic Progenitor Cells* (Third Edition, 2008), which provides guidance to manufacturers in relation to the development of technical master files (TMF) relevant to blood, blood components and haematopoietic progenitor cells. This document is available for free from the TGA website (www.tga.gov.au). The same version of this document was incorporated by reference in the former Determination;
- *Transition to new GMP requirements for medicinal products: A notice about the implications of adopting the PIC/S Guide to GMP PE009-14*, which is a notice to assist Australian sponsors and manufacturers of medicines and active pharmaceutical ingredients supplied in Australia with the transition to the current version of the PIC/S Guide to Good Manufacturing Practice. This document is available for free from the TGA website (www.tga.gov.au). It is a new document that is incorporated by reference for the first time in this Determination.

Each of these documents is incorporated as in force or existing at the time the Determination commences in accordance with paragraph 14(1)(b) of the *Legislation Act 2003*.

The Determination also incorporates the following legislative instruments, which constitute standards for the purposes of section 10 of the Act:

- *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*, which specifies minimum technical requirements in relation to donor selection, donor testing and the manufacture of human blood, blood components, tissues and cellular therapy products;
- *Therapeutic Goods Order No. 94 (Standard for Haematopoietic Progenitor Cells derived from Cord Blood) 2017*, which specifies technical requirements in relation to therapeutic goods that are haematopoietic progenitor cells derived from cord blood;

- *Therapeutic Goods (Standard for Blood and Blood Components) (TGO 102) Order 2019*, which specifies requirements in relation to therapeutic goods that are blood and blood components.

Each of these documents is incorporated as in force from time to time, in accordance with paragraph 14(1)(a) of the *Legislation Act 2003*. These instruments are available for free from the Federal Register of Legislation (www.legislation.gov.au).

Consultation

The TGA undertook targeted consultation in relation to the incorporation of the most recent version of the PIC/S Guides to Good Manufacturing Practice. A gap-analysis of the differences between the two versions of the PIC/S Guides to Good Manufacturing Practice published in 2017 and 2018 (as adopted by the former Determination and the Determination respectively) was made available by the TGA for consultation with the Technical Industry Working Group on GMP (“TIWGG”) in April 2019.

The TIWGG is a stakeholder representational group comprising members nominated by key peak industry associations Accord, the Australia New Zealand Industrial Gas Association, the Active Pharmaceutical Ingredients Manufacturers’ Association of Australia, Complementary Medicines Australia, Consumer Healthcare Products Australia and the Generic and Biosimilar Medicines Association and Medicines Australia. Feedback from the key industry associations regarding the gap analysis was generally positive and the associations supported the adoption of the most recent version of the PIC/S Guide to Good Manufacturing Practice.

The Office of Best Practice Regulation advised that a regulation impact statement was not required in relation to the making of the Determination (OBPR reference 42644).

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

The Determination 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 Determination is a disallowable legislative instrument for the purposes of the *Legislation Act 2003*, and commences on the day after registration on the Federal Register of Legislation.

Details of the *Therapeutic Goods (Manufacturing Principles) Determination 2020*

Part 1 – Preliminary

This Part provides for the name of the *Therapeutic Goods (Manufacturing Principles) Determination 2020* (“the Determination”), its commencement and authority, and a small number of other matters including, for example, setting out definitions for key terms used in the Determination.

Section 1 – Name

This section provides that the name of the instrument is the *Therapeutic Goods (Manufacturing Principles) Determination 2020*.

Section 2 – Commencement

This section provides that the Determination commences on the day after registration on the Federal Register of Legislation.

Section 3 – Authority

This section provides that the legislative authority for making the Determination is section 36 of the *Therapeutic Goods Act 1989* (“the Act”).

Section 4 – Definitions

This section provides the definitions of certain terms used in the Determination. In particular, this section defines ‘blood components’, ‘haematopoietic progenitor cells’, ‘relevant officer’ and ‘technical master file’. The section also notes that a number of terms have the meaning given in subsection 3(1) of the Act, including ‘biological’, ‘licence’ and ‘manufacture’.

Section 5 – Repeals

This section provides that each instrument that is specified in Schedule 2 to the Determination is repealed as set out in the applicable items in that Schedule.

Part 2 – Manufacturing principles

This Part determines the manufacturing principles that are to be observed in the manufacture of therapeutic goods for the purposes of section 36 of the Act.

Section 6 – Manufacturing principles—therapeutic goods other than blood, blood components, haematopoietic progenitor cells etc.

This section determines that the manufacturing principles set out in Part 1 of Schedule 1 to the Determination are to be observed in the manufacture of therapeutic goods (including active pharmaceutical ingredients and sunscreens) for use in humans, other than the therapeutic goods mentioned in paragraphs 7(a) to (d) of the Determination (that is, blood, blood components, haematopoietic progenitor cells and biologicals that do not contain live animal cells, tissues or organs).

Section 7 – Manufacturing principles—therapeutic goods that are blood, blood components, haematopoietic progenitor cells and biologicals that do not contain live animal cells, tissues or organs

This section determines that the manufacturing principles set out in Part 2 of Schedule 1 to the Determination are to be observed in the manufacture of therapeutic goods that are blood, blood components, haematopoietic progenitor cells and biologicals that do not contain live animal cells, tissues or organs.

Part 3 – Transitional

This Part sets out the transitional arrangements that apply in relation to the Determination.

Section 8 – Transitional provision

This section defines certain terms for the purposes of this Part. These terms are ‘former instrument’, ‘Transition Notice’ and ‘transition period’.

Section 9 – Transitional

This section provides that between the commencement of the Determination and 30 June 2021 (“the transition period”), the manufacturing principles determined under the Therapeutic Goods (Manufacturing Principles) Determination 2018 (“the former instrument”) may be observed by a manufacturer in relation to the manufacture of goods that are mentioned in section 6 of the Determination for that period.

In accordance with the definition of ‘transition period’ in section 8, the manufacturer must transition to the manufacturing principles determined under the Determination in accordance with the Transition Notice.

Schedule 1 – Manufacturing principles

This Schedule sets out the manufacturing principles that are to be observed for the purposes of section 36 of the Act as follows:

- Part 1 sets out the manufacturing principles to be observed in relation to the manufacture of therapeutic goods mentioned in section 6 of the Determination; and
- Part 2 sets out the manufacturing principles to be observed in relation to the manufacture of therapeutic goods mentioned in section 7 of the Determination.

Schedule 2 – Repeals

This Schedule repeals the former instrument.

Statement of Compatibility with Human Rights

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

Therapeutic Goods (Manufacturing Principles) Determination 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 legislative instrument

The *Therapeutic Goods (Manufacturing Principles) Determination 2020* (“the instrument”) is made by the Minister under subsection 36(1) of the *Therapeutic Goods Act 1989* (“the Act”).

Subsection 36(1) of the Act provides that the Minister may, from time to time, determine written principles to be observed in the manufacture of therapeutic goods for use in humans. These manufacturing principles set out the minimum requirements that are to be observed in the manufacture of therapeutic goods (other than medical devices), to ensure that therapeutic goods are produced to a high quality. The purpose of the instrument is to determine such principles.

Part 3-3 of the Act sets out requirements relating to the manufacture of therapeutic goods other than medical devices, Class 1 biologicals, or goods or persons exempt from the operation of that Part by regulations made for the purposes of section 34 of the Act. That Part contains criminal offences and civil penalty provisions that apply where a person carries out, at premises in Australia, a step in the manufacture of therapeutic goods and the person does not have a licence issued under Part 3-3.

It is a condition of each manufacturing licence that a manufacturer of therapeutic goods complies with the manufacturing principles (subparagraph 40(4)(a)(ii) of the Act refers). If the holder of a manufacturing licence breaches this (or any other) condition of the licence, the Secretary may suspend or revoke the licence (subparagraph 41(1)(a)(viii) of the Act refers). The Secretary can also refuse to grant a manufacturing licence if satisfied that the applicant for the licence will be unable to comply with the manufacturing principles (paragraph 38(1)(e) of the Act refers).

The instrument repeals and replaces the *Therapeutic Goods (Manufacturing Principles) Determination 2018* (“the former instrument”). The instrument incorporates a small number of changes to manufacturing principles determined under the former instrument, principally to:

- to incorporate the most recent version of the *Guide to Good Manufacturing Practice for Medicinal Products* (PE 009-14) (“PIC/S Guide to Good Manufacturing Practice”) published by the Pharmaceutical Inspection Co-operation Scheme (“PIC/S”) in July 2018; and
- to remove the provisions relating to therapeutic devices, as this category of therapeutic goods is now superseded (goods formerly included in this category are now regulated as other therapeutic goods or medical devices, following the introduction of a specific regulatory regime by the *Therapeutic Goods Amendment (Medical Devices) Act 2002* and the conclusion of the transitional arrangements under that Act in 2007).

The instrument also reflects contemporary drafting standards and practices on matters relating to style and form, such as the use of plain English and compliance with the Office of Parliamentary Counsel’s Drafting Directions. As such, the instrument improves readability, accessibility and presentation for stakeholders, without making any other substantive changes to the manufacturing principles that are the subject of the former instrument.

The incorporation of the most recent version of the PIC/S Guide to Good Manufacturing Practice in the Determination ensures that an appropriate level of Good Manufacturing Practice (“GMP”) applies to the manufacture of therapeutic goods manufactured or supplied in Australia. These changes reflect the need to provide guidance on the management of new technologies, to address gaps in existing requirements, to manage risks identified through inspections of manufacturing premises and to ensure continuous improvements in the way goods are manufactured.

Human rights implications

The instrument engages the right to health in Article 12 of the International Covenant on Economic, Social and Cultural rights (“ICESCR”). Article 12 of the ICESCR promotes the right of all individuals to enjoy the highest attainable standards of physical and mental health.

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 ensuring that therapeutic goods manufactured in Australia continue to be subject to an appropriate level of GMP, and are of a high quality.

Accordingly, these measures will assist to protect the safety of consumers who use therapeutic goods that are manufactured under licence in Australia.

Conclusion

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