EXPLANATORY STATEMENT

Therapeutic Goods (Manufacturing Principles) Determination 2018

Subsection 36(1), Therapeutic Goods Act 1989

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 purpose of the *Therapeutic Goods (Manufacturing Principles) Determination 2018* (the Determination) is to replace the current manufacturing principles instrument (the *Therapeutic Goods (Manufacturing Principles) Determination No. 1 of 2013* (MP 1/2013)) with a new, updated instrument. In particular, the Determination updates references to key international documents that relate to requirements for manufacturing standards for therapeutic goods.

The Determination commences on 1 January 2018.

BACKGROUND

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.

The manufacturing principles are designed to set out the minimum requirements to be observed in the manufacture of therapeutic goods other than medical devices, to ensure that therapeutic goods are produced to a high quality.

It is a condition of each manufacturing licence that manufacturers of therapeutic goods comply with the manufacturing principles (see subparagraph 40(4)(a)(ii) of the Act). If the holder of a manufacturing licence breaches this (or any other) condition the Secretary can suspend or revoke the licence (see subparagraph 41(1)(a)(viii) of the Act). 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 (see paragraph 38(1)(e) of the Act).

Under subsection 36(2) of the Act, manufacturing principles may relate to any of the matters specified in paragraphs 36(2)(a) – (e) of the Act, 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 used when producing therapeutic goods.

The Determination sets out separately requirements relating to the manufacturing practices and procedures to be adopted for the manufacture of:

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

- blood, blood components, plasma, haematopoietic progenitor cells and biologicals (except things that comprise or contain live animal cells, animal tissues or animal organs); and
- therapeutic Devices (Division 3 of the Instrument).

The Determination replaces MP 1/2013, with the following main differences compared to that earlier instrument:

- the replacement of references in MP 1/2013 to the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to Good Manufacturing Practice for Medicinal Products PE009-8 of 15 January 2009, with references to the PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 of 1 January 2017; and
- the removal of references in MP 1/2013 to transitional arrangements for goods mentioned in Division 2 of that instrument, as the transitional period nominated in that instrument has expired.

The PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 published 1 January 2017 introduces a number of new measures as compared to the PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-9 published 15 January 2009, including for example:

- greater oversight and management of all outsourced activities that may impact on the quality of products manufactured;
- new guidance and requirements in relation to the manufacture of biological medicinal substances.
- additional guidance and requirements in relation to the qualification and validation of facilities, equipment and processes;
- additional requirements relating to cleaning validation, in relation to health-based toxicological limits for determining acceptable levels of residues; and
- new requirements for the validation of the transportation of therapeutic goods.

The updating of the PIC/S Guide to Good Manufacturing Practice will ensure that an appropriate level of Good Manufacturing Practice applies to the manufacture of therapeutic goods manufactured or supplied in Australia. Good Manufacturing Practices change over time due to various reasons, such as the need to provide guidance on the management of new technologies, address gaps in existing requirements, manage risks identified through inspections of manufacturing premises and ensure continuous improvements in the way goods are manufactured.

The TGA uses internationally harmonised manufacturing standards to allow manufacturers to operate in an international environment. The TGA maintains its 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.

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.

The PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 published 1 January 2017 is available (without charge) from the TGA's website (www.tga.gov.au).

CONSULTATION

A gap-analysis of the differences between the 2009 and 2017 PIC/S Guides to GMP (as adopted by MP 1/2013, and the Determination, respectively) was made available by the TGA for consultation with the Technical Industry Working Group on GMP (TIWGG) in November 2016. 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, the Australian Self Medication Industry, Complementary Medicines Australia, the Generic and Biosimilar Medicines Association and Medicines Australia. Feedback from the key industry associations was generally positive and the associations supported the adoption of the 2017 PIC/S Guide to GMP.

REGULATION IMPACT STATEMENT

The Office of Best Practice Regulation has advised that a regulation impact statement is not required in relation to the making of the Determination, as the proposal is likely to have only minor regulatory impacts on business, community organisations or individuals (OBPR reference 22526).

INCORPORATION OF DOCUMENTS

The Determination incorporates a number of documents by reference, including Australian and international standards and guidelines. The intended incorporation of these documents, and information about their availability, is as follows:

Incorporated document	**Intended incorporation**	**How document may be obtained**
Australian Standard AS ISO 13485-2003 Medical devices – Quality management systems – Requirements for Regulatory purposes.	As published by Standards Australia on 31 December 2003.	From the website of SAI Global Limited - https://infostore.saiglobal.com/ for a fee of $211.68 pdf (a range of standards including Australian Standards are sold and distributed by SAI Global Limited). A free 9 page sample of this standard is also available on this website.
European Standard EN 556:1994 Sterilization of medical devices – requirements for medical devices to be labelled 'Sterile'.	As published by the European Committee for Standardization on 30 June 1995.	An identical version, as published by the National Standards Authority of Ireland, is available from the website of SAI Global Limited - https://infostore.saiglobal.com/ for a fee of $64.72 (pdf).
Guideline on the scientific data requirements for a plasma master file EMEA/CPMP/BWP/3794/03.	As published by the European Medicines Agency on 15 November 2006.	From the website of the European Medicine Agency (http://www.ema.europa.eu), free.
Guideline for the preparation of	As published by the Therapeutic Goods	From the TGA's website (www.tga.gov.au), free.

Technical Master Files for blood, blood components and haematopoietic progenitor cells.	Administration (TGA) on 22 July 2008.	

The Australian Standard AS ISO 13485-2003 and the European Standard EN 556:1994 are not available for free, but are available for the fees noted above. These documents are principally incorporated in the Determination because they set out levels of safety and quality in relation to the manufacturing processes. It would not be feasible from a regulatory perspective to not adopt such benchmarks on the basis that they are not available for free.

While these documents attract a fee for access, it is expected that the persons most affected by their adoption – manufacturers of the therapeutic goods to which they relate – would have access to the documents, and be familiar with their terms.

SUPPLEMENTARY MATERIAL - STATEMENT OF COMPATIBILITY WITH HUMAN RIGHTS FOR A LEGISLATIVE INSTRUMENT THAT DOES NOT RAISE ANY HUMAN RIGHTS ISSUES

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 2018

This 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 (Manufacturing Principles) Determination 2018* is made by the Minister under subsection 36(1) of the *Therapeutic Goods Act 1989*, and replaces the Therapeutic Goods (Manufacturing Principles) Determination No.1 of 2013 (MP 1/2013) – with the following main differences:

- the replacement of references in MP 1/2013 to the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to Good Manufacturing Practice for Medicinal Products PE009-8 of 15 January 2009, with references to the PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 of 1 January 2017; and
- the removal of references in MP 1/2013 to transitional arrangements for goods mentioned in Division 2 of that instrument, as the transitional period nominated in that instrument has expired.

The PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 published 1 January 2017 introduces a number of new measures as compared to the PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-9 published 15 January 2009, including for example greater oversight and management of all outsourced activities that may impact on the quality of products manufactured, new guidance and requirements in relation to the manufacture of radiopharmaceuticals and new requirements for validating the transportation of therapeutic goods. Updating the PIC/S Guide to Good Manufacturing Practice ensures that an appropriate level of Good Manufacturing Practice applies to the manufacture of therapeutic goods manufactured or supplied in Australia, and contributes to maintaining mutual confidence with regulators overseas, the promotion of quality assurance of inspections and the harmonisation of technical standards and procedures with international inspection standards.

Human rights implications

As this instrument does not involve any measures other than those outlined in the overview above, it would not appear to engage any of the applicable rights or freedoms.

Conclusion

This legislative instrument is compatible with human rights as it does not raise any human rights issues.

Adriana Platona
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