Australian Government

Department of Health
Therapeutic Goods Administration

Therapeutic Goods Act 1989

Therapeutic Goods (Manufacturing Principles)

Determination 2018

MP1/2018

I, Adriana Platona, delegate of the Minister for Health for the purpose of section 36 of the *Therapeutic Goods Act 1989* and acting under subsection 36(1) of that Act hereby:

(1) revoke the Therapeutic Goods (Manufacturing Principles) Determination No. 1 of 2013; and
(2) determine the following principles to be observed in the manufacture of therapeutic goods for use in humans, as set out in this Determination.

Dated 28 November 2017

(Signed by)

Adriana Platona
Delegate of the Minister for Health

Name of determination

1. This Determination is the Therapeutic Goods (Manufacturing Principles) Determination 2018.

Commencement

2. This Determination commences on 1 January 2018

Application

3. The manufacturing principles applicable to specific therapeutic goods are set out in the following Divisions:

    a. Division 1 – Therapeutic Goods including, Active Pharmaceutical Ingredients (API) and Sunscreens, but not Blood, Blood Components, Biologicals (except things that comprise or contain live animal cells, tissues or organs), Plasma, Haematopoietic Progenitor Cells or Therapeutic Devices;
    b. Division 2 – Blood, Blood Components, Biologicals (except things that comprise or contain live animal cells, tissues or organs), Plasma and Haematopoietic Progenitor Cells;
    c. Division 3 – Therapeutic Devices

Note: The manufacturing principles applicable to therapeutic goods that are things that comprise or contain live animal cells, tissues or organs are those set out in Division 1, and not those set out in Division 2.

Interpretation

4. In this Determination, unless the contrary intention appears:

active pharmaceutical ingredients (API) means any substance or mixture of substances intended to be used in the manufacture of a medicine and that, when used in the production of a medicine, becomes an active ingredient of that medicine. These substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

AS ISO 13485-2003 means the document entitled "AS ISO 13485-2003 Medical devices – Quality management systems – Requirements for Regulatory purposes published by the International Standards Organisation.

biological has the same meaning as in the Act.

blood means whole blood collected from a single human donor and processed either for transfusion or further manufacturing.

blood components means therapeutic components of blood (red cells, white cells, platelets, plasma) that can be prepared by centrifugation, filtration and freezing, but not including haematopoietic progenitor cells.

EN 556 means the document entitled EN 556:1994 "Sterilization of medical devices – requirements for medical devices to be labelled 'Sterile', published by the European Standards Committee (CEN) Central Secretariat.

haematopoietic progenitor cells means self-renewing or multi-potent stem cells, or both, capable of maturation into haematopoietic lineages, lineage-restricted pluri-potent progenitor cells, or committed progenitor cells.

medicine has the same meaning as in the Act.

plasma means plasma, separated from human donor blood, intended for a number of purposes including the production of further blood components, the production of which is required to be licensed under Chapter 3, Part 3-3 of the Act.

Register has the same meaning as in the Act.

standard has the same meaning as in the Act.

the Act means the *Therapeutic Goods Act 1989*, as amended from time to time.

the Australian Code of Good Manufacturing Practice means the document titled: "Australian Code of Good Manufacturing Practice for Human Blood, Blood Components, Human tissues and Human cellular therapy products" dated April 2013 and published by the TGA on its website.

the PIC/S Guide to GMP means the document titled "Guide to Good Manufacturing Practice for Medicinal Products", PE 009-13, published by the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S) dated 1 January 2017, except for the following Annexes of that document:

a. Annex 4 (Manufacture of veterinary medicinal products other than immunologicals);
b. Annex 5 (Manufacture of immunological veterinary medical products);
c. Annex 14 (Manufacture of medicinal products derived from human blood or plasma).

Technical Master File, for a therapeutic good, means:

a. compilations of scientific and technical data provided by a manufacturer which include a description of the steps of manufacture that is consistent with the description of steps of manufacture identified in the document entitled "Guideline for the Preparation of Technical Master Files for Blood, Blood Components and Haematopoietic Progenitor Cells", published by the TGA on its website; and

b. detailed scientific and technical data or information that must satisfy the Secretary that:

    i. the blood or blood components, manufactured using the steps of manufacture mentioned in paragraph (a), will meet Therapeutic Goods Order No. 81 – Standards for Blood and Blood Components; or

    ii. the haematopoietic progenitor cells derived from cord blood manufactured using the steps of manufacture mentioned in paragraph (a) will meet the standard set out in the *Therapeutic Goods Order No. 94 (Standard for Haematopoietic Progenitor Cells derived from Cord Blood) 2017*; and

    iii. donor selection, testing and the process for minimising infectious disease transmission via therapeutic goods that are human blood and blood components will meet the requirements of Therapeutic Goods Order No. 88 - Standards for donor selection, testing and minimising infectious disease transmission through therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products.

Therapeutic device has the same meaning as in the Act.

TGA means the Therapeutic Goods Administration, a business unit of the Department of Health.

Division 1 –Therapeutic Goods including, Active Pharmaceutical Ingredients (API) and Sunscreens, but not Blood, Blood Components, Biologicals (except things that comprise or contain live animal cells, tissues or organs), Plasma, Haematopoietic Progenitor Cells or Therapeutic Devices;

Note: The manufacturing principles applicable to therapeutic goods that are things that comprise or contain live animal cells, tissues or organs are those set out in Division 1, and not those set out in Division 2.

(1) This Division applies to the manufacture of therapeutic goods including API and Sunscreens, other than:

(a) blood and blood components, plasma and haematopoietic progenitor cells;

(b) biologicals (except things that comprise or contain live animal cells, tissues or organs);

(c) therapeutic devices;

(2) Subject to subclauses (3) and (4), manufacturers in Australia of therapeutic goods that are covered by this Division must follow the procedures and requirements set out in any Part of the PIC/S Guide to GMP, including any Annexes to the PIC/S Guide to GMP, that applies to the particular goods being manufactured.

(3) Where the PIC/S Guide to GMP provides that a procedure or requirement 'should' be followed, manufacturers of therapeutic goods in Australia must follow that procedure or requirement in order to comply with the PIC/S Guide to GMP, unless in relation to that particular procedure or requirement:

(a) the manufacturer demonstrates, to the satisfaction of the TGA, that the failure to adopt that procedure or requirement:

i. will not increase the risk that the goods produced as a result will or could cause harm or injury to any person, or will or could potentially have the effect of causing or contributing to such harm; and

ii. will not increase the risk of the therapeutic goods in question failing to comply with, where applicable both the standard for that therapeutic good and the conditions of the listing or registration for that therapeutic good; and

iii. will not depart from the record keeping requirements contained in the PIC/S Guide to GMP; or

(b) where an alternative procedure to the procedure or requirement set out under an applicable Part of, or Annex to, the PIC/S Guide to GMP has been adopted, the manufacturer demonstrates, to the satisfaction of the TGA, that:

i. the alternative procedure will not result in the production of therapeutic goods that could increase the risk of harm or injury to any person or will or could potentially have the effect of causing or contributing to such harm; and

ii. the alternative procedure will not increase the risk of the therapeutic goods in question failing to comply with, where applicable, both the standard for that therapeutic good and the conditions of the listing or registration; and

iii. will not depart from the record keeping requirements contained in the PIC/S Guide to GMP.

(4) For the purposes of subclause (2), the word "applies" does not include the application, to particular therapeutic goods being manufactured, of an Annex that is stated in the PIC/S Guide to GMP to be 'voluntary'.

Division 2 – Manufacturing principles for Blood, Blood Components, Biologicals (except things that comprise or contain live animal cells, tissues or organs), Plasma and Haematopoietic Progenitor Cells

(5) This Division applies to the manufacture of blood, blood components, biologicals (except things that comprise or contain live animal cells, tissues or organs), plasma and haematopoietic progenitor cells.

(6) A manufacturer of blood, blood components, plasma or haematopoietic progenitor cells must lodge a Technical Master File with, an application for a licence under Chapter 3, Part 3-3 of the Act.

(7) Blood, blood components, plasma and haematopoietic progenitor cells must be manufactured:

(a) in compliance with applicable requirements of the Australian Code of Good Manufacturing Practice; and

(b) in a manner consistent with the relevant Technical Master File lodged for the goods with the TGA by the manufacturer.

(8) Biologicals (except things that comprise or contain live animal cells, tissues or organs) must be manufactured in compliance with applicable requirements of the Australian Code of Good Manufacturing Practice.

(9) Where the Australian Code of Good Manufacturing Practice provides that a procedure or requirement 'should' be followed, manufacturers of therapeutic goods in Australia must follow that procedure or requirement in order to comply with the Australian Code of Good Manufacturing Practice.

(10) A blood processing plant that processes plasma collected from donors in Australia for products that are or will be used in Australia (the Australian product) may only be used to process plasma collected from a source outside Australia if, for that source:

(a) a plasma master file, prepared in accordance with the requirements of the European Agency for the Evaluation of Medicinal Products document entitled "Guideline on the scientific data requirements for a plasma master file (PMF) EMEA/CPMP/BWP/3794/03, revision 1(2006)" has been submitted to the Secretary by the licensee of the relevant blood processing plant; and

(b) the Secretary has advised the licensee of the plant that, based upon the plasma master file submitted for those goods, and having taken into account the plant's processes, the plasma from the source outside Australia will not contaminate the Australian product with any blood borne pathogens.

(11) The failure of a manufacturer in Australia of therapeutic goods, to which this Division applies, to follow a particular procedure or requirement set out in an applicable Part of the Australian Code of Good Manufacturing Practice will constitute a failure to comply with the Australian Code of Good Manufacturing Practice unless in relation to that particular procedure or requirement:

(a) the manufacturer demonstrates, to the satisfaction of the TGA, that the failure to adopt that procedure or requirement:

i. will not increase the risk that the goods produced as a result will or could cause harm or injury to any person, or will or could potentially have the effect of causing or contributing to such harm; and

ii. will not increase the risk of the therapeutic goods in question failing to comply with, where applicable, both the standard for that therapeutic goods and to the conditions of registration for that therapeutic good; and

iii. will not depart from any applicable record keeping requirements contained in the Australian Code of Good Manufacturing Practice; or

(b) where an alternative procedure to the procedure or requirements set out under and applicable part of the Australian Code of Good Manufacturing Practice has been adopted, the manufacturer demonstrates, to the satisfaction of the TGA, that:

i. the alternative procedure will not increase the risk that the goods produced as a result will or could cause harm or injury to any

person, or will or could potentially have the effect of causing or contributing to such harm; and

ii. the alternative procedure will not increase the risk of the therapeutic goods in question failing to comply with, where applicable, both the standard for the goods and any conditions of registration that apply to the goods; and

iii. will not depart from the record keeping requirements contained in the Australian Code of Good Manufacturing Practice.

Division 3 – Therapeutic Devices

(12) In this Division, the following therapeutic devices must be manufactured in compliance with an approved quality assurance system as follows:

(a) for a therapeutic device, other than a device incorporating human tissue

i. if the therapeutic device must be listed in the Register, it must be manufactured in compliance with AS ISO 13485-2003 other than clause 7.3 (Design and Development); or,

ii. if the therapeutic device must be registered in the Register , it must be manufactured in compliance with AS ISO 13485-2003; and

iii. if the therapeutic device is labelled 'Sterile', it must also be manufactured in compliance with EN 556.