EXPLANATORY STATEMENT

Subject - *Therapeutic Goods Act 1989*

Therapeutic Goods (Manufacturing Principles) Determination No 1 of 2007

The object of the *Therapeutic Goods Act 1989* (the Act) is to establish and maintain a national system of controls for the quality, safety, efficacy and timely availability of therapeutic goods that are used in Australia or exported from Australia. The Therapeutic Goods Administration (the TGA) is responsible for administering the Act.

Section 36 of the Act empowers the Minister to determine, as required, principles to be observed by manufacturers of therapeutic goods relating, inter alia, to standards to be maintained, the procedures to be adopted and the manufacturing practices to be employed in the manufacture of such goods. Manufacturing Principles establish the minimum requirements to be observed for the manufacture of medicinal products for human use.

Section 33 of the *Legislative Instruments Act 2003* (the LIA) requires that new compilation be registered on the Federal Register of Legislative Instruments (FRLI) in electronic form as soon as practicable after amendments to an instrument have commenced. Prior to their revocation under this instrument, attempts were made to make a technical compilation of the following legislative instruments: the Therapeutic Goods (Manufacturing Principles) Determination number 1 of 1999 (MP 1/1999), Therapeutic Goods (Manufacturing Principles) Determination No.1 of 2000 (MP 1/2000) and Therapeutic Goods (Manufacturing Principles) Determination No.2 of 2002 (MP 2/2002). However, it was not clear on the face of the amending instruments exactly which texts or clauses should be removed or inserted.

The purpose of the Therapeutic Goods (Manufacturing Principles) Determination No 1 of 2007 is to make a technical compilation of three previous Therapeutic Goods (Manufacturing Principles) Determinations described above and to carry-out a housekeeping exercise to make a number of necessary corrections and updates. A mere technical compilation of the previous Determinations without corrections and updates would result in an instrument which is ambiguous and unclear and would refer to documents which are no longer in existence.

This Determination is being made solely for the purpose of ensuring compliance and consistency with the LIA. However, the opportunity has also been taken to update outdated references and guideline documents in the previous Determinations and to make minor editorial changes such as the removal of Notes, as described in the paragraphs below.

Some guideline documents and standards referred to in the previous Determinations require updating. The International Standards applying to therapeutic devices identified as EN 46001, EN 46002, ISO 9001, ISO 9002, ISO 13485 and ISO 13488 in MP 1/1999 are now reflected in a condensed international standard referred to as AS ISO 13485-2003. Most device manufacturers in Australia and overseas already apply this standard to the manufacture of medical devices. It constitutes a conformity assessment standard for quality management systems for the manufacture of medical devices as set out in the Conformity Standards Order No. 1 of 2005 which commenced on 29 September 2005 (FRLI Registration - F2005L02892).

AS ISO 13485-2003 Medical Devices-Quality Management systems –Requirements for regulatory purposes is a stand alone standard that combines the elements of other earlier standards ISO 13485:1996, ISO 13488:1996 and ISO 9001:2000, and reflects current international practice for quality management systems for the manufacture of medical devices). The TGA consulted with key industry stakeholders on the implementation of the Conformity Standards Order No 1 of 2005 which relevantly determined that AS ISO 13485-2003 constitutes a conformity assessment standard for quality management systems for the manufacture of medical devices. The only response received by the TGA pursuant to that consultation was from the Medical Industry Association of Australia and was supportive of the proposal. AS ISO 13485-2003 and EN556:1994 can be purchased online from SAI Global Limited, which is accessible at the following website: www.saiglobal.com/shop/Script/search.asp.

MP 1/2000 refers to Therapeutic Goods Order No 66 which has been revoked by Therapeutic Goods Order No 72, which in turn was subsequently revoked by Therapeutic Goods Order No 74 (FRLI Registration F2006L00146). The Guideline for the Preparation of Technical Master Files for Blood Components published on 23 August 2000 referred to in MP 1/1999 has been replaced by the Guideline for the Preparation of Technical Master Files for Blood, Blood Components and Haematopoietic Progenitor Cells published by the TGA on its website in 2004. Industry was consulted in relation to the implementation of this Guideline and it has been used by industry for a number of years.

Under paragraph 6(d)(i) of the LIA, an instrument is a legislative instrument for the purposes of section 5 of the LIA if it is declared to be a disallowable instrument under legislation in force before the commencement of the LIA. This Determination is a legislative instrument and is subject to tabling and disallowance in the Parliament under sections 38 and 42 of the LIA.

CONSULTATION

Consultation has not been undertaken as the making of this Determination is of a minor or machinery of government nature on the basis that the remade Determination is technical in nature and does not affect the practical application of existing arrangements. This remade Determination does not substantially change existing requirements regarding standards applicable to manufacturers of therapeutic goods. The updated references in this Determination, including those which constitute the applicable manufacturing principles, were already the subject of prior consultation with industry and have been in place for several years.

This Determination is made by the delegate of the Minister for Health and Ageing in accordance with subsection 36(1) of the Act.

This Determination came into effect on the day after it was registered on the FRLI.

The details of this Determination are set out in Attachment A.

ATTACHMENT A

Section 1 provides that this Determination may be cited as the Therapeutic Goods (Manufacturing Principles) Determination No 1 of 2007.

Section 2 of this Determination provides that this Determination takes effect from the day it is registered on the Federal Register of Legislative Instruments.

Section 3 revokes the following instruments:

(a) Therapeutic Goods (Manufacturing Principles) Determination number 1 of 1999 published in the Commonwealth of Australia Gazette, No GN 37, 15 September 1999;
(b) Therapeutic Goods (Manufacturing Principles) Determination No.1 of 2000 published in the Commonwealth of Australia Special Gazette, No S 518, 28 September 2000; and
(c) Therapeutic Goods (Manufacturing Principles) Determination No. 2 of 2002 published in the Commonwealth of Australia Gazette, No GN 34, 28 August 2002.

Section 4 provides that the manufacturing principles apply to specific therapeutic goods as set out in the three Divisions of the Determination. The therapeutic goods are grouped into three Divisions namely:

(a) Division 1- medicines;
(b) Division 2 - blood, blood components, haematopoietic progenitor cells and tissues; and
(c) Division 3 - other therapeutic goods not covered by Divisions 1 to 2.

Section 5 is an interpretation provision and provides the definitions of terms and documents referred to in this Determination.

Division 1, Sections 6-7

Division 1 of this Determination reflects clauses 5, 6 and 7 of the Therapeutic Goods (Manufacturing Principles) Determination No. 2 of 2002 which require that the manufacture of medicines, except those excluded from the application of that Determination, must comply with the Australian Code of Manufacturing Practice for Medicinal Products dated 16 August 2002, the availability of which was gazetted on 21 August 2002 in the Commonwealth *Gazette*.

Section 6 provides that the manufacturing principles set out in Division 1 applies to the manufacture of medicines except active pharmaceutical ingredients, sunscreen products, blood, blood components, plasma and haematopoietic progenitor cells and human tissue. The manufacturing principles applying to active pharmaceutical ingredients are set out in Therapeutic Goods (Manufacturing Principles) Determination No.1 of 2002, while the other therapeutic goods are covered by Divisions 2 and 3 of this Determination.

Section 7 provides that medicines to which Division 1 applies must be manufactured in compliance with the Australian Code of Manufacturing Practice for Medicinal Products dated 16 August 2002.

Division 2, Sections 8-12

Division 2 of this Determination reflects clauses 1-3 under the Heading “Compliance with a Quality Assurance System of Therapeutic Goods (Manufacturing Principles) Determination No.1 of 2000, and subclause 5(9) of the Therapeutic Goods (Manufacturing Principles) Determination number 1 of 1999 which relate to requirements applying to any blood processing plant.

Section 8 provides that a manufacturer of blood, blood components, plasma and haematopoietic progenitor cells must lodge a Technical Master File with an application for a manufacturing licence under the Act. A Technical Master File is defined as the following:

a. compilations of scientific 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 Therapeutic Goods Administration, a division of the Commonwealth Department of Health and Ageing, on its website; and

b. detailed technical and scientific 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. 74 - Standard for Blood Components; or

    (ii) the haematopoietic progenitor cells derived from cord blood manufactured using the steps of manufacture mentioned in paragraph (a) will meet Therapeutic Goods Order No. 75 – Standard for Haematopoetic Progenitor Cells derived from Cord Blood.

Section 9 requires that blood, blood components, plasma and haematopoietic progenitor cells must be manufactured in compliance with the Australian Code of GMP for Human Blood and Tissues and in a manner consistent with the relevant Technical Master File lodged by the manufacture.

Section 10 requires that human tissues must be manufactured in compliance with the Australian Code of GMP for Human Blood and Tissues.

Section 12 requires that 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” 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, based upon the plasma master file, and having taken into account the plant's processes, that the plasma from the

source outside Australia will not contaminate the Australian product with any blood borne pathogens

The document entitled “Guideline on the scientific data requirements for a plasma master file (PMF) EMEA/CPMP/BWP/3794/03” can be accessed and downloaded from the TGA website.

Division 3, section 13

Division 3 of this Determination applies to therapeutic devices and sunscreen products. Section 13 of this Determination reflects subclauses 5(5) and 5(7) of MP 1/1999. However, the standard applying to the manufacture of therapeutic devices required to be listed and registered in the Australian Register of Therapeutic Goods has been updated to AS ISO 13485-2003 Medical Devices Quality management systems-Requirements for regulatory purposes.

Section 13 requires that therapeutic devices, other than human tissues or a device incorporating human tissues must be manufactured in compliance with an approved quality assurance system as follows:

i. if the therapeutic device must be listed on the Australian Register of Therapeutic Goods, 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 on the Australian Register of Therapeutic Goods, it must be manufactured in compliance with AS ISO 13485-2003; and

iii. if the therapeutic device is labeled 'Sterile', it must also be manufactured in compliance with EN 556:1994.

In relation to a sunscreen product, section 13 requires that it must be manufactured in compliance with the Sunscreen Code of GMP. The Sunscreen Code of GMP means Chapter 1 to 9 inclusive, and the glossary of the document entitled ”Australian Code of Good Manufacturing Practice for Therapeutic Goods-Sunscreen Products”, published by the Department of Human Services and Health in February 1994. This document can be accessed on the TGA website.