Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Therapeutic Goods Order No. 77 *Microbiological Standards for Medicines*

I, ROHAN HAMMETT, delegate of the Minister for Health and Ageing for the purposes of section 10 of the *Therapeutic Goods Act 1989* (the Act) and acting under that section, having consulted with the Therapeutic Goods Committee in accordance with subsection 10(4) of the Act, HEREBY DETERMINE that the matters specified in this Order constitute a standard for medicines.

Dated this 22nd day of SEPTEMBER 2008

Rohan Hammett

Delegate of the Minister for Health and Ageing

Federal Register of Legislative Instruments F2008L03574

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1 Name of Order

This Order is the **Therapeutic Goods Order No. 77** ***Microbiological Standards for Medicines.***

2 Commencement

On and from 1 January 2010, each medicine to which this Order applies must comply with this Order.

3 Introduction

This Order specifies the minimum microbiological requirements with which a medicine must comply throughout its shelf life.

The microbial attributes of a non-sterile medicine described in either section 9 of this Order or in the pharmacopoeias mentioned in this Order should not be regarded as comprehensive microbial limit specifications. In addition to being free from the microorganisms specified in this Order, the sponsor must determine the risk to the medicine from other objectionable microorganisms.

4 Interpretation

(1) In this Order:

acceptance criteria, in relation to microbiological quality, are interpreted as:

(a) 10^1 CFU: maximum acceptable count is 20;

(b) 10^2 CFU: maximum acceptable count is 200;

(c) 10^3 CFU: maximum acceptable count is 2000, and so forth.

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

antimicrobial preservation means the presence of an ingredient(s) in a medicine that inhibits the growth of microorganisms in the medicine.

British Pharmacopoeia has the same meaning as "British Pharmacopoeia" in subsection 3(1) of the Act, as amended from time to time.

CFU means colony forming units.

complementary medicine has the same meaning as "complementary medicine" in section 52F of the Act.

default standard means a pharmacopoeia mentioned under “standard” in subsection 3(1) of the Act.

European Pharmacopoeia has the same meaning as "European Pharmacopoeia" in subsection 3(1) of the Act, as amended from time to time, or if no such meaning is included in the Act, means the 6th edition including supplement 6.2 of the European Pharmacopoeia in the English language published by the Directorate for the Quality of Medicines & HealthCare of the Council of Europe.

export only medicine has the same meaning as "export only medicine" in subsection 3(1) of the Act.

herbal substance has the same meaning as "herbal substance" in regulation 2 of the Regulations.

medicine has the same meaning as "medicine" in subsection 3(1) of the Act.

monograph means the requirements of an individual or general monograph in a default standard read in conjunction with the General Notices contained in the same edition that are applicable to that monograph.

Regulations means the Therapeutic Goods Regulations 1990, as amended from time to time.

Secretary has the same meaning as "Secretary" in subsection 3(1) of the Act.

sponsor has the same meaning as "sponsor" in subsection 3(1) of the Act.

standard has the same meaning as "standard" in subsection 3(1) of the Act.

therapeutic goods has the same meaning as "therapeutic goods" in subsection 3(1) of the Act.

United States Pharmacopoeia-National Formulary has the same meaning as "United States Pharmacopoeia-National Formulary" in subsection 3(1) of the Act, as amended from time to time, or if no such meaning is included in the Act, means the 31st edition of the United States Pharmacopoeia – 26th edition of the National Formulary in the English language published by The United States Pharmacopoeial Convention.

NOTE: Where a default standard adopts a different name or number for a test or method that is included in this Order, this Order incorporates that renamed or renumbered test or method.

5 Application

(1) The requirements set out in this Order apply to all therapeutic goods that are medicines for human use and that come within the operation of the Act.

(2) However, the requirements set out in this Order do not apply to a medicine:

(a) that is exempt under section 6 of this Order; or

(b) in relation to which an exemption from compliance with this Order has been granted by the Secretary in writing for the supply, importation or export of a medicine to occur although the medicine does not conform to this Order or parts of this Order in accordance with sections 14 and 14A of the Act.

6 General Exemptions

The requirements of this Order do not apply to a medicine that:

(a) is an export only medicine; or

(b) is a personal import as described under Item 1 to Schedule 5 of the Regulations; or

(c) is a starting material used in the manufacture of medicines, except when:

(i) prepackaged for supply for other therapeutic purposes; or

(ii) formulated as a dosage form; or

(d) has not reached its final stage of manufacture.

7 Sterility and Bacterial Endotoxin testing

Where

(a) a medicine is required to be sterile or to comply with a bacterial endotoxin test by an individual or general monograph of a default standard; or

(b) a medicine through its labelling or packaging states or implies that the medicine is sterile,

the medicine must comply with the Test for Sterility, and the Bacterial Endotoxin Test if applicable, of a default standard.

8 Efficacy of antimicrobial preservation of a multidose medicine

A multidose medicine must comply with the British Pharmacopoeia, Appendix XVI C. Efficacy of Antimicrobial Preservation or the European Pharmacopoeia, Efficacy of Antimicrobial Preservation (5.1.3) except that:

(a) a liquid oral antacid medicine may comply with the relevant test in the United States Pharmacopoeia – National Formulary, chapter <51> Antimicrobial Effectiveness Test including its acceptance criteria.

9 Microbiological attributes of a non-sterile medicine

(1) A non-sterile medicine, other than a complementary medicine oral dosage form containing raw material of natural (animal, vegetal or mineral) origin, must comply with the relevant acceptance criteria for microbiological quality of one of the following:

(a) the British Pharmacopoeia, Appendix XVI. D Microbiological Quality of Pharmaceutical Preparations B. HARMONISED METHOD: MICROBIOLOGICAL QUALITY OF NON-STERILE PHARMACEUTICAL PREPARATIONS AND SUBSTANCES FOR PHARMACEUTICAL USE, when tested by the methods of:

(i) the British Pharmacopoeia, Appendix XVI B. Test for Microbial Contamination 2. Total viable aerobic count. B. HARMONISED METHOD: MICROBIOLOGICAL EXAMINATION OF NON-STERILE PRODUCTS : MICROBIAL ENUMERATION TESTS, and

(ii) the British Pharmacopoeia, Appendix XVI B. Test for Microbial Contamination 1. Tests for specified micro-organisms B. Harmonised method; or

(b) the European Pharmacopoeia, B: Harmonised Method: Microbiological Quality Of Non-Sterile Pharmaceutical Preparations And Substances For Pharmaceutical Use (5.1.4); when tested by the methods of:

(i) the European Pharmacopoeia, Harmonised Method: Microbiological Examination of Non-sterile Products: Microbial Enumeration Tests (2.6.12); and

(ii) the European Pharmacopoeia, Harmonised Method: Microbiological Examination of Non-sterile Products: Test for Specified Micro-organisms (2.6.13); or

(c) the United States Pharmacopoeia – National Formulary, chapter <1111> , MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS: ACCEPTANCE CRITERIA FOR PHARMACEUTICAL PREPARATIONS AND SUBSTANCES FOR PHARMACEUTICAL USE, when tested by the methods of:

(i) the United States Pharmacopoeia – National Formulary, chapter <61> MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS: MICROBIAL ENUMERATION TESTS; and

(ii) the United States Pharmacopoeia – National Formulary, chapter <62> MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS: TESTS FOR SPECIFIED MICROORGANISMS.

(2) A complementary medicine oral dosage form containing raw material of natural (animal, vegetal or mineral) origin must comply with the acceptance criteria for microbiological quality specified in Schedule 1 when tested by a method stated in subsection 9(1), other than:

(a) a herbal medicine consisting solely of one or more herbal substances (whole, reduced or powdered) to which boiling water is added before use, which must comply with the acceptance criteria specified in Schedule 2 when tested by a method stated in subsection 9(1).

Schedule 1

Microbial attributes for a complementary medicine oral dosage form containing raw material of natural (animal, vegetal or mineral) origin

Microbiological Quality	**Acceptance Criteria**
Total aerobic microbial count	Less than or equal to 10^4 CFU per g or per mL
Total yeast and mould count	Less than or equal to 10^2 CFU per g or per mL
Bile-tolerant Gram negative bacteria	Less than or equal to 10^2 CFU per g or per mL
Salmonella	absent in 10 g or 10 mL
Escherichia coli	absent in 1 g or 1 mL
Staphylococcus aureus	absent in 1 g or 1 mL

Schedule 2

Microbial attributes for a complementary medicine oral dosage form containing raw material of natural (vegetal) origin that is a herbal medicinal product consisting solely of one or more herbal substances (whole, reduced or powdered) to which boiling water is added before use

Microbiological Quality	**Acceptance Criteria**
Total aerobic microbial count	Less than or equal to 10^7 CFU per g
Total yeast and mould count	Less than or equal to 10^5 CFU per g
Bile-tolerant Gram negative bacteria	Less than or equal to10^2 CFU per g
Escherichia coli	absent in 1 g
Salmonella	absent in 10 g