



## **Therapeutic Goods Order No. 98 – Microbiological Standards for Medicines 2018**

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I, Jane Cook, a delegate of the Minister for Health for the purposes of section 10 of the *Therapeutic Goods Act 1989* (the Act) and acting under that section of the Act, determine that the matters specified in this Order constitute a standard for therapeutic goods of the kind identified in section 5 of this Order.

Dated 12<sup>th</sup> day of September 2018

(Signed by)

JANE COOK

Delegate of the Minister for Health

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## 1 Name

This instrument is the *Therapeutic Goods Order No. 98 – Microbiological Standards for Medicines 2018*.

## 2 Commencement

This instrument commences 1 October 2018.

## 3 Authority

This instrument is made under subsection 10(1) of the *Therapeutic Goods Act 1989*.

## 4 Interpretation

(1) In this instrument:

**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*.

**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 in the Act.

**CFU** means colony forming units.

**complementary medicine** has the same meaning as "complementary medicine" in the Regulations.

**default standard** has the same meaning as in the Act.

**European Pharmacopoeia** has the same meaning as in the Act.

**export only medicine** has the same meaning as in the Act.

**herbal substance** has the same meaning as in the Regulations.

**medicine** has the same meaning as in 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.

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**Regulations** means the *Therapeutic Goods Regulations 1990*, as in force from time to time.

**Secretary** has the same meaning as in the Act.

**sponsor** has the same meaning as in the Act.

**standard** has the same meaning as in the Act.

**therapeutic goods** has the same meaning as in the Act.

**United States Pharmacopeia-National Formulary** has the same meaning as in the Act.

- (2) 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.
- (2) However, the requirements set out in this order do not apply to a medicine that is exempt under section 6 of this order.

## 6 General exemptions

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

- (a) is an export only medicine; or
- (b) is imported into Australia for use in the treatment of the importer of the importer's immediate family, in accordance with item 1 of Schedule 5 to the Regulations; or
- (c) is a starting material used in the manufacture of medicines, except when:
  - (i) pre-packaged 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, if applicable, the Bacterial Endotoxin Test, of a default standard.

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## 8 Efficacy of antimicrobial preservation of a multidose medicine

A medicine that is an aqueous 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 an aqueous multidose medicine that is 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 Non-Sterile Pharmaceutical Preparations and Substances for Pharmaceutical use; when tested by the methods of:
    - (i) the British Pharmacopoeia, Appendix XVI B. Microbiological Examination of Non-Sterile Products: 2. Microbial Enumeration Tests; and
    - (ii) the British Pharmacopoeia, Appendix XVI B. Microbiological Examination of Non-Sterile Products: 1. Test for Specified Micro-organisms; or
  - (b) the European Pharmacopoeia, 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, Microbiological Examination of Non-Sterile Products: Microbial Enumeration Tests (2.6.12); and
    - (ii) the European Pharmacopoeia, 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 herbal medicine consisting solely of one or more herbal substances (whole, reduced or powdered) to which boiling water is added

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before use, which must comply with the acceptance criteria specified in Schedule 2 when tested with a method mentioned in subsection 9(1).



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## Schedule 1— Microbial attributes for a complementary medicine oral dosage form containing raw material of natural (animal, vegetal or mineral) origin

(subsection 9(2))

### 1 Table of acceptance criteria

| 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 |
| <i>Salmonella</i>                    | absent in 10 g or 10 mL                          |
| <i>Escherichia coli</i>              | absent in 1 g or 1 mL                            |
| <i>Staphylococcus aureus</i>         | absent in 1 g or 1 mL                            |

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**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**

(subsection 9(2))

**1 Table of acceptance criteria**

| <b>Microbiological Quality</b>       | <b>Acceptance Criteria</b>             |
|--------------------------------------|--|
| 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 to $10^2$ CFU per g |
| <i>Escherichia coli</i>              | absent in 1 g                          |
| <i>Salmonella</i>                    | absent in 10 g                         |