



**Australian Government**  
**Department of Health**  
Therapeutic Goods Administration

# Microbiological quality of medicinal cannabis products

Complying with Therapeutic Goods  
(Microbiological Standards for Medicines) (TGO  
100) Order 2018

Version 1.0, February 2020

**TGA** Health Safety  
Regulation

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## Introduction

This guidance will assist sponsors and manufacturers of medicinal cannabis products to comply with [Therapeutic Goods \(Microbiological Standards for Medicines\) \(TGO 100\) Order 2018](#), referred to in this guidance as TGO 100.

## What is TGO 100?

TGO 100 specifies the minimum microbiological quality requirements (including preservative efficacy requirements) that a medicine should comply with throughout its shelf life, unless it is exempt.



TGO 100 came into effect on 8 December 2018.

TGOs 77 and 98, which were in use before December 2018, were repealed on 1 October and 8 December 2018, respectively.

## General exemptions from TGO 100

Medicines are exempt from meeting the requirements set out in [TGO 100](#) if they meet the conditions specified in TGO 100 Clause 7 – General exemptions.

## Medicinal cannabis and TGO 100

Medicinal cannabis products, unless exempt, should **comply with TGO 100 clause 11(1)** as they contain substances that are scheduled in the Poisons Standard.

**TGO 100 Clause 11(2)**, which refers solely to complementary medicine oral dosage forms containing raw material of natural origin, is not applicable to medicinal cannabis products.

## Default standards

The [default standards](#):

- British Pharmacopoeia (BP)
- European Pharmacopoeia (Ph. Eur.)
- United States Pharmacopoeia-National Formulary (USP-NF)

are adopted as in force from time to time as permitted under subsection 10(4) of the *Therapeutic Goods Act 1989*.

## Microbiological quality criteria for medicinal cannabis products

Medicinal cannabis products **should not** contain excessive numbers of microorganisms. They should:

- be free from contamination with [specified microorganisms](#)

AND

- be free from contamination with other microorganisms that might be [objectionable](#) in the dosage form



The microbiological quality acceptance criteria in TGO 100 (and in the default standards) should not be regarded as comprehensive.

They are the minimum requirements to be met throughout the shelf life of a medicinal cannabis product.

Demonstrating the absence of only the specified microorganisms might not be sufficient to ensure the microbiological quality of a medicinal cannabis product.

## Examples of requirements

Examples of requirements for the Total Aerobic Microbial Count (TAMC), Total Yeast and Mould Count (TYMC) and absence of specified microorganisms:

- **Non-aqueous oral** dosage forms should comply with the following criteria:
  - TAMC - maximum permitted TAMC of 2000 CFU per g or per mL
  - TYMC - maximum permitted TYMC of 200 CFU per g or per mL
  - absence of *Escherichia coli* in 1 g or 1 mL
- **Aqueous oral** dosage forms should comply with the following criteria:
  - TAMC - maximum permitted TAMC of 200 CFU per g or per mL
  - TYMC - maximum permitted TYMC of 20 CFU per g or per mL
  - absence of *E. coli* in 1 g or 1 mL
- Dosage forms that are **inhaled** (either via smoking or vaping) should comply with the following criteria:
  - TAMC - maximum permitted TAMC of 200 CFU per g or per mL
  - TYMC - maximum permitted TYMC of 20 CFU per g or per mL
  - absence of bile tolerant gram-negative bacteria, *Staphylococcus aureus* and *Pseudomonas aeruginosa* in 1g or 1mL
- Dosage forms intended for **oromucosal, topical or nasal use** should comply with the following criteria:
  - TAMC - maximum permitted TAMC of 200 CFU per g or per mL
  - TYMC - maximum permitted TYMC of 20 CFU per g or per mL
  - absence of *S. aureus* and *Ps. aeruginosa* in 1g or 1mL

## Provisions for oral and inhalant dosage forms

As medicinal cannabis products are derived from plant material, compliance with TGO 100 Clause 11(1) might be challenging for some dosage forms, such as those that are taken orally or inhaled.

### Oral dosage forms

A sponsor of a medicinal cannabis oral dosage form can apply to the TGA to use the:

*Special European Pharmacopoeia (Ph. Eur.) provision for oral dosage forms containing raw materials of natural (animal, vegetal or mineral) origin for which antimicrobial pre-treatment is not feasible and for which the competent authority accepts TAMC of the raw material exceeding 1000 CFU per g or CFU per mL*

These criteria consist of:

- TAMC - maximum permitted TAMC of 20000 CFU per g or per mL
- TYMC - maximum permitted TYMC of 200 CFU per g or per mL
- bile tolerant gram negative bacteria – not more than 100 CFU per g or per mL
- absence of *E. coli* and *S. aureus* in 1 g or 1 mL
- absence of *Salmonella* in 10 g or 10 mL

TGO 100 recognises these special Ph. Eur. provision criteria from two of the default standards, i.e. the Ph. Eur. (5.1.4) and BP (Appendix XVI D) - these criteria are not included in the USP-NF.

The special Ph. Eur. provision criteria are identical to the criteria in TGO 100, Clause 11(2), Schedule 1, which are applicable to complementary medicine oral dosage forms that contain material of natural origin but which are not supplied as herbal teas (to which boiling water is added prior to ingestion).

It is preferable for medicinal cannabis oral dosage forms to comply with the special Ph. Eur. provision criteria rather than TGO 100, Clause 11(1). This is because the special Ph. Eur. provision criteria include requirements for absence of pathogenic enteric bacteria that could be present in botanical material, but not expected to be present in a pharmaceutical medicine (see also [objectionable organisms](#)).

### Applying to the TGA to use the special Ph. Eur. provision criteria

For an unapproved medicinal cannabis product, contact the [Experimental Products Section](#), Pharmacovigilance and Special Access Branch, Medicines Regulation Division.

For a medicinal cannabis product that is registered in the ARTG, contact the [Prescription Medicines Authorisation Branch](#), Medicines Regulation Division.

### Inhalant dosage forms

TGO 100 adopts the harmonised Ph. Eur., BP and USP microbiological quality criteria for inhalants. These criteria were agreed in 2005 at a time when medicinal products were not inhaled via smoking or vaping, and when inhalants were not manufactured from botanical material.

Limited information is available as a reference to propose alternative, risk-based microbiological quality criteria for inhalant dosage forms that would:

- safeguard the user of the product

and

- be achievable by industry

and

- be able to be used as a regulatory tool

There do not appear to be any well-controlled surveys of the microbiological content of medicinal cannabis dosage forms that take into account the different ways in which:

- plants are cultivated and harvested
- botanical material is processed and stored
- dosage forms are manufactured

Collaboration is necessary between regulators, sponsors and manufacturers of medicinal cannabis products to review microbiological histories for finished products and to develop suitable, risk-based microbiological specifications for inhalants.

## Applying to the TGA for an exemption to parts of TGO 100

A sponsor of an inhalant dosage form can apply to the TGA for an exemption from some, or all, of the microbiological criteria specified in TGO 100 for inhalants under Section 14 and 14A of the *Therapeutic Goods Act 1989*.

- This application for an exemption will need to be accompanied by cogent justification for the exemption and propose alternative microbiological quality criteria that would safeguard the user of the product.
- While we are obliged to consider a request for an exemption, we can reject an application if the justification to support the request for exemption is inadequate.

For guidance about making the application including what information must be provided:

- [Consent to import, supply or export therapeutic goods that do not comply with standards – information for industry](#)

## Objectionable microorganisms

In addition to being free from contamination with specified microorganisms, a medicinal cannabis product should also be free from contamination with other microorganisms that might be objectionable in the dosage form.

For example, pseudomonad-type bacteria are considered to be objectionable in aqueous dosage forms intended for inhalant, topical, nasal or oromucosal use; these dosage forms should be free from contamination with these types of bacteria. *Aspergillus species* could be considered objectionable in inhalant dosage forms.



Pseudomonad-type bacteria include bacteria that were previously identified as belonging to the genus *Pseudomonas*. Advances in molecular identification have resulted in the reclassification of some of these bacteria to other genera, including *Burkholderia*, *Ralstonia*, *Stenotrophomonas*, *Sphingomonas* and *Brevundimonas*.

When evaluating the significance of, and risk from, other objectionable microorganisms, consider:

- the formulation of the medicinal cannabis product
- route of administration
- method of application
- the population for which the product is intended, including the susceptibility of this population to infection

## Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Laboratories Branch	February 2020

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