Australian Government
Department of Health
Therapeutic Goods Administration

Quality standards for medicinal cannabis

The requirements of TGO 93

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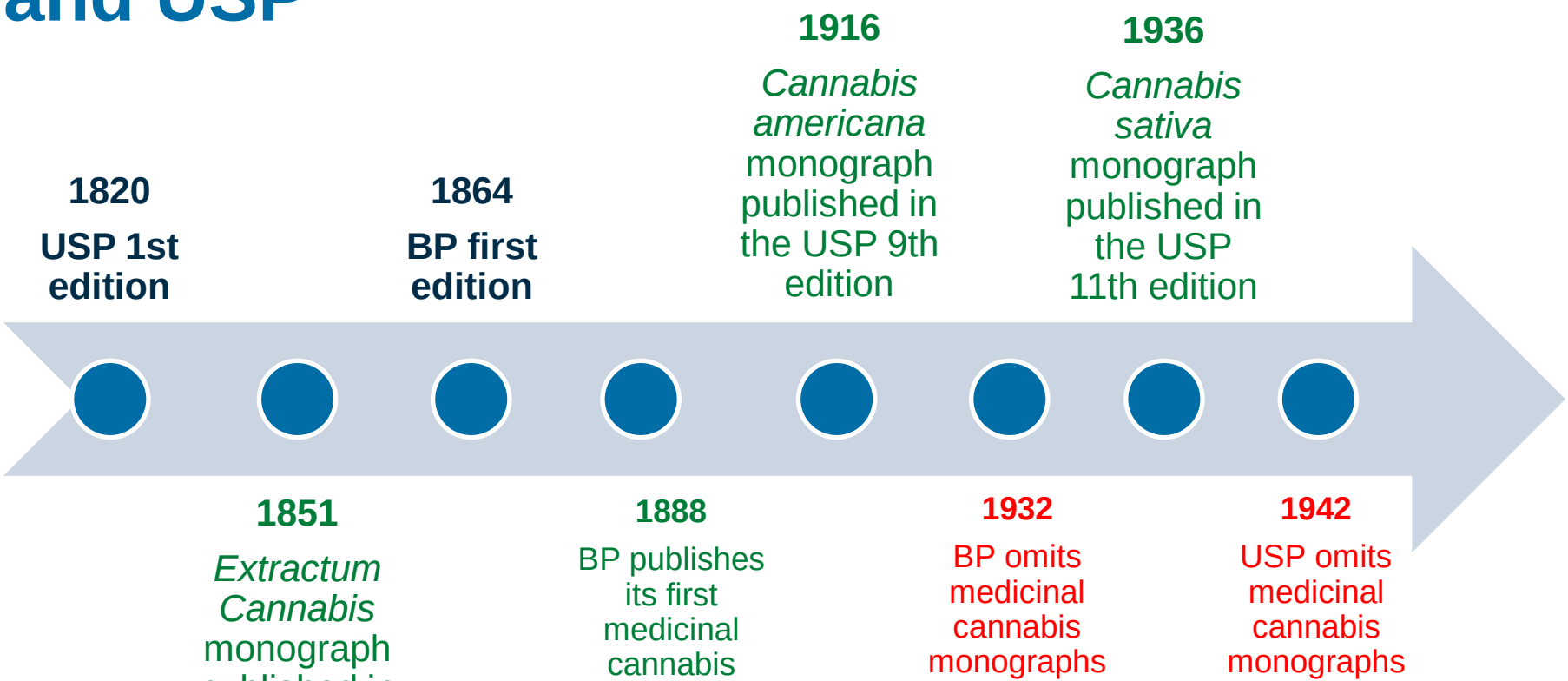
TGA Health Safety Regulation

Introduction

Therapeutic Goods Order No. 93 – *Standard for Medicinal Cannabis*

- Why create TGO 93?
- What is TGO 93?
- When does it come into effect?
- What benefits will TGO 93 bring?

History of medicinal cannabis in the BP and USP



Concerns about the quality of medicinal cannabis products

- Variation in cannabinoid content, in particular level(s) of active ingredient(s)
- Contamination with pesticides
- Microbial contamination
- Mycotoxins (aflatoxins and ochratoxin A)
- Contaminants arising from the manufacturing process e.g. toxic solvents
- Adulteration with plants
- Adulteration with synthetic psychoactive compounds
- Fortification with dronabinol
- Misidentification of the plant material – and, in particular, the variety of the plant material

Key features of TGO 93

1. Sets out requirements (minimum requirements) for the quality of:
   - medicinal cannabis products
   - the cannabis plant used in the manufacture of medicinal cannabis products (as either a starting material or as an ingredient)
   - any ingredient used in the manufacture of medicinal cannabis products

2. Sets out requirements/restrictions on the manufacturing process for medicinal cannabis products

Key definitions (section 4)

- **Medicinal cannabis products** means therapeutic goods that contain, or are manufactured from, any part of the cannabis plant.
- **Cannabis plant** means any plant, or part of a plant, of the genus *Cannabis*, including, but not limited to, the flowers, fruiting tops, seeds, stems and leaves of the plant.

What does TGO 93 apply to? (section 6)

It applies to:

- ✓ any medicinal cannabis product imported into, exported from, or supplied in Australia
- ✓ cannabis plant used in the manufacture of medicinal cannabis products (e.g. as an ingredient or as a starting material for an extract used as an ingredient)
- ✓ any other ingredients used in the manufacture of medicinal cannabis products, such as excipients
- ✓ steps and procedures carried out in the manufacture of medicinal cannabis products

What does TGO 93 not apply to?

TGO 93 does not apply to medicinal cannabis products imported by:

- x a member of a group of persons visiting Australia to participate in a national or international sporting event [Item 4 of Schedule 5A, *Therapeutic Goods Regulations 1990*]
- x a member of the military forces of another country visiting Australia for military training [Item 8 of Schedule 5A, Regulations]
- x a medical practitioner or member of a medical team accompanying a critically ill patient [Item 10 of Schedule 5A, Regulations]
- x a member of a group of persons that includes the Head of Government or Head of State of a foreign country and senior Government officials of that country, who are visiting Australia on official business [Item 11 of Schedule 5A, Regulations]

What does TGO 93 not apply to?

TGO 93 does not apply to medicinal cannabis products that are:

- x part of the medical supplies of a marine vessel or an aircraft visiting Australia for use in treatment of a passenger or crew member [Item 12 of Schedule 5A, Regulations]
- x described in item 1 of Schedule 5 to the Regulations

Adoption of the requirements of Ph.Eur. general monograph for Pharmaceutical Preparations (section 7)

TGO 93 incorporates the requirements of the Ph. Eur. general monograph for ***Pharmaceutical Preparations (2619)***

except for any requirements that are inconsistent with the Order.

Pharmaceutical Preparations (2619)

Pharmaceutical Preparations (2619) encompasses the requirements of:

- specific monographs of the Ph.Eur. for pharmaceutical raw materials (e.g. active ingredients, excipients)
- general texts (e.g. *Residual Solvents* (5.4)) and
- other general monographs of the Ph.Eur.

  including:

  - *Herbal Drugs (1433)*
  - *Herbal Drug Preparations (765)*
  - *Herbal Drug Extracts (765)*
  - *Substances for Pharmaceutical Use (2034)*
  - dosage form monographs such as *Oromucosal Preparations (1807)*

Source of active ingredients and cannabinoids (TGO 93 section 8)

All active ingredients and cannabinoids in medicinal cannabis products must be manufactured from the cannabis plant **only.**

This means that medicinal cannabis products cannot contain:

- x the synthetic form of any cannabinoid [including, for example, the synthetic form of tetrahydrocannabinol (THC), which is known as dronabinol]
- x active ingredients from any source other than the cannabis plant

Decontamination (section 9)

- ✓ Decontamination of the cannabis plant — for example, by using gamma irradiation to reduce the microbial load — is allowed provided it does not adversely affect the quality of the medicinal cannabis product.

- x Exception: use of ethylene oxide is not allowed

Adulteration (section 11)

- x The formulated medicine or any of its ingredients must not be adulterated with undeclared substances. Tobacco, calamus and synthetic cannabinoids are notable examples of adulterants.

- x The motivation for adulterating a product is irrelevant—the presence of any substance extraneous to the formulation (such as undeclared substances) — will be considered to amount to adulteration for the purposes of TGO 93.

- ✓ 'Incidental minor excipients' are not considered adulterants. These are defined in section 4 of TGO 93 as:

  an excipient or processing aid in the manufacture of ingredients for medicinal cannabis products

  or

  a processing aid in the manufacture of medicinal cannabis products

Identification of Cannabis plant (section 10)

The cannabis plant used in the manufacture of medicinal cannabis products must be positively identified and differentiate it from potential adulterants and substitutes using each of the following identification methods:

- macroscopic examination
- microscopic examination
- chromatographic procedures

Guidance on Identification testing

Identification of herbal materials and extracts - Questions & answers

www.tga.gov.au/publication/identification-herbal-materials-and-extracts

Cannabis plant tests (Schedule 1)

Sponsors/manufacturers must ensure that the cannabis plants used to manufacture medicinal cannabis products meet the requirements of Schedule 1.

Schedule 1 specifies the following parameters:

1. Aflatoxins (default Ph. Eur requirements)
2. Foreign matter (default Ph. Eur requirements – NMT 2.0%)
3. Heavy metals (arsenic NMT 3.0 ppm, cadmium NMT 0.5 ppm, lead NMT 5.0 ppm and mercury NMT 0.5 ppm)
4. Ochratoxin A (NMT 20 µg/kg)
5. Pesticides (Ph. Eur. requirements)
6. Total ash (NMT 20.0%)

Cannabis plant tests/test methods

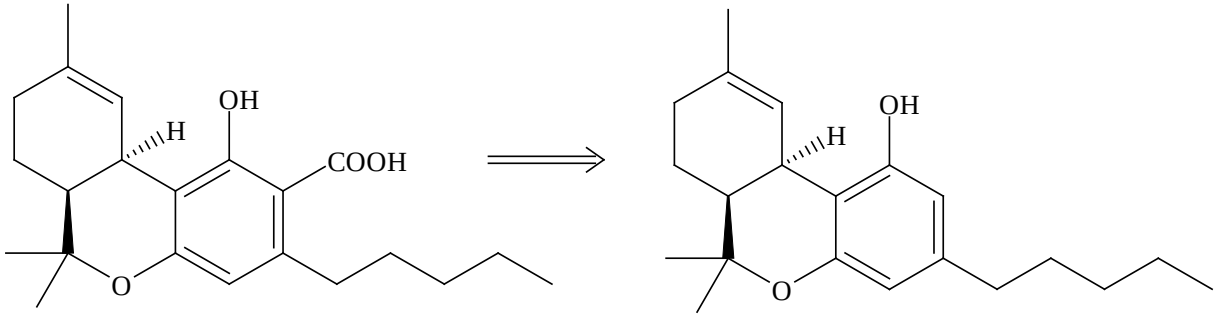
- ✓Alternative test methods?
- ✓Sample size and preparation?
- ✓Additional tests?

Assay limits for dosage forms (section 12(2))

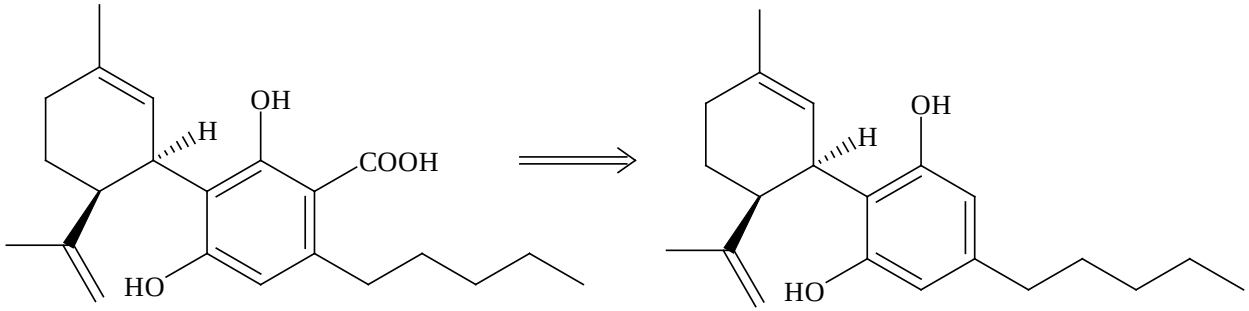
Dosage form	Average content of active ingredient* (% stated content)
Herbal final form	80.0 - 120.0
Tablets and capsules (unregistered)	90.0 - 110.0
Other dosage forms	90.0 - 110.0

* Assay calculation includes any corresponding acid of the active ingredient

Corresponding acid form



THC-acid THC



CBD-acid CBD

Assay method

- No particular test method is prescribed for calculating the average content of each active ingredient in accordance with section 12(2) of TGO 93.
- The assay method used should take into account the active ingredient, the dosage form and the formulation of the product.
- Any suitably validated test method can be used.
- Examples of literature assay methods can be found in:
  - Monograph Cannabis Flos Version 7.1 (November 28, 2014) 40953, Dutch Office of Medicinal Cannabis
  - *Recommended methods for the identification and analysis of cannabis and cannabis products* United Nations Office on Drugs and Crime.

How to validate test methods

ICH Harmonised Tripartite Guideline - Validation of Analytical Procedures: Text and Methodology Q2 (R1)

Other TGOs relating to quality that may be applicable to medicinal cannabis products

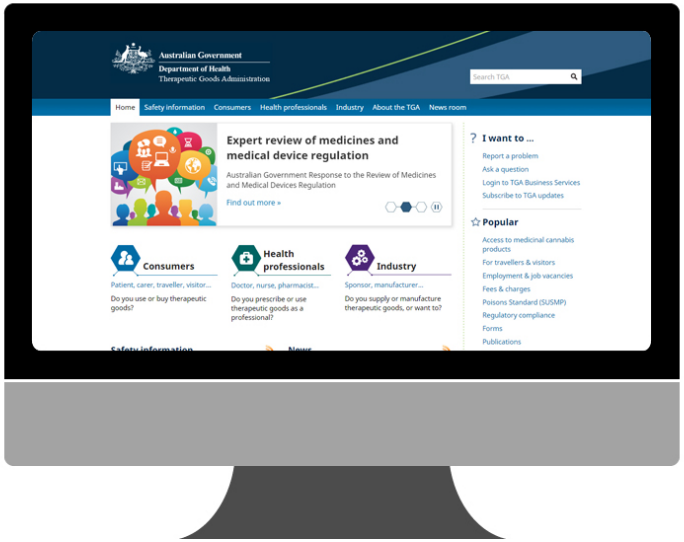
- **TGO 77 - *Microbiological Standards for Medicines***
- **TGO 78 - *Standard for Tablets and Capsules***

  TGO 78 applies to registered medicinal cannabis products in tablet or capsule form

Further information?

TGA's website www.tga.gov.au has:

- TGO 93 as well as all the other TGOs
- Guidance documents for the TGOs



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