



Australian Government
Department of Health
Therapeutic Goods Administration

Guidance on GMP compliance for the manufacture of medicinal cannabis for supply under 'approved access' provisions

Version 2.0, January 2018

TGA Health Safety
Regulation

Historical document

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Introduction

This guidance is for sponsors and manufacturers considering manufacturing non sterile medicinal cannabis products for supply under provisions of [access to medicines that have not been approved for general use](#), including medicinal cannabis for clinical trials.

This guidance does not apply to medicinal cannabis products that are listed or registered on the ARTG (Australian Register of Therapeutic Goods).

Multiple laws

Medicinal cannabis is subject to the [Therapeutic Goods Act 1989](#) as well as the [Narcotic Drugs Act 1967](#) that are both administered by the Department of Health. In addition to that, relevant states and territory legislation applies. These [legislative frameworks](#) work together while allowing for different jurisdictional objectives.

States and territory governments have a role through medicine scheduling and particular requirements on how controlled drugs including medicinal cannabis may be authorised for use in their jurisdiction.

The Department of Health regulates medicinal cannabis products through:

- the [Office of Drug Control \(ODC\)](#), which administers the Narcotic Drugs Act that regulates controlled substances to prevent diversion and illicit use
- the TGA, which administers the Therapeutic Goods Act that regulates, amongst others, the quality, safety and efficacy of medicines as well as [access to medicines that have not been approved for general use](#).

For information and guidance on the regulation of medicinal cannabis products as a controlled substance under the Narcotic Drugs Act, refer to the [Office of Drug Control website](#).

Medicinal cannabis manufacture for supply under the provisions for approved access

Approved access

Generally, medicines supplied in Australia must be approved for general use through entry in the [Australian Register of Therapeutic Goods \(ARTG\)](#). However, the Therapeutic Goods Act provides several pathways for [approved access to medicines that are not registered on the ARTG](#). These pathways are:

- [Special Access Scheme \(SAS\)](#) category B
- [Authorised prescribers](#)
- [Clinical trials](#) (CTN or CTX)

As the only medicinal cannabis product currently registered on the ARTG is not marketed in Australia, medicinal cannabis is currently only available through one of these 'approved access' pathways.

Medicines (including medicinal cannabis) supplied in Australia must also be manufactured in compliance with the [PICS Guide to Good Manufacturing Practice](#) (GMP) by a manufacturer that either:

- holds a current licence to manufacture therapeutic goods (if in Australia)
- is covered by a current GMP clearance (if overseas).

However, the Therapeutic Goods Act provides a number of ways to gain [approved access to medicines that are not registered on the ARTG](#), i.e. medicines that have not been approved for general use in Australia. With the exception of personal import, these pathways also apply to medicinal cannabis products.

Requirements for pharmacists

Pharmacists manufacturing medicinal cannabis products for approved access under the Special Access Scheme (Category B) or the Authorised Prescriber Scheme are required to hold a licence to manufacture therapeutic goods and [comply with GMP](#) unless they meet the exemption(s) under Schedule 8 of the Therapeutic Goods Regulations 1990. Currently, the only exemption to this is for pharmacists working in public hospital pharmacies. Their compliance with appropriate manufacturing requirements is managed by the hospital in the State or Territory.

Requirements for clinical trials manufacture

Pharmacists manufacturing medicinal cannabis products for supply as clinical trial materials are required to hold a licence to manufacture therapeutic goods and [comply with GMP](#) unless they meet the exemption(s) under Schedule 7 of the Therapeutic Goods Regulations 1990.

Please note

If you want to become involved in the manufacture of medicinal cannabis for approved access purposes, you should ensure that the following approvals, licences and permits under each of the relevant legislative frameworks have been provided:

- the relevant state or territory government licences or approvals
- ODC [manufacture licence](#) under the Narcotic Drugs Act in combination with the associated ODC permit(s)
- TGA approval for use under either of the following pathways:
 - [Special Access Scheme \(SAS\)](#) category B
 - [Authorised prescribers](#)
 - [Clinical trials](#) (CTN or CTX)



Terminology and definitions

Definitions for terminology used in relation to the manufacture of medicinal products including medicinal cannabis can be found at either:

- the [acronyms and glossary](#) on the TGA website
- the [glossary of the PIC/S Guide to GMP](#).

Please note

Terminology used under the Narcotic Drugs Act may differ from terminology used in the context of the Therapeutic Goods Act. For example:



In the context of the Therapeutic Goods Act the term '*production*' refers to the actual preparation of an active pharmaceutical ingredient or a finished medicinal product. As such, '*production*' is considered a subset of '*manufacture*'.

In the context of the Narcotic Drugs Act the term '*production*' refers exclusively to the harvesting of the specified plant parts and collecting these into containers for subsequent processing, which is termed '*manufacture*'. As such '*production*' is a separate step that is followed by '*manufacture*'.

Manufacturing principles

The [Manufacturing Principles](#) require all medicines to be manufactured in compliance with the manufacturing standard (the Code of GMP) unless exempted in Schedule 7 or 8 of the [Therapeutic Goods Regulations 1990](#).

Even where manufacture of medicinal cannabis products is not covered by a licence to manufacture therapeutic goods, GMP compliance is still required unless one of these exemptions applies.

Manufacturing standard

The manufacturing standard that is applicable to the manufacture of medicines is the [PIC/S Guide to Good Manufacturing Practice for medicinal products](#) (the PIC/S Guide to GMP). This standard is mandatory for the manufacture of all medicines supplied in Australia, unless exempted under the provisions of the Therapeutic Goods Act.

The PIC/S Guide to GMP applies to the active pharmaceutical ingredient (API) as well as the finished medicinal product.

Questions and answers on GMP

Please refer to the [TGA interpretation and expectations for demonstrating compliance with PIC/S PE009-13](#) on the TGA website for some further information on the interpretation of certain areas of the PICS guide to GMP.

Finished medicinal cannabis product

The finished medicinal cannabis product is the dosage form in which the medicinal cannabis is intended to be administered to the patient, for example as an oil, tincture, extract, capsule, tablet etc.

The manufacture of the finished medicinal cannabis product is required to be in compliance with [Part I of the PIC/S Guide to GMP](#), as well as the relevant parts of the [Annexes to the PIC/S Guide to GMP](#).

Active pharmaceutical ingredient (API)

The API is the active ingredient that is the starting material for the manufacturing process of the finished product. For medicinal cannabis, the API could be:

- an extracted and purified active component of the cannabis plant (for example a cannabinoid)
- an extract of specified parts of the cannabis plant
- powdered specified parts of the cannabis plant.



Please note

The term '*API starting material*' refers to the starting material from which the API is made.

The manufacture of the API is required to be in compliance with [Part II of the PIC/S Guide to GMP](#), as well as the relevant parts of the [Annexes to the PIC/S Guide to GMP](#).



Please note

If your medicinal cannabis product is being used as an API in clinical trials, compliance with chapter 19 of Part II of the PIC/S Guide to GMP is of particular importance.

GMP does not apply to the cultivation and harvesting of cannabis plants for medicinal use. The introduction chapter of Part II of the PIC/S Guide to GMP (in particular in its page 3 Table 1) provides guidance on the process steps from where GMP is expected to be increasingly applied, depending on the API manufacturing process. The relevant entries of that table are copied in the table below:

Type of manufacturing	Application of Part II of the PIC/S Guide to GMP to this type of product				
API extracted from plant	Collection of plants	Cutting and initial extraction(s)	*Introduction of the API starting material into the process	*Isolation and purification	*Physical processing and packaging

Application of Part II of the PIC/S Guide to GMP to this type of product					
Type of manufacturing					
Herbal extracts used as API	Collection of plants	Cutting and initial extraction(s)		*Further extraction	*Physical processing and packaging
API consisting of powdered herbs	Collection of plants and/or cultivation and harvesting	Cutting and commuting			*Physical processing and packaging

The shading/asterisk indicates manufacturing steps to which the PIC/S Guide to GMP applies, which means:

- for extracted cannabinoids: GMP does not apply up to cutting and initial extraction but increasingly applies from the introduction of the API starting material into the process onwards
- for herbal cannabis extracts: GMP does not apply up to cutting and initial extraction but increasingly applies from further extraction onwards
- for powdered cannabis plant parts: GMP does not apply up to cutting and commuting but increasingly applies from the moment of physical processing and packaging of the powder onwards.

You may need to seek advice from a GMP consultant or seek legal advice if you are uncertain as to where GMP is required for your manufacturing process.

Annexes to the PIC/S Guide to GMP

The [Annexes to the PIC/S Guide to GMP](#) apply to Parts I and II, i.e. to the manufacture of the active cannabis ingredient as well as to the manufacture of the finished medicinal cannabis product.

All GMP Annexes that are relevant to your manufacturing processes apply. This may depend on the dosage form manufactured, or on specific process characteristics.

GMP Annexes that are relevant to the manufacture of **all non-sterile medicinal cannabis products** are:

- Annex 7 - Manufacture of herbal medicinal products
- Annex 8 - Sampling of starting and packaging materials
- Annex 15 – Qualification and validation
- Annex 19 – Reference and retention samples
- Annex 20 – Quality risk management.

**Please note**

Annex 20 is not mandatory; it is a tool to assist you in satisfying the mandatory quality risk management clauses 1.12 and 1.13 in Part I of the PIC/S Guide to GMP, and clauses 2.20 and 2.21 in Part II of the PIC/S Guide to GMP.

GMP Annexes that **may be relevant** to the manufacture of medicinal cannabis products depending on dosage form and process characteristics are:

- Annex 9 – Manufacture of liquids, creams and ointments: only relevant for medicinal cannabis products in these dosage forms
- Annex 11 – Computerised systems: only relevant for manufacturing processes where computerised systems are used
- Annex 13 – Manufacture of investigational medicinal products: it is relevant for medicinal cannabis products for use in clinical trials.

Specific aspects relating to the manufacture and scheduling of medicinal cannabis

From 1 November 2016, the [Poisons Standard \(SUSMP\)](#) schedules medicinal cannabis products (under specified conditions) as Schedule 8: controlled substance. Where these conditions are not met, cannabis products are Schedule 9: prohibited substance.

Administration requirements

The Schedule 8 status of medicinal cannabis puts specific requirements on the adequate administration of quantities of cannabis containing materials that you:

- receive
- sample
- hold in storage at any particular point in time
- use
- supply (split up in recipients and shipments)
- discard
- destroy

These requirements apply throughout all manufacturing processes, including all handling. The PIC/S Guide to GMP also includes requirements on recording quantities of materials and the reconciliation of these at the end of manufacture.

When manufacturing medicinal cannabis products, you can use one set of records and documentation that serves both purposes as long as these records comply with the GMP requirements as well as the requirements from the product's Scheduling.

Verification requirements

The Schedule 8 status of medicinal cannabis also requires the manufacturer of medicinal cannabis products to verify that:

- Each supplier of medicinal cannabis containing goods holds current licence(s) and permit(s) under the Narcotic Drugs Act that allow the supply of each delivery to you.
- Each of the customers to which you supply medicinal cannabis products holds current licence(s) and permit(s) under the Narcotic Drugs Act that allow them to receive the delivery from you.

Both verifications are required to be conducted for each delivery and for each supplier or customer. The recommended way to meet these requirements is:

- include the verification of your supplier's narcotic drugs licence in the supplier qualification process that is required under GMP
- include the verification of the currency of that licence and the availability of the required narcotic drugs permits in your procedures on incoming goods receipt
- include the verification of your customer's narcotic drugs licence in your regular process to include customers in the customer database
- include the verification of the currency of that licence and the availability of the required narcotic drugs permits in your procedures on outgoing goods shipment.

Further technical GMP guidance

The requirements of the PIC/S Guide to GMP apply, unless the specific requirements are not applicable to the specific manufacturing activity, or equivalent level of compliance is achieved by alternative means. Any omission or alternative approach to compliance must be based on quality risk management principles. Where products are made for use in clinical trials the principles under Annex 13 should be considered.

The following technical guidance documents have been developed for the application of quality risk management in the manufacture of complementary medicines. Subject to the principles of quality risk management and Annex 13 of the PIC/S Guide to GMP, the documents contain information that may assist you in the application of quality risk management for the manufacture of medicinal cannabis products to be made available via clinical trials or investigational product pathways.

- [Supplier qualification](#)
- [Sampling and testing](#)
- [Process validation](#)

Once medicinal cannabis products are registered on the ARTG, approved access provisions will no longer apply and therefore these technical guidance documents may no longer be relevant.

Stability

Ongoing stability would not normally be applicable for the manufacture of a medicine for use in a clinical trial. However, stability would be required according to Annex 13 and in support of expiry date for the material. The clauses in Annex 13 that would be applicable for stability of a medicine that is manufactured for use in a clinical trial include 6, 9, 20, 26j and 40.

Product quality review

- for the manufacture of finished medicinal cannabis products, refer to clause 1.4 of [Part I of the PIC/S Guide to GMP](#)
- for the manufacture of medicinal cannabis as an active pharmaceutical ingredient, refer to clause 2.5 of [Part II of the PIC/S Guide to GMP](#).



Please note

The [TGA interpretation and expectations for demonstrating compliance with PIC/S PE009-13](#) includes additional information on the preparation of PQRs, which is applicable to the manufacture of medicinal cannabis products.

Related guidance and further information

- [Medicinal cannabis factsheet](#)
- [Final decision on scheduling of cannabis and tetrahydrocannabinols](#)
- [Scheduling decision FAQ](#)
- [Office of Drug Control – permits and licences to import](#)
- [Import and supply of therapeutic goods](#)
- [Import and export of controlled substances](#)

For enquiries about GMP compliance in the manufacture of medicinal cannabis, contact the [Manufacturing Quality Branch](#).

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Manufacturing Quality Branch with the Regulatory Guidance Team	October 2016
V2.0	Updated with new PIC/S GMP guidance	Manufacturing Quality Branch	January 2018

Historical document

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Reference/Publication #