MEDICINAL CANNABIS AGENCY

MANATŪ HAUORA
MINISTRY OF HEALTH

GUIDELINE ON THE REGULATION OF MEDICINAL CANNABIS IN NEW ZEALAND

Part 3

Guidance for a new medicinal cannabis product application

EDITION 3.0
July 2024

Te Kāwanatanga o Aotearoa
New Zealand Government

Citation: Ministry of Health. 2024. *Guideline on the regulation of medicinal cannabis in New Zealand: Part 3 Guidance for a New Medicinal Cannabis Product Application*. Wellington: Ministry of Health.

Published in July 2024 by the Ministry of Health
PO Box 5013, Wellington 6140, New Zealand

HP 9079

Contents

List of Tables

Section 1: Introduction

This document is the ***Guideline on the regulation of medicinal cannabis in New Zealand: guidance for a new medicinal cannabis product application***. It outlines when and how to make an application for a new medicinal cannabis product.

We recommend you read all our ***Guidelines on the regulation of medicinal cannabis in New Zealand*** in full, these can be found on our website at: https://www.health.govt.nz/publication/medicinal-cannabis-scheme-guideline-and-forms.

Please send all correspondence to medicinalcannabis@health.govt.nz.

1.1 Overview

Part 1 of the Misuse of Drugs (Medicinal Cannabis) Regulations 2019 sets the minimum quality standard requirements for medicinal cannabis products and ingredients. A medicinal cannabis product or ingredient that has been verified as meeting the minimum quality standard can be added to a medicinal cannabis licence with a supply activity, or to a licence issued under the Medicines Act 1981 (for cannabidiol (CBD) products). Once added to a licence, verified products may then be lawfully supplied in New Zealand.

A new medicinal cannabis product application is required to provide evidence that satisfies the Medicinal Cannabis Agency (the Agency) that a medicinal cannabis product or ingredient meets the minimum quality standard. If the Agency is satisfied that a product or ingredient meets the minimum quality standard, it will then recommend that the product or ingredient be added to the applicant's medicinal cannabis licence supply activity or licence under the Medicines Act 1981 (for CBD products). An additional application to amend a licence issued under the Medicines Act 1981 may be required to have a CBD product that meets the minimum quality standard added to your licence.

Note: Should you wish to apply for consent for distribution under the Medicines Act 1981 (rather than obtaining product verification) please refer to the Medsafe website for information on making New Medicine Applications at: https://www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medsafe-Evaluation-Process.asp.

A medicinal cannabis product or ingredient that the Agency has verified as meeting the minimum quality standard (rather than having consent under the Medicines Act) is an unapproved medicine under the Medicines Act 1981. For information on unapproved medicines and their supply please see Section 3.3 of Part 1: Overview of therapeutic product regulation of the *Guidelines on the Regulation of Therapeutic Products in New Zealand* at: https://www.medsafe.govt.nz/regulatory/current-guidelines.asp.

Note: initial extracts that will undergo further processing are starting material and do not need to meet the minimum quality standard. Cannabis-based ingredients and medicinal cannabis products that will only be exported (and not supplied within New Zealand) do not need to meet the minimum quality standard if they are manufactured under GMP and the importing country will accept their import. Cannabis-based ingredients and medicinal cannabis products that are only to be exported will need to

be added to the licence as 'export-only' under the supply activity. This can be done by applying to amend the licence activity.

1.2 Structure of this guideline

Section 1 (this section) provides the context for a new medicinal cannabis product (NMCP) application and the types of application you can make. It includes references to legislation and additional information that will help you complete an application.

Section 2 is a guide to preparing an NMCP application for a new cannabis-based ingredient or a medicinal cannabis product (which may be a dried product or a dosage product). This section follows the same format as the NMCP application form. The guidance covers the evidence you must provide to demonstrate to the Agency that the medicinal cannabis product or ingredient meets the minimum quality standard. Application forms can be found at: https://www.health.govt.nz/our-work/regulation-health-and-disability-system/medicinal-cannabis-agency.

Section 3 outlines the supporting data that you must submit for each type of NMCP application.

1.3 Legislation relating to the minimum quality standard requirements

The following legislation relates to the requirements of the minimum quality standard.

- Misuse of Drugs (Medicinal Cannabis) Regulations 2019.
- Misuse of Drugs Act 1975.
- Misuse of Drugs Regulations 1977.
- Medicines Act 1981.
- Medicines Regulations 1984.

1.4 Other resources relevant to this guideline

The following resources will help you to conform to the minimum quality standard.

- European Pharmacopoeia (Ph Eur) 11th edition, including supplement 11.3.
- United States Pharmacopoeia – National Formulary (2023 issue 1).
- British Pharmacopoeia (2023).
- International Council for Harmonisation of Technical Requirements for Pharmaceutical for Human Use (ICH) quality guidelines.
  - Q1A(R2) Stability Testing of New Drug Substances and Products.
  - Q2(R2) Validation of Analytical Procedures: Text and Methodology.

- New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods.
- ISO/IEC 17025:2017 Testing and Calibration Laboratories Accreditation.
- World Health Organization (WHO) Model Certificate of Analysis.

1.5 Overview of the types of applications

The two broad types of applications you can make relating to medicinal cannabis are:

- a new medicinal cannabis product (NMCP)
- a changed medicinal cannabis product (CMCP).

1.5.1 New medicinal cannabis product

You must make a NMCP application and receive approval before you can list a NMCP on your medicinal cannabis licence with supply activity or licence issued under the Medicines Act 1981. Within this category there are two types of NMCP applications.

- Cannabis-based ingredient.
- Medicinal cannabis product (dried product or dosage product).

For more information, see Section 2 and Section 3.

1.5.2 Changed medicinal cannabis product

You must make a CMCP application and receive approval for any medicinal cannabis product or cannabis-based ingredient listed on a current medicinal cannabis licence with a supply activity, or licence issued under the Medicines Act 1981 that is affected by a change to any of the matters listed in regulation 47(1)(e) of the Misuse of Drugs (Medicinal Cannabis) Regulations 2019 (the Regulations). Specifically, you must make a CMCP application when there is a change to a product or ingredients':

- trade name
- label or description that will accompany it
- composition, or formulation (the quantity or proportion of each ingredient)
- method of manufacture (including packing and testing)
- container closure system
- facilities for manufacture (including packing and testing)
- recommended method of administering, applying, or using it
- shelf life or storage conditions.

You must obtain approval from the Agency for the changes before you distribute any batches affected by the change. In your application, you must include evidence to demonstrate that the product or ingredient will continue to meet the minimum quality standard after the change. For most changes to the medicine the same type of evidence must be provided as for the NMCP.

The following changes would generally require an NMCP rather than a CMCP.

- Changing the active ingredients.
- A new combination of active ingredients.
- Change to the strength of active ingredients.
- A new dose form.

If you believe that your change does not constitute a significant change, please contact the Agency prior to submitting a request.

For further information, please see the *Guideline on the regulation of medicinal cannabis in New Zealand – Guidance for a changed medicinal cannabis product application* available at: https://www.health.govt.nz/publication/medicinal-cannabis-scheme-guideline-and-forms.

Section 2: How to submit an application for a new medicinal cannabis product

2.1 Responsibilities of the licence holder

The holder of the verification for verified product is legally responsible for the medicinal cannabis product or cannabis-based ingredient in New Zealand, including any regulatory action relating to it. The medicinal cannabis licence holder or Medicines Act 1981 licence holder is responsible for ensuring the accuracy of any information submitted to the Agency in support of any NMCP.

For this reason, an overseas company wishing to distribute a medicinal cannabis product or ingredient in New Zealand needs to have a New Zealand–based medicinal cannabis licence holder or have a Medicines Act 1981 licence holder act for them for that product or ingredient. The New Zealand licence holder is responsible for the product or ingredient, including the supply of the product or ingredient and any recall of the product from distribution.

It is the responsibility of the licence holder, before submitting an application for an NMCP and throughout the period they hold a licence, to fully understand and, if necessary, obtain appropriate advice (legal or otherwise) on their obligations, including those under the Medicines Act 1981, the Misuse of Drugs Act 1975 and the Misuse of Drugs (Medicinal Cannabis) Regulations 2019 and other associated regulations.

2.2 Submitting an application

When submitting an application for an NMCP, you must include:

- a completed NMCP application form
- a signed declaration form
- additional data depending on the type of product you are applying to be assessed.
  - Type 1: Cannabis-based ingredient
  - Type 2: Medicinal cannabis product (dried or dosage product).

For additional resources to help you compile an application, see Section 1.4. For a full summary of the application documents according to the type of product, see Appendix 1.

The forms are designed for you to complete electronically, following the guidance in this section. You must complete all fields of the form.

A unique product is identified by its:

- trade name
- dose form
- active ingredient(s)
- strength.

For each product that has a different trade name, dose form, active ingredient(s) or strength, you will need to complete a separate form and application. Different sizes of the same product (eg, 10 ml and 20 ml) are considered to be one product so can be included in one product assessment application as long as the stability data supports the proposed shelf life and storage conditions for each product size.

When submitting applications for similar products (eg, a product of varying strengths), you should state the named parent product in all application.

2.3 Proposed product details

2.3.1 Type of application

The two types of NMCP applications are:

- type 1: Cannabis-based ingredient
- type 2: Medicinal cannabis product (dried or dosage product).

Choose the type that best describes your product or ingredient.

Type 1: Cannabis-based ingredient

The type 1 application is for the assessment of a cannabis-based ingredient that is intended for further manufacture or incorporating into a dosage product. Examples of cannabis-based ingredients include dried cannabis plant material, a purified extract of cannabis (eg, delta-9-tetrahydrocannabinol (THC)) or a raw extract of cannabis that contains multiple constituents of cannabis (eg, a full spectrum extract). Applications for verification of a cannabis-based ingredient can be assessed individually or in parallel with the associated application for the dosage product in which the cannabis-based ingredient is to be used.

Type 2: Medicinal cannabis product

The type 2 application is for the assessment of a medicinal cannabis product that is intended for use in a patient. The two types of medicinal cannabis product are:

- **dried product**, which is a medicinal cannabis product that is dried cannabis and must not contain any ingredient that is not dried cannabis
- **dosage product**, which is a medicinal cannabis product in a pharmaceutical dosage form (such as a tablet, a capsule, or an oral liquid).

Choose the product that best describes your product or ingredient.

2.3.2 Proposed trade name / unique identifier (starting material for export)

The proposed trade name is the name under which your product will be distributed in New Zealand. The proposed label and all documentation should use the proposed name consistently. Where the material is starting material, rather than a trade name the material must have a unique identifier.

For cannabis-based ingredients and medicinal cannabis products (dried products and dosage products), the proposed trade name must:

- be unique (whether proprietary, non-proprietary, or a word or code), as well as being unique and distinct from any cannabis-based ingredient or medicinal cannabis product intended for export only
- not be misleading about its therapeutic effects, safety, nature, origin or composition
- not cause confusion about the products classification as a medicine (ie, must not relate to food or recreational use)
- not cause confusion with another medicine in New Zealand.

We recommend considering the naming and any associations that might be made with the name carefully. You should note that some cultivar names may be inappropriate because they are misleading, indicate product quality, or because they allude to recreational use.

2.3.3 Active ingredients

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 4

You must state the full name of all active ingredients of the proposed product in your application. When the product contains a number of different active ingredients, please ensure that each individual active ingredient is clearly identifiable on the application.

The Regulations define an active ingredient as:

- delta-9-tetrahydrocannabinol (THC)
- delta-9-tetrahydrocannabinolic acid (THCA)
- cannabidiol (CBD)
- cannabidiolic acid (CBDA)
- any other ingredient that is derived from cannabis and has a stated content of at least 1.0% by weight or volume of the ingredient or product.

Active ingredients cannot be synthetically derived. In any application for cannabis-based ingredients or medicinal cannabis products, you must demonstrate that all proposed active ingredients meet the requirements for identification, assay limits and labelling. See Section 3 for more detailed guidance.

2.3.4 Strength of active ingredients

The strength and units you give in your application should be as stated on the product label. Units must include enough detail to accurately express the strength of the product. For example, giving the percentage on its own is not enough to express strength. When expressing strength as a percentage, you should include units that indicate whether the percentage has been calculated by weight or volume – for example, ‘%w/w’ or ‘%w/v’. Please note, active ingredients may be expressed as total THC (THC+THCA) and total CBD (CBD +CBDA).

2.3.5 Dosage form

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 20

When completing the application form, the dosage form must align with that named in the European Pharmacopoeia. Dosage products must be in a pharmaceutical dosage form for which the European Pharmacopoeia (11th edition) has a general dosage form monograph.

A dosage product should have a form that is consistent with the way it is intended to be taken or administered (ie, recommended method of administration). The general monographs set out characteristics and relevant tests for particular dosage forms (eg, an oral liquid, tablet or capsule). See Section 3.2.4 for dosage product requirements.

Notes:

- Dosage form testing requirements do not apply to dried products.
- A medicinal cannabis product cannot be in a dosage form that is required to be sterile.

2.3.6 Recommended method of administration

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

This section of the form requires you to provide information on the intended method(s) of administration for the medicinal cannabis products (dried product or dosage product), where applicable.

Note: Smoking is not a permitted method of administration.

2.4 Overseas approval, declined approval or submission for approval

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

Where a product has been the subject of an application overseas (whether approval was granted or not), all details related to the submission must be provided. Include the country name and regulatory agency, along with the date of approval, declined approval or submission. Please ensure that all information is clear, and identifiable. Where the product has not been submitted for approval overseas, please clearly state this.

Note: Approval of your product by an overseas jurisdiction does not mean it meets the minimum quality standard in New Zealand. The details are provided for information purposes only, however, should you fail to provide this information, this will form part of the considerations of the Agency when considering the propriety of the application. The Agency undertakes an independent product assessment against the New Zealand minimum quality standard.

2.5 Licence holder and contact person details

A contact person may be a licence holder or be acting on behalf of a medicinal cannabis licence holder or a Medicines Act 1981 licence holder. The contact person is the person who submits the NMCP application and to whom the Agency will communicate on all matters (including the fee invoice) regarding this application for a new medicinal cannabis product.

2.5.1 New Zealand licence holder

You must submit all requested details of the licence holder (the entity responsible for the product on the New Zealand market), including the type of licence held and the licence number. The licence holder is considered the applicant for the NMCP application.

2.5.2 Contact person

The contact person is the person to whom the Agency will communicate on all matters (including the fee invoice) regarding an NMCP application. The contact person is the individual responsible for submitting the application and for responding to all correspondence. A contact person may be a licence holder, a director/partner, or a responsible person for the licensed activity.

Provide details of the contact person who is responsible for submitting the application and for responding to all correspondence. If applicable, include any letters of authorisation for a proposed contact person nominated to act on behalf of the licence holder, including details of the relationship between the contact person and the applicant.

2.6 Application fee and invoice details

The application fee is GST inclusive. The application form includes a space for comments relevant to invoicing.

The Agency's tax invoice for the NMCP fee will be sent to the licence holder as the entity legally responsible for the application.

The invoice can include a customer reference if you require it.

2.7 Product formulation and composition

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

You must submit a full statement of the product formulation or composition in table format.

When listing amounts of active ingredients or excipients, express the amounts as concentration by weight or volume using standardised units of measurement – for example, 'THC 2 mg/mL'.

When expressing active ingredients as a concentration, indicate whether the percentage has been calculated by weight or volume – for example, '%w/w' or '%w/v'.

Give details about the composition or formulation as follows.

- **Type 1: Cannabis-based ingredient:** List the active ingredients and amounts present in the cannabis-based ingredient (CBI).
- **Type 2: Dried product:** List the active ingredients and amounts present in the dried product.
- **Type 2: Dosage product:** List the full formulation of the dosage product, including all active ingredients and excipients present in the dosage product, and the amounts present.

  List each excipient as the ingredient name, amount present, and the quality standard (the British Pharmacopoeia, the European Pharmacopoeia, or the United States Pharmacopeia) – for example, 'Sweet Orange Oil, excipient, 10 mg/ml, Ph. Eur. 1811'.

Express amounts of active ingredients and excipients as either:

- an amount per dosage unit – for example, 'THC 2 mg per tablet', or
- a concentration by weight or volume using standardised units of measurement – for example, 'THC 2 mg/ml'.

Dosage products must have a named CBI that the Agency has assessed or has received a submission to assess in a NMCP application. The CBI must be clearly identifiable in the formulation table by the unique trade name of the CBI (whether it is a proprietary name, or a word or code). List the type of ingredient as CBI, specifying the amount present. If the Agency has already assessed the CBI as meeting the minimum quality standard, include the application number of the CBI under the minimum quality standard heading.

2.8 Product packaging and storage conditions

Primary packaging means the container or closure directly in contact with the medicinal cannabis product or ingredient. Secondary packaging means any box or other package surrounding the primary packaging and includes any additional features such as wallets and pouches. A description must be provided of the packaging. The description can be brief but must provide sufficient descriptions of both primary and any secondary packaging (if applicable).

The information provided must include all pack sizes and container types applicable to the application.

The shelf life and storage conditions (including in-use storage conditions) for each proposed pack must be provided, using the options listed – for example, "six months from the date of manufacture, stored at or below 25°C". The shelf life and storage conditions must be based on the results of testing the medicinal cannabis product using ICH guideline Q1A(R2) Stability Testing of New Drug Substances and Products. Please ensure the results of testing according to the ICH guideline is provided as part of the application (see Parts 3.1.5 and 3.2.8 for guidance).

2.9 Good Manufacturing Practice certification and ISO/IEC 17025:2017 accreditation

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

You must provide Good Manufacturing Practice (GMP) certification or other evidence of GMP compliance for:

- the manufacturing and packing site of each cannabis-based ingredient and medicinal cannabis product
- the testing site used to carry out the critical tests outlined in Table 1.

The certification must:

- relate to the product concerned and include the scope of activities
- be issued by Medsafe, or a regulatory authority recognised by Medsafe as listed in the Current Guidelines on the Regulation of Therapeutic Products in New Zealand (GRTPNZ): Manufacture of medicines, and meet all of the other requirements in the GRTPNZ
- have a sufficient period of validity to cover the time taken for the product to be verified, and subsequently be supplied for distribution in New Zealand. Where the certification expires during the assessment of the product, you must provide further evidence to demonstrate that the site continues to be certified.

For further guidance on GMP, see the ***Guideline on the regulation of medicinal cannabis in New Zealand: Guidance for Manufacturers and Packers***.

ISO/IEC 17025:2017: General requirements for the competence of testing and calibration laboratories accreditation is recognised as appropriate for laboratories conducting certain non-critical tests required by the Regulations. Non-critical tests are listed below.

- Microbiological contamination.
- Heavy metals.
- Pesticides.
- Absence of Aflatoxins.
- Ochratoxin A.
- Foreign matter.
- Loss on drying.
- Total ash.
- Residual solvents.

For all critical tests (assay limits for active ingredients and dosage form requirements) recognition of certification of the testing facilities to the requirements of the Code of GMP is required.

Medicinal cannabis products and cannabis-based ingredients must still be manufactured by a GMP-certified manufacturer.

Table 1: Tests carried out under GMP and/or ISO/IEC 17025:2017

Critical test-GMP	Other tests – GMP or ISO/IEC 17025:2017
Assay limits for active ingredients	Microbiological contamination
Form and dosage form	Identification of cannabis
	Identification of active ingredients
	Heavy metals
	Pesticides (imported products)
	Pesticides (domestic products)
	Absence of aflatoxins
	Ochratoxin A
	Foreign matter
	Total Ash
	Residual Solvent
	Loss on drying

Tests other than those which are critical, do not require evidence of method validation to be submitted to the Agency if the testing laboratory uses the applicable pharmacopeial method. An exception to this is in the case of identification of active ingredients. For an identification test, performed by an ISO/IEC 17025:2017 accredited laboratory for active ingredients, the Agency will require method validation in line with ICH Q2 (R2) guidance.

Whilst the information in this document is primarily related to verification of finished products or CBIs, general guidance on developing a pharmaceutical product can be found in the ICH guideline Q8(R2) Pharmaceutical Development (please be aware this guideline provides more detail than you need to include in an application to establish compliance with the minimum quality standard).

2.9.1 Manufacturing sites

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

The address of the physical site that manufactures the medicinal cannabis product or ingredient must be provided on the application form.

Please note that the address provided must be the actual address of the site of manufacture, and not the address of the company's offices (unless they are at the same location).

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

The physical address of the site that performs the testing required to demonstrate compliance with the minimum quality standard for the medicinal cannabis product or ingredient must be provided on the application form.

The address provided may also be the physical address of the manufacturer if the manufacturer is also the testing site.

Where multiple sites are performing testing, the information provided must clearly specify which test is carried out at each site.

2.9.2 Packing sites

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

The physical address of the site that packages the medicinal cannabis product or ingredient must be provided.

If the primary packing site is different to the secondary packing site, the information provided should clearly state which packing step is carried out at each site – that is, primary packing or secondary packing.

If a packing step does not apply to your application type, this must be clearly stated on the application form.

2.9.3 Site responsible for batch release

This information is about the site holding documentation for batches released onto the New Zealand market and is not necessarily the manufacturing, testing, or packing site.

If the medicinal cannabis product or ingredient is manufactured and packed overseas, provide the name and address of the company that is importing the medicine into New Zealand. The site of this importing company is termed the 'New Zealand site of batch release' and is responsible for undertaking the duties described in section 42 of the Medicines Act 1981.

Section 3: Additional data required in an application for a cannabis-based ingredient or medicinal cannabis

3.1 Additional data for Type 1: Cannabis-based ingredient

This section offers guidance on the additional data requirements for cannabis-based ingredients that you should submit as part of a NMCP application.

The additional data should be provided in the same order as this section (3.1) follows.

3.1.1 CBD product

Misuse of Drugs Act 1975, section 2A

If your cannabis-based ingredient meets the definition of a cannabidiol (CBD) product as defined in section 2A of the Misuse of Drugs Act 1975, and is therefore not a controlled drug, you must provide evidence to demonstrate this. This must include evidence to demonstrate that the ratio of specified substances falls within the definition. At a minimum, include the amount of CBD, delta-9-tetrahydrocannabinol (Δ9-THC), delta-9-tetrahydrocannabinolic acid (Δ9-THCA) and cannabinol (CBN).

You must provide evidence for at least one pilot-scale batch of the cannabis-based ingredient in the form of a Certificate of Analysis following the WHO template. The results must be expressed quantitatively with the limits of detection or limits of quantification for all tested substances.

3.1.2 Manufacturing description

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

Details of the method of manufacturing (including packaging and testing) must be submitted with your application.

The Agency expects that information would include a description of:

- the manufacturing and packaging processes, including a diagrammatic representation (eg, a flow chart) of the manufacturing process
- the equipment used, and batch formulae and sizes (pilot and commercial)
- the in-process controls, manufacturing hold times, crucial process parameters, test methods and acceptance limits at each step in the manufacturing and packaging processes.

3.1.3 Control of cannabis-based ingredient

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulations 7 and 8

This part of the application, requires submission of:

- specifications for the cannabis-based ingredient
- Certificates of Analysis for three pilot-scale batches of cannabis-based ingredient (see note below)
- method validation for all non-pharmacopeial methods from all testing sites, including all supporting data.

The specifications applied to the cannabis-based ingredient by the manufacturer must meet the minimum quality standard. Table 2 (below) sets out the tests that apply to a cannabis-based ingredient.

Laboratories and manufacturers must use the test methods published in one of the three accepted pharmacopoeias where applicable. Where the Regulations require a test method to be validated, that test method must have been validated in accordance with ICH guideline Q2(R2) Validation of Analytical Procedures: Text and Methodology. The test method validation data for non-pharmacopeial tests that each testing site will undertake for routine quality control of cannabis-based ingredients must be provided.

Representative batch analytical data for at least three batches of the cannabis-based ingredient at each of the proposed manufacturing sites must be provided. These batches must be at least pilot scale, and the data provided must include results for each specified test and demonstrate that the reported test results comply with the specifications.

The batch data must be provided in the form of a Certificate of Analysis following the WHO template. Wherever relevant, results must be expressed quantitatively rather than as 'complies' or 'passes test'.

> **Note:** A pilot-scale batch must be at least 10% of the size of a production-scale batch.
>
> For example, if a full production-scale batch of extract is 200 litres, a pilot-scale batch is 20 litres.

Table 2: Tests and specifications for cannabis-based ingredients

Test	Test method	Specification	Test method validation
Microbial contamination	Ph Eur 2.6.12, 2.6.13 and 2.6.31	Limits specified in Ph Eur 5.1.4 and 5.1.8	Required
Heavy metals	Ph Eur 2.4.27 USP <561>	≤ 3.0 ppm arsenic ≤ 0.5 ppm cadmium ≤ 5.0 ppm lead ≤ 0.5 ppm mercury	Required
Pesticides (imported products)	Ph Eur 2.8.13 USP <561>	Limits specified in Ph Eur 2.8.13	Required

Test	Test method	Specification	Test method validation
Pesticides (non-imported products)	Ph Eur 2.8.13 USP <561>	≤ 0.020 ppm Abamectin ≤ 0.020 ppm Bifenazate ≤ 0.100 ppm Bifenthrin ≤ 0.010 ppm Chlormequat chloride ≤ 0.020 ppm Daminozide ≤ 0.020 ppm Etoxazole ≤ 0.020 ppm Fenoxycarb ≤ 0.010 ppm Imazalil ≤ 0.020 ppm Imidacloprid ≤ 0.020 ppm Myclobutanil ≤ 0.020 ppm Paclobutrazol ≤ 0.050 ppm Pyrethrins (I and II) ≤ 0.010 ppm Spinosad (Spinosyn A and D) ≤ 3.000 ppm Spiromesifen ≤ 0.020 ppm Spirotetramat ≤ 0.020 ppm Trifloxystrobin	Required
Absence of aflatoxins	Ph Eur 2.8.18 USP <561>	≤ 2 µg/kg Aflatoxin B1 ≤ 4 µg/kg sum of aflatoxins B_1, B_2, G_1 and G_2	Required
Ochratoxin A	Ph Eur 2.8.22	≤ 20 µg/kg	Required
Residual solvents	Ph Eur 2.4.24 and 5.4 USP <467>	Limits specified in Ph Eur 5.4	Required
Identification of active ingredient	Chromatographic and/or spectroscopic method	Positively identified	Required
Assay of active ingredient	Chromatographic and/or spectroscopic method	Within the range specified for each active ingredient	Required

3.1.4 Container closure system

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 15

The container material for a cannabis-based ingredient must comply with one of the following.

- European Pharmacopoeia Chapters 3.1 or 3.2.
- United States Pharmacopoeia – National Formulary Chapters <660>, <661.1> or <661.2>.
- EMA Guideline on plastic immediate packaging materials.

The information provided in the application must clearly define the packaging materials used (eg, polymers, types of glass), containers, seals, closures, and any delivery device(s) supplied with the product. Specifications and schematic drawings of the proposed container system must also be provided.

You must provide sufficient information to demonstrate that the relevant tests applicable to the container material have been performed, and provide batch data for one batch in the form of a

Certificate of Analysis with data that demonstrates that the batch complies with one of the references in Table 2 above.

Any Certificates of Analysis you submit must have been signed by the manufacturer of the packaging. Wherever relevant, results must be expressed quantitatively rather than as 'complies' or 'passes test'. Please note, where a Certificate of Analysis is not available/applicable, a declaration of compliance may be accepted.

3.1.5 Stability

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 10

The application must include a proposed shelf-life that is based on the stability of the market formulations of the cannabis-based ingredient. It must be packaged as intended for storage and distribution, and have been tested in accordance with the drug substance requirements in ICH guideline Q1A(R2) Stability Testing of New Drug Substances and Products. The testing includes the ICH requirements for the number and sizes of batches used.

> **Note:** The proposed shelf-life should reflect the way the cannabis-based ingredient will be used. Consequently, the amount of stability data required to support the shelf-life may vary. For instance, if the cannabis-based ingredient is made for distribution and a six-month shelf-life applied then stability data that demonstrates requirements are met after six-months of storage would be required. However, if the cannabis-based ingredient is not stored or distributed but made and used immediately in a medicinal cannabis product, then no stability data would be required.

The application must include a detailed description of the stability trial protocol, packaging, storage conditions and test procedures.

The stability studies provided must include the following specific tests and test methods listed in the Medicinal Cannabis Regulations as minimum testing requirements.

- Microbiological contamination.
- Loss on drying (for dried products or ingredients intended for dried products only).
- Assay limits for active ingredients.

The above parameters must be tested using appropriate, clearly defined, validated (in the testing laboratory used for the stability samples), stability-indicating test procedures for their monitoring If test procedures change during the stability trials, you must provide information to justify the change and correlate the results. Update the stability data before submitting it. Wherever relevant, results should be expressed quantitatively rather than as 'complies' or 'passes test'.

The results must adequately support the proposed shelf life under the recommended storage conditions. Any extrapolation proposed must be in line with ICH guidelines.

3.2 Additional data for Type 2: Medicinal cannabis product

This section offers guidance on the additional data requirements for medicinal cannabis products (dried products and dosage products) that you should submit along with the NMCP application form.

The additional data should be provided in the same order as this section (3.2) follows.

3.2.1 CBD product

If your medicinal cannabis product meets the definition of a cannabidiol (CBD) product as defined in section 2A of the Misuse of Drugs Act 1975, and is therefore not a controlled drug, you must provide evidence to demonstrate this. This must include evidence to demonstrate that the ratio of specified substances falls within the definition. At a minimum, include the amount of CBD, delta-9-tetrahydrocannabinol (Δ9-THC), delta-9-tetrahydrocannabinolic acid (Δ9-THCA) and cannabinol (CBN).

You must provide evidence for at least one pilot-scale batch of the cannabis-based ingredient in the form of a Certificate of Analysis following the WHO template. The results must be expressed quantitatively with the limits of detection or limits of quantification for all tested substances.

3.2.2 Labelling

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 19

Medicines Regulations 1984, Part 4

Copies of the colour artwork of the proposed label(s) must be provided. The artwork does not need to be the actual size to be used on the product, but must be legible, be drawn to a specified scale and include a statement of the label dimensions and text size (in mm).

Medicinal cannabis products (dried products and dosage products) are required to meet the same requirements for packaging and labelling as other medicines in New Zealand, in accordance with Part 4 of the Medicines Regulations 1984. For specific information, please see GRTPNZ: Labelling of medicines and related products.

The medicinal cannabis product label must not include directions for use and dosing instructions. However, the following must be included:

- the name and quantitative particulars of each active ingredient as defined in the Misuse of Drugs (Medicinal Cannabis) Regulations 2019
- the principal display panels of the product labelling must contain the words ‘MEDICINAL CANNABIS PRODUCT’.

The Medicines Act 1981 defines the terms container and package. A medicine can have only one container. Bottles, tubes, ampoules, sachets, and blisters are examples of containers. A container may be enclosed in a package, and the product may include multiple layers of packaging. Cardboard boxes are a common package used for medicines.

Note: It is at the applicant's discretion as to whether a product label specifies the quantities of the active ingredients THC and THCA as 'total THC' and the active ingredients CBD and CBDA as 'total CBD' or specifies the quantities individually. If a total is specified, the label must state that the total includes both THCA and THC, or both CBD and CBDA. The label may state active ingredients as total THC or CBD content using a conversion factor of 0.877.

For example, Total content = Neutral cannabinoid + (Acidic cannabinoid × 0.877)

Package insert

You may use a separate information sheet where the container is too small to include all the required information or extra safety information on the label practically/legibly.

Over-labelling

Over-labelling a product to comply with New Zealand legislation is permitted. New Zealand and overseas sites that carry out labelling (including over-labelling) must comply with Good Manufacturing Practice requirements. All labelling activities in New Zealand must occur at a site that holds both:

- a licence to manufacture medicines or a licence to pack medicines
- a medicinal cannabis licence with a possess for manufacture activity.

Warning statements

Regulation 22 of the Medicines Regulations 1984 allows the Agency to specify warning statements that medicinal cannabis product labelling must include. No warning statements for medicinal cannabis products are currently required.

If the Agency had a proposal to require warning statements, it would consult on that proposal and notify interested parties. If it decided to introduce the requirement, the Agency would also provide a reasonable transition period.

3.2.3 Manufacturing description

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 32

You must submit details of the method of manufacturing (including packaging and testing) with your application.

The Agency expects that the information you submit would include a description of:

- the manufacturing and packaging processes, including a diagrammatic representation (eg, a flow chart) of the manufacturing process
- the equipment used, and batch formulae and sizes (pilot and commercial)
- the in-process controls, manufacturing hold times, crucial process parameters, test methods and acceptance limits at each step in the manufacturing and packaging.

3.2.4 Dosage product requirements

Misuse of Drugs (Medicinal Cannabis) Regulations 2019: Regulation 20

Dosage products must be in a pharmaceutical dosage form for which the European Pharmacopoeia has a monograph. A dosage product cannot be in a form that is required to be sterile. The dosage product must comply with the requirements of the monograph.

Laboratories and manufacturers must use the test methods published in one of the accepted pharmacopoeias for the applicable dosage form monograph. All test methods must have been validated in accordance with ICH guideline Q2(R2) Validation of Analytical Procedures: Text and Methodology. The test method validation data for non-pharmacopeial tests that each testing site will undertake for routine quality control of the product must be provided.

Provide batch data for three pilot batches in the form of a Certificate of Analysis following the WHO template. Wherever relevant, results should be expressed quantitatively rather than as 'complies' or 'passes test'.

3.2.5 Control of medicinal cannabis product

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulations 7 and 8

With your application, you must submit:

- specifications for the medicinal cannabis product
- Certificates of Analysis for three pilot-scale batches of medicinal cannabis product (see note below)
- method validation for all non-pharmacopeial methods from all testing sites, including all supporting data.

The medicinal cannabis product specifications the manufacturer applies must be in line with the minimum quality standard. See the following tables for the tests and specifications that apply to a dried product (Table 3) and dosage product (Table 4).

Laboratories and manufacturers must use the test methods specified in Table 3 and Table 4 and, where applicable, the methods are published in one of the three accepted pharmacopoeias. Where the Regulations require a test method to be validated, that test method must have been validated in accordance with ICH guideline Q2(R2) Validation of Analytical Procedures: Text and Methodology. You must provide the test method validation data for non-pharmacopeial tests that each testing site will undertake for routine quality control of the medicinal cannabis product.

Representative batch analytical data for three pilot-scale batches of the medicinal cannabis product produced must be provided. Noting that if there is more than one manufacturing site, required data must be produced for each of the proposed manufacturing sites. The information must include results for each specified test and demonstrate that all the reported test results comply with the specifications.

The batch data must be provided in the form of a Certificate of Analysis following the WHO template. Wherever relevant, results must be expressed quantitatively rather than as 'complies' or 'passes test'.

Note: A pilot-scale batch must be at least 10% of the size of a production-scale batch.

For example, if a full production-scale batch is 10,000 tablets, a pilot-scale batch is 1,000 tablets.

Table 3: Tests and specifications for dried products

Test	Test method	Specification	Test method validation
Microbial contamination	Ph Eur 2.6.12, 2.6.13 and 2.6.31	Limits specified in Ph Eur 5.1.4 and 5.1.8	Required
Heavy metals	Ph Eur 2.4.27 USP <561>	≤ 3.0 ppm arsenic ≤ 0.5 ppm cadmium ≤ 5.0 ppm lead ≤ 0.5 ppm mercury	Required
Pesticides (imported products)	Ph Eur 2.8.13 USP <561>	Limits specified in Ph Eur 2.8.13	Required
Pesticides (non-imported products)	Ph Eur 2.8.13 USP <561>	≤ 0.020 ppm Abamectin ≤ 0.020 ppm Bifenazate ≤ 0.100 ppm Bifenthrin ≤ 0.010 ppm Chlormequat chloride ≤ 0.020 ppm Daminozide ≤ 0.020 ppm Etoxazole ≤ 0.020 ppm Fenoxycarb ≤ 0.010 ppm Imazalil ≤ 0.020 ppm Imidacloprid ≤ 0.020 ppm Myclobutanil ≤ 0.020 ppm Paclobutrazol ≤ 0.050 ppm Pyrethrins (I and II) ≤ 0.010 ppm Spinosad (Spinosyn A and D) ≤ 3.000 ppm Spiromesifen ≤ 0.020 ppm Spirotetramat ≤ 0.020 ppm Trifloxystrobin	Required
Absence of aflatoxins	Ph Eur 2.8.18 USP <561>	≤ 2 µg/kg Aflatoxin B1 ≤ 4 µg/kg sum of aflatoxins B_1, B_2, G_1 and G_2	Required
Ochratoxin A	Ph Eur 2.8.22	≤ 20 µg/kg	Required
Foreign matter	Ph Eur 2.8.2	≤ 2%	Not required
Loss on drying	Ph Eur 2.2.32 USP <731>	≤ 12%	Not required
Total ash	Ph Eur 2.4.16 USP <561> BP Appendix XI.J	≤ 20%	Not required
Identification of cannabis	Macroscopic and microscopic examination	Positively identified	Not required

Test	Test method	Specification	Test method validation
Assay of active ingredient	Chromatographic and/or spectroscopic method	80–120% of its stated content (where the active ingredient is present at very low levels and difficult to control within the specified range, the Agency may allow for it to be assayed at a less than limit specified by the manufacturer)	Required

Table 4: Tests and specifications for dosage products

Test	Test method	Specification	Test method validation
Microbial contamination	Ph Eur 2.6.12, 2.6.13 and 2.6.31	Limits specified in Ph Eur 5.1.4 and 5.1.8	Required
Heavy metals	Ph Eur 2.4.27 USP <561>	≤ 3.0 ppm arsenic ≤ 0.5 ppm cadmium ≤ 5.0 ppm lead ≤ 0.5 ppm mercury	Required
Pesticides (imported products)	Ph Eur 2.8.13 USP <561>	Limits specified in Ph Eur 2.8.13	Required
Pesticides (non-imported products)	Ph Eur 2.8.13 USP <561>	≤ 0.020 ppm Abamectin ≤ 0.020 ppm Bifenazate ≤ 0.100 ppm Bifenthrin ≤ 0.010 ppm Chlormequat chloride ≤ 0.020 ppm Daminozide ≤ 0.020 ppm Etoxazole ≤ 0.020 ppm Fenoxycarb ≤ 0.010 ppm Imazalil ≤ 0.020 ppm Imidacloprid ≤ 0.020 ppm Myclobutanil ≤ 0.020 ppm Paclobutrazol ≤ 0.050 ppm Pyrethrins (I and II) ≤ 0.010 ppm Spinosad (Spinosyn A and D) ≤ 3.000 ppm Spiromesifen ≤ 0.020 ppm Spirotetramat ≤ 0.020 ppm Trifloxystrobin	Required
Absence of aflatoxins	Ph Eur 2.8.18 USP <561>	≤ 2 µg/kg Aflatoxin B1 ≤ 4 µg/kg sum of aflatoxins B_1, B_2, G_1 and G_2	Required
Ochratoxin A	Ph Eur 2.8.22	≤ 20 µg/kg	Required
Residual solvents	Ph Eur 2.4.24 and 5.4 USP <467>	Limits specified in Ph Eur 5.4	Required
Identification of active ingredient	Chromatographic and/or spectroscopic method	Positively identified	Required

Test	Test method	Specification	Test method validation
Assay of active ingredient	Chromatographic and/or spectroscopic method	90–110% of its stated content (where the active ingredient is present at very low levels and difficult to control within the specified range, the Agency may allow for it to be assayed at a less than limit specified by the manufacturer)	Required
Dosage form tests*	Refer to dosage form specific Ph Eur chapter	Refer to dosage form specific Ph Eur chapter	Required

* The European Pharmacopoeia sets out the dosage form tests, which are specific to each type of dosage form. For example, a tablet also requires disintegration testing and dissolution testing, which Chapter 0478 of the European Pharmacopoeia describes.

3.2.6 Container closure system

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 15

Container material for a medicinal cannabis product must comply with one of the following.

- European Pharmacopoeia Chapters 3.1 or 3.2.
- United States Pharmacopoeia – National Formulary Chapters <660>, <661.1> or <661.2>.
- EMA Guideline on plastic immediate packaging materials.

You must clearly define the packaging materials used (eg, polymers, types of glass), containers, seals, closures, and any delivery device(s) supplied with the product. Provide specifications and schematic drawings of the proposed container system.

You must demonstrate that the relevant tests applicable to the container material have been performed and provide batch data for one batch in the form of a Certificate of Analysis with data that demonstrates that the batch complies with one of the above options. Any Certificate of Analysis (or declaration of compliance) you submit must have been signed by the manufacturer of the packaging. Wherever relevant, express results quantitatively rather than as ‘complies’ or ‘passes test’.

3.2.7 Control of excipients

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 21

Excipients are the non-active ingredients of a product. Excipients or other ingredients (including flavours and colourants) can only be used in a dosage product if a monograph for that excipient or other ingredient exists in the European Pharmacopoeia, British Pharmacopoeia or United States Pharmacopoeia – National Formulary.

The identity and quality of all excipients (including capsule shells) must be controlled to the pharmacopeial monograph’s specifications. Laboratories and manufacturers must use the test methods published in the relevant pharmacopoeia for the applicable excipient monograph.

Adequate measures must be taken to ensure that any ingredients of animal origin (eg, gelatin, magnesium or calcium stearate, and stearic acid) used in the product are free from transmissible

spongiform encephalopathy (TSE) contamination. We recommend following European Commission and United States guidelines on TSE contamination.

Batch data for one batch in the form of a Certificate of Analysis following the WHO template must be provided and the data must demonstrate that the batch conforms with the monograph of the applicable excipient. Wherever relevant, results must be expressed quantitatively rather than as 'complies' or 'passes test'.

3.2.8 Stability

Misuse of Drugs (Medicinal Cannabis) Regulations 2019, regulation 10

The medicinal cannabis product packaged as intended for supply must have its stability tested in accordance with the ICH guideline Q1A(R2) Stability Testing of New Drug Substances and Products (including the ICH requirements for the number and sizes of batches used).

Information must be provided which describes in detail the stability trial protocol, packaging, packaging orientation (if relevant), storage conditions, and test procedures.

The testing schedule must have included all the stability-indicating organoleptic, physical, chemical, and microbiological quality parameters relevant to the dose form and type of packaging. Appropriate, clearly defined, validated (in the testing laboratory used for the stability samples) stability-indicating test procedures must be used for the monitoring of all parameters.

Stability studies must include the following specific tests and test methods that the Misuse of Drugs (Medicinal Cannabis) Regulations 2019 identify as minimum testing requirements.

- Microbiological contamination.
- Loss on drying (for dried products or ingredients intended for dried products only).
- Assay for active ingredients.
- Any test(s) listed in the European Pharmacopoeia general monograph for the relevant dosage form.

If test procedures change during the stability trials, you must justify them and correlate the results. Data for storage under the recommended conditions for at least six months must be available and must be submitted in the application.

The stability data must be updated before submitting it. Wherever relevant, express results quantitatively rather than as 'complies' or 'passes test'.

The results (and allowing for extrapolation within reasonable limits) must adequately support the proposed shelf life under the recommended storage conditions. If you do not have these results, the Agency may grant a shorter shelf-life until you can provide adequate stability data to support the proposed shelf-life.

If relevant, you must have investigated the stability of the product after first opening and shown that it is adequate for the intended use of the product.

If relevant, state adequate storage instructions and time limits for using the product after first opening on the draft product label.

3.3 Medicinal Cannabis Licence

A **Medicinal Cannabis Licence** authorises the licence holder to carry out one or more types of 'activity'. The 'possession for manufacture' activity must be specified on the licence if the holder intends to extract a cannabis-based ingredient, manufacture a medicinal cannabis product, or perform laboratory testing.

Refer to **Part 4: Guidance for Applicants for a Medicinal Cannabis Licence** of the *Guideline on the Regulation of Medicinal Cannabis in New Zealand* for information about Medicinal Cannabis Licences.

3.4 Minimum quality standard for medicinal cannabis products

All medicinal cannabis products intended for use by patients (including cannabidiol (CBD) products) must meet the minimum quality standard for medicinal cannabis. Product assessments are the method used to verify whether a product meets the minimum quality standard.

For information about the minimum quality standard and product assessments, go to: the minimum quality standard page on the Medicinal Cannabis website.

3.5 Licences issued under the Medicines Act 1981

If you hold a Medicinal Cannabis Licence and wish to manufacture a medicinal cannabis product for patients to use, you will also need to hold a **Licence to Manufacture Medicines** issued under the Medicines Act 1981. This licence permits the holder to manufacture, test, pack and label medicines.

If you hold a Medicinal Cannabis Licence but your manufacturing activities are limited to repacking products that a GMP certified facility has manufactured and that have been verified as meeting the medicinal cannabis minimum quality standard, you need a **Licence to Pack Medicines** under the Medicines Act 1981 instead of a Licence to Manufacture Medicines. This licence permits the holder to pack and label medicines only.

When you have starting materials for export, that require further industrial processing, you do not need to comply with the requirements of GMP. Neither a Licence to Manufacture Medicine nor a Licence to Pack Medicine would be required in this instance. Alternatively, if your starting material for export is supplied as bulk or as a finished packed product then you would need to comply with the requirements of GMP and a Licence to Manufacture or Licence to Pack will be required.

To obtain a Licence to Manufacture Medicines or a Licence to Pack Medicines, you must be able to demonstrate that you comply with the New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods (the GMP Code).

For more information about licences to manufacture and/or pack medicines, contact the Medsafe's Compliance Branch by sending an email to the gmp@health.govt.nz inbox. Fees for Licenses are included in the schedule of fees payable under the Medicines Act 1981.

3.6 Licence to import or export controlled drugs

You must have a licence to commercially import or export controlled drugs, including medicinal cannabis products.

For exports, the importing country must provide a 'licence to import' before Medicines Control can issue a licence to export controlled drugs.

The application fee for a licence to import or export controlled drugs is $194.22 including goods and services tax (GST) for each consignment. A licence is required for each consignment, but each consignment may contain up to four preparations or products.

Up to 30 working days is required to process an application for an import or export licence.

For further information or to receive an application form for a licence to import or export controlled drugs, contact the Advisor (Controlled Drugs), Medicines Control, on 04 816 2018 or at medicinescontrol@health.govt.nz.

Note: Import and export licences are not required for cannabis-based ingredients and medicinal cannabis products (dosage products) that meet the definition of a CBD product. However, requirements under the Medicines Act 1981 and Medicines Regulations 1984 continue to apply refer to CBD product information on Medicinal Cannabis Agency website.

Appendix 1: Application documents

summarises the documents you must include for each type of application.

Note:

- **A** indicates a document is mandatory – you must submit it with your application.
- **B** indicates a document may be relevant – you must submit it with your application if it is.
- **NA** indicates a document is not relevant – you should not submit it with your application.

Table 5: Documents required for each application type

	Cannabis-based ingredient	Dried product	Dosage product
NMCP application form	A	A	A
Good Manufacturing Practice certification/ISO accreditation	A	A	A
Manufacture description	A	A	A
Specifications	A	A	A
Test results (Certificates of Analysis)	A	A	A
Non-pharmacopoeial test method validation	A	A	A
Container closure description	A	A	A
Container closure (Certificates of Analysis)	A	A	A
Stability protocol	A	A	A
Stability data	A	A	A
Colour artwork of labels	NA	A	A
Excipients (Certificates of Analysis)	NA	NA	A
Letter of authorisation for contact person from licence holder	B	B	B
Package insert	NA	B	B