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Health Products
Regulatory Authority

Cannabis and Related Substances Legislation and Regulation

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Presentation Outline

- SAHPRA's legal remit
- Regulatory framework for scheduling and control
- International legal status of cannabis
- Legal status of cannabis in SA
- Current cannabis inscription
- Low-THC cannabis (hemp)
- Cannabidiol
- Access to cannabis for medicinal use
- Cultivation of cannabis for medicinal use
- Scenarios
- Licence application, review and inspection
- Updates on licence applications

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South African Health Products Regulatory Authority (SAHPRA)

- Replaced the Medicines Control Council (MCC) on the 1 February 2018
- Schedule 3A independent public entity with operational autonomy and accountability
- Responsible for the regulation of all medicines, including complementary medicines, medical devices and radiation control
- Mandated and governed by the Medicines and Related Substances Act, 1965 (Act 101 of 1965), as amended, and the schedules and regulations thereto, together with the guidelines made in terms of this Act.

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Regulatory Framework for Scheduling and Control of Medicines

- The sale, supply and use of a medicine or scheduled substance is subject to Section 22A of the *Medicines Act*
- All medicines are subject to a *scheduling* process on the basis of the substance(s) contained in them (their active pharmaceutical ingredients (APIs)).
- Schedules are made by the Minister, on the recommendation of the Authority, and published in the Gazette (or amended by subsequent notice in the Gazette).

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Scheduling and Control of Medicines: General Principles

- Allows for different *levels of regulatory control* over substances, whether in the form of naturally-occurring substances, APIs, or finished pharmaceutical products (medicines).
- Primary consideration is *safety* in relation to therapeutic use.
- Substances may be listed in *more than one Schedule*, based on the indication, dosage form, route of administration, strength, dose, duration, or a combination of these factors.
- Framework ensures *compliance* with international drug control Conventions to which South Africa is signatory (1961/1971/1988).

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International Legal Status of Cannabis

- South Africa is a signatory to the UN *1961 Single Convention on Narcotic Drugs*, the *1971 Convention on Psychotropic Substances*, and the *1988 Convention against Illicit Traffic in Narcotic and Psychotropic Drugs*.
- Under the *1961 Single Convention*, cannabis is classified under Schedules I and IV making it subject to special restrictions.
- The *International Narcotics Control Board* (INCB) monitors member states compliance with:
  - regulatory frameworks for enabling medical and research access
  - regulatory procedures for licensing and registration of suitable products
  - control systems for commercial cultivation of cannabis
  - specification of cannabis varieties which may be authorised for cultivation
- Attempts are currently being made globally to *ease restrictions* on cannabis and cannabis extracts under international treaties (on recommendation of the WHO Expert Committee on Drug Dependence)

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Legal Status of Cannabis in South Africa

- Cannabis is listed in the Schedules to the Medicines Act as follows:
  - *Schedule 7: cannabis and tetrahydrocannabinol (THC)*
  - *Schedule 6: THC for therapeutic use*
  - *Schedule 4: cannabidiol (CBD) for therapeutic use*
  - *Schedule 0: CBD as a supplement in a limited dose for a limited health claim; THC and CBD in processed products within prescribed limits* (by way of exclusion notice)

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Current Cannabis Inscription in Schedule 7

"Cannabis (dagga), the whole plant or any portion or product thereof, except:

- *when separately specified in the Schedules; (S6) (S4); or*
- *processed hemp fibre containing 0.1 percent or less of tetrahydrocannabinol and products manufactured from such fibre, provided that the product does not contain whole cannabis seeds and is in a form not suitable for ingestion, smoking or inhaling purposes; or*
- *processed product made from cannabis seeds containing not more than 10 milligram per kilogram (0,001 percent) of tetrahydrocannabinol and does not contain whole cannabis seeds."*

"Synthetic cannabis substances (synthetic cannabinoids) including but not limited to:

- *cannabicyclohexanol;*
- *JWH-018; JWH-073; JWH-200; CP-47497; CP 47497-C6; CP 47497-C7; CP 47497-C8; CP 47497-C9; HU-210"*

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Low-THC Cannabis (Hemp) Cultivation

- Low-THC cannabis (as a whole plant/any part thereof) is currently **not excluded** from the schedules
- Low-THC cannabis (Hemp) **fibre *is excluded*** from the Schedules provided that the hemp fibre and processed products from the hemp fibre:
  - do not contain more than **0,1 percent of THC;**
  - Is in a form not suitable for ingestion, smoking, inhaling; and
  - does not contain whole cannabis seeds
- Low-THC cannabis (Hemp) **processed products made from cannabis seeds are *excluded*** from the Schedules provided that the processed products :
  - do not contain more than **0,001 percent of THC;**
  - does not contain whole cannabis seeds

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Cannabidiol (CBD)
Clarification of the Section 36 Exclusion Notice

- Published by the Minister of Health
- Allows for the exclusion of **certain CBD preparations** from the operation of the Schedules for a time-limited period of 12 months from the date of publication of the exclusion notice (18 May 2019)
- Exemptions were made for those preparations that:
  - *(a) contain a maximum daily dose of 20 mg CBD with an accepted low risk claim or health claim; or*
  - *(b) consist of processed products made from cannabis raw plant material, where only the naturally occurring quantity of cannabinoids found in the source material are contained in the product, and which contain not more than **0,001 % of tetrahydrocannabinol (THC)** and not more than **0,0075 % total cannabidiol (CBD).***

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Cannabidiol (CBD)
Clarification of the Section 36 Exclusion Notice

Paragraph (*a*)

- CBD-containing preparations for medicinal purposes, (including complementary medicines) must satisfy the conditions prescribed in either paragraph (*a*) or (*b*).
- **NOTE:** Exclusion is from Schedule 4 to the Act.
- **Does not** infer that CBD is excluded from other requirements of the Act e.g. labelling, GMP
- **Does not** exclude any CBD-containing products which contain any other active pharmaceutical ingredients (APIs), including tetrahydrocannabinol (THC).

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Cannabidiol (CBD)
Clarification of the Section 36 Exclusion Notice

Paragraph (*a*)

- Manufacturers and importers of a CBD-containing medicine (including complementary medicine) must be in possession of a licence issued in terms of **section 22C(1)*(b)*** of the Medicines Act and comply with the relevant standards
- Such persons must be able to present verified assessment by an accredited laboratory, licenced in terms of section 22C(1)*(b)* of the Medicines Act of the CBD and/or THC content of any medicinal product, when requested to do so by the Authority.

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Cannabidiol (CBD)
Clarification of the Section 36 Exclusion Notice

Paragraph (*b*)

- A processed product containing the naturally occurring trace amounts of **THC (≤ 0,001 %)** and **CBD (≤ 0,0075 %)** is specifically excluded from the Schedules, when the product does not contain whole cannabis seeds and does not make any medicinal claim.
- Only the naturally occurring trace amounts are allowed
- **CBD as an additive or ingredient is not permissible**

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Cannabidiol (CBD)
Clarification of the Section 36 Exclusion Notice

Paragraph (*b*)

- Manufacturers and importers of CBD-containing processed products, which fall within the parameters of paragraph (*b)*, and which are not intended for medicinal purposes, do not require a licence to manufacture or import in terms of section 22C of the Act.
- **However**, they must be able to provide verifiable proof of the CBD and/or THC content of the product and comply with the provisions of other applicable legislation (for example, the Foodstuffs, Cosmetics and Disinfectants Act, 1972 (Act 54 of 1972)).

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Cannabidiol (CBD) Market

Proliferation of CBD-containing products on the market

- purported medicinal products
  - claiming treatment for a variety of diseases and symptoms
- CBD-containing foodstuffs and cosmetics
  - claiming treatment for a variety of diseases and symptoms
- Intentionally mislabelled products
  - Claiming low THC, low CBD
- Aggressive marketing and false advertising
  - Using logos, cartoons, pictorials

These are all illegally manufactured and distributed without regulatory oversight and often with unverified contents

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Access to Cannabis for Medicinal Use

- Patients who are in possession of a valid prescription for medicinal use may access cannabis in the following ways:
  1. Pharmaceutical cannabis products ***registered by SAHPRA*** (theoretical at present, as none are registered).
  2. Cannabis- or cannabinoid-containing pharmaceutical products that are not yet registered, in terms of a ***section 21*** permit. Permits will only be issued for quality-assured products containing standardised levels of cannabinoids and certified to be free of harmful contaminants, **licensed** in the country of origin. (to date, section 21 permits have been issued for products from Canada and The Netherlands)

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Registered Cannabis-containing Pharmaceutical Products

- *Dronabinol* is registered in some jurisdictions (previously including South Africa) for nausea and loss of appetite in cancer and AIDS patients.
- *Nabilone* is registered for chemotherapy-associated nausea and vomiting in some jurisdictions
- A 50:50 THC:CBD orobuccal spray (sold as *Sativex)* is registered for muscle spasms associated with multiple sclerosis and pain management in some jurisdictions
- Cannabidiol (CBD; sold as *Epidiolex*) has recently been approved in the US and EU for the treatment of seizures in paediatric patients with Lennox-Gastaut syndrome and Dravet syndrome.

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Framework: Cultivation of Cannabis for Medicinal Use

Key elements:

- Licensing of growers to enable ***controlled cultivation*** of high-THC or high-CBD cannabis
- Licensing of manufacturers to enable **controlled manufacture of cannabis-containing products**
- Availability of *standardised, quality-assured* herbal material and products for medical, scientific and research purposes.
- Clinical decision-making support for approval of medicinal use.
- Review and approval of clinical trials and related scientific research.

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Cultivation of Cannabis and Manufacture of Cannabis-related Pharmaceutical Products for Medicinal and Research Purposes

- Provides guidance on *minimum standards* required, in terms of:
  - Quality
  - Security
  - Quality systems
  - Personnel
  - Buildings and facilities
  - Compliance and enforcement
  - Documentation
- Identifies the *critical* production steps that are needed to ensure a product of reliable and reproducible quality.
- Subject to *strict monitoring* to avoid any unintended use.
- SAHPRA inspectors conduct *compliance* investigations and inspections of applicants for licensed cultivation sites.

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Cannabis for Medicinal Use Licence

- Currently, the commercial cultivation of cannabis for medicinal purposes requires a licence in terms of section 22C(1)(*b*) from SAHPRA and a section 22(9)(*a*)(i) permit from the DG of Health.
- A licence may be issued for any or all of the following activities:
  - *Cultivate cannabis and produce cannabis resin;*
  - *Extract and test cannabis, cannabis resin and/or cannabinoids;*
  - *Manufacture a cannabis-containing or cannabinoid-containing medicine;*
  - *Import, export or distribute a cannabis-containing product.*

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Scenarios

Cultivate cannabis for medicinal use and export bulk cannabis)
(sell or export to other licence holders or authorised overseas vendors)

Cultivate cannabis for medicinal use, process, package the herbal raw material and export
(export to authorised overseas vendors)

Cultivate cannabis for medicinal use, extract CBD/ THC, and manufacture a registered cannabis-containing medicine

Extract CBD/ THC/ other cannabinoids from cannabis plant
(sell to other licence holders or authorised overseas vendors)

Extract CBD/ THC/ other cannabinoids from cannabis plant and manufacture a registered cannabis-containing medicine

Extract CBD/ THC/ other cannabinoids from cannabis plant and to manufacture a CBD-containing processed product

Import a THC-containing medicine (Also require a Section 11 import permit for schedule 6 substances)

Import a CBD-containing medicine

Manufacture a registered cannabis-containing medicine (using localy procured or imported API)

Import CBD as a raw material (API)

Analytical Testing of cannabis starting materials, intermediates, bulk (cannabis herbal material) and/or finished product (cannabinoid-containing medicine)

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Section 22A(9)(*a*)(i) permit + Section 22C licence

Possess and cultivate cannabis for medicinal use and export bulk cannabis)

(sell or export to other licence holders or authorised overseas vendors)

Possess and Cultivate cannabis for medicinal use, process, package the herbal raw material and export

(export to authorised overseas vendors)

Possess and Cultivate cannabis for medicinal use, extract CBD/ THC, and manufacture a registered cannabis-containing medicine

Possess and Extract CBD/ THC/ other cannabinoids from cannabis plant

(sell to other licence holders or authorised overseas vendors)

Possess and Extract CBD/ THC/ other cannabinoids from cannabis plant and to manufacture a registered cannabis-containing medicine

Possess THC extract and manufacture a registered cannabis-containing medicine

Analytical Testing of cannabis starting materials, intermediates, bulk (cannabis herbal material)

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Section 22C licence

Import a THC-containing medicine (Also require a Section 11 import permit for schedule 6 substances)

Manufacture a registered CBD-containing medicine

Import a registered CBD-containing medicine

Import CBD as a raw material (API)

Analytical Testing of finished product and cannabinoid-containing medicine

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Section 22A(9)(*a*)(i) permit

Acquisition, use, possession of cannabis and cultivation of low-THC cannabis (hemp)

Acquisition, use, possession for research , scientific or educational purposes

Acquisition, use, possession, supply by a medical practitioner for the treatment or prevention of a medical condition in a particular patient

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Cannabis for Medicinal Use Licence

- Cultivation for any purpose other than that explicitly allowed for through the licence and permit system under the Medicines Act, is a criminal offence.
- Likewise, cultivation by non-licensees remains a criminal offence under this legislation, and the Drugs and Drug Trafficking Act (Act 140 of 1992).

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Application Process

- The application form for a licence and sample completed form can be accessed from the SAHPRA website
- New and renewal applications are made on same form
- Submit to SAHPRA offices:
  - CSIR Campus, Meiring Naude
  - SAHPRA reception
  - Building 38
- Application Fee for a licence – R 23 800
- Ensure proof of payment and all relevant required documentation is included in the application

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Review and Inspection Process

- Desktop review of application conducted by regulatory compliance officers/ inspectors
- Queries or shortcomings communicated formally to applicants
- Inspection scheduled and conducted by regulatory compliance officers/ inspectors
- Approximate timeline to inspection: 3 months
- Approximate timeline to finalization: 6 months (reduced from 12 months)

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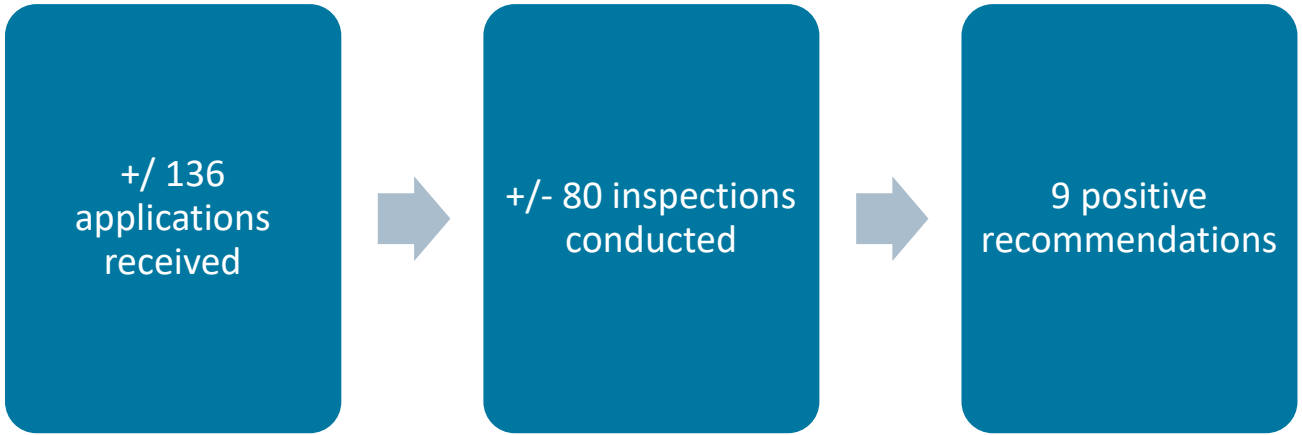
Update on Licence Applications



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