South African Health Products
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GUIDELINE FOR CULTIVATION OF CANNABIS AND MANUFACTURE OF CANNABIS-RELATED PHARMACEUTICAL PRODUCTS FOR MEDICINAL AND RESEARCH PURPOSES

This document provides the principles behind the minimum requirements in terms of quality, security and standard operating procedures relating to the cultivation of Cannabis and the manufacture and use of Cannabis-related pharmaceutical products for medicinal and research purposes that will need to be in place should an application be submitted to SAHPRA for consideration. This guideline represents SAHPRA's current thinking on the measures required to be in place to ensure that quality products are cultivated and harvested and made available to patients when prescribed by an authorised prescriber / physician. SAHPRA reserves the right to request any additional information and may make amendments in keeping with current knowledge.

Document History

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Glossary

Abbreviation/ Term	Meaning
API	Active Pharmaceutical Ingredient
CBD	Cannabidiol
CBN	Cannabinol
CCTV	Closed-Circuit Television
DALRRD	Department of Agriculture, Land Reform and Rural Development
DoH	Department of Health
EMA	European medicines Agency
FDA	Food and Drug Administration
GC	Gas Chromatography
GC-MS	Gas Chromatography Mass Spectrometry
GACP	Good Agricultural and Collection Practices
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HPLC	High Performance Liquid Chromatography
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
INCB	International Narcotics Drug Control Board
Ph. Eur	European Pharmacopoeia
PIC/S	Pharmaceutical Inspection Co-operation Scheme
SABS	South African Bureau of Standards

Abbreviation/ Term	Meaning
SAHPRA	South African Health Products Regulatory Authority
SAPS	South African Police Services
SARS	South African Revenue Service
TGA	Therapeutic Goods Administration
THC	(-)-transdelta-9-tetrahydrocannabinol
TLC	Thin Layer Chromatography
WHO	World Health Organisation

1. INTRODUCTION

The Medicines and Related Substances Act (Act 101 of 1965), as amended, herein referred to as the Medicines Act, mandates SAHPRA to regulate the availability of quality medicines which are safe and efficacious for their intended use. This mandate requires SAHPRA to apply standards for the production, distribution, sale and marketing of medicines, medical devices and Scheduled substances. In considering the availability of any medicine for human or animal use, SAHPRA assesses the balance between its benefits and risks.

In terms of Section 21 of the Medicines Act, authorised practitioners can apply to SAHPRA for permission to access and prescribe unregistered medicines when intended to treat individual patients. Cannabis-containing products intended for medicinal purposes may thus be made available, in exceptional circumstances, to specific patients under medical supervision. Authorisation is dependent on the submission of an appropriate dosage regimen, an acceptable justification for the proposed use, and regular reporting to SAHPRA.

To date, patient access to unregistered Cannabis or cannabinoid-containing medicines has been enabled by SAHPRA through importation of these products. In order to ensure the availability of standardised quality-assured locally grown Cannabis for the manufacture of suitable pharmaceutical products, the Department of Health and the SAHPRA may permit the cultivation of Cannabis solely for medicinal and research purposes. This framework, developed in consultation with the Department of Agriculture, Land Reform and Rural Development (DALRRD), is intended to control the cultivation, production and manufacturing of Cannabis-containing products intended for medicinal use in South Africa. Licensed domestic cultivation of Cannabis for medicinal use is aimed at ensuring sufficient local supply for medical, scientific and clinical research purposes and the implementation of control measures necessary to prevent diversion and misuse, as well as to ensure patient safety.

This guideline provides information relating to the standards required for the cultivation and processing of Cannabis as herbal starting material and identifies the critical production steps that are needed to ensure a product of reliable and reproducible quality.

The SAHPRA encourages and supports scientific and clinical research in order to further contribute to the evidence base for Cannabis-containing medicinal products. All studies involving Cannabis for medicinal use for clinical or scientific research purposes require a licence by the SAHPRA. Approval by an independent research ethics committee will also be required. The detailed procedure and requirements for research are available on the SAHPRA website.

2. LEGAL PROVISION LEGAL STATUS OF CANNABIS INTERNATIONAL TREATIES

The United Nations Single Convention on Narcotic Drugs (1961), herein referred to as Single Convention, aims to combat drug abuse and trafficking through coordinated international cooperation directed at limiting the possession, use, trade, distribution, import, export, manufacture and production of narcotic drugs exclusively. The Single Convention provides an international framework that recognises the medicinal value of narcotic drugs and ensures availability for such purposes while preventing diversion into illicit channels and abuse.

As a signatory to the Single Convention, South Africa is committed to comply with its obligations by controlling the cultivation of Cannabis for medicinal use and reporting to the International Narcotics Drug Control Board (INCB) on volumes of production and manufacture. These obligations require South Africa to minimise the risk

of diversion of Cannabis and to reserve its use for appropriate medical and scientific purposes only.

Under the Medicines Act and in line with the Single Convention, the use, cultivation and harvesting of Cannabis and the manufacture of Cannabis-containing products for medicinal use may only occur through a licence issued by the SAHPRA and a permit in case of manufacturing, issued by the Department of Health. These conditions allow government authorities to limit the quantities of cultivated and manufactured products based on the agreed quotas from the INCB, thus meeting a key obligation of preventing unregulated accumulation of Cannabis material.

Legislative Framework

Access to medicines and Scheduled substances in South Africa is controlled through Scheduling of the substance. Cannabis contains (-)-transdelta-9-tetrahydrocannabinol (THC) which is a narcotic substance listed under Schedule 6 of the Schedules to the Medicines Act and cultivation is allowed for through the licence and permit system under the Medicines Act. Likewise, cultivation for medical purpose by non-licensees remains a criminal offense under this and other legislation.

In addition, the Medicines Act allows SAHPRA to issue a licence to manufacture either a medicine or a Scheduled substance (Active Pharmaceutical Ingredient/API). Section 22C(1)(b) of the Medicines Act enables the cultivation and manufacture of Scheduled substances and ensures the required oversight of SAHPRA in regulating these activities. This provision allows SAHPRA to license cultivators of Cannabis for medicinal use and enables regulatory oversight in a way that is compliant with South Africa's international obligations.

The legislative framework addresses three regulatory aspects:

- Authorisation of Cannabis cultivation and production domestically, for medicinal and research purposes.
- Satisfying the requirements of South Africa's international obligations, under the Single Convention.
- Aligning the access of Cannabis-containing products for medicinal purposes with that of other controlled medicines.

3. APPLICATIONS FOR CULTIVATION OF CANNABIS FOR MEDICINAL PURPOSES

3.1 Application to the SAHPRA for a licence

An applicant may apply to the SAHPRA for a licence in terms of the provisions of Section 22C(1)(b) of the Medicines Act for any or all of the following activities:

- Cultivate/grow and produce Cannabis and Cannabis resin;
- Extract and test Cannabis, Cannabis resin and/or cannabinoids;
- Manufacture a Cannabis-containing or cannabinoid-containing medicine;
- Import a Cannabis-containing medicine;
- Export a Cannabis-containing medicine;
- Distribute a Cannabis-containing medicine.

Applications may be made on the basis of a site plan and site master file, prior to construction of the facility. However, all completed facilities will be inspected for compliance with all requirements.

3.2 Application to Director-General of Health for a permit

In addition to the licence application to SAHPRA, Applicants will also be required to apply to the Director-General of Health for a permit in terms of the provisions of Section 22A(9)(a)(i) of the Medicines Act to manufacture Cannabis for medicinal use. Section 22C(1)(b) of the Medicines Act states:

the Authority may- on application in the prescribed manner and on payment of the prescribed fee, issue to a manufacturer...of a medicine,….or scheduled substance a licence to manufacture....such medicine,...or scheduled substance, upon such conditions as to the application of such acceptable quality assurance principles and good manufacturing and distribution practices as the council may determine.

Section 22A(9)(a)(i) of the Medicines Act states:

No person shall- acquire, use, possess, manufacture, or supply any Schedule 7...substance, or manufacture any ...Schedule 6 substance unless he or she has been issued with a permit by the Director General for such acquisition, use, possession, manufacture, or supply...;

There are no restrictions on the number of licences that SAHPRA may issue, except that the overall quantities of substance produced in South Africa may not exceed the quota allocated by the INCB.

The permit system ensures that quotas issued by the INCB are adhered to. Permits will be managed fairly, relative to the expected usage in the country in order to prevent accumulation of Cannabis or Cannabis products. SAHPRA, together with the Department of Health, will order the seizure and destruction of any Cannabis produced by a licence holder when the quantity conditions of the licence are not adhered to.

3.3 Personnel Requirements

3.3.1 Suitable Fit and Proper Requirements: Applicant

The integrity of a person who is granted a licence, or who has the ability to substantially influence the conduct of activities under a licence, is fundamental to the Cannabis for medicinal use scheme.

The Applicant’s interactions and associations will be considered by SAHPRA in assessing whether the fit and proper person principle is met. Applicants will be invited in their applications to make disclosures. Once licensed, it is a condition of the licence that Applicants inform SAHPRA immediately upon becoming aware of any matter that would call into question the Applicant’s status, or that of the Applicant’s business associates' status as a fit and proper person.

3.3.2 Personnel

Licence holders must take all reasonable steps to ensure that staff members employed or engaged do not present a risk of diversion of Cannabis or compromise the cultivation, manufacture and production of Cannabis for medicinal use and Cannabis-containing products.

A person is unsuitable for employment in Cannabis-related operations if such a person:

- is under the age of 18 years
- has been convicted of a serious offence

The measures taken to ensure that employees do not fall into any of the descriptors above are the responsibility of the licence holder. Where a licence is granted, ongoing compliance with these measures must be maintained.

3.3.3 Personnel Training

It is a requirement that Applicants ensure that competent staff with appropriate skills are appointed to oversee the cultivation, production or manufacture of Cannabis for medicinal or research use. Training and hygiene policies must be developed and implemented and must include the following:

Training

Personnel must receive appropriate training before performing the tasks given to them. Production personnel must be trained in the production techniques used.

Hygiene

All personnel entrusted with handling herbal material must maintain proper personal hygiene to ensure that the quality of processing, manufacturing and production of Cannabis and Cannabis related products are not compromised. Persons suffering from infectious diseases transmittable via food, or carriers of these diseases must be precluded from accessing areas where they could come into contact with herbal material. Persons with open wounds, inflammation and skin infections must not be allowed in areas where they could come into contact with herbal material, unless they wear protective clothing or gloves. Personnel must be protected from contact with toxic or potentially allergenic herbal material by means of adequate protective clothing.

3.4 Security Requirements

Security arrangements deployed at the proposed site will form an integral part of the conditions to be considered prior to SAHPRA licence being issued and the Department of Health permit being granted. SAHPRA and the Department of Health require that Applicants develop and implement appropriate security policies and procedures for the cultivation, manufacturing and production of Cannabis and Cannabis-related products in order to prevent unauthorised access, theft or diversion. Non-compliance with any security requirements will be grounds to revoke a licence and withdraw a permit issued to an Applicant.

Applicants are advised that, in applying for a Cannabis licence, or conducting activities under a licence, it is an offence to provide false or misleading information in relation to such application or in respect of information requested by SAHPRA and or Department of Health.

3.4.1 Mandatory Requirements

There are a number of requirements prescribed in the Medicines Act and Regulations thereof, that direct a licence holder to design, implement and maintain a business operational plan that ensures the security of Cannabis and related products.

A licence or permit may be refused if the SAHPRA or the Department of Health is not satisfied that the applicant will:

- take all reasonable measures to ensure the physical security of any Cannabis cultivated or Cannabis-related product manufactured; and
- ensure that there are suitable security arrangements at all locations where activities related to the licence will be undertaken.

The Guide to Good Manufacturing Practice (GMP) for Medicines in South Africa, requires as a precondition of a licence, that adequate measures to ensure security, transport, destruction, reporting and employment of suitable persons are in place. The GMP guide also requires conditions around self-inspections, compliance and monitoring to be adhered to.

Section 22A(9)(b) of the Medicines Act allows the Director-General of Health to revoke the issued permit if any condition under which the permit was issued in not being complied with.

There are a number of critical security principles that are required to be reflected in an Applicant's security policies and procedures. These, amongst others, include the following:

- discouraging persons from attempting to breach security measures;
- preventing acts aimed at breaching security measures, including measures to delay security breaches to provide time for defence or leading to the intrusion being abandoned;
- preventative measures that allow access to authorised persons while declining access to others;
- detection measures to discover security breaches; and
- defined actions to be taken to respond to a security breach.

These principles should be supported by effective recording and information management systems that allow the licence holder to both demonstrate how security arrangements are met, and provide tools to secure evidence where there are attempts to breach security arrangements.

3.4.2 Risk of Diversion

Theft and loss are the two most likely ways in which diversion can occur and may be the result of deliberate acts or negligence.

The following scenarios may result in theft, loss or substitution of Cannabis and should be avoided:

- Unauthorised access by an external person

This is likely to be intrusion by a person or persons with no legitimate reason for accessing the site or the Cannabis material. It is likely to be a deliberate act, but may be assisted through negligence. Such scenarios might include covert attack (break-ins) and overt attack (armed holdups), and are most closely controlled through intruder resistance mechanisms.

Transport is another point of potential deliberate attack and careful consideration needs to be given to the security of the Cannabis material at this time.

- Unauthorised access by an employee or visitor

This scenario could be the result of an employee or visitor obtaining unauthorised access to an area of the Cannabis site. This could occur through deliberate deception, physical damage or negligence. It is therefore important to ensure adequate internal access controls within Cannabis sites in order to prevent unauthorised access by employees or visitors.

- Authorised access by an employee or visitor

This scenario accounts for the employee or visitor who uses their authorised access for theft or substitution of

Cannabis, or sabotages security arrangements to enable later unauthorised access.

This is an extremely difficult scenario to mitigate as it requires the imposition of controls over persons in positions of trust. Personnel security, restrictions on clothing or bags, provisions around employee searches might be the types of interventions used to avoid this scenario.

The likelihood and risk of the occurrence of these scenarios should be thoroughly considered in a security risk management plan.

Note that in the event of an intrusion, theft or loss of Cannabis, a licence holder is required to notify both the SAHPRA and the South African Police Services (SAPS) of the event as soon as possible.

3.4.3 Key Security Measures

In addition to the aforementioned principles, a number of key concepts inform the design of security systems and arrangements which should be considered, and include, amongst others:

- Access Controls

All security arrangements need to take into account the actions of employees, contractors, visitors and other persons who may have access to, or knowledge of the Cannabis cultivation or production site. Access controls are the first step in preventing access to Cannabis materials and assist in the detection and response of unauthorised activity.

Access controls should be in place to control both entry and exit to the perimeter of the facility or site, and equally important, within the facility itself. This may include locks or access passes between different sections of the facility and would need to consider the relevant level of risk of any given location. For example, a storage area for finished product may require more stringent access controls than an office area.

- Intruder resistance

Intruder resistance can be achieved through a number of physical and technological measures. Careful design, construction and ongoing maintenance are important considerations for ensuring intruder resistance. The objective is to deny, deter and delay any person or persons who may attempt to access the Cannabis cultivation/production site.

Intruder resistance refers to the concept of preventing or delaying unauthorised access or forcible attack and may also include the ability to detect attempts to tamper with the barriers.

- Crop integrity

Crop integrity means ensuring that the Applicant is growing the right number and chemo-types of plants. This will ensure the correct quality control and identification of specific marker compounds at pre-determined concentrations for the Cannabis species. In particular, cross-pollination of outdoor crops or where an enclosed air filtration system is not present, poses a high risk and requires appropriate minimisation strategies by the licence holder. Consequently, a person with a licence to produce Cannabis for purpose of hemp will not be permitted to cultivate Cannabis for medicinal purposes on the same site, in order to prevent cross-pollination. Furthermore, volunteer plants or rogue plants should be carefully controlled in outdoor sites to ensure that the permitted crop size is not contaminated or exceeded.

- Detection and response

While access controls and intruder resistance measures may prevent unauthorised access to Cannabis, the

licence holder should have measures in place to detect and respond appropriately to unauthorised access, theft or loss of Cannabis. The objective of these measures is to minimise the effect of a serious incident and, where possible, intervene to prevent any intrusion or losses. Examples of detection capability include monitored alarms and visitor escorting practices. Note that video recording of premises can be considered a detection control only when it is actively monitored.

- Procedural security measures

Effective security arrangements require integration between physical infrastructure and procedural measures. The objective of procedural security measures is to ensure that the licence holder has procedures in place that support and complement intruder resistance and detection measures, while also managing security during the handling of Cannabis in business operations. Procedural security should be reflected in operational practice and tested to ensure that this is the case.

- Disposal and destruction of Cannabis

Any Cannabis that is disposed of may still hold value on the illicit market; hence the security around disposal and eventual destruction of Cannabis remains critical to prevent diversion. In the event that a request for further processing of Cannabis by-products is made, compliance with the requirements for processed hemp fiber will apply. It is possible that licence holders will seek external assistance in disposal and destruction and any business arrangements should be carefully considered to ensure that risk is controlled.

It is important to note that the licence holder is responsible for preventing loss or theft during the destruction process, even where separate contractual arrangements are in place.

3.4.4 Transportation of Cannabis

Transport management systems with appropriate procedures and control measures must be developed and implemented. All transport activities must be recorded and reviewed. The key principle of transport security is to develop arrangements that adapt according to the risk associated with the movement. In some cases, transport of Cannabis may be outsourced to appropriate secure transport service providers. The licence holder remains responsible for the Cannabis under such arrangements.

Factors to be considered when preparing transport security arrangements include, but are not limited, to the following:

- Security requirements at the point of origin;
- Security requirements at the destination point (including handover);
- The duration of travel;
- Security considerations specific to any areas traversed;
- Size of consignment;
- Means of transport; and
- Areas where consignments may be travelling outside of the licensee's control.

The licence holder needs to be able to demonstrate effective controls around these issues before any activities can commence. Ongoing compliance with security arrangements is required to be maintained for the duration of any licence and failure to comply could result in revocation of the licence or referral of the matter to the relevant law enforcement agency.

Any changes to the arrangements must be reported to SAHPRA for assessment of the effect the changes have on the security of the Cannabis. These changes may require an amendment to the Applicant's licence.

Note: Annex A identifies some minimum security measures required to be in place. Applicants are required to develop and implement additional measures if required to address the infrastructure and operations of the specific site.

3.5 Building and Facilities

Maintenance policies for building and facilities must be developed and implemented. Buildings and facilities used in the processing of harvested crops must be clean, well ventilated and must not be used for other activities. Buildings must be designed in a manner that protects crops against pests and domestic animals.

The Cannabis for medicinal use must be stored:

- in suitable packaging materials;
- in rooms with concrete or similar floors which are easy to clean;
- on pallets;
- at a sufficient distance from walls; and
- well separated from other crops in order to prevent cross contamination.

Organic products must be stored separately from products not grown organically.

Buildings where plant processing is carried out must have changing facilities, toilets and hand washing facilities.

3.6 Equipment

Maintenance policy for equipment must be developed and implemented. Equipment used in plant cultivation and processing must be easy to clean in order to eliminate the risk of contamination. Equipment and machinery used for harvesting must be clean and in good working condition. Machine parts that come into direct contact with the harvested crop must be cleaned regularly and must be free from oil and contamination, including residual plant matter.

3.7 Production and Manufacturing

Standard operating procedures must be developed and implemented for all activities during production and manufacturing. These procedures must be reviewed at appropriate time intervals according to GMP practices.

3.7.1 Seeds and Labelling Material

Labelling of seeds and other plant material must allow for botanical identification in respect of species, variety, chemo-type and origin. The materials used must be traceable. Starting material must, as far as possible, be free from pests and disease in order to guarantee healthy plant growth. Cuttings of female plants and appropriate seed lines must be used as propagation material for the production of Cannabis.

During the entire production process (cultivation, harvest, drying, packaging), the presence of male plants and different species, varieties or different plant parts must be monitored and reported. Any unwanted or unnecessary plants and impurities found during the production process must be removed immediately.

3.7.2 Cultivation

Good Agricultural and Collection Practices must be applied in the cultivation of Cannabis, as determined by the Department of Agriculture, Land Reform and Rural Development (DALRRD) for food producing plants intended for human consumption.

Measures to be considered during cultivation include but are not limited to:

- Soil and fertilizer or alternative growth medium/ substrate;
- The reliance on irrigation; and
- The appropriate use of approved herbicides and pesticides.

3.7.3 Harvesting

Good harvesting practices with appropriate procedures, as determined by DALRRD, must be followed to ensure that the appropriate quality product is obtained for the intended use. The following are some of the measures to be considered but are not limited to those described:

- Male, damaged, and dead plants must be removed during this process. Harvesting must take place under the appropriate conditions, avoiding wet soil or extremely high air humidity. If harvesting occurs in wet conditions, additional care must be taken to avoid the adverse effects of moisture.
- During harvesting, procedures must be in place to ensure that no other plant species or Cannabis variety gets mixed with the Cannabis crop. The harvested crop must not come into direct contact with the soil.
- Directly after harvesting, the crop must be prepared for transport in clean, dry conditions (e.g. sacks, baskets, boxes). All containers must be clean and free from any residues from previous harvests; containers that are not in use must be kept in dry conditions, free of pests and inaccessible to domestic animals.
- Mechanical damage and compacting of the herbal drug that could result in undesirable quality changes must be avoided. In this respect, care should be taken to avoid: overfilling sacks/containers and stacking sacks/containers too high.
- Freshly harvested herbal material must be delivered to the processing facility as quickly as possible in order to prevent thermal degradation and mould growth.
- The harvested crop must be protected from pests and domestic animals.

3.7.3.1 Primary Processing

Primary processing includes washing, cutting before drying, decontamination, freezing, distillation, drying, etc. On arrival at the processing facility, the harvested crop must be directly unloaded and unpacked. Prior to processing, the material must not be exposed to direct sunlight (except in cases that specifically requires this) and must be protected from rain and adverse environmental conditions.

3.7.3.2 Drying

Drying conditions of crops must not adversely affect the quality such as drying on unsuitable surfaces, i.e. directly on the ground or under direct sunlight. A uniform drying speed of the crops and the prevention of mould growth by appropriate measures must be assured.

In cases where plant material is dried in the open air, the material must be spread in a thin layer, to ensure good air circulation of the drying racks placed at sufficient distance from the drying surface.

Where plant material is not dried in the open air optimal drying conditions, i.e. temperature and drying time must be followed, and recorded.

3.7.4 Packaging

The following are some of the measures to be taken during packaging operations but are not limited to those described.

Packaging procedures must be developed and implemented to ensure the integrity of the product during storage and distribution. The packaging process must be documented for quality and security purposes. Packaging of product can only occur after adequate removal and control of any sub-standard material or undesired objects.

The product must be packaged in clean, dry, uncontaminated packaging. The label of packed product must be clear, firmly fixed and made from non-toxic material. Re-usable packaging material must be well cleaned and dried prior to use. Packaging material must be stored in a clean, dry place that is free of pests and inaccessible to domestic animals. The packaging material must not contaminate the product.

3.8 Storage and Distribution

Storage and distribution procedures must be developed and implemented. Dried, packaged products and extracts must be stored in a dry, well ventilated building in which daily temperature fluctuations are limited.

Fresh products must be stored between 1 °C and 5 °C; frozen products must be kept at temperatures below -18 °C (or below -20 °C for long-term storage).

In the event of bulk transport, it is important to ensure dry conditions. To prevent mould formation or fermentation, it is advisable to use ventilated containers, transport vehicles and other ventilated facilities.

Decontamination of the storage area to combat pests must be carried out only where necessary and by authorised personnel. When frozen storage or saturated steam is used for pest control, the moisture content of the product must be controlled after treatment.

3.9 Special Provisions for the Production of Cannabis Intended for Processing into a Standardised Herbal Medicine

In this guideline, herbal medicine is understood to mean any medicine that contains exclusively herbal substance or herbal preparations as active ingredients.

A herbal medicine or preparation is regarded as one active entity in its entirety whether or not all the constituents with therapeutic activity are known.

Herbal medicine preparations are comminuted or powdered herbal preparations, extracts, tinctures, fatty or essential oils, expressed juices, processed resins or gums, etc., prepared from herbal preparations that are produced through fractionation, purification or concentration.

As a departure from the above, chemically defined isolated constituents or their mixtures are not considered herbal medicine preparations.

Herbal medicine preparations may contain other components such as solvents, diluents and preservatives.

If the Cannabis is intended for processing into a standardised herbal medicine, the Cannabis must be cultivated under such standardised conditions that the content of the constituents is constant. Protocols of the operations undertaken during the cultivation must be kept available.

The content of the main constituents, which includes Δ-9-tetrahydrocannabinol (Δ-9-THC) and cannabidiol

(CBD), is determined quantitatively. For a selection of the other constituents, fingerprinting with a suitable technique, such as GC-MS, GC, HPLC or TLC will be acceptable.

Unless it is proven that omitting the standardisation of one of the following elements results in a constant and reproducible product, at least the following must be standardised during cultivation:

- cultivar of the Cannabis plant;
- cultivation substrate;
- day length;
- light intensity;
- colour temperature of the lighting;
- atmospheric humidity;
- temperature;
- ventilation;
- plant age at the time of harvesting; and
- time of day of harvesting.

Unless it is proven that omitting the standardisation of one of the following elements results in a constant and reproducible product, at least the following must be standardised during drying:

- atmospheric humidity;
- temperature;
- ventilation; and
- drying time.

3.10 Documentation

Under the Single Convention, countries are required to inform the INCB of the quantities of Cannabis materials cultivated, produced, manufactured and used at each stage of the product supply chain to substantiate domestic requirements and forecast future requirements. Appropriate record keeping and reporting on the part of licence holders forms a core part of assisting the Department of Health in meeting these obligations. Furthermore, implementation of methodical and accurate record keeping procedures contributes to the management of the risk of diversion of Cannabis for illicit uses. To support the Department's international reporting obligation, the permit will include conditions with respect to a range of information components around both actual and estimated cultivation, production and manufacture.

Applicants must develop and implement a document management system which will allow all processes and procedures which may affect the quality of the product to be recorded in the documentation for each batch. The following in particular must at least be documented:

- the location of cultivation and the name of the person (cultivator) in charge;
- details of crops previously grown at that location;
- nature, origin and quantity of the herbal starting materials;
- the chemicals and other substances used during cultivation, such as fertilisers, pesticides and herbicides;
- irrigation water analysis;
- standard cultivation conditions, if applicable;
- particular circumstances which occurred during cultivation;
- harvesting and production which may affect the chemical composition;

- departure from standard cultivation conditions, particularly during the harvesting period;
- nature and quantity of the yield;
- date/s and time/s of day when harvesting occurred;
- drying conditions;
- measures for pest control.

Reports of soil analyses must be kept available in the dossier addressing “Location”.

All batches originating from one location must be clearly labelled (e.g. with a batch number). This must be done as early on in the process as possible. Batches originating from different geographic locations may be combined only if guaranteed to be the same, and if ensured that the mixture is homogenous. Mixing of batches must be documented. It must be recorded in the documentation for each batch that the cultivation, harvest and primary processing procedures were in accordance with these requirements.

All parties involved in the production process must demand that their suppliers document all relevant stages and elements of the production process for each batch.

Audit results must be recorded in an audit report. The audit report and concomitant analysis reports and other documents must be kept for at least ten years.

In addition to the aforementioned requirements, the following reporting and forecasting requirements must also be recorded:

- Details of cultivation area;
- Number of plants cultivated;
- Drying mechanism and average weight loss (where drying is conducted);
- Wet and dry weight of crops produced (total);
- Wet and dry weight of crops produced (components);
- End of year stock levels of crops produced (wet and dry weight);
- Transactions of Cannabis along the supply chain (including sale or physical movements);
- Purpose of production (medicinal or research – defined by the particular licence type);
- Forecast production for the next calendar year; and
- Forecast end of year stock for the next calendar year.

These reports require quantities of plants, Cannabis produced, and/or Cannabis resin produced. Note that the separation of total and component weights is to allow for the removal of the herbal flower in some production processes. In outlining the transactions along a supply chain, note that this includes any movement of materials for production or manufacture, to destruction, to consumption, or to a research purpose.

3.10.1 Record Keeping and Reporting

A licence holder should ensure that information created, sent and received in the course of conducting their business is appropriately recorded for the purposes of:

- compliance with obligations under licence conditions, the Act and Regulations;
- corporate memory and repeatable decision making;
- ensuring the integrity of information assets;
- facilitating business continuity as employees change over time;

- responding to auditing or inspectorate requirements, which may include unannounced inspections and
- meeting the security arrangements to record access to Cannabis and to Cannabis cultivation, production or manufacture sites.

The level of detail to be included in a particular record will need to factor in the complexity of the issue being addressed and any regulatory requirements that apply to the particular record.

As part of the application process Applicants are required to provide details of the arrangements in place to undertake record keeping activity.

Requirement will be included within the licence conditions and must be complied with for the duration of any Cannabis licence that is granted, including post surrender of a licence where applicable.

In the event of non-compliance with any licence requirements relating to documentation keeping, a Cannabis licence may be suspended or revoked and, if appropriate, the matter referred to the relevant law enforcement agency for further action. In addition, the licence holder must, as soon as reasonably practicable, notify SAHPRA of:

- the theft or suspected theft of Cannabis or Cannabis-related materials from a Cannabis site;
- the loss or suspected loss of Cannabis or Cannabis-related materials from a Cannabis site or any other place, including during transportation; and
- a discrepancy or suspected discrepancy in the number of Cannabis plants or quantity of Cannabis materials in the possession or under the control of a licence holder.

Should such circumstances arise, the licence holder must notify the SAHPRA and await direction. If a security breach has compromised security measures, then the licence holder must take steps to secure the Cannabis site and the Cannabis material.

The documentation requirements and key concepts related to record keeping and reporting are outlined further under Annex B – Requirements and Examples.

3.11 Good Manufacturing Practices (GMP) Related to Medicinal Cannabis and Related Products

This overview reflects on the GMP, quality, safety and efficacy requirements to be taken into consideration in the cultivation, harvesting and primary processing of Cannabis plants intended for medicinal use or in the preparation of non-sterile Cannabis-containing medicines. Cannabis for medicinal use includes:

- Cannabis,
- Cannabis materials,
- Cannabis preparations; and
- Finished Cannabis products

The cultivation method, cultivar, and primary processing of the Cannabis plant determine the ultimate properties of the active pharmaceutical ingredients (APIs). It is important to note that starting materials of herbal origin have a complex composition and can be characterised to only a limited extent through chemical or biological analysis. Therefore, an effective quality assurance system in the steps leading up to the production of the API is needed in order to guarantee reproducible quality. The goals for manufacture are to ensure that the Cannabis is:

- produced hygienically to keep microbiological contamination to a minimum;

- produced such that negative effects on the plants during cultivation, processing and storage are kept to a minimum; and
- produced under conditions that ensure that the therapeutic properties of the end product are constant and reproducible.

3.11.1 Compliance with Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP) and Good Agricultural and Collection Practices (GACP)

All manufacturers of a medicine shall comply with all relevant aspects of Good Manufacturing Practices applicable to medicines which are further described in SAHPRA Guideline, Guide to Good Manufacturing Practice (GMP) for Medicines in South Africa.

Applicants are invited to scrutinise specifically Annexure 7 which deals with the agricultural aspects relating to the production of starting materials derived from a plant.

Further to this, the PIC/S Guide to Good Manufacturing Practice (GMP) for Medicinal Products Part II adopted by the SAHPRA addresses the GMP requirements for Scheduled Substances

In addition, Applicants are invited to the WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants (http://apps.who.int/medicinedocs/pdf/s4928e/s4928e.pdf) that address the requirements for good agriculture and collection practises when dealing with the herbal products.

All conditions set forth in the above guideline pertaining to herbal products and manufacture of Scheduled Substances must be met. Applicants are advised that any alternative standards that they intend to use must be specified, referenced and justified.

Other guidelines that Applicants may refer to include:

- ICH Q7 Guideline: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients; and
- WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues. http://apps.who.int/medicinedocs/index/assoc/s14878e/s14878e.pdf

3.11.2 Quality and Safety

The list of the European Pharmacopoeia (Ph. Eur.) general monographs that may be relevant to ensure compliance with quality and safety of Cannabis include:

- Herbal Drugs (1433);
- Herbal Drug Preparations (765);
- Herbal Drug Extracts (765); and
- General monographs for dosage forms e.g. Oromucosal Preparations.
- EMA guideline - Guidance on Specifications: Test Procedures and Acceptance Criteria for Herbal Substances, Herbal Preparations and Herbal Medicinal Products/Traditional Herbal Medicinal Products (CPMP/QWP/2820/00 Rev 2).

In addition, the American Herbal Pharmacopoeia monograph on Cannabis can serve as a basis for providing standards of identity, analysis and quality control of Cannabis. Analytical tests to be performed shall include the following, but are not limited to those mentioned:

- Appearance;
- Foreign Material;

- Fineness;
- Identification A: Microscopic Properties;
- Identification B: TLC;
- Microbiological Contamination;
- Aflatoxins;
- Pesticides;
- Heavy Metals;
- Loss on Drying; and
- Assay and Related Substances.

The above tests are recommended on the basis that:

- Several plant species have morphological characteristics comparable to Cannabis, leading to contamination. Therefore, the inspection of microscopic and macroscopic characteristics can assist in distinguishing Cannabis from contaminants.
- Growth enhancers and pesticides or fungicides introduced during the cultivation and storage can be a health hazard to the consumer.
- Cannabis produced for intended medicinal purposes must also be free from foreign matter and from moulds and bacteria that have a high likelihood of pathogenicity.
- Primary cannabinoids of interest are tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN). Positive identification and quantitation of these substances, especially the THC/CBD ratio, is the primary objective to ensure reproducible potency of the product.

Analytical tests must be validated. With regard to in-house test methods, guidance on the principles and practice of validation of analytical procedures can be found at ICH Harmonised Tripartite Guideline Validation of Analytical Procedures: Text and Methodology Q2 (R1).

Guidance on the sample size and sample preparation of herbal plant material for analysis is given in Ph. Eur. method 2.8.20 Herbal Drugs: Sampling and Sample Preparation.

3.12 Compliance and Enforcement

Cannabis and its products, where a licence has been granted, shall be subject to strict monitoring to avoid any unintended usage. Monitoring of Cannabis for medicinal use has to cover the entire chain, i.e. cultivation, manufacture, import, export, distribution and access for medicinal or research purposes.

The SAHPRA Inspectorate conduct compliance and monitoring activities of all regulated parties to ensure compliance with regulations, licence and permit requirements. These activities include compliance investigations and inspecting licensed sites, as well as sites applying to be licensed to conduct regulated activities. Licensed producers and manufactures are required to comply with all applicable legislation and regulations.

In addition, where appropriate, the SAHPRA and Department of Health (DoH) work with partners including the Department of Agricultrure, Land Reform and Rural Development (DALLRD), the South African Police Services (SAPS), the South African Revenue Service (SARS) and professional regulatory bodies to help ensure controlled substances (including Cannabis) are handled effectively and remain in legal distribution channels. As appropriate, the SAHPRA refers illegal activity to the relevant authorities.

3.13 Access to Unregistered Cannabis Containing Products for Medicinal Use

In exceptional cases, unregistered Cannabis / cannabinoid-containing medicines may be prescribed by medical practitioners for medicinal purposes. The Medicines Act enables patients to access Cannabis for therapeutic purposes through the provisions of Section 21 of the Medicines Act. In order for patients to access these unregistered medicines, the registered medical practitioner/ authorised prescriber needs to apply to the SAHPRA to allow for a specific named patient to use the unregistered medicine.

As with any other unregistered medicine, the quality of the medicinal Cannabis and/or cannabinoids must be of acceptable standard, as determined by the SAHPRA. It is recommended that the medicine is registered by a regulatory authority with which the SAHPRA aligns itself, including the United States Food and Drug Administration (FDA), Australian Therapeutic Goods Administration (TGA), Health Canada, European Medicines Agency (EMA) and Swissmedic.

The Section 21 application portal and stipulated fee can be accessed on the SAHPRA website sahpra.org.za/unregistered-products/.

4. REFERENCES

The following related documents are referenced:

4.1 The Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended. http://www.SAHPRAza.com/Publications/Index/9

4.2 General Regulations made in terms of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended. http://www.SAHPRAza.com/Publications/Index/9

4.3 Guide to Good Manufacturing Practice (GMP) for Medicines in South Africa, version 5, November 2010. http://www.mccza.com/Publications/Index/1

4.4 American Herbal Products Association (2014). Recommendations to regulators: Cannabis manufacturing, packaging, labelling, and holding operations. Message posted to https://d3n8a8pro7vhmx.cloudfront.net/americansforsafeaccess/pages/7453/attachments/original/1406050488/14_0722_AHPA_Recommendation_for_Regulators_MPLH-For_Distribution.pdf?1406050488

4.5 Australian Government Department of Health, & Therapeutics Goods Administration. Good manufacturing practice - an overview. Retrieved April 29, 2013, from https://www.tga.gov.au/goodmanufacturing-practice-overview

4.6 ElSohly, M., Chandra, S., Lata, H., Williamson, E., Upton, R., & Slade, D. (2013). In Upton R., Cracker L., ElSohly M., Romm A., Russo E. & Sexton M.(Eds.), Cannabis inflorescence and Cannabis spp. standards of identity, analysis, and quality control. Scotts Valley, CA: American Herbal Pharmacopoeia.

4.7 Food and Drug Administration (2006). Guidance for industry quality systems approach to pharmaceutical cGMP regulations. Pharmaceutical CGMPs,

4.8 Health Canada. Additional information for licenced producers under the access to Cannabis for medical purposes regulations. Retrieved August 24, 2016, from http://www.hc-sc.gc.ca/dhpmps/marihuana/info/add-supp-eng.php

4.9 Health Canada. Archived-guidance document-building and production security requirements for marihuana for medical purposes. Retrieved June 19, 2013, from http://www.hc-sc.gc.ca/dhpmps/marihuana/info/bp-securit-eng.php

4.10 Health Canada. Guidance document for the industrial hemp regulations. Application for an industrial hemp licence. Retrieved November 21, 2016, from http://www.hc-sc.gc.ca/hcps/pubs/precurs/hemp_app-chanvre_dem-eng.php

4.11 HempHacker. Compliance vs. good manufacturing practices. Retrieved May 14, 2016, from http://www.hemphacker.com/tag/ich/

4.12 HempHacker. GMP Cannabis and the marijuana industry - a short introduction. Retrieved December 20, 2015, from http://www.hemphacker.com/gmp-Cannabis-and-the-marijuana-industry/

4.13 HempHacker. (2016). CGMP definitions for the Cannabis industry-21CFR part 210. Retrieved May 16, 2016, from http://hemphacker.com/cgmp-definitions-for-the-Cannabis-industry-21-cfr-part-210/ Johnson, R. (2014). Hemp as an agricultural commodity.

4.14 Ruppel, T., Kuffel, N., PerkinElmer, I., & Shelton, C. Cannabis analysis: Potency testing identification and quantification of THC and CBD by GC/FID and GC/MS. Waltham, MA 02451 USA: PerkinElmer, Inc.

4.15 Scholten, W. K. (2003). Guidelines for cultivating Cannabis for medicinal purposes [voorschriften voor de verbouw van Cannabis voor medicinale doeleinden]. Annex to the regulation of the minister of health, welfare and sport of 9 January 2003, GMT/BMC 2340685, containing policy guidelines for the decision on applications for opium act exemptions (policy guidelines opium act exemptions) (authorised English translation). Journal of Cannabis Therapeutics, 3(2), 51-61.

4.16 The Association of Public Health Laboratories Work Group. (2016). Guidance for state medical Cannabis testing programs. Silver Springs, Maryland: Association of Public Health Laboratories.

4.17 The Office of Drug Control. Medicinal Cannabis manufacturing licences and permits. Retrieved November 2, 2016, from https://www.odc.gov.au/publications/medicinal-Cannabis-manufacturelicences-and-permits

5. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the old guideline 2.44 for Cannabis Cultivation. It will be reviewed on this timeframe or as and when required.

6. ANNEXURES

6.1 ANNEXURE A: Security

Applicants should note that security conditions for growing or testing Cannabis, or manufacturing of a medicine containing cannabinoids are not limited to those outlined below and Applicants are required to develop and implement additional measures to ensure that the required security level is achieved.

1 Access Controls **Mandatory requirement:** The licence holder to maintain a set of access controls preventing unauthorized access to Cannabis, including the site as a whole and during transportation. This must include recording of movements at both internal and external perimeters.		
Expectations	**Rationale**	**Example**
Access to the Cannabis site should be limited to people required to be on site.	This is to minimise the number of people that are allowed onto the Cannabis site. The nature of the business should also be kept discreet.	No access to the general public – gates to block access. Visitor policy that documents classes of people allowed on site (and circumstances). Sign in/out registers. No external advertising of the business / Cannabis not visible to the public.
2 Intruder resistance **Mandatory requirement:** The licence holder to maintain an intruder resistant Cannabis site, designed to prevent intrusion by external parties and to prevent removal of Cannabis from within the Cannabis site.		
Expectations	**Rationale**	**Example**
The Cannabis site should be designed and maintained to deter intruders	Through its physical design, the ability to covertly access the Cannabis site is reduced and therefore intruders may be deterred from breaking in.	There should not be shrubbery immediately against fences. Sites should be well lit, and no large objects stored near access points.
The outer perimeter of the Cannabis site should have an intruder-resistant physical barrier.	To ensure that an intruder is denied, delayed or deterred from entering the Cannabis site.	Climb-proof perimeter fencing that complies with SABS standards. Mechanisms to prevent entry from above or below the Cannabis site

Cannabis should be protected by two or more layers of intruder-resistant physical barriers.	The illicit value of Cannabis requires that it has an added layer of security to deny, deter and delay an intruder. Two layers of resistance seek to control the risk of forcible attack.	For an outdoor operation, the second layer could take the form of another layer of fencing that complies with SABS standards. For an indoor operation, the Cannabis could be contained in a separate room that is securely locked.
Expectations	**Rationale**	**Example**
For outdoor sites, there should be measures in place to prevent cross-pollination.	Cross-pollination may result in different strains and cannabinoid concentrations leading to breaches of permit conditions.	Mechanisms to prevent cross-pollination such as the utilisation of distance, crop time separation, natural barriers, pollen traps or exclusions zones.
The layers of intruder-resistant physical barriers should be constructed so that they cannot be breached by a single movement or act.	This is to ensure that the two layers of security provide two points of defence against any intrusion.	The two layers of barrier should be at a distance that ensures both fences are effective in their own right. A room containing Cannabis should not share a wall with the exterior of the building unless that exterior wall has additional controls.
Any receptacle that contains Cannabis, including waste disposal units, should be contained within two layers of intruder-resistant physical barriers.	This is to ensure the physical security of bins where Cannabis may be placed or storage containers of Cannabis.	Bins are kept in a locked room or within two layers of fencing. Given that waste disposal might be only an occasional activity, additional controls are required to store material over a longer period.
Refined Cannabis (such as an extracted flower product) should be protected by two layers of intruder-resistant physical barriers, one of which should be a secure storage unit.	The term 'secure storage unit' allows for the licence holder to provide security that is appropriate to the volume of Cannabis to be stored. The additional security requirement reflects the risk of diversion of the Cannabis in this state.	A safe, vault or strong room depending on the volume of Cannabis to be stored. Additional access controls into such spaces should also be considered.
The Cannabis site should not identify the nature of activities at the Cannabis site.	It is important to not identify the existence of the Cannabis site to prevent targeting by criminals.	The site should be void of signs that identify the company or business. Vehicles that identify the company should not be visible to the public. Cannabis should not be visible from the perimeter of the site.

Expectations	Rationale	Example
The Cannabis site should be designed and maintained to prevent the theft or loss of Cannabis during daily operations.	Thorough careful physical design, the ability for an employee to access and remove Cannabis without authorization is minimized. Employees and visitors should not be presented the opportunity to remove Cannabis product. This may require the use of clothing inspections or pocketless clothing, and/or restrictions around bags and other containers.	Work areas should be separate from break areas. Physical separation of office space from Cannabis cultivation and production sites. CCTV on areas where people work with Cannabis. Avoid constructing areas that are hidden from monitoring.

3 Detection and response

The licence holder to have physical security systems and documented procedures in place to detect and respond to intrusion or unauthorized access, theft or loss of Cannabis.

The licence holder to have arrangements in place with emergency services, police and local government authorities to deal with loss or theft of Cannabis.

Expectations	Rationale	Example
The Cannabis site should have a physical intruder detection system that monitors and records activity.	This is to detect if intrusion or unauthorised access occurs and provide the evidence for any possible investigation.	CCTV Alarm system; Motion sensors. Cell Phone alert system to the Applicant of any breach of security
The licence holder should have procedures in place to maintain and test the efficacy of the security equipment and procedures.	This is to ensure that the system is working as expected.	Regular testing of security systems and drills for procedures. Regular inspections of equipment and infrastructure.
The Cannabis site should be physically visited on a daily basis.	This is to verify that a breach of security has not occurred.	Staff making daily perimeter inspections. Outsourced security services.
The licence holder should have procedures in place to rapidly respond to unauthorised access.	The procedures should outline how the licence holder uses the physical detection system with operational procedures to detect intrusion or unauthorised access.	Procedures to respond to alarms, regular and random checks of access logs, and review of CCTV footage. Training and regular drills for staff in preparation for intrusion.

Expectations	Rationale	Example
The licence holder should have procedures and clear lines of responsibility to ensure local services, police and SAHPRA are contacted in the event of a serious incident.	This is to ensure that the licence holder and employees are prepared and take the necessary steps to involve the relevant services. It is also important that local services are aware of the potential risks around criminal activity (for police) or fire or injury (emergency services).	Policies that document the events that require police intervention and procedures to follow in this event. Procedures to handle immediate threats. Procedures for contacting the SAHPRA.
The licence holder should retain a backup of all video recordings. The licence holder should retain all access records (for electronic passes) for the period of the licence.	This is to ensure that recordings can be reviewed to identify the source of theft or loss and or assistance of law enforcement during any potential investigation.	IT systems to back up CCTV recordings. Access logs on pass access (where available) are much smaller in size and may be useful in security auditing.
4 Procedural security measures **Mandatory requirement:** The licence holder to design and maintain operational policies and procedures to support physical security measures and prevent the theft or loss of Cannabis.		
Expectations	**Rationale**	**Example**
The licence holder should have policies and procedures in place to minimise the opportunity of theft or loss of Cannabis.	Ensuring staff and visitors are aware of procedures around activity on a Cannabis site reduces the risk of diversion. Divergence from standard operating procedures should be seen as a potential concern and reviewed.	Staff rotation or scheduling policy. Daily procedures for checking inventory and cross checking by a second person.
The licence holder should have policies and procedures in place for responding to unauthorised access or theft of Cannabis by an internal source.	This is so the licence holder is prepared to respond to a situation appropriately. The existence of such policies may also act as a deterrent.	Policies and procedures for staff management and referral to SAHPRA and law enforcement. Contingency plans in the event of staff suspension or termination of service.

Expectations	Rationale	Example
Cannabis should be reconciled against records once custody of the Cannabis is formally transferred, including receipt.	This is to make a clear point where responsibility is transferred and to identify any loss or theft at different stages.	Procedures for transfer and receipt of the Cannabis. Procedures to validate tamper-evident packaging along chain of custody.
The licence holder should have procedures to track the movement of Cannabis through the Cannabis site and during operational activities.	This is to ensure that theft or loss of Cannabis can be identified.	Plant stocktakes and mortality registers. Procedures that control and document the transfer, testing, or cloning of plants.

5 Disposal and destruction of Cannabis

Mandatory requirements: The licence holder to have procedures in place to ensure that all Cannabis that is not to be manufactured into a medicinal product is disposed of or destroyed in a safe and secure manner. The licence holder to provide details of the method of destruction of Cannabis and any arrangements with third parties to dispose of or destroy Cannabis.

The licence holder to have arrangements in place with emergency services, police and local government authorities to deal with disposal or destruction of Cannabis.

Expectations	Rationale	Example
The licence holder should have procedures in place that identify activities that generate Cannabis that requires disposal or destruction.	To ensure that all Cannabis is accounted for, and appropriately disposed of, or destroyed.	Standard operation procedures around destruction, including storage and transport of material to destruction.
Any equipment used for cultivation or production of Cannabis should be regularly cleaned and any Cannabis that is attached to the equipment disposed of or destroyed.	During the production process, resin may become attached to the equipment. Cleaning ensures that any Cannabis is removed from the equipment and prevents the risk of diversion.	Procedures for cleaning equipment between tasks or moving to another site. Designated waste bins for Cannabis with procedures for emptying.
Contracts with third parties should outline security requirements to ensure that Cannabis is not diverted before or during disposal or destruction.	This is to address the risk that any third party presents where Cannabis is outside of the licence holder's control.	Contract with a location that has a secure site or approval from a law enforcement agency. Record keeping from the third party to demonstrate the completion of the task.

6 Transportation of Cannabis **Mandatory requirements:** The licence holder to have procedures and contingency measures in place to ensure the transportation of Cannabis is discreet, and that security of Cannabis is maintained during transportation and at receipt at the final destination.		
Expectations	**Rationale**	**Example**
During the transportation Cannabis should be contained within two intruder-resistant physical barriers.	This expectation should be covered regardless of mode of transportation - air, road, rail or shipping.	Cannabis stowed in a secure locked receptacle in a secure vehicle. In transit, Cannabis is stowed in a secure locked receptacle within a secure locked room.
Cannabis should be transported in tamper-evident containers or packaging.	This is to ensure integrity of the consignment along the end to end transport route.	Tamper-evident tapes or seals. Security bags or pouches. Time delay access to containers.
During transportation, the Cannabis should have a physical intruder detection system that monitors and records activity.	This is to alert the person in control of the Cannabis to a possible intrusion or unauthorised access to the Cannabis.	Time delay safes/ locking systems. CCTV recordings. Alarms/ motion detection systems. Physical guarding.
A consignment of Cannabis should not be marked in such a way that identifies its contents.	This is to keep the contents of the container as discreet as possible.	No external signage or symbols on vehicles or containers that would indicate that Cannabis is being transported.
The licence holder should be able to identify who has custody of the Cannabis at any point in time during transportation.	An expectation from law enforcement agencies that the consignment be tracked. Custody control is important to prevent substitution of product.	GPS tracking chips to accompany the consignment. Barcode tracking and log systems. Procedures for reporting when Cannabis is exchanged and responsibility are securely transferred.

Expectations	Rationale	Example
The chain of custody of Cannabis during transportation should be clearly documented.	This enables any potential investigation to determine the point of weakness in the chain of security and makes people in the process accountable. This is to prevent the loss of product through negligence.	Registers with signatures and names to record people who handle Cannabis. Procedures that outline the point in time where someone accepts responsibility for the Cannabis. Training for staff involved in the process. Contractual obligations documented for third parties with responsibility for the Cannabis.
The licence holder should have procedures in place to detect the theft, substitution or loss of Cannabis during transportation.	This requirement is to address the situation where it may not be obvious that Cannabis has been removed, particularly when an employee has authorized access to Cannabis.	Procedures to reconcile inventory when Cannabis is handed from one person to another. Procedures to verify tamper proof packaging/ seals on containers.
Details of delivery schedules and routes should be disclosed only to people that have a need to know.	To prevent stealing or diversion of a consignment through leaked information.	Internal office security to conceal plans. Minimal time notification of routes or schedules to people involved.
Delivery schedules and routes should be regularly varied.	To prevent the observation of the transportation practices for the Cannabis, which could lead to heisting attempts.	Internal office security to conceal routes and schedules. Policy for regular alteration of routes and schedules and staffing.
Delivery routes should be planned to ensure the minimum number of stops along the route.	For long distance trips, some stops, for example for refuelling, may be essential. This requirement is to ensure any stops are planned and Cannabis is secure during the stops.	Routes should be the most direct possible. Vehicles should be filled with fuel before travel to avoid the need to stop for refuelling.
The vehicle should be appropriately secured during any planned stops during road transport of Cannabis.	The vehicle should be appropriately secured during any planned stops during road transport of Cannabis.	When refuelling is required, two people are present.
The licence holder should be aware when any deviation or delay occurs to a planned delivery route.	To ensure that the licence holder can respond to any possible issues and organize additional security if required.	Reporting procedures for incidents.

Expectations	Rationale	Example
The licence holder should have a contingency plan in the event that the Cannabis cannot be received at any destination.	To ensure Cannabis will be controlled and secured in the event of any failures in the planned transport route.	A backup location for storage of Cannabis that complies with site security expectations. Where possible, return of the consignment to the Cannabis site. Different routes for the return journey.
The licence holder should have contingency plans in place in the event of vehicle breakdown, incapacitation of a driver, accidents or road closures.	This is to secure drivers or third parties are prepared for any possible issues that may arise.	Regular training for staff in contingency plans. Clear reporting mechanisms.

6.2 ANNEXURE B: Record keeping and reporting

1 Record Keeping **Mandatory requirement:** It will be a condition of the licence that the licence holder has record keeping arrangements in place to record the amounts of Cannabis that, during the period of the licence, the applicant: cultivates and obtains; produces and stores; supplies to the holder of a manufacturing licence, destroys or disposes of.		
Expectations	**Rationale**	**Example**
Records should be created as close as possible to the event to which they relate, by a person with the appropriate oversight of the activity to which the record relates.	This is to ensure that record keeping is accurate and timely in order to prevent errors or neglect.	Record created by employee undertaking the stock take at the same time that the activity is being performed. Regular internal procedures for verify amounts of Cannabis on site.
Records should be maintained in a system that ensures the management of use, tracking and understanding of records.	This is to ensure that records are readily available for reporting to SAHPRA as required and accessible during inspection activities by SAHPRA.	Manual or digital filing protocols. Software systems. Version controls.
The licence holder should have procedures in place to facilitate access to records during an inspection by SAHPRA (including unannounced inspections).	Verification of records will be an important activity during an inspection. This ensures that records can be viewed.	On site records or movement of relevant records to the site for inspections. Access to digital systems.
The records should be stored in a manner that maintains continuity.	This is to prevent the loss of records through natural disaster, criminal damage or negligence.	Records backed up off site. Fire and flood proof facilities.
Employees responsible for the maintenance of records should be clearly identifiable.	This is to ensure that the people managing records understand their obligations and to enable trace back in the event of a discrepancy.	Clearly documented procedures and role accountabilities.
Distribution of records should be limited to those with a legitimate business need to access the records.	This is related to procedural measures to prevent the distribution of information further than necessary.	Policies, access controls and procedures to limit the number of people who need to know information.

Expectations	Rationale	Example
The licence holder should record details of plant mortality to reconcile with permit requirements.	This will account for any losses and enable the reconciliation of amounts of Cannabis.	Plant mortality register that lists the number of plants that die.
The licence holder should have records that document chain of custody of the Cannabis during transportation.	To ensure that the handling of Cannabis while being transported can be traced and tracked in the event of a discrepancy, theft or loss.	Registers that are signed by people involved in handling and transporting the Cannabis.
Licence holders should ensure that appropriate resources are allocated to implement and accurately maintain their record keeping arrangements.	To ensure that adequate time is available to complete records and facilitate compliance with reporting requirements.	Standard operating procedures that embed record keeping activities. Sufficient staff resources to ensure record keeping can be undertaken.
2 Reporting – stock and forecasts **Conditional requirement:** In applying for a permit, the licence holder to provide information relating to the size of a Cannabis crop, the number of plants, and the amount of Cannabis or Cannabis resin produced / intending to be produced. As part of the conditions of a licence, the licence holder will be required to provide information necessary to support the Department of Health reporting to the INCB.		
Expectations	**Rationale**	**Example**
Records should include the number of plants cultivated, the size of the growing space and the yields.	Differing means of production will result in different plant spacing, number and ultimately crop sizes.	Records of plants per permit and detail of cultivation space. Internal procedures to verify amounts of Cannabis.
The licence holder should have mechanisms to record separation of plant components and undertake both wet and dry weighing of crops.	This is to manage the risk of diversion given both the high illicit value of dried Cannabis flower, and the substantial difference in weight of Cannabis between wet and dry conditions.	Procedures to track and weigh Cannabis along the production process. Practices around internally tracking of crops.
The licence holder should maintain records of all transactions involving Cannabis distribution or movement events.	Understanding of the movements of Cannabis for supply, destruction, production or any other purpose is a diversion risk control.	Registers of Cannabis movements or transactions. Examples under plant mortality and chain of custody (above) are also relevant to this control.

The licence holder should provide annual forecasts of anticipated production and projected "end of year" stock for each calendar year.	Such forecasts will allow SAHPRA to oversee supply and prevent unnecessary stockpiling of Cannabis.	Annual reporting arrangements with the Department of Health.

3 Reporting – incidents

Mandatory requirement: The licence holder to have arrangements in place to ensure that SAHPRA is notified of actual and suspected events involving:

- A security breach at, or unauthorized access to, a Cannabis site
- A theft or loss of Cannabis
- A discrepancy in quantity of Cannabis
- A serious incident involving Cannabis.

Expectations	Rationale	Example
In the case of known or suspected criminal activity (theft or breach), the licence holder should immediately engage with their local law enforcement agency.	Law enforcement agencies are the first point of contact in response to a criminal act.	Incident response procedures contain contact details for local law enforcement agency.
The licence holder should provide SAHPRA with formal, written notification of any such events.	This is to ensure that SAHPRA can respond appropriately and to allow for consideration of any potential licence or permit breaches.	SAHPRA will work with licence holders to rectify inadvertent condition breaches.
The licence holder should notify SAHPRA immediately after identifying the event.	This is to allow SAHPRA to respond to any immediate issues. Note: Such reporting should only be made after law enforcement reporting occurs, and after actions to secure the site and / or response to safety concerns have been addressed.	SAHPRA will work with the licence holders to rectify inadvertent condition breaches.

Expectations	Rationale	Example
Licence holder should provide the SAHPRA with descriptions of the matter being reported, including but not limited to: • Details of the volume of Cannabis unaccounted for • When and how the issue was detected • When and how the event was believed to occur • The current status of security at the Cannabis site • Any action taken by the licence holder • Any records that can support investigation into the matter.	This information will assist SAHPRA in responding to the situation and ensures that the licence holder has gathered relevant facts about the matter.	Development of incident management protocols including incident report forms to submit to SAHPRA. Provision of security records, access registers and documented records of stock levels.