**REPUBLIC OF ALBANIA**

**MINISTRY OF AGRICULTURE AND RURAL DEVELOPMENT**
**MINISTER**

No.451/9, Prot. Tirana, on.20.01. 2025

# INSTRUCTION

**No. 3 , Dated 20 . 01 . 2025**

**ON**

# QUALITY CONTROL METHODS, RELATED TO CANNABINOID CONTENT, AS WELL AS PHYSICO-CHEMICAL AND MICROBIOLOGICAL CONTROL, FOR PACKAGING METHOD, FORM AND QUANTITY

Pursuant to Article 102, point 4, of the Constitution, Article 28, point 5, of Law No. 61, dated 21.7.2023, "On the control of the cultivation and processing of the *cannabis plant* and the production of its by-products for medical and industrial purposes",

**I HEREBY INSTRUCT:**

## Article 1
## Purpose

1. The purpose of this instruction is to determine the methods for quality control, physico-chemical and microbiological control for samples of the *cannabis plant* , before packaging the dry material or other subsequent stages, as well as the packaging method, form and quantity.

## Article 2
## Object

1. All permitted or licensed entities, within the meaning of Law No. 61/2023, are obliged to conduct quality control analyses for *cannabis plant* samples in accordance with the specific monographs 3028 as defined in Annex No. 1 attached to and forming part of this instruction as well as the monographs on herbal materials (2.8) of the European Pharmacopoeia (Eur.Phar) for the total levels of cannabinoids such as: *delta-9 tetrahydrocannabinol*

(THC), *cannabidiol* (CBD) and *cannabinol* (CBN); physico-chemical and microbiological control; as well as other additional analyses in accordance with the legal requirements of the importing country.

2. The criteria and procedures regarding the packaging method, form and quantity for the dried *cannabis plant* are implemented in accordance with the specific Eur-Phar, EU-GMP- and EU-GACP standard.

**Article 3**
**Definitions**

All terms defined in this instruction have the same meaning as those defined in Law No. 61/2023, "On the control of the cultivation and processing of the *cannabis plant* and the production of its by-products for medical and industrial purposes".

For the purposes of this guideline, the additional definitions have the following meanings:

1. **Δ9-Tetrahydrocannabinol (Δ9-Tetrahydrocannabinol, delta-9 THC)** – is a natural cannabinoid that appears with 4 stereoisomers ((-)-trans, (+)-trans, (-)-cis, (+)-cis) and is found in the cannabis plant.
2. **Total Δ9-Tetrahydrocannabinol (delta 9- THC total)** – refers to the total amount of delta-9 THC and delta-9 THCA calculated according to the specific monograph of the European Pharmacopoeia.
3. **Δ9-Tetrahydrocannabinolic acid (Δ-9 Tetrahydrocannabinolic acid, delta 9-THCA)** – is a natural active ingredient found in the cannabis plant in the form of the biosynthetic precursor to delta-9 THC.
4. **Cannabidiolic acid (Cannabidiolic acid, CBDA)** – is a natural active ingredient found in the cannabis plant in the form of the biosynthetic precursor to CBD.
5. **Cannabis plant** – refers to different varieties of the plant, such as cannabis sativa, cannabis indica, and cannabis ruderalis, and includes all parts of the plant.
6. **Cannabis** – refers to the flowering and fruiting tops of the cannabis plant from which the resin has not been removed.
7. **Certificate of Analysis** – is a document issued by an accredited laboratory in accordance with ISO17025 and approved according to the provisions of Law 61/2023.
8. **EU-GACP** – European Good Agricultural and Collection Practices.
9. **EU-GMP** – European Good Manufacturing Practices.
10. **Eur.Phar** – European Pharmacopoeia.
11. **GLP (Good Laboratory Practices)** – refers to a set of principles/rules aimed at ensuring the quality, integrity, and reliability of laboratory testing, applied in planning, performing, monitoring, recording, reporting, and archiving laboratory tests.
12. **Cannabidiol (Cannabidiol, CBD)** – is one of the natural cannabinoids, primarily biosynthesized in the stereoisomer (-)-trans found in the cannabis plant.
13. **Cannabinoids** – refers to the totality of substances biosynthesized in the cannabis plant, structurally similar to THC, which have an affinity for binding to specific receptors in the human body.
14. **Cannabinol (Cannabinol, CBN)** – is a natural metabolite of delta-9-Tetrahydrocannabinol.

15. **Total Cannabinol** – refers to the total amount of CBN and CBNA, calculated according to the specific monograph of the European Pharmacopoeia.
16. **Sample** – is a quantity of material taken in accordance with an approved procedure from a number of lots for laboratory testing purposes.
17. **Lot Number** – refers to an identifying number for each production batch, produced under the same conditions.
18. **Measurement Uncertainty** – refers to a range of values that accompanies a measurement result, indicating the degree of confidence and accuracy of this result. It provides information on the quality and validity of the measurement results and is expressed as a numerical value (interval), within which the measurement result lies, accompanied by a 95% confidence level.
19. **SOP (Standard Operating Procedure)** – is a detailed document that describes the specific steps to be followed to carry out a task or process consistently and in accordance with established standards.

## Article 4
## Analysis methods

1. The methods of analysis for the *cannabis* plant for medical and industrial purposes, for the determination of the total concentration of *delta-9 tetrahydrocannabinol* (THC), *cannabidiol* (CBD) and *cannabinol* (CBN), physico-chemical and microbiological control, must be in accordance with the European Pharmacopoeia (Eur.Phar), monograph 3028, according to Annex No. 1 attached and forming an integral part of this instruction, as well as with the requirements of the importing country.

2. Analyses carried out according to point 1 of this Chapter are reported referring to the dry weight of the *cannabis plant* for:

   a) Total concentration of delta-9 *tetrahydrocannabinol* (THC) and delta-9 *tetrahydrocannabinolic acid* (THCA);

   b) Total concentration of *cannabidiol* (CBD) and cannabindiol acid (CBDA);

   c) Total *cannabinol* (CBN) concentration;

   d) Physico-chemical control including macroscopic, microscopic identification and identification by high-performance thin-layer chromatography (HPTLC);

   e) Microbiological control;

   f) Pesticide residue analysis;

   g) Heavy metal levels (arsenic, mercury, lead, cadmium);

   h) Mycotoxin presence;

   i) Other analyses specified in the European Pharmacopoeia monographs.

3. Results of the analyses and measurement uncertainty (expressed as the measured value ± measurement uncertainty) are reflected in the certificate of analysis, where the confidence

limits of the performed measurements are stated. The final value of each analysis is considered the measured value with the addition of the measurement uncertainty, in accordance with the certified methodology.

4. For industrial *cannabis*, if the final result of the analysis of the representative sample exceeds a total THC concentration of 0.8%, the entire lot that this sample represents is subject to destruction according to the provisions of Law No. 61/2023.
5. The sample of the industrial *cannabis plant* , which is documented for human, animal consumption or cosmetic use, is subject to all the tests cited in point 2 of this article, taking as reference the values allowed under the legislation of the importing country.
6. Industrial *cannabis* plant , which used for sectors as defined in point 9 of Article 3 of Law No. 61/2023, except for those included in the categories of point 5 of this article, is subject only to analyses in letters “a”, “b”, “c”, “d” according to point 2 of this article.
7. The residue of the cannabis plant, after quality control, is destroyed by the laboratory in accordance with the relevant procedures, depending on the type of sample, using either incineration at over 800 degrees or chemical destruction methods, in compliance with the respective description in the Instruction "On the detailed procedure for the destruction of *cannabis* plants."
8. The procedure for the destruction of *cannabis* plant residues from the quality control sample is carried out as follows:
   - The laboratory notifies the Agency in writing within 3 working days regarding the type, quantity, THC content according to the certificate of analysis of the batch to which the residual sample material belongs, the method of destruction it intends to perform as stipulated in this Instruction, the scheduled date for destruction (in accordance with Annex No. 3 attached and integral to this Instruction), as well as the identifying details of the laboratory.
   - The Agency, within 5 (five) working days from receiving the notification from the laboratory, reviews the notification and confirms the destruction date in the presence of an authorized Agency employee.
9. The entity may perform analyses for self-control purposes in approved laboratories.

## Article 5
## Certificate of analysis

1. The laboratory begins conducting analyses within 3 (three) working days of receiving the sample, and within 2 (two) working days after their completion, the laboratory issues the certificate of analysis in accordance with the specific procedure for maintaining anonymity.
2. The certificate of analysis is prepared in three copies, two of which the laboratory officially delivers in writing to the Agency, while one copy is kept by the laboratory for a period equal to the laboratory’s accreditation period and in any case not less than 3 years from the date of issuance of the certificate of analysis, making it available for inspection.
3. The Agency, within two working days of receiving the certificate of analysis from the approved laboratory, decodes the sample sent for analysis and officially sends the certificate of analysis to the relevant subject. The Agency records the analysis results in the Register.

4. The subject must securely and systematically store the certificates of analysis, using electronic and/or physical systems for record management, facilitating traceability.
5. The certificate of analysis must contain the elements provided in standard 17025 and the laboratory's identification number and the approval act data for performing these analyses.
6. The subject must have an internal quality control system with the appropriate procedures to ensure the cultivation of cannabis plants, by-products, and final products in compliance with legal requirements.

**Article 6**
**Retesting and resampling procedure**

1. Subject licensed or permitted under Law 61/2023, may object to the results of the analysis, if it claims that one or some of the data in the analysis certificate is incorrect.

2. Retesting and resampling may not be required if the deviation from the permitted THC values is more than 10% of the specified level.

3. In the event of a dispute over the result, the subject must, within two working days from the moment of receiving the result, submit a reasoned request to the Agency in writing and electronically. In these cases, the Agency shall review the request within 3 working days and state whether retesting and/or resampling will be carried out in the approved laboratory.

4. Retesting/resampling is performed only for the parameter(s) that deviate from the specified limits. Retesting/resampling follows the same procedures and methodologies as for the initial analysis, and the corresponding results are reported according to the same procedure as for the initial analysis.

5. Retesting/resampling may be requested only once for each uncorrected production lot and the results obtained shall be considered as final results. In cases where the analysis values of the two tests have a difference greater than 10%, the analysis shall be repeated in another approved laboratory and the first laboratory shall provide the relevant explanations for the observed difference that falls outside the accreditation standards. The Agency shall take concrete actions in accordance with the provisions of the applicable legal framework up to the proposal for the revocation of the laboratory's approval by the Minister.

**Article 7**
**Corrective actions for improving the parameters of the *cannabis* plant lot related to moisture levels and microbial load**

1. The licensed or permitted entity under Law 61/2023 may correct the *Cannabis* plant lot only once , by treating the material for moisture level and microbial load, if the analysis result does not meet the permitted limits regarding these parameters.

2. Corrective actions must be included in the entity's standard operating procedures (SOPs) approved by the Agency, which include specific methods that do not affect the quality of

the material, but regulate the levels of microbial contamination and moisture in accordance with the limits of the analysis performed.

3. For the sample selected from the corrected lot, the same sampling and/or retesting procedure is carried out, which will be performed for all parameters and not only for those that deviate from the specifications in the initial analysis.

4. The final results for the corrected lot sample are non-disputable.

## Article 8
## Packaging and labeling

1. Primary and secondary packaging must ensure the quality and safety of the plant material in accordance with the following criteria and the additional requirements of the importing country.
2. The environment, the manner in which the packaging process is carried out, and the control over packaging materials for cannabis plant products, which are traded for final use in consumption or cosmetics, must comply with the EU-GMP and EU-GACP guidelines.

3. In any case, the packaging must meet the requirements according to Annex No. 2 attached and a component part of this guideline.
4. The label must have a uniform and distinguishable color, such that it creates contrast with the hazard symbol and the standardized cannabis symbol (depending on the importing country). The label must not contain product advertising or information that could mislead the consumer.
5. The language used on the label must be clear, understandable, and easily readable. The format of the label, writing style, language, and additional elements of the label content must comply with the requirements of the importing country.

## Article 9
## Special provisions

1. The method and quantity of sampling for performing analyses with accredited methods for quality control is carried out in accordance with the provisions of the Joint Instruction of the Minister of Health and the Minister of Agriculture as defined in Article 37 of Law No. 61/2023 .

## Article 10
## Final provisions

1. All institutions and entities mentioned in this instruction are responsible for implementing this instruction .

2. Annexes 1 and 2 are attached to and form an integral part of this instruction.

3. Instruction No. 12 dated 21.05.2024 of the Minister of Agriculture and Rural Development "On quality control methods, regarding the content of cannabinoid and tetrahydrocannabinol components, as well as physico-chemical and microbiological control for the method of packaging, form and quantity", is repealed .

*This instruction enters into force upon publication in the Official Gazette.*

**Minister**

**Anila DENAJ**

**07/2024:3028**

# CANNABIS FLOWER

## Cannabis flos

DEFINITION

Dried, whole or fragmented, fully developed female inflorescence of *Cannabis sativa* L.

*Content*: if the herbal drug is to be prescribed to patients as a medicinal product, the measured contents of total tetrahydrocannabinol and total cannabidiol, respectively, do not deviate from the values stated on the label by more than ± 10 per cent.

*THC-dominant type*:

– *total tetrahydrocannabinol, expressed as $\Delta^9$-tetrahydrocannabinol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): minimum 5.0 per cent (dried drug);

– *total cannabidiol, expressed as cannabidiol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): maximum 1.0 per cent (dried drug).

*THC/CBD-intermediate type*:

– *total tetrahydrocannabinol, expressed as $\Delta^9$-tetrahydrocannabinol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): minimum 1.0 per cent (dried drug);

– *total cannabidiol, expressed as cannabidiol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): minimum 1.0 per cent (dried drug);

– *total tetrahydrocannabinol / total cannabidiol ratio*: 0.2 to 5.0 (dried drug).

*CBD-dominant type*:

– *total tetrahydrocannabinol, expressed as $\Delta^9$-tetrahydrocannabinol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): maximum 1.0 per cent (dried drug);

– *total cannabidiol, expressed as cannabidiol* ($C_{21}H_{30}O_2$; $M_r$ 314.5): minimum 5.0 per cent (dried drug).

PRODUCTION

If the herbal drug is to be prescribed to patients as a medicinal product, the inflorescence is cut at the base with minimal rachis remaining.

IDENTIFICATION

A. Depending on the variety, the colour of the herbal drug varies from dark green to pale yellow or from light brown to reddish-brown. The whole female inflorescence is a dense or more or less lax panicle, comprising sessile or almost sessile, elongated bracts (about 10 mm long) with dentate margins, intermingled with the flowers. The fragmented inflorescence, comprises parts of the axis of the inflorescence, the bracts and panicle, together with individual flowers or floral organs. The female flowers are very small (about 2 mm) with a short pedicel. The perianth is monosepalous and apetalous. The sepal, often referred to as the bracteole, is wrapped around the unilocular ovary which bears two styles, each terminating in a fine, orange-brown stigma that is longer than the calyx. The inflorescence is more or less densely pilose, with covering trichomes and glandular trichomes that produce a sticky resin with an aromatic odour.

B. Microscopic examination (*2.8.23*), on the milled or ground herbal drug (not sieved). The colour varies from dark green to yellowish-green or from light brown to reddish-brown. Examine under a microscope using *chloral hydrate solution R*. The milled or ground herbal drug shows the following diagnostic characters (Figure 3028.-1): very numerous glandular or covering trichomes, free or attached to epidermis, of different types: a) whole glandular trichomes, with a multiseriate, multicellular stalk and a multicellular head covered by a domed cuticle (transverse section [E]), or fragments of these trichomes comprising the stalk or head [A] only; some have a very short stalk [Ha], others are sessile; some still have the domed cuticle over the glandular cells (surface view [Da], transverse section [Ea]) while others no longer have it [A]; b) small glandular trichomes with a uni- or biseriate stalk and a uni-, bi- or quadricellular head containing orange-yellow droplets (surface view [Bc, Ca, J], side view [Cb, La, Lb]); c) cystolithic [Fa, Ka] and non-cystolithic unicellular covering trichomes; the conical, cystolithic covering trichomes have either thickened walls, a broad base and a curved, pointed end, with a clearly visible, lumpy, globular calcium carbonate deposit (surface view [Ba], transverse section [Ka]), or a narrower base and markedly pitted walls [Fa]; the non-cystolithic covering trichomes are more elongated and have thickened, smooth walls [Hb]; fragments of the upper epidermis of the bracts (surface view [B, F, L]) sometimes covered by a fine, striated cuticle composed of polygonal cells with rigid walls [Bb], cystolithic covering trichomes [Ba, Fa] and small glandular trichomes (surface view [Bc], side view [La, Lb]); the upper epidermis is usually associated with palisade parenchyma with some cells containing small cluster crystals of calcium oxalate [Bd]; fragments of the lower epidermis of the bracts [D] comprising cells with slightly sinuous walls [Db], anomocytic stomata (*2.8.3*) [Dc], small glandular trichomes [Dd] and glandular trichomes with a multicellular stalk and a multicellular head [Da]; fragments of the lamina of the bracts (transverse section [K]) comprising the upper epidermis covered by a cuticle [Kb], with rectangular cells and cystolithic covering trichomes [Ka], and the palisade parenchyma layer with some cells containing a small cluster crystal of calcium oxalate [Kc]; fragments of the lower epidermis of the bracteoles [H] with slightly wavy cells [Hc], glandular trichomes with a short stalk [Ha], anomocytic stomata [Hd], non-cystolithic covering trichomes [Hb] and small glandular trichomes [He]; small cluster crystals of the underlying mesophyll are clearly visible in the fragments of the bracteole epidermises [Hf ]; fragments of the orange-brown stigmas showing epidermal cells with very fine, faintly visible walls, terminating in large papillae with a rounded end [G]; fragments of the axis of the inflorescence [N] comprising cellulose fibres, spiral [Na] or annular vessels, and cells of the pith with

reticulate walls [Nb], some of which contain cluster crystals of calcium oxalate of about 30 µm in diameter; free cluster crystals of calcium oxalate [M].

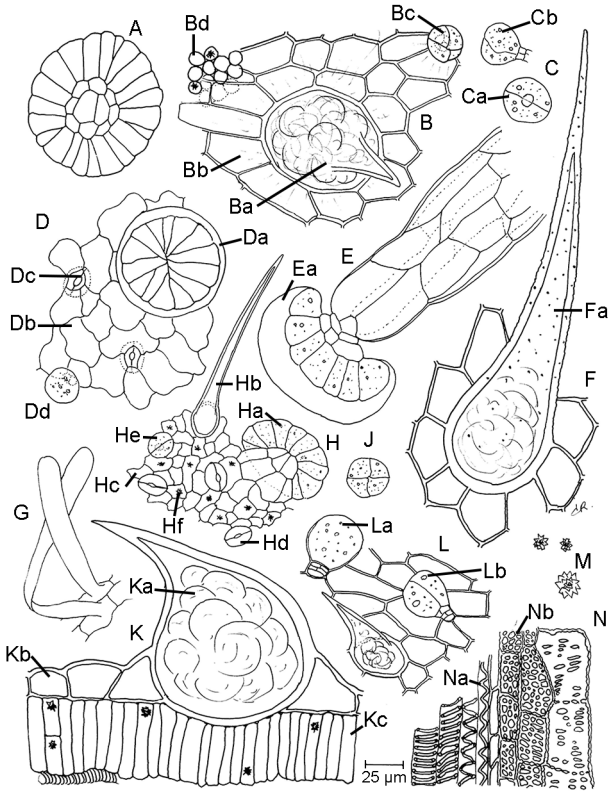


Figure 3028.-1. – *Illustration for identification test B of milled or ground herbal drug of cannabis flower*

C. High-performance thin-layer chromatography (*2.8.25*).

*Test solution.* Introduce 0.5 g of the cut or milled herbal drug (not sieved) into a test tube and add 5.0 mL of *methanol R*. Stopper the tube and mix using a vortex mixer for 10 s. Sonicate for 5 min, then mix using a vortex mixer for 10 s. Repeat this operation twice. Centrifuge and use the supernatant.

*Reference solution (a).* Dissolve 5.0 mg of *cannabidiol R* in 1.0 mL of *Δ⁹-tetrahydrocannabinol solution R*.

*Reference solution (b).* Dilute 0.25 mL of reference solution (a) to 1.0 mL with *methanol R*.

*Reference solution (c).* Dissolve 1 mg of *cannabidiol R* and 1 mg of *cannabidiolic acid R* in *methanol R* and dilute to 1 mL with the same solvent.

*Intensity marker*: reference solutions (a) and (b):

– $\Delta^9$-tetrahydrocannabinol.

*Plate*: *TLC octadecylsilyl silica gel $F_{254}$ plate R* (2-10 µm).

*Mobile phase*: *water R*, *glacial acetic acid R*, *methanol R* (10:10:80 *V/V/V*).

*Application*: 2.0 µL, as bands of 8 mm.

*Development*: 70 mm from the lower edge of the plate.

*Drying*: in a current of air at room temperature for 5 min.

*Detection*: treat with *vanillin reagent R*, heat at 100 °C for 3 min and then allow to cool for 3 min; examine in daylight.

*System suitability*: reference solution (c):

– the chromatogram shows in the middle third 2 distinct zones, which may be touching; the lower zone (cannabidiolic acid) and the upper zone (cannabidiol) are grey to reddish-violet.

*Results*: see below the sequence of zones present in the chromatograms obtained with reference solution (a) and the test solution. Furthermore, in the chromatogram obtained with the test solution, other very faint zones may be present. If present, the zone due to $\Delta^9$-tetrahydrocannabinolic acid is more intense than the zone due to $\Delta^9$-tetrahydrocannabinol. If present, the zone due to cannabidiolic acid is more intense than the zone due to cannabidiol.

| Top of the plate | | | |
|---|---|---|---|
| Cannabidiol: a reddish-violet zone | | A reddish-violet zone, faint to very faint (cannabidiol)<br>A reddish-violet zone, intense (cannabidiolic acid) | A reddish-violet zone, faint to very faint (cannabidiol)<br>A reddish-violet zone, intense (cannabidiolic acid) |
| $\Delta^9$-Tetrahydrocannabinol: a reddishviolet zone | A reddish-violet zone, faint to equivalent ($\Delta^9$-tetrahydrocannabinol) | A reddish-violet zone, faint ($\Delta^9$-tetrahydrocannabinol) | A grey to reddish-violet zone, very faint, may be absent ($\Delta^9$-tetrahydrocannabinol) |
| | A reddish-violet zone, intense ($\Delta^9$-tetrahydrocannabinolic acid) | A reddish-violet zone ($\Delta^9$-tetrahydrocannabinolic acid) | A reddish-violet zone, very faint ($\Delta^9$-tetrahydrocannabinolic acid) |
| **Reference solution (a)** | **Test solution (THC-dominant type)** | **Test solution (THC/CBD-intermediate type)** | **Test solution (CBD-dominant type)** |

TESTS

**Total CBN**. Liquid chromatography (*2.2.29*).

*Test solution (a).* To 0.50 g of the cut or milled herbal drug (not sieved) in a suitable centrifuge tube fitted with a screw cap, add 40 mL of *ethanol (96 per cent) R* and shake for 15 min. Centrifuge at about 1700 *g* and transfer the clear supernatant into a flask. Repeat the extraction twice with 25 mL of *ethanol (96 per cent) R*. Combine the supernatants and dilute to 100.0 mL with *ethanol (96 per cent) R*. Filter through a membrane filter (nominal pore size 0.22 µm).

*Test solution (b).* Dilute 1.0 mL of test solution (a) to 10.0 mL with *methanol R*.

*Reference solution (a).* Dissolve 20.0 mg of *cannabidiol for cannabis CRS* in *methanol R* and dilute to 100.0 mL with the same solvent.

*Reference solution (b).* Dilute 5.0 mL of reference solution (a) to 20.0 mL with *methanol R*.

*Reference solution (c).* Dilute 10.0 mL of reference solution (a) to 25.0 mL with *methanol R*.

*Reference solution (d).* To 50 mg of *cannabis flower for system suitability HRS* in a suitable centrifuge tube fitted with a screw cap, add 4 mL of *ethanol (96 per cent) R* and shake for 15 min. Centrifuge the solution at about 1700 *g* and transfer the clear supernatant into a flask. Repeat the extraction twice with 2.5 mL of *ethanol (96 per cent) R*. Combine the supernatants and dilute to 10 mL with *ethanol (96 per cent) R*. Filter through a membrane filter (nominal pore size 0.22 µm).

*Reference solution (e).* Dilute 1 mL of reference solution (d) to 10 mL with *methanol R*.

*Column*:

– *size*: *l* = 0.15 m, Ø = 4.6 mm;

– *stationary phase*: *end-capped solid core polar-embedded octadecylsilyl silica gel for chromatography R* (2.7 µm);

– *temperature*: 35 °C.

*Mobile phase*: 0.1 per cent *V/V* solution of *trifluoroacetic acid R*, *acetonitrile for chromatography R* (41:59 *V/V*).

*Flow rate*: 2.0 mL/min.

*Detection*: spectrophotometer at 228 nm.

*Injection*: 5 µL of test solution (a) and reference solutions (b) and (d).

*Run time*: 5.0 times the retention time of cannabidiol.

*Identification of peaks*: use the chromatogram obtained with reference solution (b) to identify the peak due to cannabidiol; use the chromatogram supplied with *cannabis flower for system suitability HRS* and the chromatogram obtained with reference solution (d) to identify the peaks due to $\Delta^9$-tetrahydrocannabinol, $\Delta^9$-tetrahydrocannabinolic acid, cannabidiolic acid, cannabinol, cannabinolic acid, cannabichromene, cannabigerol and cannabigerolic acid.

*Relative retention* with reference to cannabidiol (retention time = about 6.9 min): cannabidiolic acid = about 1.10; cannabigerol = about 1.17; cannabinol = about 1.48; cannabigerolic acid = about 1.63; $\Delta^9$-tetrahydrocannabinol = about 1.76; cannabinolic acid = about 2.38; cannabichromene = about 2.48; $\Delta^9$-tetrahydrocannabinolic acid = about 2.78.

*System suitability*: reference solution (d):

– *resolution*: minimum 2.0 between the peaks due to cannabigerolic acid and $\Delta^9$-tetrahydrocannabinol;

– *peak-to-valley ratio*: minimum 1.5, where $H_p$ = height above the baseline of the peak due to cannabigerol and $H_v$ = height above the baseline of the lowest point of the curve separating this peak from the peak due to cannabidiolic acid; minimum 5.0, where $H_p$ = height above the baseline of the peak due to cannabinolic acid and $H_v$ = height above the baseline of the lowest point of the curve separating this peak from the peak due to cannabichromene.

Calculate the percentage content of total CBN, using the following expression:

$$\frac{((A_1 \times 0.405) + (A_3 \times 0.901 \times 0.876)) \times m_2 \times p}{A_2 \times m_1 \times 4}$$

$A_1$ = area of the peak due to cannabinol in the chromatogram obtained with test solution (a);

$A_2$ = area of the peak due to cannabidiol in the chromatogram obtained with reference solution (b);

$A_3$ = area of the peak due to cannabinolic acid in the chromatogram obtained with test solution (a);

$m_1$ = mass of the herbal drug to be examined used to prepare test solution (a), in grams;

$m_2$ = mass of *cannabidiol for cannabis CRS* used to prepare reference solution (a), in grams;

$p$ = percentage content of cannabidiol in *cannabidiol for cannabis CRS*;

0.405 = correction factor of cannabinol with reference to cannabidiol;

0.901 = correction factor of cannabinolic acid with reference to cannabidiol;

0.876 = ratio of the molecular mass of cannabinol to that of cannabinolic acid.

*Limit*:

– *total CBN*: maximum 1.0 per cent.

**Foreign matter** (*2.8.2*): maximum 2 per cent; if the herbal drug is to be prescribed to patients as a medicinal product, it does not contain any seeds and the whole herbal drug does not contain any leaves more than 1.0 cm in length.

Carry out the determination using 25-50 g.

**Loss on drying** (*2.2.32*): maximum 12.0 per cent, determined on 1.000 g of the cut or milled herbal drug (not sieved) by drying over about 100 g of *molecular sieve R* at a pressure between 1.5 kPa and 2.5 kPa at 40 °C for 24 h.

**Arsenic** (*2.4.27*): maximum 0.2 ppm if the herbal drug is to be prescribed to patients as a medicinal product.

**Cadmium** (*2.4.27*): maximum 1.0 ppm, or maximum 0.3 ppm if the herbal drug is to be prescribed to patients as a medicinal product.

**Lead** (*2.4.27*): maximum 5.0 ppm, or maximum 0.5 ppm if the herbal drug is to be prescribed to patients as a medicinal product.

**Mercury** (*2.4.27*): maximum 0.1 ppm.

ASSAY

*This procedure has been validated for an analytical range of 0.2 per cent to 32.0 per cent of $\Delta^9$-tetrahydrocannabinol, $\Delta^9$-tetrahydrocannabinolic acid, cannabidiol and cannabidiolic acid respectively.*

Liquid chromatography (*2.2.29*) as described in the test for total CBN, with the following modifications.

*Injection*: test solution (b) and reference solutions (c) and (e).

*System suitability*: reference solution (e):

– *resolution*: minimum 2.0 between the peaks due to cannabidiol and cannabidiolic acid.

Calculate the percentage content of total tetrahydrocannabinol, expressed as $\Delta^9$-tetrahydrocannabinol, using the following expression:

$$\frac{((A_1 \times 1.097) + (A_3 \times 0.691 \times 0.877)) \times m_2 \times p \times 4}{A_2 \times m_1}$$

$A_1$ = area of the peak due to $\Delta^9$-tetrahydrocannabinol in the chromatogram obtained with test solution (b);

$A_2$ = area of the peak due to cannabidiol in the chromatogram obtained with reference solution (c);

$A_3$ = area of the peak due to $\Delta^9$-tetrahydrocannabinolic acid in the chromatogram obtained with test solution (b);

$m_1$ = mass of the herbal drug to be examined used to prepare test solution (a), in grams;

$m_2$ = mass of *cannabidiol for cannabis CRS* used to prepare reference solution (a), in grams;

$p$ = percentage content of cannabidiol in *cannabidiol for cannabis CRS*;

1.097 = correction factor of $\Delta^9$-tetrahydrocannabinol with reference to cannabidiol;

0.691 = correction factor of $\Delta^9$-tetrahydrocannabinolic acid with reference to cannabidiol;

0.877 = ratio of the molecular mass of $\Delta^9$-tetrahydrocannabinol to that of $\Delta^9$-tetrahydrocannabinolic acid.

Calculate the percentage content of total cannabidiol, expressed as cannabidiol, using the following expression:

$$\frac{(A_1 + (A_3 \times 0.596 \times 0.877)) \times m_2 \times p \times 4}{A_2 \times m_1}$$

$A_1$ = area of the peak due to cannabidiol in the chromatogram obtained with test solution (b);

$A_2$ = area of the peak due to cannabidiol in the chromatogram obtained with reference solution (c);

$A_3$ = area of the peak due to cannabidiolic acid in the chromatogram obtained with test solution (b);

$m_1$ = mass of the herbal drug to be examined used to prepare test solution (a), in grams;

$m_2$ = mass of *cannabidiol for cannabis CRS* used to prepare reference solution (a), in grams;

$p$ = percentage content of cannabidiol in *cannabidiol for cannabis CRS*;

0.596 = correction factor of cannabidiolic acid with reference to cannabidiol;

0.877 = ratio of the molecular mass of cannabidiol to that of cannabidiolic acid.

STORAGE

In an airtight container.

LABELLING

The label states the percentage contents of total tetrahydrocannabinol and total cannabidiol.

In addition, the label states if the herbal drug is to be prescribed to patients as a medicinal product.

**Annex No. 2**

**Requirements for the Packaging and Labeling of *Cannabis* plant materials, by-products, and final products.**

## I. Packaging of *Cannabis* plant materials, by-products, and final products

1. General criteria for packaging are as follows:

a) must be resistant to damage;

b) must be opaque and impervious to light;

c) must prevent *cannabis* contamination;

ç) for products where the packaged item is dried *cannabis*, it must ensure storage in dry conditions;

d) must include safety features that guarantee the consumer the product has not been opened before delivery;

dh) must be made of inert material (chemically inactive) that does not release substances into the product;

e) the internal and external surfaces of the packaging must not include any advertising elements related to the cultivating or producing entity;

ë) the color of the internal and external surfaces of the packaging must be uniform and meet the following criteria:

i. must not be coated with a metallic layer or contain metallic elements in the paint, except in cases where the packaging is made of metal;

ii. must not be fluorescent or contain fluorescent elements in the paint or pigments that absorb ultraviolet radiation and release it as longer-wavelength radiation (such as pantone 800 series);

iii. must provide sufficient contrast with the health hazard symbol and the *cannabis* symbol;

f) the texture of the packaging surfaces must be uniform, without reliefs, decorative stripes, engravings, or other irregular elements, except for those necessary to facilitate opening or to assist persons with disabilities;

g) no part of the packaging should include hidden elements designed to alter its appearance, such as heat-activated ink or other features visible only with technological tools, except for anti-counterfeiting elements;

gj) the inner or outer surfaces of product containers or their external packaging must not include elements designed to alter the surface of the container or packaging;

h) packaging must not emit scents;

i) the packaging must include a barcode/track-trace code element in a rectangular format, printed in black and white;

j) the external packaging must not include:

i. other food products;

ii. more than one *cannabis* variety;

iii. more than one primary packaging, except in cases where individually packaged *cannabis*-containing food products are included, and the total does not exceed the allowed total THC limit for the importing country.

2. For *cannabis* plants sold in bulk, the packaging:

a) Must ensure the safe transport of its contents;

b) Should use vacuum-sealed or hermetically closed, light-resistant barrels for *cannabis* flowers and by-products intended for use in the pharmaceutical, food, or cosmetic industries;

c) Should use large bags or crates for other parts of the *cannabis* plant, such as stems, seeds, or their by-products, intended for industrial use, except for the purposes mentioned in point “b” of this section.

3. For *cannabis* plants intended for retail sale, the packaging:

a) Must include safety seals;

b) Must prevent access by minors;

c) Must be portioned so that the total THC content per dose or package does not exceed the limits of the importing country;

ç) Must accurately reflect the THC content on the label;

d) Must suit the form and intended use of the *cannabis* plant part, by-product, or product being packaged.

**II. Labeling of *Cannabis* plant materials, by-products, and final products**

1. The label must include the elements specified in point 6 of Article 28, as well as the following characteristics:

a) chemical/generic/official name;

b) trade name, if applicable;

c) license/permit number of the producing entity;

ç) batch number;

d) storage conditions: referring to elements such as temperature, light, or humidity (e.g., store in a dry place, avoid direct light, etc.);

dh) net weight of dry mass: the net weight of the *cannabis* plant expressed numerically in grams or kilograms and within the following tolerance limits:

i. for quantities from 0 g to 2 g, the tolerance is 10%;

ii. for quantities over 2 g, the tolerance is 5%.

e) total THC concentration and total CBD concentration, per unit and for the entire packaged amount;

ë) usage instructions and purpose;

f) warnings to keep out of reach of children;

g) health hazard warnings;

gj) content of additional substances, if any;

h) nutritional values, allergen sources, and sulfite content if intended for consumption;

i) barcode/track-trace code.