Quality issues and Medicinal Cannabis in The Netherlands

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Office of Medicinal Cannabis (OMC)
CIBG; Ministry of Health, Welfare and Sport
The Netherlands

December 2022

- Pressure from society (patients, patients groups, parliament) against prohibition of medicinal use;

**Existing practice at that time:** patients use illegal cannabis from Dutch coffeeshops:

- No quality control;
- No medical coaching of patients;
- Patients at the mercy of illicit trade.
OMC - legislation

• The OMC comes under the Ministry of Health, Welfare and Sport;

• An agency according to art. 28 of the Single Convention (UN) and is, to the exclusion of others, authorized:
  > to import and export medicinal cannabis from the Netherlands;
  > to sell and deliver it;
  > to have it available, with the exception of stocks maintained by those who have a license to cultivate, work up and/or convert.

• Medicinal cannabis is a controlled substance and can be prescribed and dispensed.
Pharmaceutical characteristics:

- Pharmaceutical raw material (API);
- Not registered as a medicine;
- Standardized herbal medicinal product;
- Opium Act.

Route of administration / application:

- Inhalation, vaporization;
- Oral application (tea);
- Compounding pharmacies: oil production

Available on prescription in the pharmacy:
Main responsibilities of the OMC

• Ensure constant quality of medicinal cannabis produced which meets pharmaceutical standards;

• Establish an effective procedure for distribution comparable with GDP-rules for registered pharmaceutical products;

• Prevent leakage to the criminal circuit (tracking procedure / recordkeeping);

• Ensure availability of medicinal cannabis.
Production and distribution model

Office of Medicinal Cannabis (OMC)

Growers → Packager → Logistics Service Provider

Laboratory

Irradiation company

Distribution invoicing collection → Pharmacy
**Contracted third parties:**

Cultivation : Bedrocan BV

Packaging and distribution : Fagron BV

(Gamma) Irradiation : Steris

Analytics / lab. analyses : Ofichem Group

Quality covers all parties involved.
Growers and Quality (control)

- Mandatory compliance to GAP-rules and guidelines;
- GMP-certification obligatory; supervised by Dutch Health Inspectorate - OMC;
Logistics – packaging and distribution

• Partner with experience in packaging and labelling of pharmaceutical products as well as raw materials;

• Quality standards and certification: GDP-certified and FDA-certified company;

• Recordkeeping procedure for tracking medicinal cannabis to the patient.
Clean rooms
Laboratory analysis

› Partner experienced with API’s and analytical testing methods;

› GMP-certification obligatory; supervised by Dutch Health Inspectorate - OMC; (FDA-audited)

› Dutch monograph available; (concept European Pharmacopeia monograph)

› Validated testing methods;

› Certificate of analysis for every batch tested;

› Approval by the OMC;
Products – varieties cannabis flos

• Cannabis flos, variety **Bedrocan**: 22% THC, <1% CBD

• Cannabis flos, variety **Bedrobinol**: 13,5% THC, <1% CBD

• Cannabis flos, variety **Bedica** granulated: 14% THC, <1% CBD

• Cannabis flos, variety **Bediol** granulated: 6,3% THC, 8% CBD

• Cannabis flos, variety **Bedrolite** granulated: <1% THC, 7,5% CBD
# Certificate of Analysis

**Product:** Bedrocan

**Batch number:** A5.01.F.45.190821

**Analytical monograph:** OMC Monograph Cannabis Flower / Version 8.0 / November 01, 2021

**Analysis number or code:** 33905

**Report date:** 26 December 2021

<table>
<thead>
<tr>
<th>Test</th>
<th>Method</th>
<th>Specification</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characters</strong></td>
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</tr>
<tr>
<td>Odour</td>
<td>EP 2.3.4</td>
<td>Characteristic for cannabis flower</td>
<td>Compiles</td>
</tr>
<tr>
<td>Appearance</td>
<td>Visual</td>
<td>Leaves do not shoot out more than 20% of the length of the flower and stalks are mostly cut off directly under the bottom site of the flowers</td>
<td>Compiles</td>
</tr>
<tr>
<td><strong>Identification</strong></td>
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<tr>
<td>Identification A</td>
<td>Visual</td>
<td>Brown green clustered flowers of 1.5 to 3.0 cm length</td>
<td>Compiles</td>
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<tr>
<td>Identification B</td>
<td>Monograph</td>
<td>Gland hairs are mainly observed</td>
<td>Compiles</td>
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<tr>
<td>Identification C</td>
<td>EP 2.2.27</td>
<td>The main spot obtained with test solution has comparable retention time with reference solution and is coloured red (THCA)</td>
<td>Compiles</td>
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<tr>
<td><strong>Heavy metals</strong></td>
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<tr>
<td>Lead</td>
<td>EP 2.4.27 EP 2.2.58</td>
<td>≤ 20.0 ppm</td>
<td>&lt; 5 ppm</td>
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<tr>
<td>Cadmium</td>
<td></td>
<td>≤ 0.5 ppm</td>
<td>&lt; 0.125 ppm</td>
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<tr>
<td>Mercury</td>
<td></td>
<td>≤ 0.5 ppm</td>
<td>&lt; 0.125 ppm</td>
</tr>
<tr>
<td>Arsenic</td>
<td></td>
<td>FIO</td>
<td>&lt; 0.05 ppm</td>
</tr>
<tr>
<td>Nickel</td>
<td></td>
<td>FIO</td>
<td>0.13 ppm</td>
</tr>
<tr>
<td>Zinc</td>
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<td>FIO</td>
<td>35 ppm</td>
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<td><strong>Assay and Related substances</strong></td>
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</tr>
<tr>
<td>CBD</td>
<td>Monograph EP 2.2.29</td>
<td>FIO</td>
<td>&lt; 0.05 %</td>
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<tr>
<td>CBDA</td>
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<td>FIO</td>
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<tr>
<td>THC</td>
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<td>FIO</td>
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<tr>
<td>THCA</td>
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<td>FIO</td>
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<td>CBD total equivalent</td>
<td>Monograph EP 2.2.29</td>
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<td>0.1 %</td>
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<tr>
<td>THC total equivalent</td>
<td>Monograph EP 2.2.29</td>
<td>22.0 % [17.6 – 26.4]</td>
<td>18.4 %</td>
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<tr>
<td>CBN</td>
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<tr>
<td>CBNA</td>
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<tr>
<td>CBN total equivalent</td>
<td>Monograph EP 2.2.29</td>
<td>≤ 1.0 %</td>
<td>&lt; 0.1 %</td>
</tr>
</tbody>
</table>

**Quality Control**

R. Vree Egberts, BSc

28 DEC 2021

**Quality Assurance**

R. Schutter, MSc

28 DEC 2021
This lot complies with the requirements of the current version of the specification sheet and is analysed conform OMC Monograph Cannabis Flower / Version 8.0 / November 01, 2021. The analyses are performed in compliance with EU-GMP.
**Dutch Monograph (version 8.0, 2021)**

Applicable for:
- Fragmented dried flowering tops;
- Fragmented and granulated dried flowering tops;

<table>
<thead>
<tr>
<th>Test</th>
<th>EP 2.2.27</th>
<th>EP 2.2.32</th>
<th>EP 2.8.13</th>
<th>EP 2.4.27 / 2.2.58</th>
<th>EP 2.2.29</th>
<th>EP 2.6.12 / 2.6.13</th>
<th>Monograph</th>
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<td>Heavy Metals</td>
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<td>Assay and related substances</td>
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<td>Microbial contamination</td>
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<td>Aflatoxines</td>
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</tbody>
</table>
- Cannabis flos, variety Bedrocan
  - Approx. 19% dronabinol,
  - <1% cannabidiol,
  - other cannabinoids very low

- Cannabis flos, variety Bedrobinol
  - Approx. 12% dronabinol,
  - <1% cannabidiol,
  - other cannabinoids very low

- Cannabis flos, variety Bediol, granulated
  - Approx. 6% dronabinol and 7.5% cannabidiol,
  - other cannabinoids very low
Bediol granulated
Experiences over time (2003-2022) I

- Indoor versus outdoor cultivation;

- Standardization needs fully controlled environment;

- Growing without microbiological contamination not possible;

- Standardization and inter-batch variability in THC / CBD concentration: 20%; dedicated growth conditions;
Experiences over time (2003-2022) II

- Drying process is a critical step in production cycle;
- Pesticide contamination in rural areas;
- Take samples with utmost precision and protocolized;
- Stability of internal standard(s) in assay;
Current priorities for cannabis quality

• Adherence to coming EP Monograph on cannabis flos (for example limits set for heavy metals);

• Optimization of homogenization of cannabis flos;

• Discussion on harmonization - standardization of ‘Good agriculture Practices’ for medicinal cannabis;
Medicinal cannabis complies with pharmaceutical quality guidelines

• Standardized product with constant content (tetrahydrocannabinol, cannabidiol and other)

• Very low concentration of degradation compounds (e.g. CBN)

• Free of contamination
  – Micro-organisms
  – Pesticides
  – Heavy metals
  – Aflatoxines
Thank you for your attention!