United Nations E/CN.7/2019/12

Economic and Social Council

Distr.: General
1 February 2019

Original: English

Commission on Narcotic Drugs
Sixty-second session
Vienna, 14–22 March 2019
Item 9 (a) of the provisional agenda*
Implementation of the international drug control treaties: changes in the scope of control of substances

Changes in the scope of control of substances: proposed scheduling recommendations by the World Health Organization on cannabis and cannabis-related substances

Note by the Secretariat

Summary

The present document contains recommendations for action to be taken by the Commission on Narcotic Drugs pursuant to the international drug control treaties.

In accordance with article 3 of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, the Commission will have before it for consideration a recommendation by the World Health Organization (WHO) to delete cannabis and cannabis resin from Schedule IV of that Convention.

In accordance with article 3 of the 1961 Convention and article 2 of the Convention on Psychotropic Substances of 1971, the Commission will have before it for consideration a recommendation by WHO to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention and to delete the substance from Schedule II of the 1971 Convention.

In accordance with article 3 of the 1961 Convention and article 2 of the 1971 Convention, the Commission will have before it for consideration a recommendation by WHO to add tetrahydrocannabinol (isomers of *delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention, subject to the Commission's decision on whether to add dronabinol and its stereoisomers to Schedule I of the 1961 Convention, and a recommendation to delete tetrahydrocannabinol from Schedule I of the 1971 Convention.

In accordance with article 3 of the 1961 Convention, the Commission will have before it for consideration a recommendation by WHO to delete extracts and tinctures of cannabis from Schedule I of the 1961 Convention.

In addition, the Commission will have before it for consideration a recommendation by WHO that preparations considered to be pure cannabidiol should

* E/CN.7/2019/1.

not be scheduled under the international drug control conventions, and a recommendation that, to that effect, a footnote should be added to the entry for cannabis and cannabis resin in Schedule I of the 1961 Convention to read "Preparations containing predominantly cannabidiol and not more than 0.2 per cent of *delta*-9-tetrahydrocannabinol are not under international control."

Furthermore, in accordance with article 3 of the 1961 Convention, the Commission will have before it for consideration a recommendation by WHO to add to Schedule III of that Convention preparations containing *delta*-9-tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as preparations of cannabis that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that *delta*-9-tetrahydrocannabinol (dronabinol) cannot be recovered by readily available means or in a yield that would constitute a risk to public health.

I. Consideration of the notification from the World Health Organization concerning scheduling under the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, and the Convention on Psychotropic Substances of 1971

1. Pursuant to article 3, paragraphs 1 and 3, of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, the Director-General of the World Health Organization (WHO), in correspondence dated 23 July 2018, notified the Secretary-General of the United Nations of the outcome of the critical review of cannabidiol (CBD) undertaken by the WHO Expert Committee on Drug Dependence at its fortieth meeting. In that regard, the Director-General notified the Secretary-General of a recommendation to the effect that preparations considered to be pure CBD should not be scheduled under the international drug control conventions (see annex I for the relevant extract of that notification).

2. In accordance with the provisions of article 3, paragraph 2, of the 1961 Convention, on 29 August 2018, the Secretary-General transmitted to all Governments a note verbale, to which the notification dated 23 July 2018 and the information submitted by WHO in support of that recommendation were annexed.

3. Pursuant to article 3, paragraphs 1 and 3 to 6, of the 1961 Convention and article 2, paragraphs 1, 4 and 6, of the 1971 Convention, the Director-General of WHO, in correspondence dated 24 January 2019 (received 28 January 2019), notified the Secretary-General of the outcome of the critical review of cannabis and cannabis-related substances undertaken by the WHO Expert Committee on Drug Dependence at its forty-first meeting. In that connection, the Director-General notified the Secretary-General of the recommendations regarding the review of cannabis and cannabis-related substances, which were as follows (see annex II for the relevant extract of that notification):

(a) To delete cannabis and cannabis resin from Schedule IV of the 1961 Convention;

(b) To add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention; and to delete it from Schedule II of the 1971 Convention, subject to the Commission's adoption of the recommendation to add it to Schedule I of the 1961 Convention;

(c) To add tetrahydrocannabinol (THC) (isomers of *delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention, subject to the Commission's adoption of the recommendation to add dronabinol and its stereoisomers to Schedule I of the 1961 Convention; and to delete THC from Schedule I of the 1971 Convention, subject to the adoption of the recommendation to add it to Schedule I of the 1961 Convention;

(d) To delete extracts and tinctures of cannabis from Schedule I of the 1961 Convention;

(e) To give effect to the recommendation of the Expert Committee on Drug Dependence at its fortieth meeting that preparations considered to be pure CBD should not be scheduled under the international drug control conventions, by adding a footnote to the entry for cannabis and cannabis resin in Schedule I of the 1961 Convention to read "Preparations containing predominantly cannabidiol and not more than 0.2 per cent of *delta*-9-tetrahydrocannabinol are not under international control";

(f) To add to Schedule III of the 1961 Convention preparations containing *delta*-9-tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as preparations of cannabis that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that *delta*-9-tetrahydrocannabinol

(dronabinol) cannot be recovered by readily available means or in a yield that would constitute a risk to public health.

4. In accordance with the provisions of article 3, paragraph 2, of the 1961 Convention and article 2, paragraph 2, of the 1971 Convention, on 1 February 2019, the Secretary-General transmitted to all Governments a note verbale, to which the notification dated 24 January 2019 and the information submitted by WHO in support of those recommendations were annexed. Furthermore, on 29 January 2019, the Secretariat informally submitted the notification and the information submitted by WHO in support of those recommendations in advance to all permanent missions to the United Nations in Vienna.

Action to be taken by the Commission on Narcotic Drugs

5. The notification from the Director-General of WHO is before the Commission for its consideration, in accordance with the provisions of article 3, paragraphs 3 to 6, of the 1961 Convention, which read as follows:

> 3. Where a notification relates to a substance not already in Schedule I or in Schedule II,
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> (i) The Parties shall examine in the light of the available information the possibility of the provisional application to the substance of all measures of control applicable to drugs in Schedule I;
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> (ii) Pending its decision as provided in subparagraph (iii) of this paragraph, the Commission may decide that the Parties apply provisionally to that substance all measures of control applicable to drugs in Schedule I. The Parties shall apply such measures provisionally to the substance in question;
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> (iii) If the World Health Organization finds that the substance is liable to similar abuse and productive of similar ill-effects as the drugs in Schedule I or Schedule II or is convertible into a drug, it shall communicate that finding to the Commission, which may, in accordance with the recommendation of the World Health Organization, decide that the substance shall be added to Schedule I or Schedule II.
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> 4. If the World Health Organization finds that a preparation, because of the substances which it contains, is not liable to abuse and cannot produce ill-effects (paragraph 3) and that the drug therein is not readily recoverable, the Commission may, in accordance with the recommendation of the World Health Organization, add that preparation to Schedule III.
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> 5. If the World Health Organization finds that a drug in Schedule I is particularly liable to abuse and to produce ill-effects (paragraph 3) and that such liability is not offset by substantial therapeutic advantages not possessed by substances other than drugs in Schedule IV, the Commission may, in accordance with the recommendation of the World Health Organization, place that drug in Schedule IV.
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> 6. Where a notification relates to a drug already in Schedule I or Schedule II or to a preparation in Schedule III, the Commission, apart from the measure provided for in paragraph 5, may, in accordance with the recommendation of the World Health Organization, amend any of the Schedules by:
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> (a) Transferring a drug from Schedule I to Schedule II or from Schedule II to Schedule I; or
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> (b) Deleting a drug or a preparation, as the case may be, from a Schedule.

6. The notification from the Director-General of WHO is also before the Commission for its consideration in accordance with the provisions of article 2, paragraph 6, of the 1971 Convention, which reads as follows:

If a notification under paragraph 1 relates to a substance already listed in one of the Schedules, the World Health Organization shall communicate to the Commission its new findings, any new assessment of the substance it may make in accordance with paragraph 4 and any new recommendations on control measures it may find appropriate in the light of that assessment. The Commission, taking into account the communication from the World Health Organization as under paragraph 5 and bearing in mind the factors referred to in that paragraph, may decide to transfer the substance from one Schedule to another or to delete it from the Schedules.

7. With respect to the decision-making process regarding the decisions to be taken in accordance with article 3, paragraphs 3 to 6, of the 1961 Convention, the attention of the Commission is drawn to rule 58 of the rules of procedure of the functional commissions of the Economic and Social Council, which stipulates that decisions are to be made by a majority of the members present and casting an affirmative or negative vote. Members who abstain from voting are considered as not voting.

8. With respect to the decision-making process regarding the decisions to be taken in accordance with article 2, paragraph 6, of the 1971 Convention, the attention of the Commission is drawn to article 17, paragraph 2, of the 1971 Convention, which stipulates that the decisions of the Commission provided for in articles 2 and 3 are to be taken by a two-thirds majority of the members of the Commission. From a practical point of view, this means that, for a decision to be adopted, an affirmative vote of at least 35 members of the Commission is required.

9. The Commission should therefore decide:

(a) Whether or not it wishes to delete cannabis and cannabis resin from Schedule IV of the 1961 Convention;

(b) Whether or not it wishes to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention, and whether or not it wishes to delete dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) from Schedule II of the 1971 Convention, subject to the Commission's adoption of the recommendation to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention;

(c) Whether or not it wishes to add THC (isomers of *delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention, subject to the Commission's adoption of the recommendation to add dronabinol and its stereoisomers to Schedule I of the 1961 Convention and whether or not it wishes to delete THC (isomers of *delta*-9-tetrahydrocannabinol) from Schedule I of the 1971 Convention, subject to the adoption of the recommendation to add THC (isomers of *delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention;

(d) Whether or not it wishes to delete extracts and tinctures of cannabis from Schedule I of the 1961 Convention;

(e) Whether or not it wishes to add a footnote to the entry for cannabis and cannabis resin in Schedule I of the 1961 Convention to read "Preparations containing predominantly cannabidiol and not more than 0.2 per cent of *delta*-9-tetrahydrocannabinol are not under international control";

(f) Whether or not it wishes to add to Schedule III of the 1961 Convention preparations containing *delta*-9-tetrahydrocannabinol, produced either by chemical synthesis or as preparations of cannabis that are compounded as pharmaceutical preparations with one or more ingredients and in such a way that the *delta*-9-tetrahydrocannabinol cannot be recovered by readily available means or in a yield that would constitute a risk to public health.

Annex I

Extract of the notification dated 23 July 2018 from the Director-General of the World Health Organization to the Secretary-General containing a recommendation on cannabidiol, including the relevant extract from the report on the fortieth meeting of the Expert Committee on Drug Dependence

With reference to article 3, paragraphs 1 and 3, of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, I am pleased to submit the recommendations of the Expert Committee on Drug Dependence at its fortieth meeting, as follows:

Cannabidiol
The Committee recommended that preparations considered to be pure cannabidiol (CBD) should not be scheduled under the international drug control conventions.

Cannabis plant and resin
The Committee concluded that there is sufficient evidence to proceed to a critical review.

Extracts and tinctures of cannabis
The Committee concluded that there is sufficient evidence to proceed to a critical review.

***Delta*-9-tetrahydrocannabinol**
The Committee concluded that there is sufficient evidence to proceed to a critical review.

Isomers of tetrahydrocannabinol
The Committee concluded that there is sufficient evidence to proceed to a critical review.

The recommendations and the assessments and findings on which they are based are set out in detail in the report on the fortieth meeting of the Expert Committee on Drug Dependence of the World Health Organization (WHO).

Extract from the report on the fortieth meeting of the Expert Committee on Drug Dependence

Cannabidiol

CBD is one of the naturally occurring cannabinoids found in cannabis plants.

There are no case reports of abuse or dependence relating to the use of pure CBD. No public health problems have been associated with CBD use.

CBD has been found to be generally well tolerated, with a good safety profile. Adverse effects of CBD use include loss of appetite, diarrhoea and fatigue.

Therapeutic applications of CBD are being researched for a variety of clinical uses. Research in this area is most advanced in the treatment of epilepsy. In clinical trials, one pure CBD product has demonstrated effectiveness for treating some forms of epilepsy, such as Lennox-Gastaut Syndrome and Dravet Syndrome, that are often resistant to other forms of medication. Since the Committee met, a pure CBD product has received marketing approval by the Food and Drug Administration of the United States of America.

CBD is not specifically listed in the schedules of the 1961, 1971 or 1988 United Nations international drug control conventions. However, if prepared as an extract or tincture of cannabis, it is controlled in Schedule I of the 1961 Convention.

There is no evidence that CBD as a substance is liable to similar abuse and similar ill-effects as substances in the 1961 or 1971 Conventions such as cannabis or THC, respectively.

The Committee recommended that preparations considered to be pure CBD should not be scheduled.

Cannabis plant and resin

Cannabis is defined as the flowering tops or separated resin of the *Cannabis sativa* plant. Cannabis contains 121 reported phytocannabinoids, with the most prominent of these compounds being Δ^9-THC (THC) and CBD. THC is thought to be the principal intoxicant constituent of cannabis.

When consumed acutely, cannabis causes adverse effects such as dizziness and impaired motor control and cognitive function. Cannabis can cause driving impairment. There are particular reported risks for children such as respiratory depression, tachycardia and coma. The adverse effects of cannabis consumption are similar to those produced by THC alone.

Most of the adverse effects associated with cannabis result from chronic use. Regular cannabis use is associated with increased risk of mental health disorders such as anxiety, depression and psychotic illness. Chronic regular cannabis use is particularly problematic for young people as a result of the effects on the developing brain.

Cannabis can cause physical dependence in humans, as evidenced by the onset of cannabis withdrawal symptoms upon abstinence. Withdrawal syndromes include mood changes, irritability and sleep impairment. Clinical diagnostic guidelines such as DSM-5 and ICD-10 recognize cannabis use disorder.

The Committee considered information regarding the therapeutic indications of cannabis and ongoing research for its possible medical applications. Several countries permit the use of cannabis for the treatment of medical conditions such as back pain, sleep disorders, depression, post-injury pain and multiple sclerosis. Research with cannabis on its potential medical applications is ongoing.

Cannabis plant and cannabis resin are placed in Schedule I and Schedule IV of the 1961 Convention. Substances that are included in both Schedules I and IV of the 1961 Convention are particularly liable to abuse and to produce ill-effects. Other substances included in both Schedules I and IV are fentanyl analogues and other opioids considered especially dangerous.

The evidence presented to the Committee did not indicate that cannabis plant and cannabis resin were liable to produce ill-effects similar to these other substances that are in Schedule IV of the 1961 Convention. The inclusion of cannabis and cannabis resin in Schedule IV may not appear to be consistent with the criteria for Schedule IV.

The Committee concluded that there is sufficient evidence to proceed to a critical review of cannabis plant and cannabis resin at a future meeting of the Expert Committee on Drug Dependence and explore further the appropriateness of their current scheduling within the 1961 Convention.

Extracts and tinctures of cannabis

Extracts and tinctures of cannabis are substances that have been extracted from the *Cannabis sativa* plant. These include preparations such as cannabis oils, teas and nabiximols (an extract with approximately equal quantities of THC and CBD). These substances can be administered through various routes, including through oral consumption and smoke inhalation.

Evidence around the dependence potential of extracts and tinctures of cannabis varies by substance. There are no published studies that have evaluated the dependence potential of nabiximols, but there is limited evidence of a withdrawal syndrome upon abrupt cessation (e.g., sleep disruption or mood changes). The frequent use of butane hash oil has been associated with physical dependence. The psychoactive constituent Δ^9-THC present in a majority of extracts has been separately examined and has been shown to have dependence potential.

There are few published studies that have evaluated the abuse potential of cannabis extracts in animals or humans. There are, however, studies that have investigated the abuse potential of various components of extracts and tinctures of cannabis. While particular components, such as Δ^9-THC, have demonstrated abuse potential, other components in these preparations, such as CBD, do not have abuse potential.

The Committee recognized that the term “extracts and tinctures” as cited in the 1961 Convention encompasses preparations that have psychoactive properties, as well as those that do not have such properties. The Committee also recognized that the psychoactive properties of these preparations are due to Δ^9-THC and possibly isomers of THC, substances which are currently scheduled in the Convention on Psychotropic Substances of 1971. Among the substances that are not psychoactive within the preparations that are derived as extracts or tinctures of cannabis, some, such as CBD, have promising therapeutic indications.

Cannabis extracts and tinctures are placed in Schedule I of the 1961 Single Convention on Narcotic Drugs.

The Committee noted that the category “Extracts and tinctures of cannabis” encompasses a variety of very diverse formulations with varying ratios of cannabis components, in particular THC, and with or without psychoactive properties.

The Committee therefore concluded that there is sufficient information to progress extracts and tinctures of cannabis to critical review at a future meeting of the Expert Committee on Drug Dependence in order to address the necessity of continuing to include the nomenclature “extracts and tinctures of cannabis” in the 1961 Convention.

Delta-9-tetrahydrocannabinol

Delta-9-tetrahydrocannabinol (THC) refers to four stereoisomers of Δ^9-THC. One of these stereoisomers is known by the International Nonproprietary Name (INN) dronabinol, and has recognized therapeutic uses.

Chronic administration of Δ^9-THC can induce physical dependence in laboratory animals and in humans. This has been evidenced by the presence of withdrawal effects in animals and human subjects.

The subjective effects of Δ^9-THC when administered orally resemble those of cannabis. However, there is little evidence that oral Δ^9-THC is used for non-medical purposes so as to cause a public health problem.

Δ^9-THC (dronabinol) has approval in a number of countries for therapeutic indications, including anorexia associated with weight loss in patients with acquired immune deficiency syndrome (AIDS) and for nausea and vomiting associated with cancer chemotherapy. Δ^9-THC (dronabinol) is routinely administered orally.

Δ^9-THC and its stereoisomers are listed in Schedule II of the 1971 Convention.

In previous reviews by the Expert Committee on Drug Dependence, Δ^9-THC and especially dronabinol had been considered in a synthetic form as a pharmaceutical preparation.

However, the Committee recognized that Δ^9-THC, in particular its active and naturally occurring stereoisomer, dronabinol, today also refers to the main psychoactive component of cannabis and cannabis-derived psychoactive products. In this form, dronabinol produces similar ill-effects, dependence and abuse potential to cannabis, which is controlled under the 1961 Convention. A substance liable to similar

abuse and productive of similar ill-effects as that of a substance already scheduled within the 1961 Convention would normally be scheduled in the same way as that substance.

The Committee concluded that there is sufficient information to progress Δ^9-THC to critical review at a future meeting of the Expert Committee on Drug Dependence in order to address the appropriateness of its scheduling under the Conventions.

Isomers of tetrahydrocannabinol

There are currently six isomers of tetrahydrocannabinol (THC) listed in Schedule I of the 1971 Convention.

Of the six THC isomers reviewed here, the abuse potential of only two, Δ^8-THC and Δ6a,10a-THC, have been evaluated in a few human studies. These studies found that the acute intoxicating effects of these substances are similar to those of Δ^9-THC, but they are less potent.

There are no reports that THC isomers induce physical dependence. There are no reported medical or veterinary uses of these isomers.

There is no evidence that any of these listed isomers are being abused or are likely to be abused so as to constitute a public health or social problem. However, the Committee noted the potential difficulty of differentiating these six isomers (listed in Schedule I of the 1971 Convention) from Δ^9-THC (listed in Schedule II of the 1971 Convention) using standard methods of chemical analysis, due to their chemical similarities. The Committee further noted that this is an important factor to consider in the scheduling of these isomers.

The Committee concluded that there is sufficient information to progress the isomers of THC to critical review at a future meeting of the Expert Committee on Drug Dependence and to explore further the relevance of their current scheduling under the 1971 Convention.

Annex II

Extract of the notification dated 24 January 2019 from the Director-General of the World Health Organization to the Secretary-General on cannabis and cannabis-related substances, containing scheduling recommendations on substances controlled under the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, and the Convention on Psychotropic Substances of 1971, including the relevant extract from the report on the forty-first meeting of the Expert Committee on Drug Dependence

With reference to article 3, paragraphs 1, 3, 5 and 6, of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, and article 2, paragraphs 1, 4 and 6, of the Convention on Psychotropic Substances of 1971, I am pleased to submit recommendations of the Expert Committee on Drug Dependence at its forty-first meeting regarding the review of cannabis and cannabis-related substances, as follows:

Cannabis and cannabis-related substances

Cannabis and cannabis resin

- To be deleted from Schedule IV of the 1961 Convention

Dronabinol (*delta*-9-tetrahydrocannabinol)

- To be added to Schedule I of the 1961 Convention
- To be deleted from Schedule II of the 1971 Convention, subject to the adoption by the Commission on Narcotic Drugs of the recommendation to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention

Tetrahydrocannabinol (isomers of *delta*-9-tetrahydrocannabinol)

- To be added to Schedule I of the 1961 Convention, subject to the adoption by the Commission of the recommendation to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention
- To be deleted from Schedule I of the 1971 Convention, subject to the adoption by the Commission of the recommendation to add tetrahydrocannabinol to Schedule I of the 1961 Convention

Extracts and tinctures

- To be deleted from Schedule I of the 1961 Convention

Cannabidiol preparations

- To give effect to the recommendation of the Expert Committee on Drug Dependence at its fortieth meeting that preparations considered to be pure cannabidiol (CBD) should not be scheduled within the international drug control conventions, by adding a footnote to the entry for cannabis and cannabis resin in Schedule I of the 1961 Convention to read “Preparations containing predominantly cannabidiol and not more than 0.2 per cent of *delta*-9-tetrahydrocannabinol are not under international control.”

Preparations produced either by chemical synthesis or as preparations of cannabis that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that *delta*-9-tetrahydrocannabinol (dronabinol) cannot be recovered by readily available means or in a yield which would constitute a risk to public health

- To be added to Schedule III of the 1961 Convention

The assessments and findings on which they are based are set out in detail in the report on the forty-first meeting of the Expert Committee on Drug Dependence.

Extract from the report on the forty-first meeting of the Expert Committee on Drug Dependence

5. Cannabis and cannabis-related substances

5.1 Cannabis and cannabis-resin

In the 1961 Convention, cannabis and cannabis resin are described, respectively, as the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted, and as the separated resin, whether crude or purified, obtained from the cannabis plant. References to cannabis below will be taken to also include cannabis resin. Of the many compounds in cannabis, *delta*-9-tetrahydrocannabinol (Δ^9-THC) is the principal psychoactive constituent of cannabis, while CBD is also present but is not psychoactive.

Following consumption of cannabis, the adverse effects experienced include dizziness and impairment of motor control and cognitive function. As a result of the effects on movement and cognition, cannabis use can impair driving. There are particular risks of cannabis use reported for children, such as respiratory depression, tachycardia and coma. The adverse effects of cannabis consumption are similar to those produced by Δ^9-THC alone.

There are also a number of adverse effects associated with long-term cannabis use, particularly increased risk of mental health disorders such as anxiety, depression and psychotic illness. Chronic regular cannabis use is particularly problematic for young people because of its effects on the developing brain.

Cannabis can cause physical dependence in people who use the drug daily or near daily. This is evidenced by the onset of cannabis withdrawal symptoms that occur upon abstinence; these symptoms include gastrointestinal disturbance, appetite changes, irritability, restlessness and sleep impairment. Clinical diagnostic guidelines such as DSM-5 and ICD-10 recognize cannabis dependence and other disorders related to cannabis use.

The Committee considered information regarding the therapeutic indications of cannabis and ongoing research into its possible medical applications. A number of countries permit the use of cannabis for the treatment of medical conditions such as chemotherapy-induced nausea and vomiting, pain, sleep disorders and spasticity associated with multiple sclerosis. The Committee recognized the limited robust scientific evidence on the therapeutic use of cannabis. However, some oral pharmaceutical preparations of cannabis have therapeutic advantages for treatment of conditions such as certain forms of pain and epilepsy. Preparations of cannabis are defined as a mixture, solid or liquid containing cannabis and are generally subject to the same measures of control as cannabis and cannabis resin as per article 2, paragraph 3, of the 1961 Convention.

Cannabis and cannabis resin are included in Schedule I and Schedule IV of the 1961 Convention. Substances that are included in both these Schedules are particularly liable to abuse and to produce ill-effects and have little or no therapeutic use. Other substances that are included in both Schedules I and IV are fentanyl analogues, heroin and other opioids that are considered especially dangerous. Use of

all these substances is associated with a significant risk of death, whereas cannabis use is not associated with such risk.

The evidence presented to the Committee did not indicate that cannabis plant and cannabis resin were particularly liable to produce ill-effects similar to the effects of the other substances in Schedule IV of the 1961 Convention. In addition, preparations of cannabis have shown therapeutic potential for treatment of pain and other medical conditions, such as epilepsy and spasticity associated with multiple sclerosis. In line with the above, cannabis and cannabis resin should be scheduled at a level of control that will prevent harm caused by cannabis use and at the same time will not act as a barrier to access and to research and development of cannabis-related preparations for medical use.

The Committee concluded that the inclusion of cannabis and cannabis resin in Schedule IV is not consistent with the criteria for a drug to be placed in Schedule IV.

The Committee then considered whether cannabis and cannabis resin were better placed in Schedule I or Schedule II of the 1961 Convention. While the Committee did not consider that cannabis is associated with the same level of risk to health as most of the other drugs that have been placed in Schedule I, it noted the high rates of public health problems arising from cannabis use and the global extent of such problems, and for these reasons recommended that cannabis and cannabis resin continue to be included in Schedule I of the 1961 Convention.

Recommendation 5.1: The Committee recommended that cannabis and cannabis resin be deleted from Schedule IV of the 1961 Convention.

5.2 Dronabinol (*delta*-9-tetrahydrocannabinol; Δ^9-THC)

The main psychoactive substance in the cannabis plant is one of the four stereoisomers of *delta*-9-tetrahydrocannabinol (Δ^9-THC). This substance has therapeutic uses and is sometimes known by its international non-proprietary name, dronabinol. It is currently placed in Schedule II of the 1971 Convention.

At the time of the adoption of the 1961 Convention, scientific research had not identified Δ^9-THC as the main psychoactive compound in cannabis. Subsequently, Δ^9-THC was included in the 1971 Convention at its inception. In previous reviews by the Expert Committee on Drug Dependence, the active and naturally occurring stereoisomer of Δ^9-THC known as dronabinol had been considered in a synthetic form as a pharmaceutical preparation. Following a recommendation from the Expert Committee on Drug Dependence at its twenty-seventh meeting, dronabinol was placed in Schedule II of the 1971 Convention. The Commission on Narcotic Drugs, however, did not adopt a subsequent recommendation to place dronabinol in Schedule III of the 1971 Convention.

The Committee noted that, whereas in these previous reviews by the Expert Committee on Drug Dependence, Δ^9-THC, and especially its active stereoisomer dronabinol, had been considered in a synthetic form as a pharmaceutical preparation, Δ^9-THC today also refers to the main psychoactive component of cannabis and the principal compound in illicit cannabis-derived psychoactive products. Some of these products contain Δ^9-THC at concentrations as high as 90 per cent. Butane hash oil is an example of a high-purity Δ^9-THC illicit cannabis-derived product that has recently emerged and is being used by heating and inhalation of the vapour. In such high-purity, illicitly-derived forms, Δ^9-THC produces ill-effects, dependence and abuse potential that is at least as great as for cannabis, which is placed in Schedule I of the 1961 Convention.

A substance liable to similar abuse and productive of similar ill-effects as that of a substance already scheduled within the 1961 Convention would normally be scheduled in the same way as that substance. As Δ^9-THC is liable to similar abuse as cannabis and has similar ill-effects, it meets the criteria for inclusion in Schedule I of the 1961 Convention. It was further recognized that cocaine, the principal active compound in coca, is contained along with coca leaf in Schedule I of the

1961 Convention, and morphine, the principal active compound in opium, is placed with opium in the same schedule. Placing Δ^9-THC, the principal active compound in cannabis, in the same schedule as cannabis would be consistent with this approach.

Based on requests received from Member States and information received from other United Nations agencies, the Committee understood that placing Δ^9-THC under the same Convention and in the same Schedule as cannabis, Schedule I of the 1961 Convention, would greatly facilitate the implementation of the control measures of the Conventions in Member States. Accordingly:

Recommendation 5.2.1: The Committee recommended that dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) be added to Schedule I of the 1961 Convention.

As indicated in the "Guidance on the WHO review of psychoactive substances for international control", to facilitate efficient administration of the international control system, it is not advisable to place a substance under more than one Convention. Accordingly:

Recommendation 5.2.2: The Committee recommended the deletion of dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) from the 1971 Convention, Schedule II, subject to the Commission's adoption of the recommendation to add dronabinol and its stereoisomers (*delta*-9-tetrahydrocannabinol) to Schedule I of the 1961 Convention.

5.3 Tetrahydrocannabinol (isomers of *delta*-9-tetrahydrocannabinol)

There are currently six isomers of tetrahydrocannabinol (THC) listed in Schedule I of the 1971 Convention. These six isomers are chemically similar to *delta*-9-tetrahydrocannabinol (Δ^9-THC), which is currently listed in Schedule II of the 1971 Convention, but which the Committee has recommended deleting from this Schedule and including in Schedule I of the 1961 Convention.

While these six isomers are chemically similar to Δ^9-THC, there is very limited to no evidence concerning the abuse potential and acute intoxicating effects of these isomers. There are no reports that the THC isomers listed in Schedule I of the 1971 Convention induce physical dependence or that they are being abused or are likely to be abused so as to constitute a public health or social problem. There are no reported medical or veterinary uses of these isomers.

While the Committee recognized that available evidence has not demonstrated abuse and ill-effects of these isomers similar to those associated with Δ^9-THC, it noted that, due to the chemical similarity of each of the six isomers to Δ^9-THC, it is very difficult to differentiate any of these six isomers from Δ^9-THC using standard methods of chemical analysis. The Committee understood that placing these six isomers under the same Convention and in the same Schedule as Δ^9-THC would facilitate the implementation of international control of Δ^9-THC, as well as assist Member States in the implementation of control measures at the country level. Accordingly:

Recommendation 5.3.1: The Committee recommended that tetrahydrocannabinol (understood to refer to the six isomers currently listed in Schedule I of the 1971 Convention) be added to Schedule I of the 1961 Convention, subject to the Commission's adoption of the recommendation to add dronabinol (*delta*-9-tetrahydrocannabinol) to the 1961 Convention, in Schedule I.

As indicated in the "Guidance on the WHO review of psychoactive substances for international control", to facilitate efficient administration of the international control system, it is not advisable to place a substance under more than one Convention. Accordingly:

Recommendation 5.3.2: The Committee recommended that tetrahydrocannabinol (understood to refer to the six isomers currently listed in Schedule I of the 1971 Convention) be deleted from the 1971 Convention, subject to the Commission's

adoption of the recommendation to add tetrahydrocannabinol to Schedule I of the 1961 Convention.

5.4 Extracts and tinctures of cannabis

Extracts and tinctures of cannabis are preparations that are produced by application of solvents to cannabis and that are currently placed in Schedule I of the 1961 Convention. These include both medical preparations such as that containing an approximately equal mixture of *delta*-9-tetrahydrocannabinol (dronabinol; Δ^9-THC) and CBD and non-medical preparations with high concentrations of Δ^9-THC such as butane hash oil. While the medical extracts and tinctures are administered orally, those produced and used illicitly are normally inhaled following heating and vaporization.

The Committee recognized that the term "extracts and tinctures of cannabis", as cited in the 1961 Convention, encompasses these diverse preparations that have psychoactive properties as well as those that do not. The Committee also recognized that the variability in psychoactive properties of these preparations is due principally to varying concentrations of Δ^9-THC, which is currently scheduled in the 1971 Convention, and that some extracts and tinctures of cannabis without psychoactive properties and including predominantly CBD have promising therapeutic applications. The fact that diverse preparations with a variable concentration of Δ^9-THC are controlled within the same entry, "Extracts and tinctures", and the same Schedule, is a challenge for responsible authorities that implement control measures in countries.

As per the 1961 Convention, preparations are defined as mixtures, solids or liquids containing a substance in Schedule I or II and are generally subject to the same measures of control as that substance. The Committee noted that, by this definition, the 1961 Convention may cover all products that are "extracts and tinctures" of cannabis as "preparations" of cannabis and also, if the Committee's recommendation to move dronabinol to Schedule I of the 1961 Convention was followed, as "preparations" of dronabinol and its stereoisomers. Accordingly:

Recommendation 5.4: The Committee recommended deleting extracts and tinctures of cannabis from Schedule I of the 1961 Convention.

5.5 Cannabidiol preparations

At its fortieth meeting, the Expert Committee on Drug Dependence considered a critical review of CBD and recommended that preparations considered to be pure CBD should not be scheduled within the international drug control conventions. CBD is found in cannabis and cannabis resin but does not have psychoactive properties and has no potential for abuse and no potential to produce dependence. It does not have significant ill-effects. CBD has been shown to be effective in the management of certain treatment-resistant, childhood-onset epilepsy disorders. It was approved for this use in the United States of America in 2018 and is currently under consideration for approval by the European Union.

CBD can be chemically synthesized or it can be prepared from the cannabis plant. The approved medication (Epidiolex) is a preparation of the cannabis plant. The Committee noted that medicines without psychoactive effects that are produced as preparations of the cannabis plant will contain trace amounts of *delta*-9-tetrahydrocannabinol (Δ^9-THC; dronabinol). The CBD preparation approved for the treatment of childhood-onset epilepsy, Epidiolex, contains not more than 0.15 per cent Δ^9-THC by weight and has no effects indicative of potential for abuse or dependence. In keeping with the recommendation that preparations considered pure CBD not be controlled, and recognizing that trace levels of Δ^9-THC may be found in such preparations, such as the concentration of 0.15 per cent in Epidiolex, while acknowledging that chemical analysis of Δ^9-THC to an accuracy of 0.15 per cent may be difficult for some Member States:

Recommendation 5.5: The Committee recommended that a footnote be added to Schedule I of the 1961 Convention to read "Preparations containing predominantly cannabidiol and not more than 0.2 per cent of *delta*-9-tetrahydrocannabinol are not under international control."

5.6 Pharmaceutical preparations of cannabis and dronabinol (*delta*-9-tetrahydrocannabinol)

There are currently two main types of registered medicines that contain *delta*-9-tetrahydrocannabinol (Δ^9-THC; dronabinol).

One type is a preparation of cannabis that contains both the psychoactive Δ^9-THC and the non-psychoactive CBD in approximately equal concentrations, e.g., Sativex. This is used for the treatment of spasticity due to multiple sclerosis.

A second type contains only Δ^9-THC as the active compound and is used for the treatment of anorexia associated with weight loss in patients with acquired immune deficiency syndrome (AIDS) and for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional anti-emetic treatments.

Currently approved medicines with Δ^9-THC as the only active compound use synthetically produced Δ^9-THC, e.g., Marinol and Syndros, although it is possible in the future that medicines with equivalent amounts of Δ^9-THC could be prepared from cannabis. There is no difference in the therapeutic effects or adverse effects of synthetic Δ^9-THC compared to Δ^9-THC from the cannabis plant.

These medicines are all taken orally and are approved for use in a number of countries.

The evidence concerning the use of these Δ^9-THC-containing medicines is that they are not associated with problems of abuse and dependence and they are not diverted for the purpose of non-medical use.

The Committee recognized that such preparations are formulated in a way that they are not likely to be abused and there is no evidence of actual abuse or ill-effects to an extent that would justify the current level of control associated with Schedule I of the 1961 Convention for cannabis-based preparations such as Sativex and the level of control associated with Schedule II of the 1971 Convention, for preparations using synthetic *delta*-9-THC, e.g., Marinol and Syndros.

In order not to impede access to these medicines, and in reference to article 3, paragraph 4, of the 1961 Convention:

Recommendation 5.6: The Committee recommended that preparations containing *delta*-9-tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as preparations of cannabis that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that *delta*-9-tetrahydrocannabinol (dronabinol) cannot be recovered by readily available means or in a yield which would constitute a risk to public health, be added to Schedule III of the 1961 Convention.