4TH INTERSESSIONAL MEETING COMMISSION ON NARCOTIC DRUGS 62ND SESSION
RECOMMENDATIONS BY THE WHO ON CANNABIS Y CANNABIS RELATED SUBSTANCES
(24TH JUNE 2019)

General Comment

Mexico reiterates its full support to the work undertaken by WHO, including through its Experts Committee on Drug Dependence (ECDD), in undertaking its responsibilities derived from the international conventions.

Mexico welcomes that finally the CND is the position of starting its examination on cannabis, bearing in mind as every single State Party knows, that is original inclusion the scheduling lists over six decades ago was not supported by a scientific analysis. The CND has not only the opportunity but rather the duty to fulfil its commitments, as established both in the conventions and the relevant General Assembly and ECOSC resolutions which govern its work.

Annex 1- Extract from the Report of the 41st Expert Committee on Drug Dependence: Cannabis and cannabis-related substances

5. Cannabis and cannabis-related substances

General comments:

1. *Do the medical and scientific communities have the same tools now that they had when the Convention was drafted?*
2. *Does the knowledge about the different components of Cannabis is the same in 2019 than 50 or 60 years ago?*
3. *Could you confirm if the "single species concept" was still widely accepted by the time of the drafting of the Convention?*
4. *Could you confirm if the original concept of Cannabis as a "single species" has finally been fully overcome? Should it be not the case, could you elaborate in which circles is this outdated notion still in vogue?*
5. *Is there now a better understanding by the scientific and medic communities both of the different components of Cannabis, well beyond the differentiation captured in the Single Convention, as well as the differences of their characteristics and properties?*
6. *Is there a different perception regarding the Poppy plant and seeds, opium and heroin, or the Coca plant and leaves versus cocaine than there is between Cannabis as a plant and as a narcotic drug? Did this deference prevail in the Convention? What were the reasons?*

5.1 Cannabis and cannabis resin

In the 1961 Single Convention on Narcotic Drugs, 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. Reference to cannabis below will be taken to also include cannabis resin. Of the many compounds in cannabis, delta-9tetrahydrocannabinol (Δ9-THC) is the principal psychoactive constituent of cannabis, while cannabidiol (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 Δ9-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 recognised 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 2.3 of the 1961 Single Convention on Narcotic Drugs

Cannabis and cannabis resin are included in Schedule I and Schedule IV of the 1961 Single Convention on Narcotic Drugs. 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 Single Convention on Narcotic Drugs. 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 preparation 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 Single Convention on Narcotic Drugs. While the Committee did not consider that cannabis is associated with the same level of risk to health of 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 Single Convention on Narcotic Drugs.

• *Recommendation 5.1: The Committee recommended that Cannabis and Cannabis Resin be deleted from Schedule IV of the 1961 Single Convention on Narcotic Drugs*.

Questions:

- if Δ9-THC is the only psychoactive constituent of cannabis then, why continue to refer to Cannabis as whole, when addressing the narcotic effects of a particular substance?
- could you elaborate on why Δ9-THC was paragoned to fentanyl, heroin and other opioids, given that in terms of toxicity and mortality are completely different? Is there any medical or scientific reason, other than ignorance, that could continue to justify the inclusion of THC within the same List as those substances?

- if the Committee “did not consider that cannabis is associated with the same level of risk to health of most of the other drugs that have been placed in Schedule I”... it “recommended that cannabis and cannabis resin continue to be included in Schedule I of the 1961 Single Convention on Narcotic Drugs”.
- if toxicity and mortality are out of the question, what are the other “public health problems arising from cannabis use and the global extent of such problems and for these reasons”? What is the metric for determining that there are “high rates”? What would be the difference between those “health problems” and problems arising from the consumption of other substances such as sugar, not to mention alcohol or tobacco, or modern practices such as “work burn out”?

5.2 Dronabinol (delta-9-tetrahydrocannabinol; Δ9-THC)

The main psychoactive substance in the cannabis plant is one of the four stereoisomers of delta-9tetrahydrocannabinol (Δ9-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 on Psychotropic Substances.

At the time of the adoption of the 1961 Single Convention on Narcotic Drugs, scientific research had not identified Δ9-THC as the main psychoactive compound in cannabis. Subsequently, Δ9-THC was included in the 1971 Convention on Psychotropic Substances at its inception. In previous ECDD reviews, the active and naturally occurring stereoisomer of Δ9-THC known as dronabinol had been considered in a synthetic form as a pharmaceutical preparation. Following a recommendation from the 27th ECDD, dronabinol was placed in Schedule II of the 1971 Convention on Psychotropic Substances. The Commission on Narcotic Drugs however did not adopt a subsequent recommendation to place dronabinol in Schedule III of the 1971 Convention on Psychotropic Substances.

The Committee noted that whereas in these previous ECDD reviews Δ9-THC, and especially its active stereoisomer dronabinol, had been considered in a synthetic form as a pharmaceutical preparation, Δ9THC 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 Δ9-THC at concentrations as high as 90%. Butane hash oil is an example of a high purity Δ9-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, Δ9-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 Single Convention on Narcotic Drugs.

A substance liable to similar abuse and productive of similar ill-effects as that of a substance already scheduled within the 1961 Single Convention on

Narcotic Drugs would normally be scheduled in the same way as that substance. As Δ9-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 Single Convention on Narcotic Drugs. It was further recognised that cocaine, the principal active compound in coca is placed along with coca leaf in Schedule I of the 1961 Single Convention on Narcotic Drugs and morphine, the principal active compound in opium, is placed with opium in the same schedule. Placing Δ9-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 UN agencies, the Committee understood that placing Δ9-THC under the same Convention and in the same schedule as cannabis, Schedule I of the 1961 Single Convention on Narcotic Drugs, 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 Single Convention on Narcotic Drugs.*
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 on Psychotropic Substances, 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 Single Convention on Narcotic Drugs*

Questions:

- If Δ9-THC was already identified by 1971 as being the only narcotic agent present in cannabis, why did the international regime on cannabis control was never updated?
- What would be the rationale for ECDD to compare the "active and naturally occurring stereoisomer of Δ9-THC known as dronabinol" to synthetic versions? Is it even scientifically sound to address together and paragon any natural product with synthetic ones?
- Does Δ9-THC at concentrations as high as 90% of exists naturally or is the result of human manipulation or bioengineering? If it is not the case, is it scientifically sound to address the natural concentrations of Δ9-THC together with manipulated versions?
- Are you familiar with the work on sugar and yeast of companies such as San Francisco based CB Therapeutics?
- Could you elaborate on the last paragraph in relation to the requests received by Member States and information by UN agencies? Who,

what and why? Could you elaborate on why listing dronabinol and Δ9-THC "would greatly facilitate the implementation of the control measures of the Conventions in Member States"?

- *Bearing in mind that ECDD undoubtedly affirms that cannabis cannot be associated to the same level of risk to health tan other substances scheduled in Lista 1 of the Single Conventions, at the same time it recommends to place individually dronabinol and TCH on that List. Is it not a contradiction?*

5.3 Tetrahydrocannabinol (isomers of delta-9-tetrahydrocannabinol)

There are currently six isomers of tetrahydrocannabinol (THC) listed in Schedule I of the 1971 Convention on Psychotropic Substances. These six isomers are chemically similar to delta-9tetrahydrocannabinol (Δ9-THC), which is currently listed in Schedule II of the 1971 Convention on Psychotropic Substances, but which the Committee has recommended deleting from this Schedule and including in Schedule I of the 1961 Single Convention on Narcotic Drugs.

While these six isomers are chemically similar to Δ9-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 recognised that available evidence has not demonstrated abuse and ill effects of these isomers similar to those associated with Δ9-THC, it noted that, due to the chemical similarity of each of the six isomers to Δ9-THC, it is very difficult to differentiate any of these six isomers from Δ9THC using standard methods of chemical analysis. The Committee understood that placing these six isomers under the same Convention and in the same Schedule as Δ9-THC would facilitate the implementation of international control of Δ9-THC, as well as assist Member States in the implementation of control measures at 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 on Psychotropic Substances) be added to Schedule I of the 1961 Single Convention on Narcotic Drugs, subject to the Commission's adoption of the recommendation to add dronabinol (delta-9-tetrahydrocannabinol) to the 1961 Single Convention on Narcotic Drugs 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 on Psychotropic Substances) be deleted from the 1971 Convention on Psychotropic Substances, subject to the Commission's adoption of the recommendation to add tetrahydrocannabinol to Schedule I of the 1961 Single Convention on Narcotic Drugs.*

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 Single Convention on Narcotic Drugs. These include both medical preparations such as that containing an approximately equal mixture of delta-9-tetrahydrocannabinol (dronabinol; Δ9-THC) and cannabidiol and non-medical preparations with high concentrations of Δ9-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 vaporisation.

The Committee recognised that the term Extracts and Tinctures of Cannabis as cited in the 1961 Single Convention on Narcotic Drugs encompasses these diverse preparations that have psychoactive properties as well as those that do not. The Committee also recognised that the variability in psychoactive properties of these preparations is due principally to varying concentrations of Δ9-THC, which is currently scheduled in the 1971 Convention on Psychotropic Substances, and that some extracts and tinctures of cannabis without psychoactive properties and including predominantly cannabidiol have promising therapeutic applications. The fact that diverse preparations with a variable concentration of delta-9 THC are controlled within the same entry "Extract and Tinctures" and the same schedule, is a challenge for responsible authorities that implement control measures in countries.

As per the 1961 Single Convention on Narcotic Drugs, preparations are defined as mixtures, solid, or liquid 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 Single Convention on Narcotic Drugs 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 Single Convention on Narcotic Drugs 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 Single Convention on Narcotic Drugs.*

5.5 Cannabidiol preparations

At its 40th Meeting the ECDD considered a critical review of cannabidiol and recommended that preparations considered to be pure cannabidiol should not be scheduled within the International Drug Control Conventions. Cannabidiol 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. Cannabidiol 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 in 2018 and is currently under consideration for approval by the EU.

Cannabidiol 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 (Δ9-THC; dronabinol). The cannabidiol preparation approved for the treatment of childhood-onset epilepsy, Epidiolex, contains not more than 0.15% Δ9-THC by weight and has no effects indicative of potential for abuse or dependence. In keeping with the recommendation that preparations considered pure cannabidiol not be controlled and recognising that trace levels of Δ9-THC may be found in such preparations, such as the concentration of 0.15% in Epidiolex, while acknowledging that chemical analysis of Δ9-THC to an accuracy of 0.15% may be difficult for some Member States:

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

- *How did the ECDD came to the range of 0.2% of THC for making this recommendation?*
- *Could it not be somewhat arbitrarily to set a specific percentage?*

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

There are currently two main types of registered medicines that contain delta-9-tetrahydrocannabinol (Δ9-THC; dronabinol).

One type is a preparation of cannabis that contains both the psychoactive Δ9-THC and the nonpsychoactive cannabidiol in approximately equal concentrations e.g. Sativex. This is used for the treatment of spasticity due to multiple sclerosis.

A second type contains only Δ9-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 antiemetic treatments.

Currently approved medicines with Δ9-THC as the only active compound use synthetically produced Δ9-THC, e.g. Marinol, Syndros, although it is possible in the future that medicines with equivalent amounts of Δ9-THC could be prepared from cannabis. There is no difference in the therapeutic effects or adverse effects of synthetic Δ9-THC compared to Δ9-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 Δ9-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 recognised 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 Single Convention on Narcotic Drugs for cannabis based preparations such as Sativex and the level of control associated with Schedule II of the 1971 Convention on Psychotropic Substances, 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 3.4 of the 1961 Single Convention on Narcotic Drugs

• *Recommendation 5.6: The Committee recommended that preparations containing delta-9tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as a preparation 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 on Narcotic Drugs*

Questions:

- *Could you reconfirm that the statement "There is no difference in the therapeutic effects or adverse effects of synthetic Δ9-THC compared to Δ9-THC from the cannabis plant", refers exclusively to the current versions of synthetic Δ9-THC approved for medical use? Hence, would it be safe to affirm that new versions of synthetic Δ9-THC should be addressed on their own?*
- *Could you elaborate further on what would be covered by the term "pharmaceutical preparations of cannabis" in relation to this recommendation.*