February 15, 2020

Secretariat to the Governing Bodies
Division for Treaty Affairs
United Nations Office on Drugs and Crime
P.O. Box 500
Vienna International Centre
1400 Vienna, Austria

Re: WHO/ECDD Recommendation of CBD rescheduling

Dear Sir or Madam:
Community Alliances for Drug Free Youth (CADFY) has grave concerns regarding the specifics of the World Health Organization (WHO) and its Expert Committee on Drug Dependence (ECDD) recent analysis on the abuse potential and appropriate scheduling of cannabis and cannabidiol (CBD).

CADFY is writing to provide further information concerning the composition of Epidiolex®, which may in part have contributed to ECDD's considerations in reaching its recommendation concerning the scheduling status of preparations containing predominantly cannabidiol. In section 5.5 (Cannabidiol Preparations) of Annex 1 of ECDD's 41st Report, ECDD recommended the following:

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.

That recommendation appeared to have been based in large part on ECDD's understanding of the abuse potential data relating to Epidiolex®. This is understandable, since the Epidiolex® U.S. development program has produced the most robust body of scientific data on cannabidiol. The Report stated that: "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 recognizing 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."

Meaning of the Term "Preparation"

The ECDD's use of the term "preparation" has been widely interpreted by the general public (including the manufacturers of CBD products) to mean a finished product containing cannabidiol. In Article 1 (1)(s) of the Single Convention on Narcotic Drugs 1961, the term "preparation" is broadly defined: "'Preparation' means a mixture, solid or liquid, containing a drug." Furthermore, Section 2 differentiates "preparations" from the drugs which they contain. For example, Article 2(3) states that "Preparations other than those in Schedule III are subject to the same measure of control as the drugs which they contain." Furthermore, cannabis extracts and tinctures are separately listed as "drugs" in Schedule I.

Therefore, it is not surprising that many would interpret the ECDD's use of the term to refer to finished products.

Content of Epidiolex® as a Finished Product

To the extent that the ECDD intended to use the term "preparation" to apply to finished products, the recommendation may have been influenced by **inadequate information concerning the composition of Epidiolex®**.

Epidiolex® is manufactured from a high-CBD containing crude extract, which subsequently undergoes a purification process that removes all but tiny amounts of THC and other cannabinoids. This process results in a crystalline powder comprised of purified CBD. This crystalline powder forms the **Active Pharmaceutical Ingredient** (API). The API is then formulated in sesame oil and other excipients to form the finished product, Epidiolex®.

In Epidiolex®, it is the **crystalline API that has a concentration of 0.1% w/w THC**. **Then the THC concentration in the API is diluted 10-fold** in the **finished product** by the process of formulation in sesame oil and other excipients to form the final product, Epidiolex®.

Epidiolex® is comprised of 100mg of CBD per milliliter, and 100 ml per bottle of finished preparation. Therefore, there are 10,000mg of CBD per bottle. Since the THC content of the bottle is 0.1% w/w of the API weight (essentially the total crystalline CBD content), there would be at most 10mg of THC in a bottle.

As a result of the ambiguity in the ECDD's intended meaning in its use of the term "preparation," it is unclear whether the 0.2% THC limit that the committee recommends refers to THC

(1) as a percentage of the total weight/content of the Active Pharmaceutical Ingredient (i.e. weight by weight or "w/w"),

(2) as a percentage of mass to volume (i.e. grams/milliliter X 100 or "w/v)," of a finished product or

(3) as a percentage of the total weight of the finished product (w/w of the finished product).

If THC is not measured as a percent of the Active Pharmaceutical Ingredient (purified, crystalline CBD), the THC content can be measured in finished products in two ways. First, the THC content of a finished product can be measured on a weight to volume basis, i.e. grams/milliliter X 100. Under that approach, the THC content of the Epidiolex® bottle **is 0.01%** w/v, **which is 20 times less than the maximum THC level recommended by ECDD to be allowed in CBD preparations**.

Second, the weight of THC in the finished preparation can instead be measured **as a percentage of the total weight of the preparation** (taking into account the specific gravity of the oil, such as sesame oil). It is important for ECDD to clarify its meaning of the use of the term "preparation" **because, if THC percentage is measured in finished products, CBD "preparations" containing 0.2% THC would contain significant amounts of THC.**

By way of perspective, a user who ingested 3 ml of a CBD finished product/preparation with 0.2% THC (there are 5 ml in a teaspoon) could be consuming 5.5mg-6mg THC. A single CBD gummy bear weighing 4 grams could contain 8mg THC. Under Oregon's recreational cannabis laws, a serving of a THC-containing cannabis edible (such as a gummy candy or a single square of a chocolate bar) cannot exceed 5 mg of THC. Oregon has determined that 5 mg of THC is sufficient to produce psychoactivity, particularly in an inexperienced or infrequent user or an elderly person.

This level of THC (0.2%), if measured as other than the % of THC to the total content of crystalline CBD/API (w/w), would therefore be able to produce psychoactivity, depending on the amount taken in a single administration and also depending on whether a product is taken orally, oromucosally or inhaled (as with vaping), and would produce potential impairment in unsuspecting individuals, who believe they are consuming a product that has no intoxicating potential, thus posing a public health risk.

Preparations "Considered to be" Pure Cannabidiol

In his January 24, 2019, letter to the Secretary General of the U.N. (attached), Dr. Tedros Adhanom Ghebreyesus, Director General of WHO, stated that, to give effect to the ECDD recommendation, "preparations **considered to be** pure cannabidiol" should not be scheduled. The phrase "considered to be" is rather ambiguous.

CADFY assumes that the phrase contemplates that a determination will be made by the appropriate agency of a member State that a preparation (finished product or API) is, indeed, pure CBD. For example, the U.S. Food and Drug Administration has made such a pre-marketing determination with regard to Epidiolex®, and if FDA permits CBD to be sold in dietary supplements, it is likely that the safety and quality (which would include the content) of each product will need to be reviewed by FDA through the "New Dietary Ingredient" notification process. CADFY assumes it does **not** mean that the determination would be made solely by a manufacturer of cannabidiol products, which determination has not reviewed and approved or affirmed by a national regulatory agency.

Conclusion

CADFY believes that it is important for ECDD to clarify the intended meaning of its use of the term "preparation" and also to state specifically how it intended that the THC content would be expressed—w/w in the API, w/v in the finished product, w/w of the finished product, or mg/ml and mg/dose. Furthermore, ECDD should clarify which entity must make the determination that a preparation is "considered to be" pure CBD. CADFY believes that THC should effectively not be present in foods and dietary supplements and a 0.2% THC in finished products would pose dangers to public health. CADFY further believes that this information should be communicated to the Commission on Narcotic Drugs and the International Narcotics Control Board. Thank you so much for your assistance.

Respectfully,
John Redman
CEO CADFY