idpc
International Drug Policy Consortium

Advocacy Note

November 2017

Contribution for the pre-review of CBD and Tramadol at the 39th WHO Expert Committee on Drug Dependence

Introduction

The Expert Committee on Drug Dependence (ECDD) of the World Health Organization (WHO) will hold its 39th meeting from 6th to 10th November 2017 in Geneva.[1] The ECDD is mandated by the 1961 and 1971 UN drug conventions with the task of undertaking scientific reviews of substances and recommending their appropriate scheduling to the Commission on Narcotic Drugs (CND), taking into account both risks related to non-medical use and therapeutic usefulness.

In the context of the proliferation of new psychoactive substances, the principle of scientific review is of greater importance than ever. In this regard, scheduling plays a key role in both restricting non-medical use of controlled substances and ensuring access to controlled medicines. The UNGASS Outcome Document[2] gives due prominence to ensuring access to controlled medicines with an entire chapter dedicated to the issue, thereby raising the profile of the ECDD, which work in maintaining the principle of scientific review is critical and fully supported by IDPC.

At its 39th session, the ECDD will review a number of psychoactive substances and make recommendations to the UN Secretary General on whether and how these substances should be internationally controlled. Sixteen substances[3] will be under review at the upcoming meeting, including cannabidiol (CBD) and tramadol. In this advocacy note, IDPC offers some analysis and key recommendations on these two substances to inform the ECDD's meeting.

The ECDD pre-review of tramadol

Medical and non-medical uses of tramadol

Tramadol is a centrally-acting analgesic which was first synthesised in Germany by Grunenthal GmbH in 1962. It is used in over 100 countries,[4] and regarded as a relatively safe-acting analgesic, although it can result in various forms of intoxication when administered at high doses. These include central nervous system depression, coma, tachycardia, cardiovascular collapse and respiratory depression (including respiratory arrest). Tramadol is nonetheless used worldwide to treat both acute (for example, post-operative pain) and chronic pain (such as cancer) of moderate to severe intensity. It is also used in the treatment of opioid withdrawal, usually when other substances such as methadone and buprenorphine are unavailable. Although tramadol can produce dependence, withdrawal symptoms are mild.[5]

Tramadol is not included in the 20th WHO Model List of Essential Medicines,[6] but it is listed in various medical guidelines for pain management – for example in the WHO guidelines for cancer pain relief.[7] It is also included in several national lists of essential medicines, for instance in Bhutan, Botswana, several provinces of China, Congo, Cook Islands, Côte d'Ivoire, Croatia, Dominican Republic, Ecuador, Egypt, Ghana, Honduras, India, Iraq, Jamaica, Macedonia, Maldives, Moldova, Montenegro, Morocco, Myanmar, Namibia, Peru, Philippines, Rwanda, Serbia, Seychelles,

Box 1. ECDD pre-reviews and critical reviews of substances

The ECDD carries out two types of review in order to make its recommendations: the pre-review and the critical review. The pre-review is a preliminary exercise, carried out in order to decide on the necessity or otherwise of a critical review. This will depend on whether the pre-review indicates that a substance may require scheduling under the Conventions, though no recommendation can be arrived at by a pre-review. If no such information is identified, the ECDD will recommend that insufficient data exists to necessitate a critical review.[8]

Slovakia, Slovenia, Sri Lanka, Sudan, Tajikistan, Thailand, Timor-Leste, Togo, Trinidad and Tobago, Tanzania and Uruguay.[9]

The increase in attention to tramadol is largely the result of the upsurge in its non-medical use and trafficking, mainly in North Africa and the Middle East, in particular Egypt, Iran, Jordan, Lebanon, Qatar, Libya, Mauritius, Saudi Arabia, Nigeria and Togo.[10] The substance is reportedly mainly used as self-medication – a point on which we will come back in this note.[11] Although the substance is not under international control, it is domestically controlled by those countries where non-medical use takes place on a large scale, for instance in Egypt, Saudi Arabia, Qatar, Bahrain, Mauritius and Jordan – and Lebanon is currently considering putting the substance under national control. Egypt has been most vocal on its concerns about the non-medical use of tramadol, which led it to adopt domestic controls and to submit a conference paper at the 2017 Commission on Narcotic Drugs (CND).[12]

Previous ECDD reviews of tramadol

Tramadol has already undergone several pre-reviews by the WHO ECDD. It was first pre-reviewed at the Expert Committee's meeting held in 1992, where it was not recommended for critical review.[13] At the following pre-review in 2000, is was recommended for critical review, but at the 33rd ECDD meeting, it was not warranted for international control. Instead, it was recommended that the WHO would keep the substance under surveillance.[14]

A further pre-review followed in 2006. The ECDD concluded that despite the recent increase in tramadol use, it continued to have therapeutic usefulness and showed low levels of abuse. The Committee concluded that there were no sufficient grounds for a critical review.[15]

The latest pre-review to date was conducted in 2014 at the occasion of the 34th session of the ECDD. There, the ECDD did not modify its 2006 recommendation. In its final report, it concluded:

> 'Based on the evidence available regarding dependence, abuse and risks to public health, the Committee recommended that a critical review of tramadol is not warranted at this time'.[16]

Implications of scheduling tramadol

The tramadol market has grown rapidly over the past 20 years, in particular in Asia and the Middle East, and there is evidence of its increasing use for non-medical purposes. However, data also shows that tramadol has played a key role in filling a gap caused by over-restrictive drug controls on opioids, making the latter largely unavailable for medical purposes. Tramadol's role for medical purposes – both as legally prescribed and as self-medication – should therefore not be underestimated. This should be strongly taken into consideration when discussing the scheduling of tramadol in the international drug control treaties, as such a move would severely restrict its availability for legitimate medical uses.[17]

In preparation for the 36th ECDD meeting, Grunenthal GmbH submitted comments to the WHO, raising concerns about the impact that tramadol scheduling would have on what is now widely known as the global epidemic of pain:

> 'Pain experts unanimously share the concern that the negative effects of an international control on tramadol's medical availability will cause more pain patients to suffer. Developing countries will be the ones most severely affected – there scheduling has a huge impact on medical availability, controlled strong opioids are barely available and patients in these regions already suffer from severe under-treatment of pain'.[18]

Recommendations on tramadol

IDPC recommends that tramadol remains under WHO surveillance, but that the ECDD does not request its scheduling in the international drug control treaties to ensure its continued availability to respond to moderate to severe pain, especially in developing countries.

The ECDD pre-review of CBD

Cannabis in the UN drug control treaties

Historically, scientific assessment by the UN on cannabis has been scarce. Cannabis was last reviewed in 1935 under the League of Nations-administered system of the interwar period. This review, however, lacked a solid scientific base, being primarily focused on morality and racial stereotypes. No further official UN review has been conducted on cannabis to date, and the substance 'cannabis' (the flowering or fruiting tops of the cannabis plant) and 'cannabis resin' are currently listed under the strictest schedules of the 1961 Single Convention on Narcotic Drugs (Schedule I), with little or no recognised therapeutic value (Schedule IV). While the cannabinoids THC and delta-9-THC are scheduled under the 1971 Convention on Psychotropic Substances, CBD is not specifically listed in the schedules of either the 1961 or 1971 conventions. However, as pointed out in the pre-review report, 'cannabidiol that is produced as an extract of cannabis' could be seen to fall under the category of 'cannabis resin, extracts and tinctures' included in Schedule I of the 1961 Convention,[19] even though the Yellow List's description seems to restrict that category to 'the separated resin, crude or purified, obtained from the cannabis plant'.[20]

This level of international control over cannabis represents a glaring historical anomaly,[21] especially in light of the far-reaching scientific and social shifts which have occurred in the past decades.[22] Today, medicinal cannabis is at the forefront of discussions on drug policy reform, and over 40 jurisdictions worldwide (from 16 countries) have already moved to regulate the substance for medical purposes, including Argentina, Brazil, Canada, Chile, Colombia, the Czech Republic, Germany, Israel, Jamaica, Mexico, the Netherlands, Peru, Puerto Rico, the UK, several US states and Uruguay.

The International Narcotics Control Board (INCB) itself has recognised the medicinal properties of cannabis.[23] According to the INCB, the 'licit use of cannabis has increased considerably since 2000. Since then, more and more countries have started to use cannabis and/or cannabis extracts for medical purposes, in addition to scientific research. In 2000, total production was 1.3 tons; by 2015, it had increased to 100.2 tons'.[24] Reported requirements for 2017 indicate further growth to nearly 160 tons.[25]

ECDD considerations on cannabis and CBD

Cannabis and its derivatives have never been subjected to a scientific review by the WHO ECDD. However, the debate has moved forward within the Expert Committee over the past three years, with the WHO providing updates to the ECDD on cannabis in 2014[26] and 2015.[27] Based on those updates, the ECDD 'requested the Secretariat to begin collecting data towards a pre-review of cannabis, cannabis resin, extracts and tinctures of cannabis at a future meeting. Furthermore, it specifically requested the Secretariat to place emphasis on any therapeutic advantages that they may have relative to other existing therapeutics'.[28]

At its 38th session in 2016, the ECDD 'recommended that these pre-reviews be evaluated at a specific ECDD meeting dedicated to cannabis and its component substances to be held within the next eighteen months from the 38th meeting'.[29] The pre-review of CBD at its upcoming 39th session in November 2017 is a first step in this process.[30] This comprehensive scientific assessment is long-overdue, and IDPC welcomes the move from the ECDD to convene a special cannabis meeting in May 2018.

Recommendations on CBD

The pre-review report on CBD has found 'no effects indicative of any abuse or dependence potential', that it has demonstrated to be 'an effective treatment of epilepsy', that it 'may be a useful treatment for a number of other medical conditions', and that 'there is no evidence of rec-

reational use of CBD or any public health related problems associated with the use of pure CBD'.[31] The Expert Peer Review No. 2 also concludes:

> 'Based on available evidence CBD lacks psychoactivity, reinforcing properties and abuse liability. On the other hand, emerging findings suggest promising therapeutic usefulness. Scheduling this substance could impact accessibility for scientific and medical research'.[32]

We agree with Expert Peer Review No.1 that the pre-review 'does not justify scheduling of the substance'.[33] We request, however, that the announced pre-review of 'cannabis extracts and tinctures'[34] on the agenda of the upcoming special cannabis ECDD meeting in May 2018 clarifies the status of CBD within that broad category and, in light of the outcomes of the pre-review, considers a re-definition that explicitly excludes CBD in order to end the current ambiguity.

Procedural concerns

There are procedural issues that IDPC wishes to raise ahead of the November 2017 session. On the webpage of the 39th session of the ECDD, a note states that 'Depending on the outcome of the pre-review, the Expert Committee on Drug Dependence (ECDD) may proceed to a critical review at the same ECDD meeting'.[35] In specific cases, the WHO can rule that a pre-review for a substance is not needed and it can proceed directly to a critical review. This is possible in three instances: in the case of a notification of a party, upon review request by the CND, or when 'information is brought to WHO's attention that a substance is clandestinely manufactured, of especially serious risk to public health and society, and of no recognized therapeutic use by any Party'.[36]

While the WHO Guidance on substance review, approved by the WHO Executive Board in January 2010, provides for the option to skip a pre-review and immediately undertake a critical review in those cases, the note on the website seems to indicate that during the same meeting the ECDD could now also decide to treat a pre-review as if it were a critical review and proceed to make scheduling recommendations on the basis of a pre-review only. If that were indeed the case, that would be a worrying and unauthorised change of the standing rules of procedure, which explicitly state that the 'pre-review is a preliminary analysis and findings at this stage should not determine whether the control status of a substance should be changed'.[37]

Moving in that direction would be particularly problematic for substances like tramadol and CBD, which require an appropriate period of time to consider all available evidence regarding both illicit use and harms, medical and scientific usages, and potential impacts of placing them under international control. Moving immediately to scheduling recommendations on the basis of a pre-review without the additional scrutiny of a critical review would significantly undermine the scientific basis of the ECDD's scheduling recommendations.

Acknowledgements

This advocacy note was drafted by IDPC's Head of Research and Communications, Marie Nougier. The author wishes to thank, for their valuable contributions and comments, Martin Jelsma and Tom Blickman (Transnational Institute), Christopher Hallam (IDPC) and Dave Bewley-Taylor (IDPC & Global Drug Policy Observatory).

Endnotes

1 Expert Committee on Drug Dependence, Tramadol Pre-review Report, 39th Meeting, Geneva, 6-10 November 2017, http://www.who.int/medicines/access/controlled-substances/PreReview_Tramadol.pdf

2 Available here: https://www.unodc.org/documents/postungass2016/outcome/V1603301-E.pdf

3 For the full list, please see: World Health Organization, 39th Expert Committee on Drug Dependence (ECDD), WHO Headquarters, Geneva, Switzerland, 6 to 10 November 2017, http://www.who.int/medicines/access/controlled-substances/substances-to-considered_at39thECDD.pdf

4 Grunenthal gmbH, (February 2017), *Tramadol: Comments on the EML application for inclusion of opioid analgesics for cancer pain: fentanyl, methadone, tramadol, 21st WHO Expert Committee on the selection and use of essential medicines,* http://www.who.int/selection_medicines/committees/expert/21/applications/Grunethal_tramadol.pdf?ua=1

5 World Health Organization (2015), *WHO Expert Committee on Drug Dependence thirty-sixth report*, http://apps.who.int/iris/bitstream/10665/153834/1/WHO_TRS_991_eng.pdf?ua=1&ua=1

6 See: WHO Model List of Essential Medicines, 20th List (March 2017) (Amended August 2017), http://www.who.int/medicines/publications/essentialmedicines/20th_EML2017_FINAL_amendedAug2017.pdf?ua=1

7 See: World Health Organization (1996), *Cancer pain relief, second edition: with a guide to opioid availability*, http://whqlibdoc.who.int/publications/9241544821.pdf

8 For more information about the process and international scheduling, see: Hallam, C., Bewley-Taylor, D. & Jelsma, M. (June 2014), *Scheduling in the international drug control system*, Series on Legislative Reform of Drug Policies No. 25 (Transnational Institute & International Drug Policy Consortium), http://fileserver.idpc.net/library/DLR_scheduling.pdf

9 World Health Organization (2014), *National Medicines List/Formulary/Standard Treatment Guidelines,* http://www.who.int/selection_medicines/country_lists/en/index.html

10 International Narcotics Control Board (2013), *INCB annual report 2013,* https://www.incb.org/documents/Publications/AnnualReports/AR2013/English/AR_2013_E.pdf

11 United Nations Office on Drugs and Crime (2017), *UNODC world drug report 2017*, https://www.unodc.org/wdr2017/field/Booklet_2_HEALTH.pdf

12 'Conference room paper submitted by the Arab Republic of Egypt on strengthening international cooperation in addressing the non-medical use and abuse, the illicit manufacture and the illicit domestic and international distribution of tramadol' E/CN.7/2017/CRP.4 (13 March 2017), https://www.unodc.org/documents/commissions/CND/CND_Sessions/CND_60/CRPs/ECN72017_CRP4_V1701497.pdf

13 World Health Organization (1993), *WHO Expert Committee on Drug Dependence twenty-eighth report,* http://apps.who.int/iris/bitstream/10665/37029/1/WHO_TRS_836.pdf

14 World Health Organization (2003), *WHO Expert Committee on Drug Dependence thirty-third report,* http://apps.who.int/iris/bitstream/10665/42655/1/WHO_TRS_915.pdf

15 World Health Organization (2006), *WHO Expert Committee on Drug Dependence thirty-fourth report,* http://apps.who.int/iris/bitstream/10665/43608/1/9789241209427_eng.pdf

16 World Health Organization (2014), *WHO Expert Committee on Drug Dependence thirty-sixth report,* http://apps.who.int/iris/bitstream/10665/153834/1/WHO_TRS_991_eng.pdf?ua=1&ua=1

17 Kramer, T., Jensema, E., Jelsma, M. & Blickman, T. (2014), *Bouncing back: Relapse in the Golden Triangle* (Transnational Institute), https://www.tni.org/files/download/tni-2014-bouncingback-web-klein.pdf

18 Grunenthal gmbH, (February 2017), *Tramadol: Comments on the EML application for inclusion of opioid analgesics for cancer pain: fentanyl, methadone, tramadol, 21st WHO Expert Committee on the selection and use of essential medicines,* http://www.who.int/selection_medicines/committees/expert/21/applications/Grunethal_tramadol.pdf?ua=1

19 World Health Organization (2017), *Cannabidiol (CBD), Pre-Review Report, Agenda Item 5.2, Expert Committee on Drug Dependence, Thirty-ninth Meeting, Geneva, 6-10 November 2017*, p. 20, http://www.who.int/entity/medicines/access/controlled-substances/5.2_CBD.pdf

20 Yellow List, List of Narcotic Drugs under International Control, Annex to Forms A, B and C, (56 th edition, July 2017), http://www.incb.org/incb/en/narcotic-drugs/Yellowlist_Forms/yellow-list.html

21 For more information, see: Hallam, C., Bewley-Taylor, D. & Jelsma, M. (June 2014), *Scheduling in the international drug control system*, Series on Legislative Reform of Drug Policies No. 25 (Transnational Institute & International Drug Policy Consortium), http://fileserver.idpc.net/library/DLR_scheduling.pdf

22 See, for example: DrugScience (2016), *Cannabis and cannabis resin: Pre-review report – A document prepared for the World Health Organization Expert Committee on Drug Dependence thirty-eight meeting*, http://www.drugscience.org.uk/assets/files/WHOcannabisreport.pdf

23 International Narcotics Control Board (2017), *The therapeutic use of cannabis*, https://www.incb.org/documents/News/Alerts/Alert_on_Control_of_Narcotic_Drugs_June_2017.pdf

24 INCB, *Report 2016, Estimated World Requirements for 2017 - Statistics for 2015*, p.22

25 This includes: 67 tons for Canada, 44.5 tons for Colombia, 33.5 tons for the USA, 8 tons for Israel, 1.5 tons for Germany, 1.5 tons for Macedonia, 1.1 tons for Italy, 0.4 tons for the Netherlands, 0.3 tons for Spain, and many others with smaller amounts. See: International Narcotics Control Board (2016), *Report 2016, Estimated World Requirements for 2017 - Statistics for 2015, Annex II. Estimated requirements of narcotic drugs*, pp. 267-308, https://www.incb.org/incb/en/narcotic-drugs/Technical_Reports/narcotic_drugs_reports.html

26 See: World Health Organization (2015), *WHO Expert Committee on Drug Dependence thirty-sixth report,*http://apps.who.int/iris/bitstream/10665/153834/1/WHO_TRS_991_eng.pdf

27 See: World Health Organization (2016), *WHO Expert Committee on Drug Dependence thirty-seventh report,* http://apps.who.int/iris/bitstream/10665/206452/1/WHO_TRS_998_eng.pdf

28 Ibid., p. 32

29 Commission on Narcotic Drugs (2016), *Extract from the Report of the 38th Expert Committee on Drug Dependence, convened from 14 to 18 November 2016, at*

WHO headquarters in Geneva, E/CN.7/2016/CRP.13, p. 8, http://www.unodc.org/documents/commissions/CND/CND_Sessions/CND_59Reconvened/ECN72016_CRP13_V1610192.pdf

30 http://www.who.int/medicines/access/controlled-substances/ecdd_38_meeting/en/

31 World Health Organization (2016), *Cannabidiol (CBD) pre-review report, Agenda Item 5.2*, http://www.who.int/entity/medicines/access/controlled-substances/5.2_CBD.pdf

32 World Health Organization (2017), *Expert Peer Review for Cannabidiol (CBD), Expert Peer Review No.2*, http://www.who.int/entity/medicines/access/controlled-substances/5.2_CBD_PeerReview2.pdf

33 World Health Organization (2017), *Expert Peer Review for Cannabidiol (CBD), Expert Peer Review No.1,* http://www.who.int/entity/medicines/access/controlled-substances/5.2_CBD_PeerReview1.pdf

34 Commission on Narcotic Drugs (2016), *Extract from the Report of the 38th Expert Committee on Drug Dependence, convened from 14 to 18 November 2016, at WHO headquarters in Geneva*, E/CN.7/2016/CRP.13, http://www.unodc.org/documents/commissions/CND/CND_Sessions/CND_59Reconvened/ECN72016_CRP13_V1610192.pdf

35 See the bottom of the page: http://www.who.int/medicines/access/controlled-substances/ecdd_39_meeting/en/

36 World Health Organization (2010), *Guidance on the WHO review of psychoactive substances for international control*, p. 11, http://www.who.int/medicines/areas/quality_safety/GLS_WHORev_PsychoactSubst_IntC_2010.pdf

37 World Health Organization (2010), *Guidance on the WHO review of psychoactive substances for international control*, p. 10, http://www.who.int/medicines/areas/quality_safety/GLS_WHORev_PsychoactSubst_IntC_2010.pdf

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About IDPC

The International Drug Policy Consortium is a global network of non-government organisations that specialise in issues related to illegal drug production and use. The Consortium aims to promote objective and open debate on the effectiveness, direction and content of drug policies at national and international level, and supports evidence-based policies that are effective in reducing drug-related harm. It produces briefing papers, disseminates the reports of its member organisations, and offers expert advice to policy makers and officials around the world.

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Report design by Mathew Birch - mathew@mathewbirch.com

Funded, in part, by:

OPEN SOCIETY FOUNDATIONS