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English only

Commission on Narcotic Drugs
Sixty-fifth session
Vienna, 14–18 March 2022
Item 5 (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**,***

Note by the Secretariat

1. In accordance with article 3 of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol (1961 Convention), the Commission will have before it for consideration recommendations by the World Health Organization (WHO) to place brorphine and metonitazene in Schedule I of the 1961 Convention. Further, pursuant to article 2 of the Convention on Psychotropic Substances of 1971 (1971 Convention), the Commission will have before it for consideration recommendations by the WHO to add eutylone to Schedule II of the 1971 Convention.

2. In accordance with article 3, paragraphs 1 and 3, of the 1961 Convention, and article 2, paragraphs 1 and 4, of the 1971 Convention, the Director-General of WHO, in the correspondence dated 18 November 2021, notified the Secretary-General of these recommendations.

3. Pursuant to article 3, paragraph 2, of the 1961 Convention, and article 2, paragraph 2, of the 1971 Convention, the notification and the information submitted by WHO in support of its recommendations were transmitted to all States parties to the 1961 Convention and the 1971 Convention in annex to a note verbale dated 8 December 21.

4. As of 1 March 2022, the Governments of the following 10 States parties had provided comments on the WHO recommendations under the 1961 Convention and the 1971 Convention: Cyprus, Egypt, El Salvador, Ghana, Holy See, Jamaica, Madagascar, Saudi Arabia, Serbia and the Russian Federation.

5. The Government of Cyprus stated that it had no objection on the scheduling of the substances recommended by WHO to be placed under international control under the 1961 Convention.

* E/CN.7/2022/1.
** This conference room paper is to be read in conjunction with document E/CN.7/2022/10.
*** This document has not been edited.

6. The Government of Egypt informed that brorphine and metonitazene, as well as kratom and phenibut were not included in the schedules annexed to the 1960 Egyptian Anti-Narcotics Law 182. Eutylone was included in the second section of schedule 1 annexed to the Egyptian Anti-Narcotics Law, according to Egyptian Drug Authority decision number 4 in 2020 (item 1). The Government of Egypt further informed that there were no products registered in the Egyptian Drug Authority, or under registration, that contained these substances.

7. The Government of El Salvador informed that in El Salvador there was to date no known therapeutic use of brorphine, metonitazene and eutylone and therefore the inclusion of these substances in the respective schedules according to the recommendation of the WHO was considered appropriate. Further, there was no registered industrial, medical or scientific use of these substances in El Salvador, and the pharmaceutic industry in El Salvador did not synthesize or produce these substances, so that there would not be any impact on economic, social, legal administrative and other factors. To the contrary, the risk of diversion of these substances for the illicit fabrication of other drugs would be decreased.

8. The Government of Ghana expressed its agreement with the scheduling recommendations as reflected above.

9. The Holy See informed that it agreed with the scheduling recommendations as reflected above.

10. The Government of Jamaica stated that it had no objection to recommendations to add brorphine and metonitazene to schedule I of the 1961 Convention. The Government noted that brorphine had a chemical structure similar to bezitramide, an opioid listed in Schedule I of the Convention. While it was observed that brorphine was not known to have any therapeutic use and was liable to abuse and therefore prima facie could be scheduled under schedule IV, it was also recognized that brorphine was liable to have similar abuse potential and ill effects as opioids that were controlled under schedule I of the Convention, for example morphine and fentanyl. Therefore Jamaica offered no objection to the recommendation to add brorphine to schedule I of the Convention.

11. The Government of Jamaica further noted that metonitazene belonged to the series of 2-benzylbenzimidazole opioid compounds. Like brorphine, metonitazene also had no known therapeutic use and whilst there were no controlled studies on the abuse potential, it was expected to have abuse liability. Jamaica also recognized that the mechanism of action and effects of metonitazene indicated that it was liable to have similar abuse potential and ill effects as opioids that were controlled under schedule I of the 1961 Convention. Accordingly, the Government offered no objection to adding metonitazene to schedule I of the 1961 Convention. The Government stated that locally, Jamaica had little experience with both brorphine and metonitazene, but that the administrative control mechanisms, including permitting, licensing and monitoring systems over these substances would be maintained.

12. The Government of Jamaica further stated that Jamaica offered no objection to the Committee’s recommendation to add eutylone to Schedule II of the 1971 Convention. It noted that eutylone was physically indistinguishable from methylenedioxymethamphetamine (MDMA). Though similar in appearance, it was noted that eutylone produced a weaker effect to MDMA when taken by consumers seeking to get the equal effect of MDMA and might therefore lead to fatal consequences such as overdosing. In view of the physical similarities to MDMA, it was stated that testing capacity was necessary. It was also noted that eutylone was not known to have any therapeutic use, which could make the substance considerable for the same rigid controls as other substances scheduled in schedule I. Notwithstanding, where schedule II substances were characterized as substances whose abuse liability constituted a substantial risk to the public health and which had little to moderate therapeutic usefulness and where strict control and regulatory mechanisms were imposed on substances added to schedule II of the 1971 Convention, Jamaica offered no objection to the recommendation. The Government of Jamaica also stated that

locally the applicable administrative control mechanisms were established and in force.

13. The Government of Madagascar stated that it had no objection with regard to the scheduling recommendations as reflected above.

14. The Government of Saudi Arabia confirmed its support for the WHO proposal to schedule the above-mentioned substances under the Single Convention on Narcotic Drugs of 1961 and the Convention on Psychotropic Substances of 1971, given that their scheduling had no effect in economic, social, legislative or administrative terms and did not contradict the measures to be applied against any person who violated the articles of the Drugs and Psychotropic Substances Act and its implementing regulations.

15. The Government of Serbia provided a recommendation on brorphine. The Government stated that structurally related compounds had been known for decades and some of them were approved drugs (pimozide and benperidol, both antipsychotics; domperidone (antiemetic) and others). Most of these compounds, while pharmacologically active, were not known as specific opioid agonists. However, a number of the analogues, disclosed in patents and elsewhere, were described as strong analgesics, although never marketed. The new series of compounds, disclosed in a paper from 2018[1] were structurally modified, as to acquire specific opioid agonist activity. Several of them were shown to be more potent than morphine, with brorphine being the most active, with the opioid activity some 10 times that of morphine. The chemical synthesis of the whole novel class was considered relatively simple and disclosed in detail in the cited paper. Since the general class had been known for decades, the various synthetic procedures were published in patents and scientific papers,[2] thus making them freely available to anyone. The precursor chemicals were generally readily accessible general-purpose chemicals and could not be controlled. Therefore, the compounds from this novel class could be synthesized illicitly on a considerable scale in relatively modestly equipped laboratories. Considering all those technical aspects, the Government considered it reasonable to expect similar analogues on the illicit markets in the coming years. It was noted that brorphine appeared on the illicit market only several months (in early 2019, if not earlier)[3] after it was first disclosed in the mentioned paper. This fact suggested that the individuals involved in this criminal enterprise were likely highly qualified and informed experts. The Government made reference to a report provided by the Drug Enforcement Administration of the USA, in which numerous seizures were reported starting from early 2019, as well as its presence in a number of drug-related deaths. The Government therefore stated that brorphine presented exceptionally high risks both to the individuals who abused it and society in general. Therefore, the Government expressed the view that brorphine should be scheduled immediately, word-wide, as a dangerous opioid drug without any legitimate use. However, it was noted that this should not preclude the legitimate scientific research on brorphine itself and its analogues, in a quest to find opioid analgesics with better pharmacological profile, including those with reduced addiction liability and less pronounced respiratory depression.

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[1] Optimization of a Series of Mu Opioid Receptor (MOR) Agonists with High G Protein Signaling Bias; Nicole M. Kennedy, Cullen L. Schmid, Nicolette C. Ross, Kimberly M. Lovell, Zhizhou Yue, Yen Ting Chen, Michael D. Cameron, Laura M. Bohn, and Thomas D. Bannister; Journal of Medicinal Chemistry 2018, 61 (19), 8895– 8907; DOI: 10.1021/acs.jmedchem.8b01136.

[2] Derivaten van piperidylbenzimidazolinone. Janssen Pharmaceutica. (1965) Belgian Patent BE663433; Bezitramide (R 4845), a new potent and orally long-acting analgesic compound. Janssen, P. A. J., Niemegeers, C. J. E., Schellekens, K. H. L., Marsboom, R. H. M., Hérin, V. V., Amery, W. K. P., Admiraal, P. V., Bosker, J. T., Crul, J. F., Pearce, C., and Zegveld, C. (1971); Arzneim.-Forsch. 21, 862−867; The chemical anatomy of potent morphine-like analgesics. In Drugs Affecting the Central Nervous System Janssen, P. A. J., and Van der Eycken, C. A. M. (1968) (Burger, A., Ed.), Vol. 2, pp 25−60, Marcel Dekker, Inc., New York.

[3] Temporary Placement of Brorphine in Schedule I; https://deadiversion.usdoj.gov/fed_regs/rules/2021/fr0301_4.htm.

16. The Government of the Russian Federation stated that it had no objections regarding the recommendations of the World Health Organization to place brorphine, metonitazene and eutylone under control. The Government further informed that eutylone was a derivative of the substance *N*-[1-(2H-1,3-benzodioxol-5-yl)-propan-2-yl]-*N*-methylhydroxylamine (FLEA), which was included in the list of narcotic drugs, psychotropic substances and their precursors whose circulation was prohibited in the Russian Federation in accordance with national legislation and international treaties to which the Russian Federation is a party, also known as list I, as approved by the Decree of the Government of the Russian Federation No. 681 dated 30 June 1998. With regard to brorphine and metonitazene, the Government informed that it was planning to establish, in accordance with a draft decree, national control measures, similar to those applicable to the narcotic drugs included in the afore mentioned list I.