United Nations E/CN.7/2007/10

Economic and Social Council

Distr.: General
22 January 2007

Original: English

Commission on Narcotic Drugs
Fiftieth session
Vienna, 12-16 March 2007
Item 7 (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

Note by the Secretariat

Summary

The present document contains recommendations for action 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, and article 2 of the Convention on Psychotropic Substances of 1971, the Commission will have before it for consideration two proposals from the World Health Organization concerning recommendations to include oripavine in Schedule I of the 1961 Convention as amended and to transfer dronabinol and its stereoisomers from Schedule II to Schedule III of the 1971 Convention.

* E/CN.7/2007/1.

V.07-80285 (E) 070207 080207

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

1. Pursuant to article 3, paragraphs 1 and 3 (iii), of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol,[1] the World Health Organization (WHO) notified the Secretary-General on 18 September 2006 that it was of the opinion that oripavine should be included in Schedule I of that Convention (see annex).

2. In accordance with the provisions of article 3, paragraph 2, of the 1961 Convention as amended, the Secretary-General transmitted to all Governments a note dated 13 October 2006 containing the text of that notification, together with the assessments and recommendations submitted by WHO. As at 19 January 2007, 12 States had responded to the notification. The Governments of Algeria, Belgium, Brazil, Cyprus, the Czech Republic, Denmark, Germany, Hungary, Lithuania, Pakistan, Peru and Turkey provided comments on economic, social, legal, administrative or other factors relevant to the possible inclusion of oripavine in Schedule I of the 1961 Convention as amended.

3. The Government of Algeria reported that it had no objection to placing oripavine in Schedule I of the 1961 Convention as amended, taking into account the potential abuse of the substance and the mental health risks associated with it.

4. The Governments of Belgium, the Czech Republic, Germany, Pakistan and Turkey reported that they had no objections to the possible scheduling of oripavine under the 1961 Convention as amended.

5. The Government of Brazil reported that the substance was not yet under control in Brazil and that it supported the proposal by WHO.

6. The Governments of Cyprus and Peru expressed their agreement that oripavine should be included in Schedule I of the 1961 Convention as amended, based on evidence submitted by WHO that the substance had the potential to be converted into thebaine and other substances listed in Schedule I of the 1961 Convention as amended.

7. The Government of Denmark reported that there were no factors that the Danish authorities found relevant to communicate regarding the inclusion of oripavine in Schedule I of the 1961 Convention as amended.

8. The Government of Hungary reported that because oripavine was a natural poppy alkaloid, which, together with morphine, thebaine and codeine, could be found in the poppy plant in low concentration, it could be considered a natural precursor of morphine. The Government of Hungary considered the inclusion of oripavine in Schedule I of the 1961 Convention as amended to be acceptable but not necessary; its position on the issue was neutral. However, the Government of Hungary considered the inclusion of oripavine in the national schedule to be problematic from the legal and administrative standpoint. According to the

[1] United Nations, *Treaty Series*, vol. 976, No. 14152.

Government, the control measures on substances in Schedule II of the Convention are just as rigorous. Thus, it would seem logical to include oripavine in Schedule II rather than Schedule I. For example, in Hungary, poppy straw, which is the natural source of opium alkaloids, was included in the national legislation corresponding to Schedule II.

9. The Government of Lithuania reported that there were no medicinal preparations containing oripavine in the country, that oripavine was not used for scientific purposes and that no instances of illegal use of the substance were known. The Government of Lithuania had no objection to including oripavine in Schedule I of the 1961 Convention as amended.

Action by the Commission on Narcotic Drugs

10. The notification from the Acting Director-General of WHO will be before the Commission on Narcotic Drugs for consideration in accordance with the provisions of article 3, paragraph 3 (iii), of the 1961 Convention as amended, which reads as follows:

> "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."

11. With regard to the decision-making process, 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 shall be made by a majority of the members present and voting. From a practical point of view, that means that, for a decision to be adopted, an affirmative vote of at least 27 members of the Commission is required, on the assumption that all members are present and vote.

12. The Commission should therefore decide whether or not, at the present stage, it wishes to include oripavine in Schedule I of the 1961 Convention as amended, or, if not, what other action, if any, might be required.

II. Consideration of a notification from the World Health Organization concerning scheduling under the Convention on Psychotropic Substances of 1971

13. Pursuant to article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances of 1971,[2] WHO notified the United Nations on 18 September 2006 that it was of the opinion that dronabinol (INN) and its stereoisomers should be transferred from Schedule II to Schedule III of the 1971 Convention (see annex).

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[2] United Nations, *Treaty Series*, vol. 1019, No. 14956.

14. In accordance with the provisions of article 2, paragraph 2, of the 1971 Convention, the Secretary-General transmitted to all Governments a note dated 13 October 2006 containing the text of the notification, together with the assessments and recommendations submitted by WHO. As of 19 January 2007, 13 States had responded to the notification by the Secretary-General. The Governments of Algeria, Belgium, Brazil, Cyprus, the Czech Republic, Denmark, Germany, Hungary, Lithuania, Pakistan, Peru, the Syrian Arab Republic and Turkey provided comments on economic, social, legal, administrative or other factors relevant to the possible transfer of dronabinol and its stereoisomers from Schedule II to Schedule III of the 1971 Convention.

15. The Government of Algeria reported that it was in favour of transferring dronabinol and its stereoisomers from Schedule II to Schedule III of the 1971 Convention in view of the therapeutic usefulness of the substance.

16. The Government of Belgium reported that it had no objection to the proposed rescheduling but pointed out that the problem of the distinction between tinctures and extracts of cannabis listed under Schedule I of the 1961 Convention as amended and the mixture of *delta* cannabinols remained, because it is often difficult to make the distinction between the two at the level of control.

17. The Government of Brazil reported that dronabinol had already been placed under special control in the national list of psychotropic substances and that the rescheduling of the substance would not lead to any economic, social, legal or administrative problems in the country.

18. The Governments of the Czech Republic, Germany, Pakistan, Peru, the Syrian Arab Republic and Turkey reported that they had no objections to the possible rescheduling of dronabinol and its stereoisomers under the 1971 Convention.

19. The Government of Denmark reported that there were no factors that the Danish authorities found relevant to communicate with regard to the transfer of dronabinol from Schedule II to Schedule III of the 1971 Convention.

20. The Government of Hungary did not support the transfer of dronabinol (*delta*-9-tetrahydrocannabinol (THC)) and its stereoisomers from Schedule II to Schedule III of the 1971 Convention. The Government of Hungary submitted the following response to the note by the Secretary-General:

> “In our view it is not necessary to transfer dronabinol from Schedule II to Schedule III in order to enhance its medical use. Amphetamine, methamphetamine and methylphenidate are also included in Schedule II of the 1971 Convention, while morphine, codeine etc. are included in Schedule I of the 1961 Convention. All of these substances are used as active substances of medicines.
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> “In our opinion, the evidence for the infrequent abuse of therapeutic dronabinol is not very well established. It might be due to the low quantity of licit manufacture and the low volume of therapeutic use. Another possibility is that the present situation regarding the abuse of dronabinol (*delta*-9-THC), which is the active substance of cannabis, does not give a clear picture about the real scale of abuse of *delta*-9-THC. Namely, the majority of abusers illegally use the easily accessible and much cheaper cannabis (in the form of marihuana) to get the needed *delta*-9-THC.

"In Hungary, the decisions of judges are based on the quantity of dronabinol (as the primary active substance responsible for the physiological effects of cannabis) in the seized drug (including Schedules I, II and IV of the 1961 Convention and Schedules I and II of the 1971 Convention). The forensic laboratories are measuring this active substance to verify the relevant amount. In the case of transferring dronabinol to Schedule III, this active substance will not be considered a drug from the criminal aspect any more, and for the penal law, it is becoming an irrelevant substance. A cardinal question is, instead of dronabinol, what can we measure in order to support the decision of the judges, e.g. the gross quantity of cannabis, but when and in which condition of dryness? This amendment raises several procedural questions.

"It is hardly justifiable to transfer dronabinol from Schedule II (with this decision, it will not be considered a drug from the criminal aspect in Hungary anymore) which is recognized – also by WHO – as the primary substance responsible for the physiological effects of cannabis – and to leave out other cannabinoid compounds (for example, *delta*-8-THC and its isomers) that are found in a much lower concentration and have different but, on the average, much lesser physiological effects than the main component, dronabinol.

"In the case the amendment comes into force, in Hungary it would be necessary to change nearly the entire basis of the legal system using the definitions and the legal terms 'large' and 'small' quantities, by changing definitions, legal categories and procedures. The altering of the present coherent and well-working legal system would mean disproportionate and unnecessary additional work, legal insecurity and contradictions in the statutory interpretation.

"As is intended by WHO, cannabis, cannabis resin and cannabis oil will remain in Schedule I of the 1961 Convention as amended. How can we classify and identify them if the most characteristic, primary substance responsible for the physiological effects of those substances was legally not considered to be an illicit drug anymore?"

21. The Government of Lithuania reported that there were no medicinal preparations containing dronabinol in the country, that the substance was not used for scientific purposes and that no instances of illegal use of that substance were known. However, the Government expressed concern that a less rigid control regime for dronabinol might create possibilities for the illegal use of the substance in future, as dronabinol was the main psychoactive ingredient of cannabis.

Action by the Commission on Narcotic Drugs

22. The notification from WHO will be before the Commission for consideration in accordance with the provisions of article 2, paragraphs 5 and 6, of the 1971 Convention, which read as follows:

"5. The Commission, taking into account the communication from the World Health Organization, whose assessments shall be determinative as to medical and scientific matters, and bearing in mind the economic, social, legal, administrative and other factors it may consider relevant, may add the

substance to Schedule I, II, III or IV. The Commission may seek further information from the World Health Organization or from other appropriate sources.

"6. 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."

23. With regard to the decision-making process, 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 shall be taken by a two-thirds majority of the members of the Commission". From a practical point of view, that means that, for a decision to be adopted, an affirmative vote of at least 35 members of the Commission is required.

24. The Commission should therefore decide whether it wishes to transfer dronabinol and its stereoisomers from Schedule II to Schedule III of the 1971 Convention or, if not, what other action, if any, might be required.

Annex

Notification dated 18 September 2006 from the Acting Director-General of the World Health Organization to the Secretary-General concerning the proposal for international control in respect of oripavine and rescheduling of dronabinol

The Acting Director-General of the World Health Organization presents his compliments to the Secretary-General of the United Nations and has the honour to submit, in connection with article 2, paragraphs 1, 4 and 6, of the Convention on Psychotropic Substances of 1971, assessments and recommendations of the World Health Organization, as set forth in appendices I and II hereto, concerning the proposed international control in respect of dronabinol (INN) and its stereoisomers, which should be rescheduled from Schedule II to Schedule III of the 1971 Convention, and oripavine, which should be placed in Schedule I of the Single Convention on Narcotic Drugs of 1961.

Appendix I

Recommendation on dronabinol (INN)

Substance identification

Dronabinol (INN) is (6a*R*,10a*R*)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6-*H*-dibenzo[*b*,*d*]pyran-1-ol. It is the (6a*R*,10a*R*)-stereoisomer of *delta*-9-tetrahydrocannabinol and is also designated (–)-*trans*-*delta*-9-tetrahydrocannabinol.

Other stereoisomers of *delta*-9-tetrahydrocannabinol are: (6a*R*,10a*S*)-, (6a*S*,10a*R*)- and (6a*S*,10a*S*)-, also known as (–)-*cis*-, (+)-*cis*- and (+)-*trans*-, respectively. *Delta*-9-tetrahydrocannabinol has two racemates, (6a*RS*,10a*RS*)- and (6a*RS*,10a*SR*)-, also known as (±)-*trans*- and (±)-*cis*-, respectively.

Originally, all isomers of tetrahydrocannabinol were included in Schedule I of the 1971 Convention. This was later amended to include seven named constitutional isomers and their respective stereochemical variants. The term "constitutional isomers" used above has recently been introduced by the International Union of Pure and Applied Chemistry (IUPAC) to replace the traditionally used term "positional isomers".

The term "stereochemical variants" used in the 1971 Convention and mentioned above is equivalent to the term "stereoisomers", which is at present much more widely used in the chemical and related literature. Both terms cover geometric isomers and optical isomers.

Previous review

Delta-9-tetrahydrocannabinol was included in Schedule I of the 1971 Convention at the time of its adoption. At its twenty-sixth meeting, the Expert Committee on Drug Dependence recommended that dronabinol be moved to Schedule II, while keeping

the other isomers and their stereochemical variants in Schedule I.[a] This proposal was rejected at the eleventh special session of the Commission on Narcotic Drugs, and the Committee reviewed the question again at its twenty-seventh meeting, when it recommended that all stereochemical variants of *delta*-9-tetrahydrocannabinol be rescheduled to Schedule II.[b] This recommendation was adopted by the Commission on Narcotic Drugs at its thirty-fourth session.[c] At its thirty-second meeting, the Committee pre-reviewed dronabinol and recommended its critical review for consideration of the rescheduling on the grounds that the rate of abuse of dronabinol was extremely low.[d]

Delta-9-tetrahydrocannabinol was critically reviewed by the Expert Committee on Drug Dependence at its thirty-third meeting, in September 2002.[e] On the basis of the available data, the Committee considered that dronabinol should be rescheduled to Schedule IV of the 1971 Convention. However, no further procedural steps were taken. Therefore, the existing critical review report was updated, including information from recent scientific publications, to enable the Committee to finalize the process of critical review.

Similarity to known substances and effects on the central nervous system

Dronabinol is the main active principle of cannabis and has similar effects on mood, perception and the cardiovascular system. The cannabis plant contains a "natural mixture" of around 70 different cannabinoids and also contains flavonoids and terpenes, as well as many other substances. Therefore, the pharmacological properties of natural cannabis and dronabinol are not identical.

Dependence potential

Animal studies have demonstrated that, like other drugs of abuse, dronabinol acts as a drug reinforcer. Physical dependence, as shown by withdrawal syndrome following chronic administration, has also been demonstrated. Reinforcing effects and physical dependence have also been described in human studies.

Actual abuse and/or evidence of likelihood of abuse

The abuse of dronabinol is currently rare, and there have been very few specific reports of its occurrence. In response to the WHO questionnaires, only the United States of America mentioned instances of abuse of *delta*-9-tetrahydrocannabinol. At present, the quantity produced by licit manufacture is limited. In the United States, which is the major manufacturing country, the abuse of dronabinol medicinal preparations is reported to be very low, and there are no reports of diversion of the pharmaceutical product.

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[a] *WHO Expert Committee on Drug Dependence: Twenty-sixth Report*, WHO Technical Report Series, No. 787 (Geneva, World Health Organization, 1989).

[b] *WHO Expert Committee on Drug Dependence: Twenty-seventh Report*, WHO Technical Report Series, No. 808 (Geneva, World Health Organization, 1991).

[c] *Official Records of the Economic and Social Council, 1991, Supplement No. 4* (E/1991/24), chap. II, sect. A.1.

[d] *WHO Expert Committee on Drug Dependence: Thirty-second Report*, WHO Technical Report Series, No. 903 (Geneva, World Health Organization, 2001).

[e] *WHO Expert Committee on Drug Dependence: Thirty-third Report*, WHO Technical Report Series, No. 915 (Geneva, World Health Organization, 2003).

Therapeutic usefulness

Dronabinol preparations have been used in a limited number of countries in the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments and in the treatment of anorexia associated with weight loss in patients with acquired immunodeficiency syndrome (AIDS). It has also been indicated in the treatment of chronic pain (e.g. for multiple sclerosis, neuropathic disorders and arthritis), neurological disorders and appetite loss in cachexia and is being evaluated for use in various other clinical situations.

Recommendation

The Committee reconsidered the recommendation made at its thirty-third meeting after considering the updated critical review report. The Committee concluded that dronabinol constitutes a substantial risk to public health. However, this risk is different from those related to cannabis—controlled under the 1961 Convention. The substance has a moderate therapeutic usefulness, and, as a result of continuing clinical research, its medical use is likely to increase. Therefore, the Committee recommended that dronabinol (INN) and its stereoisomers should be rescheduled from Schedule II to Schedule III of the 1971 Convention.

To avoid legal and forensic chemical problems that may arise in some countries when placing stereoisomers of the same substance under different control systems, the Committee indicated that the recommendation pertains to all stereoisomeric forms of *delta*-9-tetrahydrocannabinol as specified above.

Appendix II

Recommendation on oripavine

Substance identification

Oripavine, 3-*O*-demethylthebaine or 6,7,8,14-tetradehydro-4,5-*alpha*-epoxy-6-methoxy-17-methylmorphinan-3-ol is a phenanthrene alkaloid contained in species of the *Papaver* plant. It is a major metabolite of thebaine.

Previous review

Oripavine was pre-reviewed at the thirty-third meeting of the Expert Committee in 2002.[a] The reason for pre-review in 2002 was that oripavine is a substance that is convertible into thebaine, and because thebaine is, in turn, convertible into morphine. Thebaine and morphine are both in Schedule I of the 1961 Convention. Owing to uncertainties regarding the scheduling of oripavine based on the additional possibility of applying the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, the Committee did not finalize this review at its thirty-third meeting but asked WHO for clarification on issues related to the conversion of precursors into scheduled substances. Subsequent

[a] *WHO Expert Committee on Drug Dependence: Thirty-third Report*, WHO Technical Report Series, No. 915 (Geneva, World Health Organization, 2003).

clarification of these issues allowed the Committee to come to a conclusion at its thirty-fourth meeting.

Recommendation

The Committee decided that oripavine is a substance that is easily convertible into thebaine and other substances controlled in Schedule I of the 1961 Convention. Hence, the Committee recommended that oripavine be scheduled, like the substances mentioned, in Schedule I of the 1961 Convention.