UNITED NATIONS

ECONOMIC AND SOCIAL COUNCIL

GENERAL

E/CN.7/209
17 November 1950

ORIGINAL: ENGLISH

COMMISSION ON NARCOTIC DRUGS
Fifth session
Item 13 of the provisional agenda

NOTIFICATIONS BY THE GOVERNMENTS OF TURKEY AND THE UNITED STATES OF AMERICA UNDER ARTICLE 1, PARAGRAPH 1, OF THE PROTOCOL OF 19 NOVEMBER 1948 BRINGING UNDER INTERNATIONAL CONTROL DRUGS OUTSIDE THE SCOPE OF THE CONVENTION OF 13 JULY 1931 FOR LIMITING THE MANUFACTURE AND REGULATING THE DISTRIBUTION OF NARCOTIC DRUGS, AS AMENDED BY THE PROTOCOL OF 11 DECEMBER 1946

The Secretary-General has the honour to communicate to the Commission of Narcotic Drugs the following notifications received from the Governments of Turkey and the United States of America which he has transmitted under Article 1, paragraph 1 of the above-mentioned Protocol to the other states Parties thereto and to the World Health Organization.

1. Turkey

The Acting Head of the Turkish Permanent Delegation to the United Nations presents his compliments to the Secretary-General of the United Nations, and, acting on the instructions of the Government of Turkey and in pursuance of Article 1, paragraph 1 of the Protocol of 19 November 1948 bringing under international control drugs outside the scope of the Convention of 13 July 1931 for limiting the manufacture and regulating the distribution of narcotic drugs, as amended by the Protocol of 11 December 1946, has the honour to request the Secretary-General to be good enough to transmit to the other States Parties to the said Protocol of 19 November 1948, to the Commission on Narcotic Drugs of the Economic and Social Council, and to the World Health Organization the request of the Government of Turkey for the following drug to be subjected to the control provided for by the Convention of 13 July 1931, as amended by the Protocol of 11 December 1946:

/The hydrochloride

The hydrochloride of 1-methyl-4-phenyl piperidine-4-carboxylic acid ethyl ester (known under the names of Dodonal, Dolantin, Pethidine, Piridosal, etc.)

The Government of Turkey considers that the opinions expressed by the World Health Organization on this drug entirely justify the application to it of the procedure provided for in the Protocol of 19 November 1948. These opinions of the World Health Organization are to be found in the report to the Expert Committee on Habit-forming Drugs on its first session (Official Records of the World Health Organization No. 19) and in the report of the Expert Committee on Drugs Liable to Produce Addiction (World Health Organization Technical Report Series No. 21).

New York, 13 July 1950

2. United States of America

The Representative of the United States on the Commission on Narcotic Drugs of the United Nations presents his compliments to the Secretary-General of the United Nations and has the honour to submit on behalf of his Government pursuant to Paragraph 1 of Article 1 of the Protocol signed at Paris on 19 November 1948, bringing under international control drugs outside the scope of the Convention of 13 July 1931, as amended by the Protocol signed at Lake Success on 11 December 1946, a notification that each of the following named drugs, all of which are or may be used for medical or scientific purposes and to which the Convention of 13 July 1931 does not apply, is considered liable to the same kind of abuse and productive of the same kind of harmful effects as the drugs specified in Article 1, paragraph 2, of the said Convention:

1. 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester. (in the form of the hydrochloride, known under the names of Dolantin, Demerol, Pethidine, Isonipecaine, etc.).

4-(3-hydroxyphenyl)-1-Methyl-4-piperidyl ethyl ketone hydrochloride (known as Kato-bemidone).

1-methyl-4-metahydroxyphenyl-piperidine-4-carboxylic acid ethyl ester. (known as Bemidone).

-1,3-dimethyl-4-phenyl-4-propionoxy piperidine (known as NU-1196, or Nisentil).

B-1,3-dimethyl-4-phenyl-4-propionoxy piperidine. (Otherwise identified by symbol NU-1779).

4,4-Diphenyl-6-Dimethylamino-Heptenone-3. (Also known as Methadon, Amidone, Dolophine, Adanon, etc.).

/4,4-

4,4-Diphenyl-5-Methyl-6-Dimethylamino-hexanone-3
(known as Isoamidone)

6-dimethylamino-4, 4-diphenyl-3-heptanol
(Otherwise identified by symbol N.I.H.-2933).

6-dimethylamino-4,4-diphenyl-3-acetoxyheptane
(Otherwise identified by symbol N.I.H.-2953).

6-morpholino-4,4-diphenyl-3-heptanone,
(Also known as CB-11, Heptanone or Heptalgin).

It is understood that all of the foregoing substances have heretofore been considered carefully by the Expert Committee on Habit-Forming Drugs of the World Health Organization and that the Committee, in the light of technical information before it, found that each of the substances was definitely habit-forming. Each of the aforementioned substances has heretofore been made subject to the Federal narcotic laws of the United States.

2.a) 3-hydroxy-N-methyl morphinan
(otherwise known only under the symbol identification NU-2206)

It will be recalled that this drug was mentioned in a Report from the Expert Committee on Habit-Forming Drugs of the World Health Organization, issued 10 February 1949 (corrected copy issued 16 March 1949). The Committee found that German and Swiss chemists had produced by direct synthesis the compound under discussion, in which the structure of naturally occurring morphine alkaloid had been nearly attained. The Committee outlined in what respect the new compound differed chemically from morphine, and noted that the new compound had been shown in the laboratory to possess marked analgesic action, greater than that of morphine itself, and to exhibit many of the other characteristics of morphine action.

There are enclosed two copies of a Report on this new drug by Dr. Harris Isbell, Director of Research, United States Public Health Service Hospital, Lexington, Kentucky. It will be noted, that as a result of his clinical tests, Dr. Isbell concludes that the new drug has addiction liability which is approximately equal to that of morphine.

Although the new drug bears such a degree of chemical similarity to morphine that it might possibly be considered a chemical derivative of morphine, the procedure provided by Article 11 of the 1931 Convention may not be applied to this drug. This drug has been made subject to the Federal narcotic laws of the United States.

/b) B-1-methyl

b) B-1-methyl-3-ethyl-4-phenyl-4-propionoxy piperidine (Otherwise identified by symbol NU-1932).

According to the memorandum by Professor H. Fischer, Professor of Pharmacology at the University of Zurich, Member of the Permanent Central Opium Board and Drug Supervisory Body, and the note submitted to the Expert Committee on habit-forming drugs of the W.H.O. by Dr. P. O. Wolff, this drug has an effect similar to that of morphine and about four to eight times stronger (document E/OB/3/Rev.1, E/DSB/5/Rev.1 and Bulletin of the W.H.O., 1949, 2.193-204). It has been made subject to the Federal Narcotic laws of the United States.

3. Dihydrocodeine;

Acetyldihydrocodeine.

With respect to Dihydrocodeine the Commission on Narcotic Drugs made the following statement at its second session:

> "The Commission had considered the advisability of preparing for the approval of the Council a draft protocol for placing Dihydrocodeine (paracodine) under international control. In view, however, of the urgent recommendation for the immediate drafting of an instrument to bring under international control drugs not covered by Conventions at present in force, the Commission decided to draft this new instrument in such a way as to include control over Dihydrocodeine". (Report to the Economic and Social Council, document E/575, page 15).

In a Report from the Expert Committee on Habit-Forming Drugs of the World Health Organization, issued 10 February 1949, the Committee expressed the opinion that Acetyldihydrocodeine is convertible to Dihydrocodeine which, in turn, is convertible to Dihydromorphine, a habit-forming drug. The Committee considered the statement with respect to conversion to a habit-forming drug applied equally to other esters of Dihydrocodeine and their salts. In another Report of the Expert Committee, issued 16 January 1950, the Committee confirmed its opinion with respect to the addition-producing properties of Acetyl-dihydrocodeine and Dihydrocodeine.

These two drugs are already subject to the Federal narcotic laws of the United States.

H. J. Anslinger

17 October 1950

3-HYDROXY-N-METHYLMORPHINAN (NU-2206)

(Reports of Dr. Harris Isbell, Director of Research, U.S. Public Health Service Hospital, Lexington, Ky.)

FROM LEXINGTON REPORT OF 31 AUGUST 1949

Five men began to receive 3-hydroxy-N-methylmorphinan (NU-2206) during August. Preliminary single dose tests had shown that it produced euphoria and relief of abstinence from morphine. The maximum dose is to be 15 mgm., 4 times daily. At the end of August, it is apparent that the picture of morphinan intoxication is quite similar to morphine addiction. When the drug was first administered, the patients were exhilerated and showed increased psychomotor activity. Later, as the dose was increased, they became more sedated and finally went "on the nod". All the patients have exhibited mycsis and injection of the conjunctivae. They itched and scratched, had increased rectal temperature and increased respiratory rates. Nausea and weight loss have also been noticed.

FROM LEXINGTON REPORT OF 30 SEPTEMBER 1949

The men attained maximum dosage level of 60 mgm. daily on 17th day of experiment. The maximum dosage was continued for additional 21 days. Complete tolerance to the sedative action did not develop, although very definite partial tolerance was observed. Following abrupt withdrawal very definite signs of abstinence appeared at about the rate as signs of abstinence from morphine. Signs including yawning, lacrimation, rhinorrhea, gooseflesh, mydriasis, vomiting, anorexia and rapid weight loss. The over-all severity of abstinence appeared to be quite similar to that of abstinence in individuals who received about 240 mgm. of morphine for 30 days. These signs indicate that the drug has addiction liability which is approximately equal to that of morphine.

EXCERPTS FROM LEXINGTON REPORT OF 30 NOVEMBER 1949

"(d) Intravenous injections of morphinan. In previous studies with this particular compound, definite euphoria was seen following subcutaneous administration but, in other experiments using different men, very little evidence of euphoria was apparent after intravenous injection. The study of the effects of both subcutaneous and intravenous injections in 10 individuals under blind conditions has been undertaken. It is already quite apparent that the drug produces very marked euphoria when given intravenously, but the effect is not obtained nearly as rapidly as following intravenous injections of morphine or methadone."
