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ORIGINAL: ENGLISH

COMMISSION ON NARCOTIC DRUGS

SECOND SESSION

SUMMARY RECORD OF THE CLOSED MEETING

Held at Lake Success, New York, on Thursday, 24 July 1947, at 2.30 p.m.

Present:

Chairman:	Colonel C. H. L. SHARMAN, C.M.G., (Canada)
	C.B.E., I.S.O.
Rapporteur:	Dr. Szeming SZE (China)
	Dr. Mahmoud Labib (Egypt)
	H. E. M. Gaston Bourgois (France)
	Mr. H. N. Tandon (India)
	Mr. A. G. Ardalan (Iran)
	Dr. Secundino Ramos y Ramos (Mexico)
	Mr. J. H. Delgorge (Netherlands)
	Dr. Cemal Kiper (Turkey)
	Mr. I. E. Komenev (Union of Soviet Socialist Republics)
	Major W. H. Coles (United Kingdom)
	Mr. Harry J. Anslinger (United States)
	Mr. Stane Krasovec (Yugoslavia)
	Mr. Herbert L. May (President of the Permanent Central Opium Board)
	Dr. W. P. Forrest (Interim Commission of the World Health Organization)
	Dr. Nathan Eddy (United States Public Health Service)
	Dr. Lyndon Small (United States Public Health Service)

/Secretariat:

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UNITED NATIONS

Secretariat: Mr. Leon Steinig (Representing the Assistant Secretary-General in charge of Social Affairs)

Mr. F. H. Logan (Assistant Director of the Division of Narcotic Drugs)

Mr. V. Pastuhov (Secretary of the Commission)

Items 15 and 8 of the Agenda: Study of Measures to be taken with a view to bringing under international control Narcotic Drugs not covered by Convention at present in force. (Documents E/CN.7/80 and E/CN.7/81)

The CHAIRMAN called on Dr. Eddy and Dr. Small to explain the present position of the new synthetic drug amidone.

Dr. EDDY (United States Public Health Service) said: "The consideration of first importance is the morphine-like character of the action of amidone whereby it is able to reproduce in animals and man almost all of the actions produced by morphine itself. These morphine-like actions of amidone include:

1. Powerful analgesic action which extends to almost all types of pain. Relative to morphine, amidone is about one and a half times more effective as an analgesic.
2. Morphine-like sedative action. In this respect amidone is weaker than morphine.
3. A morphine-like subjective reaction, euphoria, which is readily produced in former morphine addicts and occasionally in patients seeking pain relief. The former addicts describe this subjective reaction as entirely comparable to that experienced with morphine. Most commonly they describe the effect of amidone as very like that produced by heroin especially when amidone is given intravenously, a mode of administration which they prefer.
4. The ready production of tolerance to all of the morphine-like effects. Tolerance has been attained to amounts of amidone ten times greater than the starting dose.
5. The smooth and complete satisfaction of morphine addicts by substitution of amidone for morphine in the proportion of one part of amidone for two parts of morphine to which the addict is accustomed. This substitution can be carried out without the addict being aware of the change.
6. The production in post-addicts by intentional and prolonged administration of increasing amounts of amidone of a state like that produced by similar administration of morphine, and the occasional production of a similar state in patients by prolonged administration of amidone for the relief of pain. I know of the production of such a state in only one patient.

7. The occurrence of a characteristic abstinence picture when amidone is stopped abruptly after prolonged administration. This differs from the morphine abstinence picture in its time relationship and in its intensity, but it is definite and characteristic.

Because of the morphine-like subjective reaction, because of the smoothness with which it substitutes for morphine in addicts and because of the definite and characteristic abstinence picture, one must conclude that amidone is an addicting drug and dangerous, like morphine, from the standpoint of habituation."

The CHAIRMAN considered Dr. Eddy's statement of the utmost importance and said that from the standpoint of the drug control officer it had to be realized that as the new drugs replaced existing drugs and came on to the legitimate market there was a great danger that they would slip on to the illicit market. He cited the case of Canada where the price of morphine on the legitimate market was ten dollars an ounce, whereas on the illicit market the price was \$8,700. He enquired if the manufacture of amidone presented great difficulties and if data were available as to the amount required to produce morphine-like poisoning.

Dr. EDDY replied that experiments on animals had proved that the toxic effect was considerably greater. In man the respiratory effect was relatively less, but nearly the same amount of amidone as of morphine would probably produce death by respiratory depression.

Dr. SZE (China) asked if there were any scientific opinions contesting that amidone was habit-forming.

Dr. EDDY replied that he had knowledge of dependence in one case only in clinical administration for pain relief. Amidone was still in the experimental stage, but had been used by medical practitioners for about one year for pain relief, and investigators administering the drug for this purpose had said that they had seen no symptoms of dependence. This, however, did not mean that it was not habit-forming. Physicians had investigated the drug for pain-relief and had limited the amounts administered to that need.

In reply to Dr. LABIB (Egypt) concerning the countries where amidone was manufactured, since it was not manufactured in Egypt, the CHAIRMAN said that it was not produced in Canada.

Mr. ANSLINGER (United States) stated that so far this drug was not classified as a narcotic drug. The formula had been found in Germany among some pharmaceutical documents. At present it was being manufactured only experimentally and was not yet licensed for distribution. Nevertheless it would be licensed in two months and declared a dangerous drug by the President. Owing to the nature of the United States Constitution it would not be possible to limit the manufacture of amidone except under international obligations. Some twenty firms would manufacture this drug,

although one firm could produce an amount sufficient for the needs of the whole world. The plans for the manufacture of amidone were being expedited, for it was hoped that the drug would eventually replace morphine and eliminate the purchase of opium except for certain items that required opium, such as papaverine, opium powders, tinctures and the like.

Amidone would be declared a narcotic, its distribution would be controlled and its export probably prohibited. Before long, however, amidone would be produced in every country manufacturing opium today.

Mr. KRASOVEC (Yugoslavia) asked to what extent amidone could replace morphine for medical purposes.

Dr. EDDY replied that it could do so to a very large extent. There were very few exceptions to the reproduction of morphine pictures by amidone. It had a more powerful analgesic effect and the same effect on the gastro-intestinal tract as morphine. In the absence of all supplies of morphine, amidone could replace it one hundred per cent.

Dr. KIPER (Turkey) asked how the minimum and maximum daily therapeutic doses were calculated.

Dr. EDDY replied that it was primarily used as an analgesic for pain relief, but generally speaking two parts of amidone would be equal to three parts of morphine. In cases of addiction, one part amidone would be a complete substitute for four parts of morphine.

The CHAIRMAN said that there was no doubt that the work of the Commission was vitally affected by the discovery of this new drug. The whole picture was changed unless there was some certainty that the world would settle down to a percentage such as thirty, fifty or one hundred per cent substitution of amidone for morphine. In the latter event, the whole opium production of the world in so far as morphine was concerned would disappear.

In reply to Mr. DEEGORGE (Netherlands), Dr. Eddy said that a number of scientific papers had been published within the past year on this drug and reports on its clinical use for the relief of pain would continue to be published in the ordinary way.

In reply to Mr. May (President of the Permanent Central Opium Board), Dr. Eddy stated that amidone far surpassed demerol in its activity.

In reply to the CHAIRMAN, Dr. Eddy stated that its comparison with codeine was a different matter, since codeine was commonly administered orally and morphine by hypodermic injection. If given orally, amidone produced in fifty per cent of the cases secondary reactions such as vomiting, dizziness, etc. These effects interfered with satisfactory oral use and would limit the extent to which amidone would substitute for codeine for oral use. Physicians might extend the use of amidone for pain relief much more widely than simple replacement of morphine if they gained the impression that

would like the relief obtainable with morphine but one avoided its use because of the danger of addiction. In this field, amidone might be used widely unless its similar danger was closely recognized.

Amidone had no local anaesthetic action of importance. Its intravenous administration had recently been recommended as the route of choice but this was not likely to be generally accepted.

Dr. Small (National Institute of Health) then made the following statement:

"There has not yet been sufficient actual manufacturing experience to obtain good cost of production figures for amidone, but I can give you some idea of their magnitude. Amidone hydrochloride has been offered wholesale by one drug manufacturer at \$250. per kilo. This is less than the price of morphine. Pilot plant operations on amidone have naturally resulted in much greater expense, but it is anticipated that large factory operation will ultimately reduce the figure materially. It might not be out of line to take \$100. to \$150. per kilo as the cost, depending on the scale of manufacture. The cost of production of morphine depends almost entirely on the price of opium which fluctuates widely in the world market. During the last few years the production cost has varied from \$175. to \$332. per kilo.

"One manufacturer states: 'We could manufacture amidone in any desired quantities. Our present plans are for a factory having a capacity of 25 kilos per day of eight hours. Obviously this could be increased so that the entire world requirements for amidone could be supplied from a single factory.'

"An able, but unscrupulous, chemist with equipment and materials available on the open market could undoubtedly produce substantial amounts of amidone secretly. Considerable amounts could be made in large glass apparatus. Factory equipment consists chiefly of stirred stills of conventional design. The manufacturers and users of stills and condensers of more than trivial capacity must register the equipment with the Treasury Department, Alcohol Tax Unit, and must report changes in location and so forth.

"Starting materials that may be used by a skilled chemist include the following: Propylene oxide, dimethylamine, dimethylaminopropanol, dimethylaminochloropropane, thionyl chloride, benzil chloride, benzaldehyde, benzoin, benzilic acid, benzil, diphenylacetic acid and ester, diphenylacetonitrile, diphenylmethane, ethyl halides, sodium, magnesium, anhydrous ether, gamma-dimethylaminoalpha, alpha-diphenylvaleronitrile and gamma-dimethylamino-alpha, alpha-diphenylvaleric acid ester. Many of these materials are ordinary

articles of commerce, but some are rather specific intermediates. The presence of dimethylaminopropanol, dimethylaminodiphenylvaleric acid ester or the corresponding nitrile might be considered suspicious.

He added that some of the chemicals which he had mentioned and which were not on the market, could be compounded very easily from common chemicals on the legitimate market. Any good organic chemist could write out two hundred varieties or more of amidone which would not be covered by amidone or any description of amidone. It was therefore quite clear that any international agreement must be drawn up in such a manner as to cover all these possible component drugs.

M. BOURGOIS (France) cited as an instructive consideration for any agreement the case of the firm Rhone-Poulenc manufacturing a drug known as dolosal. These new products were made of components which in the main could be bought in any grocer's shop. The firm in question had been obliged to carry on operations in a separate workshop, although the amount produced was very small. There were two factories producing analogous products. There were no clinical observations as yet, and only a few doctors were carrying on experiments. The French medical faculty had not yet been made aware of these products.

In reply to Dr. KIPER (Turkey), Dr. SMALL stated that amidone would remain stable over a period of years if not exposed to the light.

The CHAIRMAN asked if, assuming that a factory was engaged in the illicit manufacture of heroin, it could switch to amidone easily. Would a more highly qualified chemist be necessary?

Dr. SMALL replied that amidone, being more difficult to produce, needed a higher standard of skilled workmanship. The starting materials were cheap, but the synthesis was not easy, although any skilled chemist could produce the drug. There was also the possibility of explosion.

Dr. SZE (China) asked, since the number of allied substances was so large, what phrasing could be used in an international instrument.

Dr. SMALL preferred to leave that to diplomats working in co-operation with experts. The formula should state that every drug found to be of similar dangerous effect should automatically come under the treaty.

Mr. MAY (President of the Permanent Central Opium Board) asked if the effect, rather than the composition, should be the test.

Dr. SMALL replied in the affirmative.

Mr. STEINIG (Director of the Division of Narcotic Drugs) suggested the following formula:

"Every narcotic drug which is used, or may be used, for medical purposes, and which is liable to produce drug addiction, but is not covered by the 1931 Convention, should come under international control."

Dr. SMALL thought it would be advisable to include a definition of the extent to which a drug was habit-forming. In reply to Dr. SZE (China) he said that there was at present a chemical formula which might cover the majority of like substances, but this might not be so in a year's time. Such a formula would therefore be dangerous.

Dr. RAMOS Y RAMOS (Mexico) requested that a summary of the statements made by Dr. Small and Dr. Eddy, accompanied by a few general considerations concerning the physico-chemical characteristics of amidone and by a comparison with morphine as a medical and toxic drug capable of producing addiction, should be circulated among the members, together with data concerning the possibilities of illegal and legal manufacture, import, export, and the like. This would enable the members of the Commission to put further questions to the experts and thus to obtain a clear picture of the elements for a comprehensive international instrument.

M. BOURGOIS (France) stated that a similar situation had arisen in France and the Government had automatically placed the products in question in the category of dangerous drugs. The solution had been made possible by the valuable documents supplied by the representative of the United States. It had been simple since only one authority was concerned.

Mr. DELGORGE (Netherlands) thought it impossible for the Commission to take definite steps as yet. It should first apply to the World Health Organization for an opinion.

Dr. FORREST (Interim Commission of the World Health Organization) stated that the Interim Commission had set up a committee of experts on habit-forming drugs, of which Dr. Eddy was a member. Application could be made to this committee for an opinion.

The CHAIRMAN said that there was a definite need to exercise control as soon as possible for it was not possible to allow amidone to be sold freely. The United States was one country where production was immediately possible.

Mr. ANSLINGER (United States) stated that the formula was not patented in the United States and did not fall within the category of captured technology; it was therefore available to anyone on payment of twenty-five cents. Obviously, the drug would not be manufactured only in the United States, but very shortly in Europe and elsewhere. The immediate problem was the tremendous surplus manufacture in the United States. Safeguards would be employed to prevent diversion. By next year manufacture would be undertaken in many countries if no steps were taken to limit it and there would be a flood of amidone in the licit and illicit markets. Diversion was bound to
/occur

occur even in the United States. The Commission now saw itself faced with the possibility of losing much of the ground which it had gained by limiting the manufacture of morphine, if no steps were taken. The formula was available in Germany and Switzerland, and experiments were certainly being conducted. The urgency of limiting manufacture was therefore manifest. Control of distribution by means of medical prescriptions would not limit manufacture. There must be supervision of the manufacturer himself, otherwise there was great danger of losing all the advantages so far gained from the Narcotics Limitation Convention.

The CHAIRMAN said that it was his duty to point out that even if the Commission urgently recommended the need of control there would be a long delay before action was taken. Reports to governments would have to be made, entailing consultations, correspondence and so on. If a recommendation were made to the Economic and Social Council at its present session, it would take eighteen months before effective international control were established. By that time, manufacture would be in full swing with the result that the situation would be a nightmare for narcotic control officers.

Dr. SZE (China) said that members had all been impressed by the time factor. The statements made by Dr. Eddy and Dr. Small had convinced everyone, and he therefore moved that the Commission should go on record now as recommending immediate and urgent action. As a preliminary measure he would urge members to take unilateral action with their governments.

Mr. ANSLINGER (United States) seconded this motion.

Dr. LABIB (Egypt) was quite satisfied that amidone must be considered a dangerous drug. The drug would be seized unless accompanied by an import license and intended for medical use.

The CHAIRMAN observed that the need was for a combination of the individual action of States. However excellent Ministerial orders might be, smuggling would be carried on. He reminded the representative of Egypt that some 12,000 kilos of opium were seized in countries adjacent to Egypt in recent years. It was clear that the manufacture of amidone must be controlled so as to prevent export, import and all smuggling.

Mr. DELGORGE (Netherlands) asked if governments could be invited to stop manufacture pending effective measures.

The CHAIRMAN did not think this sufficient and put the motion of the Chinese representative to the vote, namely, "that this Commission is of the opinion that it is urgent to take action respecting the manufacture and distribution of amidone."

DECISION: The motion was adopted.

/The CHAIRMAN

The CHAIRMAN stated that the principle had now been established.

Mr. ANSLINGER (United States) then read his proposal for an amendment to the 1931 Convention:

"Article 1 of the Convention for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs is hereby amended by adding to Group I, Sub-Group (a), the following paragraph (v):

- (v) Any other drug, however produced, which shall be found by the World Health Organization to have an addiction-forming or addiction-sustaining liability similar to morphine or cocaine, as of the date such finding is communicated through the Secretary-General of the United Nations to the respective High Contracting Parties."

The CHAIRMAN declared the meeting open at 4.00 p.m.
