Information on the extent of association of 37 benzodiazepines with illicit activities during the period 1984-1989, available to the 27th meeting of the WHO Expert Committee on Drug Dependence in 1980, clearly indicated a higher incidence of association with illicit activities of both diazepam and flunitrazepam in comparison with other benzodiazepines. At that time, however, the data were not evaluated in relation to drug availability. After and adjustment for the amounts manufactured and for potency, flunitrazepam further stands out in both seizures and the number of illicit cases involving the drug, whereas diazepam is no longer outstanding.

Information on drug involvement in illicit activities after 1980, received from governments in response to the WHO questionnaire in 1994, is limited, and does not allow a comparison among a large number of benzodiazepines. However, the recent report from Interpol and the increasing trend in the United States of America, despite the lack of licit medical supplies in that country, together with several recent reports showing flunitrazepam as being the main non-opioid drug abused by opioid abusers in major European cities, further substantiate its high abuse liability. 5. Therapeutic usefulness

Flunitrazepam is useful for the treatment of insomnia. It is also indicated as a preanaesthetic medication to assist in the induction and maintenance of anaesthesia. Flunitrazepam has a therapeutic usefulness similar to other benzodiazepine hypnotics, within the range from moderate to great. 6. Recommendation

Flunitrazepam has a greater likelihood of abuse than other benzodiazepines. Although there is some element of self-medication for opioid withdrawal, the abuse of flunitrazepam by opioid abusers complicates the clinical picture, leading to multiple drug dependence. Its abuse is prevalent also among youths and cocaine abusers. In addition to its oral and intravenous use, abuse by "snorting" has recently been reported. As yet, no other benzodiazepine has been reported as being abused by three different routes of administration: oral, nasal and intravenous. Flunitrazepam abuse has been associated with dependence and other behavioural problems. Illicit activities involving flunitrazepam are increasing even in the United States of America, where it is available illegally despite the lack of marketing for therapeutic use.

Based on the available data concerning its pharmacological and toxicological profile, dependence potential and likelihood of abuse, and paying particular regard to the above characteristics, the degree of seriousness of the public health and social problems associated with the abuse of flunitrazepam is assessed to have become substantial. On the basis of this and the assessment of its therapeutic usefulness, it is recommended that flunitrazepam be rescheduled into Schedule III of the Convention on Psychotropic Substances, 1971.

## Mesocarb

1. Substance identification

Mesocarb (INN; CAS 34262–84–5), is chemically 3-( $\alpha$ -methlylphenethyl)-*N*-(phenylcarbamoyl)syndone imine, is also known as Pharbamocarb, Sidnocarb and Sydnocarb. Mesocarb has one asymmetric carbon atom in the molecule, so that two stereoisomeric forms and one racemate are possible.

2. Similarity to already known substances and effects on the central nervous system

Chemically, mesocarb is a sydnone imine having an amfetamine-like moiety in its molecule. Of the two optical isomers of mesocarb, only the levorotatory isomer exerts a stimulant effect on the central nervous system. This effect is significantly weaker than that of dexamfetamine. Mesocarb produces locomotor stimulation, anorectic activity, enhancement of conditioned reflexes, and shortening of the period of action of hypnotic agents. In addition, there are several pharmacological studies on mesocarb used in combination with other substances in animals, such as mesocarbacetylsalicylic acid combination. Mesocarb has been reported to increase work capacity and improve cardiovascular function while maintaining normal oxygen consumption. Adverse reactions are similar to those of other CNS stimulants. Several studies in humans have shown that mesocarb increases resistance to environmental stress such as cold temperature, low gravity, and low oxygen levels in the air.

3. Dependence potential

Animal studies indicate that mesocarb has discriminative stimulus effects similar to CNS stimulants such as dexamfetamine and cocaine, as well as some reinforcing effects in monkeys, suggesting a low to moderate dependence potential.

4. Actual abuse and/or evidence of likelihood of abuse

There is some evidence to indicate that mesocab is abused in sports, and its use has been banned by the International Olympic Committee.

Though reportedly discontinued, information from the International Narcotics Control Board indicated that large quantities of a pharmaceutical preparation containing mesocarb and acetylsalicylic acid were illegally exported to western Africa. Although epidemiological data are not available, it is believed that most, if not all, of the exported combination products was abused. On the basis of available information, mesocarb is assessed to have an appreciable abuse liability.

5. Therapeutic usefulness

Mesocarb is used in several countries, mainly in eastern Europe, as a stimulant to counteract acute intoxication by depressants; for the treatment of hyperactivity and nocturnal enureses in children; and as an "energizer" to enhance resistance to environmental stress. The therapeutic usefulness of mesocarb is estimated to be within the range between little and moderate. 6. Recommendation

Although no epidemiological data are available on health problems associated with

the actual abuse of mesocarb, mesocarb is abused in sports, and illicit activities involving mesocarb have been reported. Based on this and the available data concerning its pharmacological and toxicological profile, dependence potential and likelihood of abuse, the degree of seriousness of the public health and social problems associated with the abuse of mesocarb is assessed to be significant. On the basis of this and the assessment of its therapeutic usefulness, it is recommended that mesocarb be included in Schedule IV of the Convention on Psychotropic Substances, 1971.

## Methcathinone

1. Substance identification

Methcathinone (CAS 5650–44–2) chemically 2-(methylamino)-1phenylpropan-1-one, is also know as ephedrone and metylcathinone. It has one chiral centre, so that two stereoisomeric forms and one racemate are possible. 2. Similarity to already known substances and affects on the central nervous system

Methcathinone is the *N*-methyl derivative of cathinone, and is closely related to metamfetamine. Animal studies have shown that methcathinone produces CNS stimulant effects similar to those produces by amfetamine, metamfetamine, cathinone and cocaine. Of the two optical isomers, the levorotatory form is more active. 3. Dependence potential

Drug discrimination and selfadministration studies in animal indicate that methcathinone has a dependence potential similar to central nervous system stimulants such as amfetamine and cocaine. Case reports and a study conducted in the United States of America on methcathinone abusers also suggest that methcathinone has a high dependence potential similar to that of metamfetamine.

4. Actual abuse and/or evidence of likelihood of abuse

Significant abuse of methcathinone has been reported in Estonia, Latvia, the Russian Federation, and in some countries of the Commonwealth of Independent States as well as in the United States of America. Methcathinone is readily manufactured from ephedrine by oxidation. Methcathinone is assessed to have a high abuse liability. 5. Therapeutic usefulness

Methcathinone has not been marketed for therapeutic purposes. Its therapeutic usefulness is assessed to be very limited, if any.

## 6. Recommendation

Studies from the United States of America and the Russian Federation have confirmed that methcathinone abuse results in adverse health effects similar to those associated with the abuse of metamfetamine, including fatal cases of acute intoxication. Illicit activities involving methcathinone, including clandestine manufacturing, are also reported widely.

Based on the available data concerning its pharmacological and toxicological profile, dependence potential and likelihood of abuse, and paying particular regard to the above characteristics, the degree of