Health Canada Santé Canada

STATUS DECISION OF CONTROLLED AND NON-CONTROLLED SUBSTANCE(S)

Substance: I - 2,3-Methylenedioxymethamphetamine
II - 3,4-Dihydroxymethamphetamine
III - 3-Fluoromethamphetamine

Based on the current information available to the Office of Controlled Substances, it appears that the above substance is:

Controlled	✓
Not Controlled	☐

under the schedules of the *Controlled Drugs and Substances Act* (CDSA) for the following reason(s):

- The substances are amphetamines and captured under item I of Schedule III to the CDSA. In the case of 3-fluoromethamphetamine, the substance could also be captured under 18 of Schedule I to the CDSA.

Prepared by: _____ Date: Dec 10th 2010
Evelyn Soo

Verified by: _____ Date: _____
Marianne Tang

Approved by: _____ Date: _____
DIRECTOR, OFFICE OF CONTROLLED SUBSTANCES

This status was requested by: "third party information removed as per agreement with applicant"

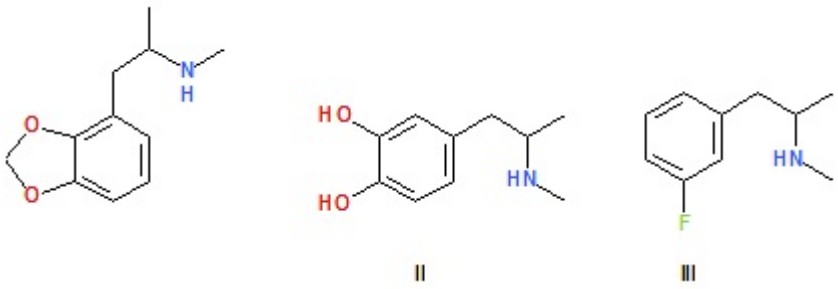
Drug Status Report

Drug: I - 2,3-Methylenedioxymethamphetamine
II - 3,4-Dihydroxymethamphetamine
III - 3-Fluoromethamphetamine

Drug Name Status: I - 2,3-Methylenedioxymethamphetamine
II - 3,4-Dihydroxymethamphetamine
III - 3-Fluoromethamphetamine are the common names.

Chemical Name: I - N-alpha-Dimethyl-1,3-benzodioxole-4-ethanamine
II - 4-[2-(Methylamino)propyl]-1,2-benzenediol
III - 3-Fluoro-N.a-dimethylbenzeneethanamine

Chemical Structure:



II III

Molecular Formula: I - $C_{11}H_{16}ClNO_2$; II - $C_{10}H_{16}ClNO_2$; III - $C_{10}H_{14}FN$

CAS-RN: I - 168968-01-2; II - 438625-60-6; III - 1182818-14-9

Pharmacological class / Application: Amphetamine-related

International status:

US: 2,3-Methylenedioxymethamphetamine, 3,4-Dihydroxymethamphetamine and 3-fluoromethamphetamine are not currently listed in the Schedules to the US *Controlled Substances Act.* However, they may be considered controlled due to the "controlled substances analogue" provision of the CSA.

United Nations: The substances are not listed on the Yellow List - List of Narcotic Drugs under International Control, the Green List - List of Psychotropic Substances under International Control. nor the Red List - List of Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances Under International Control.

Canadian Status: 2,3-Methylenedioxymethamphetamine, 3,4-dihydroxymethamphetamine and 3-fluoromethamphetamine are not currently listed in the CDSA. The substances are all considered to be amphetamines; specifically 2,3-methylenedioxymethamphetamine is an positional isomer of N–methyl–3,4–methylenedioxyamphetamine (MDMA)[1] while 3-fluoromethamphetamine is a structural analogue of methamphetamine where for the purpose of forming status decisions, an analogue is considered to be a substance of significant structural similarity to one included in the Schedules to the CDSA. With regard to 3,4-dihydroxymethamphetamine, the substance has been reported in the scientific literature to be major metabolite of MDMA[2].

"Amphetamines, their salts, derivatives, isomeres and analouges of salts of derivatives, isomers and analogues" are controlled under item 1 of Schedule III to the CDSA. Considering that 2,3-methylenedioxymethamphetamine is an isomer of MDMA and 3,4-dihydroxymethamphetamine is a metabolite of MDMA, both substances are considered captured under item 1(9) of Schedule III as an isomer or derivative of MDMA, respectively. In the case of 3-fluoromethamphetamine, the substance is amphetamine and therefore would be included under item 1 of Schedule III to the CDSA. However, as an analogue of methamphetamine, 3-fluoromethamphetamine could also be considered to fall under the heading "Methamphetamine (N,α-dimethylbenzeneethanamine), its salts, derivatives, isomers and analogues and salts of derivatives, isomers and analogues" of item 18 of Schedule I to the CDSA.

Recommendation: 2,3-Methylenedioxymethamphetamine, 3,4-dihydroxymethamphetamine and 3-fluoromethamphetamine are included under item 1of Schedule III to the CDSA and are controlled substances. 3-fluoromethamphetamine may also be considered controlled under item 18 of Schedule I to the CDSA.

Date: 10 December 2010

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[1]Montgomery, T. et al. (2007) Comparative potencies of 3,4-methylenedioxymethamphetamine (MDMA) analogues as inhibitors of [3H]noradrenaline and [3H]5-HT transport in mammalian cell lines, Br. J. Pharmacol. **152**:1121-1130.

[2]Ortuno, SM et al. (2001) 3,4-Dihydroxymethamphetamine (HHMA). A major in vivo 3,4-methylenedioxymethamphetamine (MDMA) metabolite in humans, Chem. Res. Toxicol. **14**:1203-1208.