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

Substance:    Midazolam derivatives

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 derivatives of midazolam and therefore included under item 18(22.1) of Schedule IV to the CDSA.

Prepared by: _____________________________     Date: Sept 21\textsuperscript{th} 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 - Midazolam 2,5-dioxide
II - Midazolam 2,5-dioxide-d6
III - Midazolam-d5
IV - Midazolam-d6
V - 1',4-dihydroxymidazolam
VI - 1',4-dihydroxymidazolam-d4
VII - 1'-hydroxy midazolam
VIII - 1'-hydroxy midazolam-d5
IX - 1'-hydroxy midazolam-13C-3
X - 1'-hydroxy midazolam-beta-D-glucuronide
XI - 4-acetoxy midazolam
XII - 4-hydroxy midazolam
XIII - 4- hydroxy midazolam-beta-D-glucuronide
XIV - 5,6- dihydromidazolam

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XI - 4-acetoxy midazolam
XII - 4-hydroxy midazolam
XIII - 4- hydroxy midazolam-beta-D-glucuronide
XIV - 5,6- dihydromidazolam are common names

Chemical Name:

I - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5- a][1,4]benzodiazepine 2,5-dioxide
II - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5- a][1,4]benzodiazepine 2,5-dioxide-d6
III - 8-chloro-6-(o-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine-d5
IV - 8-chloro-6-(o-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine-d6
V - 8-Chloro-6-(2-fluorophenyl)-4-hydroxy-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol
VI - 8-Chloro-6-(2-fluorophenyl)-4-hydroxy-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-d4
VII - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol
VIII - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-d5
IX - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-13C-3
X - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-beta-D-glucuronide
XI - 4-Acetoxy-8-chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine
XII - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepin-4-ol
XIII - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepin-beta-D-glucuronide
XIV - 8-Chloro-6-(2-fluorophenyl)-5,6-dihydro-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine

Chemical structure:
**Molecular Formula:** I - C_{18}H_{13}ClFN_{3}O_{2}; II - C_{18}D_{6}H_{7}ClFN_{3}O_{2}; III - C_{18}D_{5}H_{8}ClFN_{3}; IV - C_{18}D_{4}H_{9}ClFN_{3}; V - C_{18}H_{13}ClFN_{3}O_{2}; VI - C_{18}D_{4}H_{1}ClFN_{3}O_{2}; VII - C_{18}H_{13}ClFN_{3}O_{2}; VIII - C_{18}D_{4}H_{1}ClFN_{3}O_{2}; IX - C_{2}C_{1}H_{15}ClFN_{3}O; X - C_{2}H_{3}ClFN_{3}O; XI - C_{2}H_{15}ClFN_{3}O; XII - C_{18}H_{13}ClFN_{3}O; XIII - C_{2}H_{2}ClFN_{3}O; XIV - C_{18}H_{15}ClFN_{3}

**Pharmacological class / Application:** Pharmaceutical-related substances

**CAS-RN:** I - 59468-87-0; II - 1215321-98-4; III - 59467-70-8; IV - NONE; V - 64740-68-7; VI - NONE; VII - 59468-90-5; VIII - NONE; IX - NONE; X - 81256-81-7; XI - 59468-84-7; XII - 59468-85-8; XIII - 81256-82-8; XIV - 59468-07-4

**International status:**

US: The substances are not listed specifically in the Controlled Substances Act and are not mentioned anywhere on the DEA website.

United Nations: The substances are not listed on the Yellow List - List of Narcotic Drugs under International Control nor the Green List - List of Psychotropic Substances under International Control.

Canadian Status: The above substances are all derivatives of midazolam, which is presently listed under as item 18(22.1) in Schedule IV to the CDSA under the item heading “Benzodiazepines, their salts and derivatives, including”. Therefore, the substances must be included under item 18(22.1) of Schedule IV to the CDSA.

**Recommendation:** Midazolam 2,5-dioxide, midazolam 2,5-dioxide-d6, midazolam-d5, midazolam-d6, 1’4-dihydroxymidazolam, 1’4-dihydroxymidazolam-d4, 1'-hydroxy midazolam, 1'-hydroxy midazolam-d5, 1-hydroxy midazolam-13C-3, 1'-hydroxy midazolam-beta-D-glucuronide, 4-acetoxymidazolam, 4-hydroxy midazolam, 4-hydroxy midazolam-beta-D-glucuronide and 5,6-dihydromidazolam are all under item 18(22.1) of Schedule IV to the CDSA and are controlled substances.

**Date:** 21st September 2010