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

Substance: I- Midazolam impurity A  
II- Midazolam impurity B  
III- Midazolam impurity E  
IV- Midazolam impurity G  
V- Midazolam impurity H

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 impurities of midazolam and all contain the core structure of the 1,4-benzodiazepines and are therefore captured under Item 18 of Schedule IV to the CDSA.

Prepared by: ________________________________ Date: _____________
Vincent Marleau

Verified by: ________________________________ Date: _____________
Mark Kozlowski

Approved by: ________________________________ Date: _____________
DIRECTOR, OFFICE OF CONTROLLED SUBSTANCES

This status was requested by: Nacer Silarbi, OCS
Drug Status Report

Drug:
I- Midazolam impurity A
II- Midazolam impurity B
III- Midazolam impurity E
IV- Midazolam impurity G
V- Midazolam impurity H

Drug Name Status:
I- Midazolam impurity A
II- Midazolam impurity B
III- Midazolam impurity E
IV- Midazolam impurity G
V- Midazolam impurity H are the common names.

Chemical Name:
I- (6RS)-8-chloro-6-(2-fluorophenyl)-1-methyl-5,6-dihydro-4H-imidazo[1,5-a][1,4]benzodiazepine
II- (6RS)-8-chloro-6-(2-fluorophenyl)-1-methyl-6H-imidazo[1,5-a][1,4]benzodiazepine
III- [(2RS)-7-chloro-5-(2-fluorophenyl)2,3-dihydro-1H-1,4-benzodiazepin-2-yl]methanamine
IV- 8-chloro-1-methyl-6-phenyl-4H-imidazo[1,5-a][1,4]benzodiazepine (desfluoromidazolam)
V- 6-chloro-4-(2-fluorophenyl)-2-methylquinazoline

Chemical structure:

Molecular Formula:  I- C_{18}H_{15}ClFN_3; II- C_{18}H_{15}ClFN_3; III- C_{18}H_{15}ClFN_3; IV- C_{18}H_{10}ClFN_2;
V- C_{18}H_{14}ClN_3.

CAS-RN: I- N/A; II- N/A ; III- N/A ; IV- N/A ; V- N/A.
Pharmacological class / Application: Pharmaceutical-related impurity

International status:

US: Midazolam impurity A, midazolam impurity B, midazolam impurity E, midazolam impurity and midazolam impurity H are not listed specifically in the Schedules to the US 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, 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: Midazolam impurity A, midazolam impurity B, midazolam impurity E, midazolam impurity and midazolam impurity H are not listed specifically in the schedules to the CDSA. The substances are synthetic impurities of midazolam, which is currently listed as sub-item 18(22.1) in Schedule IV to the CDSA under the heading “Benzodiazepines and their derivatives”. The substances also contain the core structure of the 1,4-benzodiazepines and are therefore considered captured under sub-item 18(22.1) of Schedule IV to the CDSA. A number of synthetic impurities relating to midazolam were reviewed previously and also considered captured under item 18 of Schedule IV to the CDSA.

Recommendation: Midazolam impurity A, midazolam impurity B, midazolam impurity E, midazolam impurity and midazolam impurity H are included under item 18 of Schedule IV to the CDSA and are controlled substances.

Date: September 11th, 2012.