

Drug Status Report

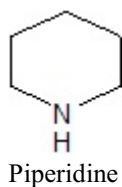
Drug: Piperidines

This report was prompted by a request from a client for status determinations of several closely related substances which are shown in the Appendix.

Chemical Names and **Chemical structures** for the substances are shown in the Appendix. The names are consistent with the structures.

Regulatory Status:

Piperidine (structure below) and its salts are Class A precursors in Canada. They were included in the list of precursors because piperidine is a precursor to phencyclidine¹. It is included in Table II to the UN's Red List.



None of the substances in the Appendix are salts of piperidine.

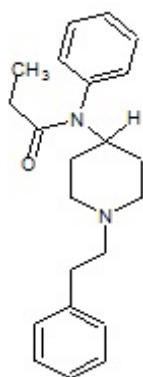
The piperidine radical is incorporated into several drug substances. Item 3 of Schedule I to the CDSA is "Phenylpiperidines, their intermediates, salts, derivatives and analogues and salts of intermediates, derivatives and analogues." A previous status report on 4-(fluorophenyl)-piperidine proposed an interpretation of the item heading for phenylpiperidines. This report which is attached indicated the three existing root structures which are characteristic of substances currently listed at phenylpiperidines. None of the substances in the Appendix contains these root structures.

Item 5 of Schedule I is "Amidones, their intermediates, salts, derivatives and salts of intermediates and derivatives." While some of these substances do contain the piperidine group, it is not characteristic of the class; other amine radicals such as dimethylamino and morpholino are incorporated, in place of piperidine, into these substances.

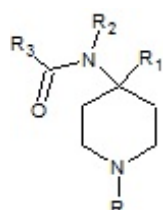
Only two of the three ampromides (item 12) specifically listed on Schedule I contain piperidine radicals so the presence of the piperidine cannot be considered essential or characteristic of this class of substances.

¹ See the Regulatory Impact Analysis Statement attached to SOR/2002-359.

Item 16 of Schedule I is “Fentanyls, their salts, derivatives and analogues and salts of derivatives and analogues.” The structure of fentanyl is shown below. A review of the current family of fentanyls indicates that all members have one common root structure. This fentanyl root structure is shown below and must be considered essential in order to consider a substance a member of the fentanyl family of drugs and hence included in this item of Schedule I. The substituents R through R₃ may be hydrogen, alkyl or aryl groups.



Fentanyl

Fentanyl Root
Structure

None of the substances included in the Appendix contain the fentanyl root structure.

Recommendation: Based on this comparison with substances and families of substances currently included in the schedules to the CDSA, none of the substances shown in the Appendix is subject to the CDSA.

August 2, 2007

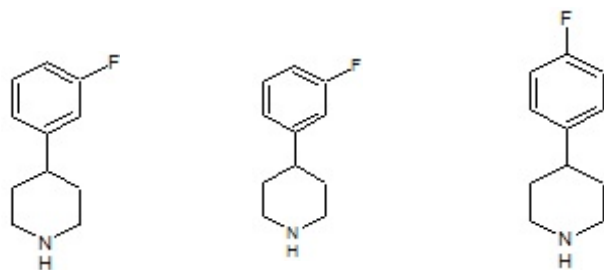
Drug Status Report

Drug: 4-(Fluorophenyl)piperidine

Drug Name Status: 4-(Fluorophenyl)piperidine is the common name

Chemical Name: 4-(2-Fluorophenyl)piperidine; 4-(3-fluorophenyl)piperidine; 4-(4-fluorophenyl)piperidine

Chemical structure:



There are three possible positional isomers of 4-fluorophenylpiperidines.

Molecular Formula: $C_{11}H_{14}FN$

Pharmacological class / Application: fine chemical

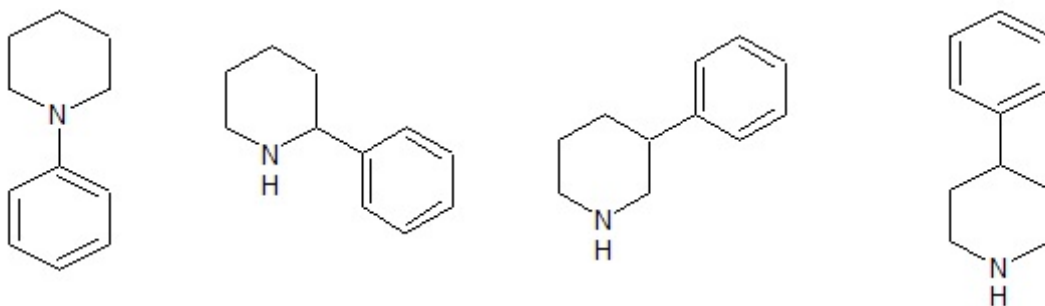
International status:

US: 4-(Fluorophenyl)piperidines are not currently listed explicitly on the schedules to the US Controlled Substances Act and are not mentioned on the DEA website.

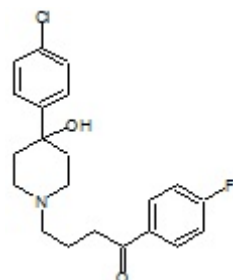
United Nations: The substances are not listed on the Yellow List - List of Narcotic Drugs under International Control nor the Green List - List of Psychotropic Substances under International Control.

Canadian Status: "Phenylpiperidines, their intermediates, salts, derivatives and analogues and salts of intermediates, derivatives and analogues" is listed as item 3 of Schedule I.

"Phenylpiperidine" may refer to the following four positional isomers.

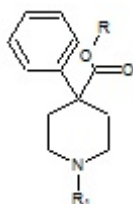


Strictly interpreted, the text of item 3 of Schedule I includes a wide range of chemical substances. For example, haloperidol (structure below), a drug not currently subject to the CDSA, would be included if an unrestricted interpretation of item 3 is used. Many other chemicals used commonly in chemical procedures would also become subject to the CDSA.

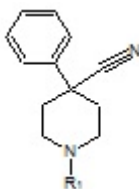


Haloperidol

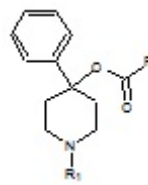
It would seem reasonable to interpret the text of item 3 of Schedule I in the context of the CDSA. Item 3 of Schedule I intends to include a class of narcotic analgesic drugs. This class of drugs, as defined by the specific substances given as examples in subitems 1 through 24 is characterized by the following three chemical structure elements.



Root 1



Root 2



Root 3

Root 1 includes drugs (anileridine, diphenoxylate, pethidine, etc.) of this class where a carboxylic acid function exists at the four position of the piperidine. Root 2 includes methylphenyl-isonipecotnitrile, a precursor to pethidine. Root 3 includes drugs (alphaprodine, betameprodine, etc.) where an ester is attached at the four position of the piperidine ring. Other members in the class are differentiated by the type of group attached at R₁ and other substituents attached to the piperidine and phenyl rings. Limiting the interpretation of item 3 to include only substances with these three root structures will continue to control narcotic analgesics without capturing common chemicals and other drugs.

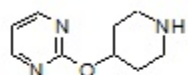
Recommendation: The isomers of 4-(fluorophenyl)piperidine are not included in item 3 of Schedule I and are not controlled substances.

March 15, 2007

Appendix

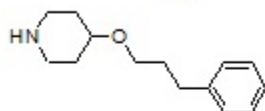
2-(Piperidin-4-yloxy)pyrimidine

1 g



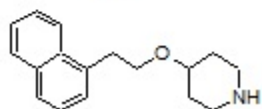
4-(3-Phenylpropoxy)piperidine

1 g



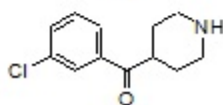
4-[2-(1-Naphthyl)ethoxy]piperidine

1 g



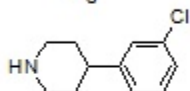
4-(3-Chlorobenzoyl)piperidine

1 g



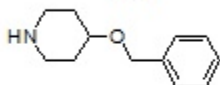
4-(3-chlorophenyl)piperidine

1 g



4-(Benzoyloxy)piperidine

30 g



1-Boc-4-bromomethylpiperidine

10 g

