

1-(3-chlorophenyl) piperazine (mCPP)
Expert peer review on pre-review report

35th Expert Committee on Drug Dependence, Hammamet, Tunisia
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1. Comments based on the review report

a. Evidence on dependence and abuse potential

Abuse and dependence potential can be assessed in laboratory studies in experimental animals, in human laboratory studies, in clinical populations of people known or suspected of using the drug, and in epidemiological studies. The pre-review report notes that in drug discrimination studies in animals, mCPP was found to mimic other complex piperazines, namely 1-(3-trifluoromethylphenyl) piperazine (TFMPP), ethanol and MDMA. There are no known published reports of the abuse and dependence potential in laboratory studies human beings. There are reports of abuse of the drug by humans and it is noteworthy that mCPP is available on the black market in a number of regions in the world and that it has attracted a number of “street” brand names. Furthermore it is being used in place of MDMA in illicit preparations of the latter (as “Ecstasy”). It is not known whether mCPP produces a dependence syndrome (by ICD 10 or DSM IV criteria) in human beings. Epidemiological studies do not report mCPP use to the best of this reviewer’s knowledge and there are therefore no estimates of dependence potential as judged by “conversion” rates (the percentage of users who go on to persistent, dependent-pattern use).

b. Consequences to individual and society because of misuse

mCPP has psychostimulant, anxiety-provoking and hallucinogenic effects. The effects are noted 45-90 minutes after oral administration and include euphoria, illusions (colour enhancement), circum-oral paraesthesia, and in higher doses overt hallucinosis equivalent to primary hallucinogens such as lysergic acid diethylamide (LSD). There are reports of coma following mCPP use but it is likely that other substances were taken by these individuals. There are no reports of fatal intoxication. Increases in body temperature and in anxiety, and also depression are reported, particularly in older subjects. Among patients with psychiatric disorders a greater degree of anxiety, euphoria, perceptual changes, and hostility were observed compared with healthy control subjects.

c. Magnitude of the problem in countries (misuse, illicit production, smuggling etc)

There are extremely limited data to gauge the impact of mCPP at a population level. It has been reported from numerous countries including the USA and most European countries, but no estimates of its prevalence are available. There are also no data on the extent of its illicit manufacture and trafficking. Although it has many different street names, which suggest it is quite widely available in drug-using subcultures, it appears to have a niche presence rather than being a widespread drug of abuse such as MDMA (such as Ecstasy).

d. Need of the substance for medical (including veterinary) practice

mCPP is a known metabolite of a number of antidepressants including trazodone and nefazodone. It is not known to what extent the therapeutic effect of these antidepressants

are mediated specifically by mCPP. However given the fact that mCPP has been shown to cause depression, it would suggest that the therapeutic benefits of drugs such as trazodone are mediated by the parent drug or other biologically active metabolites. mCPP has not, as the reviewer comments, “been the subject of a marketing authorization”, with the single exception of Iraq where it would appear to be registered as an antidepressant. It is reported that in Germany mCPP is used as an intermediate in the production of trazodone and related chemical suppliers. More information is needed on the alternative means of manufacturing these medications.

e. Need of the substance for other purposes (e.g. industrial)

Other than the use mentioned above as an intermediate in the production of trazodone and related substances, there is no use of mCPP for industrial or other purposes.

f. Measures taken by countries to curb misuse

There are no international controls on mCPP under any of the international drug control conventions. In some countries mCPP is controlled under national legislation that regulates the availability of substances of abuse.

g. Impact if this substance is scheduled

It seems that there is more potential for harm from mCPP than any benefit and that if alternative methods of manufacturing trazodone and its analogues can be identified, there would seem to be no adverse consequences on it being declared a prohibited substance.

2. Additional information to the pre-review report

As the author of the pre-review report emphasizes, there are few data on mCPP that allow conclusions to be drawn on the extent of its abuse and dependence potential. In particular it would be helpful if there were studies of its use among known drug-using populations, including people frequenting the “club and party scene”. Subsequently questions on mCPP use could be incorporated into national epidemiological surveys if the initial studies in drug-using populations identified it was of significant concern. Standard measures of dependence potential in human beings such as conversion ratios could then be calculated to guide further investigations and policy decisions.

3. Other comments or opinions

It seems that mCPP is of relatively minor significance compared with other illicit drugs according to the available data. Reports of drug users indicate that it is not a preferred substance when alternatives such as MDMA (such as Ecstasy) and more potent hallucinogens

are available. Reports of it causing anxiety as a predominant response and also inducing depression would suggest that it is likely to be attractive only to a small minority of individuals.

4. Expert reviewer's recommendation on the need for a critical review

On the basis of the pre-review, there seems to be a paucity of data available on mCPP. Consideration could be given to a critical review of the group as a whole, of substituted piperazines, which are being considered by the 35th Expert Committee on Drug Dependence. mCPP does not merit a critical review as an individual substance, especially considering the resources needed for such a review.