1-(3-trifluoromethylphenyl)piperazine (TFMPP)

Expert peer review on pre-review report

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

a. **Evidence on dependence and abuse potential**
   There are few animal studies on the dependence potential of TFMPP. One study found that TFMPP possesses neither rewarding properties nor reinforcing effects and did not substitute for cocaine or amphetamine. A few published studies in humans concerning psychological effects of TFMPP indicate the substance to be a mild stimulant with slight mood elevation and some perceptual shift. The pre-review report concluded that TFMPP is unlikely to possess an abuse or dependence potential.

b. **Consequences because of misuse**
   User reports and study information indicate that TFMPP is commonly used in conjunction with other psychoactive piperazines, mostly as admixture to N-benzyl-piperazine (BZP). There are some reports of non-fatal intoxication where TFMPP is implicated as a cause of hospital admission, but usually there is lack of laboratory confirmation. In the relatively few instances of fatalities involving TFMPP, in no cases was it involved alone, but BZP was also found. It was not possible to specifically determine the toxicological significance of TFMPP. It was also not possible to relate any particular concentration of TFMPP to specific effects or outcome.

c. **Magnitude of problem in countries**
   A WHO survey concerning the use of TFMPP carried out in 2008 was answered by 49 countries. Among the responding countries, 3 countries, Denmark, France and Germany reported on the use in a harmful way, 16 countries considered that it is used, but not in a harmful way, while in 17 countries its use was unknown. No specific data could be collected in the pre-review report on the extent of use of TFMPP in countries where it is available as a “party pill”, it is found usually in combination with BZP.

d. **Need of TFMPP for medical practice**
   TFMPP is not used in any country as a human medicine or in veterinary practice.

e. **Need of TFMPP for other purposes**
   TFMPP is a synthetic chemical which may be used as an intermediate material or for analytical purposes. It was previously used as a chemical intermediate in the synthesis of antrafenine, but this product is no more marketed.

f. **Measures taken by countries to curb misuse**
   TFMPP is not controlled internationally under the 1971 Convention on Psychotropic Substances. According to the pre-review report TFMPP is controlled under national legislation in Belgium, Denmark, Greece, New Zealand and Sweden.

g. **Impact if TFMPP is scheduled**
   Scheduling TFMPP will have no impact on medical (and veterinary) practice, as the substance is not used in medical or veterinary practice.
2. Additional information to the pre-review report

Some statements of the pre-review report may be expanded by additional information. Data concerning pharmacokinetics of TFMPP are confirmed in a paper of Vorce et al (1) who found urine concentrations of up to 26μg/ml TFMPP in human subjects. In 2002, the U.S. Drug Enforcement Administration (DEA) classified TFMPP as a Schedule I controlled substance as an emergency order. Since 2004 it was omitted from the schedule and at present (March 2012) it remains in USA as an unscheduled compound (2). In the European Monitoring Center for Drugs and Drug Addictions (EMCDDA) there is a low level of interest in TFMPP. In EMCDDA drug profile series, it is mentioned in the review of BZP and other piperazines, but without any specific details related to TFMPP (3).

References
(2) U.S. DEA, Schedules of controlled substances - accessed in March 2012
(3) EMCDDA drug profiles - accessed in March 2012.

3. Other comments or opinions

When assessing the advisability of taking any further steps that may lead to scheduling of TFMPP it should be taken into account that the substance is mostly used as an additive to other psychoactive drugs, mostly BZP, and that there are practically no clinical studies indicating (or disproving) its abuse and dependence potential.

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

There is no need for a critical review of TFMPP as it seems to posses no abuse or dependence potential and there is no information on extended harmful use.