

Expert Committee on Drug Dependence
Thirty-sixth Meeting
Geneva, 16-20 June 2014



1. Comments based on the review report

a. Evidence on dependence and abuse potential

Dependence Potential

Review states currently not available in the literature.

Abuse Potential

In humans: studies are not available.

In Vitro: The review has described that 4-MEC shares monoamine uptake/5-HT releasing properties. However, it was unclear if this extends to abuse liability encountered with psychomotor stimulants like methamphetamine or cocaine. Observably, research is lacking and there is data missing in relation to mechanism of action. Yet that does not exclude its abuse potential as will be noticed in the following sections.

b. Risks to individual and society because of misuse

c.

Risks to individual

Review states published literature reports on toxicity are not available. As for adverse reactions in humans there has been a reference to three case reports. All case reports showed different levels of 4-MEC in the blood analysis. One (152ng/ml and 0.12g/dl ethanol) resulted in fatal traffic accident of a 30 year old male, the next case was a male who developed 'psychomotor agitation' and his blood analysis had multiple 'legal highs' including a level of 56ng/ml of 4-MEC. His cause of death was referred to 'damage to important centers of the brain'. Although, with such mixture of substances in his blood it would be difficult to attribute the exact role 4-MEC played in his death, but does not exclude it. The third case report was about the possession of a white powder which turned out to be 4-MEC. It's easy to extrapolate from the reports the role of 4-MEC in substance abuse but it's inconclusive to its potential risk. In the WHO questionnaire on the evaluation of 4-MEC, a total of 65 Member States answered the questionnaire for 4-MEC. Of these, only 29 respondents had information on 4-MEC. Nineteen out of 29 respondents confirmed that there was recreational/harmful use of 4-MEC. In the report, one respondent referred to the year 2012, where 18 deaths due to all cathinones were reported as well as 4 emergency room visits by another respondent. Four respondents reported withdrawal, tolerance and other adverse effects or medical illnesses caused by 4-MEC. These include hallucinations, delusions, palpitations, blurred

vision, psychosis, dizziness, confusion, agitation and fits. Hence, from the report it is clearly illustrated the high risks to the individuals.

Risks to society

The Review referred to the “Drug Enforcement Administration, after reviewing the scientific literature, 3-factor analysis, consultation of NFLIS, law enforcement, Customs and Border Protection and other sources, confirmed that 4-MEC appeared to sufficiently prevalent to pose a public health risk.” Furthermore, in the WHO questionnaire report on the evaluation of 4-MEC and as described by one respondent ‘a survey of college students in 2012 by the Monitoring the Future (MTF) showed that 0.2% of full-time college students used synthetic cathinone substances. The use of synthetic cathinone substances among 8th, 10th, and 12th grade students and young adults (non-college peers aged 19 to 28-years-old) was 0.8%, 0.6%, 1.3%, and 0.8%, respectively.’ The respondent also referred to a press release from the American Association of Poison Control Centers (AAPCC). There were 306 exposure calls related to synthetic cathinones in 2010, 6,137 calls in 2011, and 2,691 calls in 2012. 4-MEC, and others are synthetic cathinones that emerged on the United States’ illicit drug market around the time of the temporary scheduling of mephedrone, MDPV, and methylone on October 21, 2011. 4-MEC is among popular recreational drugs. The respondent confirmed that evidence of these synthetic cathinone substances are being abused is indicated by law enforcement encounters of these substances. It was highlighted that forensic laboratories have analyzed drug exhibits received from state, local, and Federal law enforcement agencies and confirmed the presence of 4-MEC, 4-MePPP, a-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or a-PBP in these exhibits. The respondent further added that STRIDE registered 1,732 drug exhibits pertaining to the trafficking, distribution and abuse of 4-MEC and others from January 2010 to November 2013. Specifically, in 2010, STRIDE contains four reports related to 4-MEC and none for the other nine substances described earlier. However, in 2011, there were 205 reports related to these 10 substances, and in 2012, there were 1,302 reports. From January to November 2013 there were 221 reports (excluding naphyrone). National Forensic Laboratory Information System (NFLIS) registered over 8,000 reports from state and local forensic laboratories identifying these substances in drug related exhibits for the period from January 2010 to November 2013 across 42 states. Specifically, in 2010, NFLIS registered 13 reports from 5 states containing many of these synthetic cathinone substances. In 2011, there were 800 reports from 32 states related to these substances registered in NFLIS, in 2012 there were 5,485 reports from 41 states, and from January to November 2013 there were 2,509 reports from 41 states.’ This further supports the critical review on 4-MEC to the extent of the problem to society.

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

The review highlights reports (up to 10.3.2014) that have been received from the European early-warning system on new drugs that 4-MEC was encountered in seizures or as a used substance in 20 European countries. Furthermore, in the U.S.A, the review described four different credible reporting systems as a source of information for the misuse of 4-MEC these are “The Drug Enforcement Administration (DEA) disclosed that

377 exhibits were reported for 4-MEC between January 2010 and December 2013 which was based on STRIDE (System to Retrieve Information from Drug Evidence) database queries. The National Forensic Laboratory Information System (NFLIS) registered 1952 reports containing 4-MEC between January 2010 and December 2013. Between April 2010 and November 2013, a total number of 78 encounters (shipments) with 4-MEC were identified by U.S. Customs and Border Protection." Regardless of the limited/lacking information on the pharmacokinetics and mechanism of action of 4-MEC, the evidence is strong on misuse. In addition, the review stated that "4-MEC was reported to be the most common substance found in pills sold as 'ecstasy' in the region of Oceania." Hence, the magnitude of the problem is big.

In the questionnaire report, on illicit activities related to 4-MEC, two respondents reported clandestine manufacture and one reported the synthesis of the product itself. Five respondents reported processing into the consumer product, 11 countries reported trafficking, four countries diversion and 12 countries an internet market. Again this report further supports the critical review on the extent of the problem.

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

The review stated no information available and referred to the WHO questionnaire on 4-MEC, where it reported that out of 65 respondents, none reported medical or veterinary use.

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

In the same questionnaire report, four respondents stated that 4-MEC was used in medical/scientific research or as analytical standard.

g. Measures taken by countries to curb misuse

The review described that the EMCDDA received confirmation that 4-MEC is controlled in the following countries: 18 European countries, in Turkey, in the USA, Singapore and New Zealand. In addition, in the questionnaire report, 26 respondents had 4-MEC controlled under 'legislation that was intended to regulate its availability.' Eighteen had it under "controlled substance act". Four had it under "medicines law" and the other four had it under different legislations.

h. Impact if this substance is scheduled

The review states not applicable, and on referring to the outcome of the questionnaire report in relation to scheduling, 25 out of 29 respondents that had information on 4-MEC reported that if 4-MEC was placed under international control, they would have the laboratory capacity to identify the substance. Which means the majority that had information on 4-MEC would put an effort to have laboratory capacity to have it identified.

2. Additional information to the critical review report

Section on risk to society: The most common ingredients of “legal highs” 4-MEC ranked 6th. The study was conducted in Poland. [Zuba, D and Byrska B (2013). Prevalence and co-existence of active components of ‘legal highs’. Drug Testing and Analysis; 5(6): 420.]

3. Other comments or opinions

None.

4. Expert reviewer’s view on scheduling with rationale

To include in Schedule I (1971 Convention of psychotropic substance): Substances whose liability to abuse constitutes an especially serious risk to public health and which have very limited, if any, therapeutic usefulness. With reference to section 1b and 1c, the extent of the problem is very clearly described. In addition, according to the review more than 18 countries have it controlled and according to the questionnaire report at least 26 countries have legislation to control it.