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COVER NOTE

From:	Françoise Le Bail
date of receipt:	4 September 2014
To:	Ambassador Stefano Sannino cc Rafael Fernandez-Pita
Subject:	Request for risk assessment on a new psychoactive substance: 4,4'-DMAR (4-methyl-5-(4-methylphenyl)-4,5-dihydrooxazol-2-amine)

Delegations will find attached a request from the Commission for a risk assessment on a new psychoactive substance 4,4'-DMAR (4-methyl-5-(4-methylphenyl)-4,5-dihydrooxazol-2-amine).

Encl.:

Ref. Ares(2014)2309324 - 11/07/2014

EUROPEAN COMMISSION
DIRECTORATE-GENERAL JUSTICE

Director-General

Brussels, 11 JUIL. 2014
DG JUST/B3/EM/mdc/ARES (2014)

Dear Ambassador,

On 25 June 2014, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Europol presented to the Council, the Commission and the European Medicines Agency (EMA) a Joint Report on the new psychoactive substance 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine (MT-45). This Joint Report, drawn up in accordance with Article 5(1) of the Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances[1], provides an overview of the available information on detections, patterns of use and incidents reported on this substance.

According to the Joint Report, a considerable number of hospitalisations and deaths related to MT-45 were reported in one Member State, in a short period of time. The Joint Report also points out that few studies are available on the pharmacology and toxicity of this substance, which is comparable to morphine, and gives rise to further questions, including with regards to the characteristics, associated risks and availability on the market of this substance.

I consider that the health and social risks posed by the manufacture, trafficking and use of MT-45, as well as the involvement of organised crime and possible consequences of control measures, should be assessed through a risk assessment, as foreseen by Article 6 of Decision 2005/387/JHA.

His Excellency
Ambassador Stefano Sannino
Permanent Representative of Italy to the European Union
Rue du Marteau, 5-11
1000 - Bruxelles
Belgique

[1] OJ L 127, 20.5.2005, p.32.

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
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I should be grateful if you would notify this request to conduct a risk assessment of MT-45 to the Members of the Council and to the Horizontal Drugs Group.

Yours sincerely,

F. Le Bail

Françoise LE BAIL

Annex 1: Findings of the Joint Report and summary of the procedure under Council Decision 2005/387/JHA.

Annex 2: EMCDDA-Europol Joint report on 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine (MT- 45).

Annex 3: Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances.

Copy: Mr Rafael Fernandez-Pita, Director-General, Secretariat-General of the Council

ANNEX 1 - FINDINGS OF THE JOINT REPORT AND SUMMARY OF THE PROCEDURE

1.1 THE FINDINGS ON *1-cyclohexyl-4-(1,2-diphenylethyl)piperazine* (MT- 45)

- MT-45 is an *N,N*-disubstituted piperazine compound, having a cyclohexane ring attached to one nitrogen and a 1,2-diphenylethyl moiety attached to the other nitrogen. MT-45 is a synthetic opioid, developed as analgesic in the 1970s by a Japanese company.

- MT-45 has been available on the Union drug market since at least October 2013 and three Member States reported detections in seizures, biological and/or collected samples.

- 28 seizures were reported in one Member State, in either white or off-white powder form or detected in plant material. In two of these cases another new psychoactive substance was also present.

- A total of 21 deaths associated with this substance have been reported in one Member State, in a short period of time between November 2013 and April 2014. All cases were male, aged between 19 and 43, most of them found dead at home. In 17 of the cases, MT-45 was found in combination with at least one other psychoactive substance; in 4 of the cases no other substances were detected. MT-45 was identified as the cause of death in 8 cases.

- The same Member State reported 13 non-fatal intoxications occurring during 2013 and 2014, in which males aged between 18 and 37 were involved.

- There is a lack of studies examining the pharmacology and toxicology of MT-45 in humans. In several studies in animals, the analgesic activity was found to be comparable to morphine and its acute toxicity was determined in male mice and rats observing mortality within seven days. No data are available on the chronic toxicity and the studies that examined the abuse liability and dependence potential of this substance indicate that MT-45 substitutes for morphine in morphine-dependent animals.

- Information from the serious adverse events and users' websites suggest that MT-45 may be used as a drug on its own and in combination with other psychoactive substances, being mainly used in the home environment. The routes of administration include oral and nasal, as well as intravenous or intramuscular injection and rectal administration.

- The subjective effects of MT-45 in humans are not well documented in literature, but according to self-reported experiences from websites, they appear to be similar to those related with opiate-like effects, as the sensation of feeling high followed by sedation, nausea and, in some cases, analgesia. Some self-reported users experiences on websites suggest withdrawal-like symptoms.

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- MT-45 is subject to control measures under drug control, medicines or other consumer protection legislation in 4 Member States.

1.2 SUMMARY OF THE PROCEDURE AS LAID DOWN IN COUNCIL DECISION 2005/387/JHA

Council Decision 2005/387/JHA on the information exchange, risk-assessment and control of new psychoactive substances, hereafter referred to as the 'Council Decision', establishes a mechanism for subjecting substances to control across the Union.

Under this, when a new substance has been notified by a Member State, Europol and EMCDDA consider - on the basis of a set of predefined criteria - whether the gathering of further information is necessary. If so, a Joint Report on the specific substance is drawn up by the agencies in consultation with the European Medicines Agency (EMA) and based on information from the Member States (Article 5). The Joint Report is submitted to the Council, the Commission and the EMA within **ten weeks.** Within **four weeks** from receipt of the Joint Report, the Commission or at least one quarter of the Member States may submit a written request to the Council asking for a Risk Assessment to be conducted. The Council decides by a majority of its Members (Article 6(1)) whether to request the Scientific Committee of the EMCDDA for conduct a risk assessment.

Procedure for a Risk Assessment

As the Joint Report on MT-45 was dated 25 June 2014, the written request of the Commission or of the Member States to conduct Risk Assessments should be transmitted to the Council by 23 July 2014.

If a risk assessment is requested, the EMCDDA must submit the risk assessment reports within 12 weeks.

Within **six weeks** from the date of submission of the risk assessment report, the Commission shall present to the Council an initiative to have the new psychoactive substance subjected to control measures or to present a report explaining it is not necessary to do so.

In accordance with Article 8(3) of the Council Decision, the Council shall decide, by qualified majority and acting on an initiative presented to paragraph 1 or 2 of this Article, whether to submit the new psychoactive substance to control measures.

Grounds for not carrying out a Risk Assessment

Article 7 of the Council Decision describes a number of circumstances under which a Risk Assessment of a new psychoactive substance is not to be carried out – in particular if the substance is under an advance stage of assessment within the United Nations system and if it is a medicine.

According to the Joint Report, the substance MT-45 is not currently under assessment and has not been under assessment within the United Nations system (Art. 7.1).

Furthermore, MT-45 has no medical use (human or veterinary) in the EU and there is no marketing authorisations granted (existing, on-going or suspended) in the Member States

which responded to the EMA (Art. 7.3). Also there are no indications that this substance has other use apart from in scientific research and as analytical reference standards. However, in the absence of an EU database on the synthetic routes of all registered medicinal products, the collection of information cannot be exhaustive.

Therefore, there are no grounds for excluding MT-45 from Risk Assessment.

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