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**EMCDDA–Europol Annual Report on the implementation of
Council Decision 2005/387/JHA**

**In accordance with Article 10 of Council Decision 2005/387/JHA on information
exchange, risk assessment and control of new psychoactive substances**

Overview	3
1. Introduction.....	4
2. Arrangements for information exchange	5
2.1 Reporting form on new psychoactive substance – Article 3(g) of the Decision.....	5
2.2 Criteria for the launch of a Joint Report – Article 5 of the Decision.....	5
2.3 Cooperation with the EMEA and the pharmacovigilance system.....	5
2.4 Cooperation with the United Nations system.....	6
3. Implementation of the Decision and results.....	6
3.1 New psychotropic substances notified in 2005.....	6
3.2 EMCDDA–Europol Joint Report on mCPP	7
4. Implementation issues arising from the initial experiences.....	9
4.1 Scope and deadlines set by the Decision.....	9
4.2 The case of mCPP.....	9
4.3 Possible difficulties to be encountered	10
4.4 Interpretation of Article 7 of the Decision.....	10
4.5 Reference materials.....	11
5. Conclusion.....	11
Annexes	12

Overview

This document jointly presented by the EMCDDA and Europol provides the first Annual Report on activities in support of the Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances.

This Decision establishes a mechanism for the rapid exchange of information on new psychoactive substances appearing on the European Union drugs market. The Decision replaces and broadens the scope of the 1997 Joint Action on new synthetic drugs. Details on the scope of the Decision and the implementation arrangements can be found in the first two sections of the report.

During 2005, 14 new psychoactive substances were officially notified through the information exchange mechanism set up by the Decision. These were all psychotropic substances (synthetic drugs) similar to those listed in Schedules 1 and 2 of the 1971 UN Convention on Psychotropic Substances. Of these 14 substances, three are of particular note, methyldone, DPIA and mCPP, as exhibiting characteristics that suggest that they are particularly appropriate for active monitoring and further vigilance. The reasons why this is so are elaborated in the body of this report.

In particular, the case of mCPP, which is used in the manufacture of at least one medicinal product, and in line with Article 7.3 of the Decision not recommended for formal risk assessment, raises some important issues for the future implementation of the Council Decision. For this reason the case of mCPP is considered in detail in this report as are the implications for the future operation of the Decision.

In the conclusion of this report it is noted that there are challenges to overcome in respect to identifying comprehensive information sources to allow a clear identification of the use of notified substances in the preparation of medicinal products by the pharmaceutical industries.

1. Introduction

Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances ⁽¹⁾ (hereinafter the 'Decision') establishes a mechanism for the rapid exchange of information on new psychoactive substances that may pose public health and social threat, thus allowing European Union institutions and Member States to act on all new narcotic and psychotropic drugs that appear on the European Union drug scene. The Decision also provides for an assessment of the risks associated with these new substances so that measures applicable in the Member States for the control of narcotic and psychotropic substances ⁽²⁾ can also be applied to new psychoactive substances.

The Decision broadens the scope of, and replaces, the 1997 Joint Action ⁽³⁾, which was devoted exclusively to new synthetic drugs. The Decision, however, maintains the three-step approach piloted by the Joint Action: information exchange/early warning, risk assessment and decision-making.

Under the terms of the Decision, the EMCDDA and Europol, in close collaboration with their networks – the Reitox national focal points (NFPs) and Europol national units (ENUs) respectively – were assigned a central role in detecting new psychoactive substances (Article 4). Furthermore, in cooperation with the European Medicines Agency (EMA), the responsible institutions may collect, analyse and present information on a new psychoactive drug in the form of a Joint Report (Article 5). The Report provides evidence-based advice to the Council and the Commission on the need to request a risk assessment of any new psychoactive substance. Such a risk assessment examines the health and social risks posed by the use of, the manufacture of, and traffic in, a new psychoactive substance, the involvement of organised crime and the possible consequences of control measures. In order to carry out the risk assessment, the EMCDDA convenes a special meeting under the auspices of its Scientific Committee (Article 6).

To ensure greater transparency in the implementation of the Decision, Article 10 stipulates that 'The EMCDDA and Europol shall report annually to the European Parliament, the Council and the Commission on the implementation of this Decision. The report will take into account all aspects required for an assessment of the efficacy and achievements of the system created by this Decision. The report shall, in particular, include experience relating to coordination between the system set out in this Decision and the pharmacovigilance system.'

In compliance with the above provision, the EMCDDA and Europol herein present the first Annual Report on the implementation of the Decision for the period 21 May to 31 December 2005. The report outlines the results of the implementation and describes some issues arising from the initial experiences.

⁽¹⁾ Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances was published in the Official Journal of the European Union on 20 May 2005 (L 127/32-37) and took effect the following day, i.e. on 21 May 2005.

⁽²⁾ In compliance with the provisions of the 1961 UN Single Convention on Narcotic Drugs and the 1971 UN Convention on Psychotropic Substances.

⁽³⁾ Joint Action of 16 June 1997 concerning the information exchange, risk assessment and control of new synthetic drugs (Official Journal L 167, 25.06.1997).

2. Arrangements for information exchange

To ensure a smooth transition from the Joint Action to the mechanism set up by the Decision, and to operationalise the implementation, specific arrangements have been made to facilitate the exchange of information between the two responsible institutions and their respective networks.

2.1 Reporting form on new psychoactive substance – Article 3(g) of the Decision

The EMCDDA–Europol reporting form has been designed as an official tool for notification of a new psychoactive substance under the Decision. The reporting form is a concise document, appropriate both for the Reitox NFPs and for the partner ENUs. Furthermore, the EMCDDA and Europol have pledged that, as a rule, all information that they officially receive from Member States through reporting forms shall be immediately transmitted to all partners.

2.2 Criteria for the launch of a Joint Report – Article 5 of the Decision

To provide for a consistent approach and to help ensure a high degree of transparency of the decision-making process under the information exchange mechanism of the Decision, the EMCDDA and Europol have elaborated the criteria to be considered in order to justify the collection of further information that will lead to the production of a Joint Report. The following set of criteria has been agreed:

1. the amount of the material seized;
2. evidence of organised crime involvement;
3. evidence of international trafficking;
4. analogy with better-studied compounds;
5. evidence of the potential for further (rapid) spread; and
6. evidence of cases of serious intoxication or fatalities.

The first three criteria fall within the competence of Europol, whereas criteria 4 to 6 lie within the competence of the EMCDDA. The decision to initiate a Joint Report is taken only following a thorough joint assessment and requires the two institutions to agree on the need for such a report.

2.3 Cooperation with the EMEA and the pharmacovigilance system

At a meeting in Lisbon in June 2005, participants of the Reitox early warning system (EWS) as well as representatives of Europol and the EMEA discussed the likely increased role of the EMEA (Articles 5, 6 and 7). The EMEA provided an overview of the European pharmacovigilance system, which involves surveillance of authorised medicinal products through the collection and evaluation of information on adverse drug reactions (ADRs) under normal conditions of use, as well as on misuse and abuse that may have an impact on the evaluation of benefits and risks.

An outcome of the meeting was that the EMCDDA and the EMEA agreed to consider a stronger cooperation with the pharmacovigilance system. In addition, it was agreed that it is the responsibility of the NFPs to establish links with the relevant National Competent Authorities (NCAs) in their country in order to initiate cooperation with the pharmacovigilance system at a national level.

2.4 Cooperation with the United Nations system

Within the United Nations system, assessment on the medical aspects of substances in relation to their ability to cause dependence is carried out by the Expert Committee on Drug Dependence (ECDD) of the World Health Organization (WHO). The WHO advises the Commission on Narcotic Drugs (CND) whether or not to include these substances in any of the schedules of the 1961 or 1971 UN Conventions.

Article 5.2(e) of the Decision requires the EMCDDA–Europol Joint Report to include information on ‘whether or not a new substance is currently under assessment, or has been under assessment by the UN system’. To obtain such information, the EMCDDA has established a permanent communication channel with the Department of Medicines Policy and Standards, which prepares the ECDD’s work at the WHO headquarters in Geneva.

3. Implementation of the Decision and results

3.1 New psychotropic substances notified in 2005

In 2005, the information exchange under both legal instruments – the 1997 Joint Action and Council Decision 2005/387/JHA – took place without interruption. As of 21 May the new EMCDDA–Europol reporting form was formally introduced to the networks and became a standard tool for notification of a new psychoactive substance.

During 2005, a total of 14 new psychoactive substances were officially notified for the first time to the EMCDDA and/or Europol (see Annex 1). The substances notified in 2005 were all psychotropic (synthetic) drugs, similar to those listed in Schedule 1 and Schedule 2 of the 1971 UN Convention on Psychotropic Substances. All newly-notified substances belonged to three major chemical groups – phenethylamines, tryptamines and piperazines. Various substances from these groups have been previously notified through the early warning system in the framework of the Joint Action. Furthermore, it is worth noting that, of the nine new synthetic drugs that underwent risk assessment between 1997 and 2004 under the Joint Action ⁽⁴⁾, all six substances that were subsequently controlled at European Union level were phenethylamines ⁽⁵⁾.

Subsequently, all 14 new compounds were added to the list of substances monitored by the EMCDDA and Europol, but three can be singled out as exhibiting characteristics that suggest that they are particularly appropriate for active monitoring and further vigilance: methylone, DPIA and mCPP (for the latter see section 3.2).

Methylone: 3,4-methylenedioxymethcathinone (MDMCAT) is the benzylic ketone derivate of 3,4-methylenedioxymethamphetamine (MDMA). Methylone and related compounds can be described as ring-substituted cathinones, where cathinone, the parent compound and a scheduled drug in the 1971 UN Convention on Psychotropic Substances, is an active constituent of khat. Methylone was reported by the Dutch NFP in the beginning of 2005 – it appeared in the end of 2004 in the Netherlands

⁽⁴⁾ The related risk assessment reports are available in English at <http://www.emcdda.eu.int/?nnodeID=431>

⁽⁵⁾ Council Decision of 13 September 1999 defining 4-MTA as a new synthetic drug which is to be made subject to control measures and criminal penalties (1999/615/JHA) (Official Journal L 244/1, 16.9.1999); Council Decision of 28 February 2002 concerning control measures and criminal sanctions in respect of the new synthetic drug PMMA (Official Journal L 63/14 6.3.2002); and Council Decision 2003/847/JHA of 27 November 2003 concerning control measures and criminal sanctions in respect of the new synthetic drugs 2C-I, 2C-T-2, 2C-T-7 and TMA-2 (Official Journal L 321/64, 6.12.2003).

under the name 'Explosion' where it is sold in liquid form via the internet and in the so-called 'smartshops' ⁽⁶⁾ as an 'air freshener' (room odouriser in plastic tubes with vanilla oil). During the same period methylone was also reported from Sweden where it was encountered as tablets sold on the internet. Methylone is reported to be ingested by users in order to achieve psychoactive effects. Behaviourally and pharmacologically the substance resembles MDMA, but the observed subjective effects are not completely identical. Concerns exist that methylone has a potential for further spread and therefore it will be actively monitored in 2006.

The occurrence of di-(β-phenylisopropyl)amine (DPIA) in two seizures containing only this substance in Malta; and tablets containing DPIA and MDMA in Slovenia, is unusual. DPIA is a substance well known to forensic scientists and for many years it has been a useful marker in impurity profiling of illicit amphetamine produced through the Leuckart route. Therefore, the finding of tablets containing only DPIA or in combination with MDMA is a new phenomenon which is worthy of active monitoring.

3.2 EMCDDA–Europol Joint Report on mCPP

A significant new development in 2005 was the appearance and rapid spread of the new psychoactive substance 1-(3-chlorophenyl)piperazine (mCPP). mCPP is one of a family of aryl-substituted piperazines that includes benzylpiperazine (BZP), 1-(4-methoxyphenyl)-piperazine (MeOPP) and m-trifluoromethyl phenylpiperazine (TFMPP). All of these have also been notified through the early warning system, in the case of BZP as early as 1999 and in the case of MeOPP in 2005 (by Sweden in April and by Denmark in October). It is likely that, as mCPP (see below) many of the psychoactive piperazines are metabolites of licensed medicinal products.

However, mCPP was the only psychoactive piperazine identified in a number of Member States (18) and one third state – Norway ⁽⁷⁾ within a period of less than a year (see Annex 2). In fact, mCPP has been more widely identified by Member States than any other new psychoactive substance since the early warning system started to monitor new (synthetic) drugs in 1997. However, the large number of identifications could be also due to increased awareness of the drug and the enhanced detection capacities and activities of the national early warning systems and the law enforcement agencies.

The first official notifications of mCPP detections were received by the EMCDDA and Europol in February and March 2005 from France and Sweden respectively. Information about the two notifications was immediately exchanged between the EMCDDA, Europol and the Member States; furthermore, the Commission and the EMEA were duly informed. Subsequently, mCPP was added to the list of monitored psychoactive substances and further information about detections in seizures, biological samples and actively collected samples ⁽⁸⁾ was accumulated and exchanged between the two responsible organisations and the Member States.

In August 2005, Europol and the EMCDDA examined the collected information on mCPP through a joint assessment based upon the criteria laid down (see section

⁽⁶⁾ Stores selling non-scheduled psychoactive substances.

⁽⁷⁾ In January 2006, the EMCDDA and Europol were informed that mCPP has been identified in a further Member State (Ireland) and in one accession country (Romania). There is unconfirmed information that Italy is the latest Member State which has made a mCPP seizure in 2006. Furthermore, the EMCDDA was informed that mCPP is known to have been identified in Switzerland.

⁽⁸⁾ Samples collected for monitoring and research purposes.

2.2). It was agreed that the information collected so far satisfied criteria 1, 2, 3 and 5; thus, the two organisations concluded that sufficient information had been accumulated to merit the production of a Joint Report as stipulated by Article 5.1 of the Decision.

The EMCDDA and Europol collected information, according to their competences, through their networks in the Member States – the Reitox NFPs and the ENUs. By the deadline Europol had received replies from 23 Member States and one third state (two Member States, Austria and Greece, did not provide information), while the EMCDDA received information from all 25 Member States and Norway.

As mCPP is not a centrally authorised medicinal product, the EMEA in order to determine the marketing authorisation status (authorised, suspended or pending) of mCPP as a human or a veterinary medicinal product, collected information through the NCAs in the Member States responsible for national authorisation of medicinal products. In addition, the EMEA, in consultation with the EMCDDA, requested information from the pharmacovigilance system on all spontaneously reported adverse drug reactions (ADRs) associated with the use or misuse of trazodone-containing medicinal products (trazodone is an antidepressant substance that is known to be metabolised to mCPP). Furthermore, in anticipation of Article 7.3 of the Decision, a preliminary search of the patent literature revealed that mCPP could (theoretically) be used in the synthesis of at least four active substances found in authorised medicinal products (trazodone, nefazodone, etoperidone and mepiprazole). Therefore, in order to determine the true situation, the EMEA asked its Mutual Recognition Facilitation Group (MRFG) whether or not mCPP is used in the manufacture of medicinal products containing these substances. In the event of a positive response for any of the four substances, information was requested regarding the active substance; the manufacturer of the active substance; the trade name of the medicinal product; and the holder of marketing authorisation for the medicinal product.

The conclusions and recommendations of the Joint Report were prepared by the two responsible organisations – the EMCDDA and Europol – in consultation with the EMEA. Thus, the first Joint Report under the new legal framework was submitted to the Council, the Commission and the EMEA on 28 October 2005 within the deadline stipulated by the Decision (see Annex 3).

In line with the provisions of Article 7.3 of the Decision, the report recommended that no risk assessment be carried out, on account of evidence that mCPP is used in the manufacture of at least one medicinal product. In addition, in the report is also noted that, despite the fact that at present 'there is little evidence of significant public health or social risks, these could be thoroughly examined only through a scientific risk assessment taking into account the principles of proportionality and precaution'.

Based on the Joint Report, the Commission and the Horizontal Working Party on Drugs of the Council agreed that 'no risk assessment should be carried out'. 'However, given the concern mCPP is causing, and as provided for by article 7.3 of the Decision, the scope for further action, such as a scientific analysis, will be examined by the Commission in close cooperation with the EMCDDA and EMEA. The Commission will inform the Council on the results of this examination' (see Annex 4). Nevertheless, in the meantime, two more Member States (Hungary and Denmark) have chosen to introduce national control measures in respect of mCPP in line with their drug control legislation.

4. Implementation issues arising from the initial experiences

4.1 Scope and deadlines set by the Decision

The substances notified by the Member States to the EMCDDA and/or Europol after the Decision came into effect, i.e. after 21 May 2005, would have been notified under both the current and the previous legal instrument – the 1997 Joint Action and Council Decision 2005/387/JHA.

The system that has been set up under the Joint Action is well positioned to carry out the timely and thorough collection of the available information about the types of substances that until now have been notified within the framework of the Decision. Thus, the majority of the notified substances do not pose new challenges to the two main implementing institutions – the EMCDDA and Europol and their networks. Equally establishing the authorisation status of new psychoactive substances (including medical products) in the European Union (Article 5.3) is relatively easy as each Member State has its own individual database, while the EMEA maintains a database of products authorised via the Centralised Procedure. However, the case of mCPP raised some issues regarding the type of information that the EMCDDA and the EMEA are expected to generate or collect.

4.2 The case of mCPP

- 4.2.1 There is no marketing authorisation for mCPP in the European Union. However, as this substance has been widely used in experimental human pharmacology and is commercially available, it was relatively straightforward for the EMCDDA to establish that mCPP is a synthetic substance that occurs as a metabolite of trazodone and several related antidepressant substances and that it is (potentially) used as an intermediate or starting material in their manufacture. In the case of mCPP the information necessary was readily available and the number of substances of interest was low, making it relatively easy for the EMEA to perform a targeted screening (see section 3.2 above) to confirm the true situation.
- 4.2.2 In the case of mCPP the cooperation between the system set up by the Decision and the pharmacovigilance system can be assessed as positive. The EMEA requested information from the pharmacovigilance system on all spontaneously reported adverse drug reactions associated with the use or misuse of trazodone-containing medicinal products. Twelve Member States (the Czech Republic, Denmark, Finland, France, Hungary, Ireland, Italy, Portugal, Slovakia, Sweden, the Netherlands and the UK) that replied to the EMEA's request said that no spontaneously reported ADRs (relating to the terms misuse or abuse) had occurred in association with the use of trazodone. The cooperation between the two systems will need to be developed further at national level too.
- 4.2.3 Europol faced serious problems in obtaining information needed for the drafting of the Joint Report. Some Member States only provided the information following several reminders; two Member States did not provide information at all. A Joint Report can only provide a full picture of the situation, and can only be produced in time, respecting deadlines as set out in the Decision, if all Member States fully comply with their obligations.

4.3 Possible difficulties to be encountered

- 4.3.1 Implementation of the Decision may become more difficult, as establishing whether new substances are used in the manufacture of medicinal products might present a substantial challenge. Such type of information may not come to light until a very late stage of the implementation of the Decision, for example, until the risk assessment procedure is under way or even until control measures have been implemented ⁽⁹⁾.
- 4.3.2 In addition, whether or not a substance is used to manufacture a medicinal product in the European Union is a difficult question to answer in the full terms of the legislation (Article 7.3). According to the EMEA, the Member States or the EMEA do not maintain databases of the reagents/intermediates that can be used in the manufacture of the ingredients of all human and veterinary medicinal products they have authorised (or which are suspended or pending authorisation). This makes the search almost unfeasible at present. To attempt to obtain such information directly from manufacturers would inevitably result in a delay in the procedure, except if a focused screening procedure is possible, as was case for mCPP.
- 4.3.3 The Decision provides an explicit legal basis for the EMEA to ask from the Member States for the information mentioned under Article 5.3. However, no similar provision is mentioned under Article 7.3, so the collection and exchange of such information between the Member States and EMEA may be carried out only 'by analogy'. For example, in the case of mCPP, the EMEA requested the information needed in Article 7.3 'by analogy with Article 5.3'.

4.4 Interpretation of Article 7.3 of the Decision

Two different interpretations of Article 7.3 of the Decision can be made.

- 4.4.1 The Joint Report on mCPP adopted an approach that considers this chemical as a new psychoactive substance *per se*, albeit one that happens also to be used as either a starting or intermediate material in the synthesis of the active substance ⁽¹⁰⁾ trazodone, which is found in a number of medicinal products. The Joint Report also considered that the use of mCPP in the production of the active substance trazodone is in essence the same as its use in the production of medicinal products that contain trazodone. Hence, the report recommended referring the substance to the Commission and the EMEA in order to assess the need for further action.
- 4.4.2 A different interpretation could lead to the understanding that mCPP is a precursor used to synthesise an active substance (or API) – trazodone, which is then manufactured into licensed medicinal products, i.e. tablets, capsules, etc. The term 'medicinal product' has a specific legal meaning under the Directives for human or veterinary products (Directives 2001/83/EC and 2001/82/EC as amended, respectively) and it does not mean an API. Thus, an alternative course of action could have been to refer mCPP to the Drugs Precursors Committee ⁽¹¹⁾, rather than to the EMEA, because, strictly speaking, it is not an API that can be formulated into a medicinal product.

⁽⁹⁾ In some cases the potential delay might be due to commercial sensitivity of such type of information.

⁽¹⁰⁾ In technical terms the 'active pharmaceutical ingredient' (API).

⁽¹¹⁾ The committee set up by Article 10 of Council Regulation (EEC) No 3677/90 of 13 December 1990.

4.5 Reference materials

It is likely that synthetic psychoactive substances will continue to be predominantly notified in the framework of the information exchange mechanism set up by the Decision. The availability of reference materials (seized substances or reference substances) is of the utmost importance if forensic and toxicology laboratories are to identify new psychoactive substances, especially in the case of a new synthetic drug about which limited scientific literature is available. However, in contrast to the exchange of samples of seized drugs, for which a procedure has been created at European Union level by a Council Decision of 28 May 2001 ⁽¹²⁾, there is no European Union system for the synthesis of reference substances. If a system that can successfully function in the long term is to be implemented, it will be important to consider how coordination can be established and how access to reference materials can be facilitated.

5. Conclusion

Council Decision 2005/387/JHA has been in effect for slightly more than half a year (seven months). It is likely that in the coming year new implementation challenges will emerge, primarily related to types of substances or to medicinal products that have not been reported so far under the information exchange mechanism.

In view of the new experiences and the lessons learned through the implementation of the 1997 Joint Action and the Decision, the EMCDDA and Europol have undertaken to prepare new guidelines for the information exchange/early warning. The guidelines will assist the early warning system partners in introducing the new working methods taking into account the individual countries' specific needs and situations. Furthermore, in this context the EMCDDA is attempting to develop a more integrated approach with Member States to enable the collection, monitoring and exchange of information on emerging trends in the use of existing substances and on possible public health-related measures.

A risk assessment procedure is still to be launched under the new legal instrument, it is therefore essential to adapt the guidelines for risk assessment so as to make them appropriate for various types of new psychoactive substances that might come into the scope of the Decision.

⁽¹²⁾ The system organises the exchange of substances under control between European Union Member States through national control points.

Annexes

Annex 1 – Notifications of new substances to the EMCDDA and Europol in 2005 under the terms of 1997 Joint Action and Council Decision 2005/387/JHA

Annex 2 – Member States reporting to Europol and EMCDDA on mCPP 2005/2006

Annex 3 – doc. 14409/05 CORDROGUE 73 – Europol–EMCDDA Joint Report on a new psychoactive substance: 1-(3-chlorophenyl)piperazine (mCPP)

Annex 4 – doc. 15832/05 CORDROGUE 88 – Follow-up to Europol-EMCDDA Joint Report on a new psychoactive substance: mCPP