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Subject:	EMCDDA-Europol 2013 Annual Report on the implementation of Council Decision 2005/387/JHA

Delegations will find enclosed the above-mentioned Annual Report, in accordance with Article 10 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances.



European Monitoring Centre
for Drugs and Drug Addiction



EMCDDA–Europol 2013 Annual Report on the implementation of Council Decision 2005/387/JHA

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

1. Background to this report

As part of the response to new psychoactive substances within the European Union (EU), the *Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances* (hereafter 'the Council Decision') established a mechanism for the rapid exchange of information on substances that may pose public health and social threats, including the involvement of organised crime. This provides a legal basis for the institutions of the EU and the Member States to monitor all new narcotic and psychotropic substances that appear on the European drug scene. Where necessary, the Council Decision also provides for an assessment of the risks associated with these new substances, so that control measures deriving from Member States' obligations to the United Nations drug control conventions ⁽¹⁾ can also be applied to new psychoactive substances.

Under Article 4 of the Council Decision, the EMCDDA and Europol, in close collaboration with their respective expert networks, the Reitox National Focal Points and Europol National Units, are assigned a central role in detecting, notifying and monitoring new psychoactive substances. The information exchange element of the Council Decision has been implemented by the EMCDDA and Europol as the *European Union Early Warning System on New Psychoactive Substances* (hereafter 'Early Warning System'). In addition, where necessary, and in cooperation with the European Medicines Agency (EMA), the EMCDDA and Europol may collect, analyse and present information on a new psychoactive substance in the form of a *Joint Report* (Article 5). This report provides evidence to the Council of the European Union and the European Commission on the need to request a *risk assessment* on a new psychoactive substance. Such a risk assessment examines the health and social risks posed by a new substance including: the use of, manufacture of, and, traffic in, a new psychoactive substance; the involvement of organised crime; and, the possible consequences of control measures. In order to conduct the risk assessment, the EMCDDA convenes a special meeting under the auspices of its Scientific Committee, extended with additional experts as necessary (Article 6).

To ensure transparency in the implementation of the Council 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'.

⁽¹⁾ The 1961 United Nations Single Convention on Narcotic Drugs and the 1971 United Nations Convention on Psychotropic Substances.

In compliance with Article 10, the EMCDDA and Europol herewith present the eighth such annual report which covers the period 1 January to 31 December 2013. The report outlines the results of the implementation, describes key issues arising from accumulated experiences, and also serves as a monitoring tool. In order to facilitate the reading of the report, the reader is referred to the full text of the Council Decision ⁽²⁾.

The report is written as a standalone document with annexes kept to a minimum. Annex provides the list of new psychoactive substances notified for the first time in 2013. This includes the systematic chemical name, the reporting country, and date of notification for each substance. Further information on these substances is available from the EMCDDA and Europol.

2. New psychoactive substances in 2013

Since 1997, the EMCDDA and Europol have played a central role in the response to new psychoactive substances. Together, the two agencies, supported by their networks and other partners, have operated the world's only regional early warning system on new psychoactive substances; a system that has underpinned the ability to identify and respond to new psychoactive substances that pose social and public health harms within the EU.

During 2013, 81 new psychoactive substances were reported for the first time within the EU (section 4.1). This compares to 74 in 2012 ⁽³⁾, 49 in 2011 and 41 in 2010.

It should come as little surprise to most people that the majority of new psychoactive substances are intended as 'legal' replacements to controlled drugs. 2013 provided further evidence that entrepreneurs and increasingly organised crime groups (OCGs) are expanding on the types of substances they plan to offer as 'legal' alternatives. Of particular concern to the EMCDDA and Europol in this respect are the new synthetic opioids — such as AH-7921, MT-45, carfentanil and ocfentanil — reported in the past two years.

Until about a decade ago, most new psychoactive substances that emerged were typically sold on the drug illicit market. Sometimes this was as drugs in their own right or as a new type of 'ecstasy', but often they were sold surreptitiously as amphetamine and MDMA. Only a handful was reported each year. Usually these were stimulant-type or hallucinogenic drugs produced in Europe or the United States either in small amounts in amateur laboratories or on a commercial scale in clandestine laboratories by organised crime groups. Sometimes new substances also emerged from the diversion of medicines. Importantly, this continues to be the case, with some of these substances simply acting as temporary substitutes for established controlled drugs that are in

⁽²⁾ Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk-assessment and control of new psychoactive substances, OJ L 127, 20.5.2005, p. 32.

⁽³⁾ The 2012 annual report listed 73 substances as notified through the Early Warning System in 2012; this figure should have been 74. The synthetic cannabinoid JWH-302 (1-pentyl-3-(3-methoxyphenylacetyl)indole), was identified by Germany in August 2012 but was not included in the 2012 annual report.

short supply, such as MDMA; while others such as 4-methylamphetamine appear to be produced by accident arising from the use of uncontrolled precursors in the production of amphetamine.

Only a few years ago the issue of new psychoactive substances was regarded as having limited significance to drug policy. In the past few years, however, there have been phenomenal changes in this market. Today the question of how to respond to the challenges posed by the emergence of new drugs has become a major concern within the EU and at the international level.

The sale of new psychoactive substances through an open market took off in mid-2000s with the stimulants 1-benzylpiperazine (BZP, a piperazine derivative) and methylone, followed by mephedrone (cathinone derivatives). This marked the start of the modern 'legal highs' and the 'research chemicals' market. Many of the new substances that are destined for these markets are produced in bulk outside of the EU (e.g. China and India) and imported into Member States, where they are processed, packaged and sold. Europol has received reports that such operations occur in a number of Member States. The marketing and distribution of these drugs has reached a new level of sophistication. This includes through the internet (with next day delivery to consumers), bricks and mortar 'head shops' in towns and cities, as well as by street level drug dealers.

Globalisation and the new opportunities provided by developments in information technology have transformed many aspects of the new psychoactive substance market. A key player here is the Internet. Commerce and communication are no longer constrained by physical or geographical boundaries. This has also meant that the back catalogue of chemical substances developed by the pharmaceutical and medical research industries, and, whose psychoactive properties may make them attractive to consumers, is easily accessible to those wishing to identify such substances. Manufacturers in the chemical industries in China and India are able to synthesise the substances in bulk amounts. New trends also diffuse more rapidly, and a market-place for psychoactive substances has been created that exists, to a large extent, outside the established regulatory frameworks.

As noted, 81 new psychoactive substances were reported for the first time within the EU during 2013. Twenty-nine of these substances were synthetic cannabinoids⁽⁴⁾. This brings the total number of synthetic cannabinoids reported since December 2008 to 104, making them the largest group of substances monitored by the Early Warning System; the large number clearly illustrating the continuing attempts by manufacturers to produce new substances in order to circumvent drug control measures. Also reported in 2013 were: 14 phenethylamines, 7 synthetic cathinones, 7 arylalkylamines, 5 opioids, 2 benzodiazepines, a tryptamine, an aminoindane, an arylcyclohexylamine, a piperidines/pyrrolidine, a piperazine, and 12 substances that do not conform to the previous groups.

⁽⁴⁾ The term 'synthetic cannabinoids' is used here to include: synthetic cannabinoid receptor agonists (such as JWH-018 which is a CB₁ and CB₂ receptor agonist); allosteric modulators (such as Org 27569) that change the structure of the cannabinoid receptors leading to altered activity when a ligand binds to the receptors; and, substances that act as inhibitors of the fatty-acid amide hydrolase (FAAH), which catalyses the intracellular hydrolysis of the endocannabinoid anandamide (such as URB597).

Nine of the new substances reported in 2013 are used as the active pharmaceutical ingredients in medicines. The monitoring of such substances under the Council Decision can provide essential early warning on the emerging misuse and abuse of medicines authorised within the EU and also in third countries ⁽⁵⁾. An example of this in 2013 was the report from Italy that tropicamide, which is used in medicine to dilate the pupils, was being injected by opioid users. A review of the available information suggests that the injection of tropicamide has been reported in some eastern European countries. It appears to be used to self-treat opioid withdrawal symptoms and for its euphorogenic and hallucinogenic effects.

A substantial part of the market in new psychoactive substances is those that are sold on the open market in head shops and online shops as 'legal highs' and 'research chemicals'. In 2013 the EMCDDA's monitoring of the Internet ⁽⁶⁾ identified 651 online shops selling these types of products to consumers in the EU (section 3.1.3). Europol has also gathered information from Member States on investigations regarding the online distribution of new substances in order to better understand how this market operates and the threats posed it.

Adding to the complexity of this online market is the sale of new substances as 'food supplements'. This includes the plant *kava kava* and the medicine *phenibut*. These 'supplements' are of particular concern because the retailers and products are typically not covered by existing drug monitoring systems, effectively creating a blind spot in our understanding of the market. Some of these products are widely available on popular e-commerce sites, online health food shops, as well as in fitness equipment shops. In some cases these 'supplements' are marketed as 'natural' exploiting the general belief that they are safe and healthy options for consumers. One product that that was sold as a sport supplement and analysed in 2013 was found to contain a derivative of methamphetamine (substance 17, Annex). This product has been sold in a number of countries including Sweden, the United Kingdom, and the United States.

2013 was also the year that sales of controlled drugs on the 'hidden' deep web, such as the now defunct Silk Road, really came to the public's attention. Less well known is that new psychoactive substances are also sold on the deep web, and work is required to better understand the importance to the EU drug market of such distribution networks, including sales to consumers.

Of serious concern is that illicit production within the EU has been reported to Europol in 2013. Hungary, Poland and Slovakia have all reported the dismantling of illicit facilities where synthesis, processing and/or tableting of new psychoactive substances was taking place. These reports demonstrate that the processing of new substances within EU is not limited to mixing and packaging, but that organised crime groups have invested resources in illicit production facilities.

⁽⁵⁾ The terms 'misuse' and 'abuse' are used in their regulatory sense within the medicine regulatory system. See: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/05/WC500143294.pdf

⁽⁶⁾ Monitoring was limited to retailers on the surface web selling direct to consumers.

The number and type of new psychoactive substances reported each year is critical to understanding the development and growth of the market. These numbers, however, fail to convey the enormous amount of work undertaken by the Early Warning System Network at national and EU-level. For the EMCDDA and Europol, each report of a new substance requires that the information and analytical data is checked and assessed, that literature searches are run to see what is known about the substance, and that a technical profile is created on the European Database on New Drugs (EDND) at the EMCDDA. Simultaneously, the information is recorded and analysed by the Focal Point Synergy at Europol which is the hub for law enforcement data on synthetic drug crime including new psychoactive substances. From there, the substance is formally notified to the Early Warning System Network allowing laboratories, law enforcement, healthcare agencies, researchers, practitioners and policy makers to receive this critical data. This stage also marks the point at which the EMCDDA and Europol begin to monitor the new substance. Currently more than 380 new substances are monitored. The EDND, which is updated on a daily basis, plays a critical role in this monitoring by providing round-the-clock access on the latest information on new substances including, chemistry, pharmacology, toxicity, law enforcement seizures and epidemiology to the Early Warning System Network.

In 2013, the EMCDDA and Europol also produced four Joint Reports on very different substances, both in terms of their chemistry, pharmacology, and individuals who use them: AH-7921, an opioid with similar effects to morphine; 25I-NBOMe, a potent hallucinogen; MDPV, a stimulant which in animal studies appears to be more potent and longer lasting than cocaine; and methoxetamine, a dissociative sold as a 'legal' and 'safer' alternative to ketamine (section 4.2). Reflecting the growing diversity of the market, 2013 marked the first time that formal action on an opioid (AH-7921) has been required at the EU-level. Also in 2013, a risk assessment was conducted by the EMCDDA's Scientific Committee on the stimulant 5-IT after 24 deaths associated with its use were reported over a short time period (section 4.3).

While it is clear that many new substances will not gain a foothold as drugs in their own right and spread to broader groups of users, they are still capable of causing serious harm. The largely unknown pharmacology can pose serious risks to users. This is compounded by both the growing range of substances and the generally high availability. These problems are especially apparent when they are sold as 'legal highs' with no information provided to the user of the actual substance(s) present, and as a result of an increasing number finding their way to the black market where they are sold as ecstasy, cocaine, ketamine, heroin or LSD to unsuspecting users. In addition, while much focus has been given on the use of new substances by recreational users, they are also being used by problem drug users, including those who inject. This situation is presenting challenges for service providers, including low threshold services such as needle and syringe programmes that often have limited experience of these drugs and their effects. Little is also known about the treatment requirements of users of new psychoactive substances, which in part may reflect the fact that many have emerged only recently.

Estimating the prevalence of use of new psychoactive substances continues to present challenges, especially through general population surveys. In some cases, such as with the synthetic cannabinoids, there is a clear discordance between the large number of multi-kilogram seizures

reported to the Early Warning System and the levels of use reported in surveys. During 2013, the EMCDDA continued to work with its partners on ways to strengthen epidemiological methods and indicators related to the use of new substances. This includes exploring the development of indicators based on waste water analysis.

Reports of serious adverse events from the Early Warning System Network — such as non-fatal intoxications that require hospital treatment and deaths — provide signals of emerging harms. Reflecting the growing number of such reports, in 2013 the EMCDDA began to develop a framework to strengthen the toxicovigilance component of the Early Warning System. This system will facilitate the identification and reporting of serious events as well as optimise the reported data in order to best analyse these signals. Ultimately this should allow the Member States and the EU to respond earlier to emerging harms. While there is a still long way to go in its full development, the EMCDDA has already begun to improve the quality of data that is reported by the Early Warning System Network related to serious adverse events. In addition, as a component of this system, the EMCDDA is developing a framework that allows it to more systematically monitor the media to pick up on these signals as early as possible and from a broader number of sources, including from countries outside of Europe. In fact the EMCDDA monitors the scientific and medical literature on a daily basis for reports of serious adverse events as well as data from nonclinical studies that help explain the cause of these events. These data are analysed and prioritised and are then fed into the broader monitoring process.

In 2013, the EMCDDA issued 16 public health alerts and advisories to the Early Warning System Network (section 4.4). Many of these concerned serious adverse events, particularly deaths, and/or hazards that had the potential to cause serious harm. Notably alerts were issued on three potent new opioids – AH-7921, carfentanil, ocfentanil — that appear to have only been sold on the drug market for the past two years or so. The EMCDDA and Europol are highly concerned about the number and type of new synthetic opioids reported to the Early Warning System in the past two years. Five of these opioids are fentanyl, a family of drugs that have already caused hundreds of deaths in Europe and the United States since they first appeared as 'designer drugs' sold as 'synthetic heroin' or 'China white' in California in the late 1970s. Adding to this concern is that some of the new opioids have already been sold as replacements to heroin. This includes a seizure made in Lithuania containing carfentanil (substance 6, Annex) which is usually used to tranquillise large animals such as elephants, and a seizure of ocfentanil in the Netherlands (substance 62, Annex).

In September, Europol initiated the collection of available information on the new substance 4,4'-DMAR, after eight deaths were reported by Hungarian police to be associated with the substance. 4,4'-DMAR is a derivative of the designer drug 'U4Euh' (4-methylaminorex) and the weight-loss medicine aminorex which was withdrawn after it caused an epidemic of pulmonary hypertension. As a result of the information provided by Hungary, Europol and the EMCDDA issued alerts to their respective partners within the Early Warning System Network (see 'Update from 2014', below).

The effective exchange of information on new psychoactive substances underpins an effective response. During 2013 the EMCDDA and Europol provided formal training in order to strengthen

early warning both at the national and EU-level. Reflecting the globalised nature of this phenomenon, international cooperation with third countries was strengthened further. This included the bilateral exchange of technical information with law enforcement and healthcare agencies from the United States, Japan, Australia, among others. The importance of these global partnerships continues to be highlighted by the exchange of information on serious adverse events. In 2013, alerts were issued related to outbreaks of serious adverse events associated with synthetic cannabinoids that were reported to the EMCDDA by law enforcement agencies in the United States. While during the Third International Forum on New Drugs, experts from around the world came together to exchange experiences, identify information gaps and research needs, as well as anticipate future developments and challenges.

Update from 2014

There appears to be no slowdown in the growth of the phenomenon. As of May, 37 new psychoactive substances have been reported to the Early Warning System.

The eight deaths associated with 4,4'-DMAR reported by Hungary in 2013 were joined by reports of a further 18 deaths from the United Kingdom in February 2014, leading the EMCDDA and Europol to launch a Joint Report on 4,4'-DMAR in the same month. The substance continues to be intensively monitored by the Early Warning System. Twenty seven deaths associated with the substance have now been reported; a particular concern in this respect is that more than 260 kg of 4,4'-DMAR has been seized in the Netherlands, and that in some countries it has been sold as ecstasy on the illicit drug market. The availability of 4,4'-DMAR may also mark an astonishing development in the 'research chemical' market after the suggestion that the distributors have conducted testing of the substance in animals, with the data from these tests being used as part of the marketing. If this is correct then distributors may be attempting to consolidate a 'legal' market in new substances.

Also in 2014, 21 deaths and thirteen non-fatal intoxications associated with the new opioid MT-45 have been reported. Of particular concern in this respect is that this substance appears to have only been sold on the drug market for the past six months or so. On the basis of these reports a Joint Report on MT-45 was launched in April by the EMCDDA and Europol (substance 74, Annex). The substance continues to be intensively monitored by the Early Warning System.

The growing involvement of organised crime groups apparently drawn by the large profits from this market is of serious concern to Europol. Analysis of intelligence reports provided by the Member States indicates that in the near future criminal groups based within the EU will expand their involvement in the trade, manufacture, trafficking and distribution of new psychoactive substances.

There is little doubt that enhanced monitoring systems within some national early warning systems are playing a key role in the early identification of serious adverse events and other harms by the Early Warning System. Such systems will require adequate resources if they are to continue to

supply this essential data and scale-up to provide enhanced coverage. Resources will also be required in order to replicate these enhancements in other settings and regions.

For the past few years the EDND has begun to feel the strain as a result of both the huge increase in the amount and types of data now being reported. Resources are urgently required in order to ensure it can meet the needs of the EU in both in the near future and longer-term.

3. Implementation arrangements and cooperation with the European Union Pharmacovigilance system

3.1 Specific implementation arrangements

3.1.1 Assistance to national early warning systems

In 2013, the EMCDDA and Europol continued to provide support to the national early warning systems within the National Focal Points and Europol National Units in order to assist them in the identification of new substances. Assistance related to new psychoactive substances from the Member States as well as Institutions and agencies of the EU was also provided.

The analytical data available to the Early Warning System Network continued to be expanded during 2013. In addition, data and information is now routinely provided on an informal basis by international partners, including Australia, the United States and Japan. This is an important aspect of the exchange of information and emphasises the global nature of the phenomenon.

The EMCDDA also collects national risk assessments on new psychoactive substances which are made available on the EDND in order to help identify emerging harms as well as inform policy responses in the Member States. Similarly, legislative developments related to new substances reported by the Member States are also recorded and tracked.

Training was also provided to some of the Member States (section 3.1.4).

3.1.2 Annual meeting of the Early Warning System Network

The 13th annual meeting of the Reitox Early Warning System Network took place on 27 June 2013. The meeting was organised in conjunction with the second Europol law-enforcement meeting on new psychoactive substances and the Third International Multidisciplinary Forum on New Drugs.

Over 70 representatives from the Early Warning System Network and Europol networks in the 28 Member States, Turkey and Norway attended the forum as well as delegates from 10 third countries. Experts from a wide range of disciplines also attended. This included both from academic and operational backgrounds, such as epidemiology, forensic science, healthcare, law-

enforcement, criminology and policy. The forum aimed to identify information gaps and research needs, anticipate future developments and challenges and explore the role that can be played by law enforcement. Topics discussed included:

- historical context, public health perspective, motivations of users, the role of law enforcement, challenges for drug policy;
- national, regional and global perspectives on new drugs, including presentations on significant developments and initiatives taking place around the globe;
- how emerging harms can be detected, monitored and understood by the work of forensic science, toxicology and healthcare disciplines;
- the role of law enforcement in the response to new drugs, including the difficulties faced by the growing interplay between new drugs and illicit drug markets;
- good practice and novel approaches, including what can be learned from the users of new drugs; and,
- the response to new drugs, which included a discussion of the recent policy developments in New Zealand.

3.1.3 *Monitoring of the online availability of new psychoactive substances*

In 2013 the EMCDDA, in partnership with some of the National Focal Points, undertook an Internet monitoring exercise in 18 languages of the EU, Norwegian and Russian. The aim of the exercise was to provide a snapshot of the online sale of new psychoactive substances to consumers within the EU. The snapshot identified 651 shops which typically sold new substances as 'legal high' products or 'research chemicals'; in some cases products were also identified that were sold as 'food supplements'. In comparison, the previous snapshot exercise in January 2012 identified 693 shops, while the snapshots conducted in January 2011 and 2010, identified 314 and 170 shops, respectively ^(7, 8).

A targeted Internet snapshot in English was also conducted in 2013 to provide data to support the risk assessment of 5-IT (section 4.3.1).

⁽⁷⁾ EMCDDA (2011), Online sales of new psychoactive substances/'legal highs': summary of results from the 2011 multilingual snapshots, EMCDDA, Lisbon. Available at: <http://www.emcdda.europa.eu/publications/scientific-studies/2011/snapshot>

⁽⁸⁾ It is important to note that the data between different snapshots may not be directly comparable, due to changes in the methodology which have increased the quality and coverage of these surveys over time; in addition, changes in technology, such as the algorithms used by search engine, can also affect the comparability between different snapshots.

3.1.4 Supporting activities

During 2013 the EMCDDA and Europol continued to be prominently involved in organising events and participating in activities that are designed to develop the Early Warning System Network and provide support to others working in the field of new psychoactive substances. These events and activities provide a platform to improve collaboration among partners and promote best practice in order to strengthen early warning activities. Significant activities carried out in 2013 are provided below.

In April a Reitox Academy training event examining contemporary approaches to drug monitoring was organised in Prague, Czech Republic for Western Balkan countries and Turkey. The EMCDDA provided a keynote lecture on new psychoactive substances, including the critical role that Internet plays in this phenomenon. The event also incorporated a training session on monitoring the supply of new psychoactive substances on the Internet. A pilot internet snapshot in Balkan languages (Montenegrin, Macedonian, Bosnian, Serbian, Albanian, Croatian and Turkish) was implemented during the training.

In May training was provided at the 'Workshop on New Psychoactive Substances, the Health Dimension', in Zagreb, Croatia, funded under the European Commission's TAIEX instrument and organised by the Croatian Office for Combatting Drug Abuse. Also in May the annual meeting of the Drugs Working Group of the European Network of Forensic Science Institutes (ENFSI) was held in Dubrovnik, Croatia, in which the EMCDDA actively participated as an associate member of the network.

In June the EMCDDA assisted Europol by providing a training input at the Cefpol–Europol International Illicit Synthetic Drug Laboratory Dismantling Course, held at the national police training centre in Legionowo, Poland.

In September the Second International Conference on Novel Psychoactive Substances took place in Swansea, United Kingdom. As well as co-organising the event, the EMCDDA participated with two keynote speeches and chaired or co-chaired the plenary and parallel sessions of the Conference.

In October a meeting of forensic drug experts representing different institutions took place at the EMCDDA in Lisbon, Portugal. During this meeting the participants explored the possibilities to improve processes, particularly in relation to the interaction of the forensic community with the Early Warning System.

In November the EMCDDA attended the Spanish national early warning system meeting in Madrid to provide a European overview and best practice example to strengthen the national network.

The EMCDDA also organised or participated in a number of meetings with dedicated sessions on new psychoactive substances, reflecting the relevance of this area for traditional illicit drug areas and established key epidemiological indicators. This included meetings covering general population surveys, drug-related deaths, and problem drug use. In May, the EMCDDA organised the first international multidisciplinary conference on detecting illicit drugs in wastewater 'Testing the waters', with a dedicated session on the potential of sewage analysis for identifying and monitoring population-level trends of new drugs in wastewater. In October, the EMCDDA co-organised with COPOLAD a thematic twinning training on analysis, interpretation and dissemination of drug-related data to facilitate decision making.

3.2 Cooperation with the EMA and the Pharmacovigilance system

During 2013, the EMA and EMCDDA continued to regularly exchange information on new psychoactive substances according to their respective obligations under the Council Decision and EU pharmacovigilance legislation as well as the working arrangement between the two agencies ⁽⁹⁾. This included *ad hoc* reports relating to the misuse and abuse of medicinal products, or the active pharmaceutical ingredients used therein, that had been notified as new psychoactive substances, in order to support the Pharmacovigilance system. At the request of the EMCDDA, the EMA provided pharmacovigilance data on phenibut (notified in 2010) and information on authorised medicinal products containing tropicamide as well as pharmacovigilance data on these products related to their misuse, including by injection (substance 25, Annex 2). Formal consultations and exchange of information took place in order to prepare the Joint Reports on 25I-NBOMe, AH-7921, MDPV and methoxetamine (section 4.2). In addition, at the request of the EMA, the EMCDDA undertook a data collection exercise with the Early Warning System Network in order to provide information on the misuse and abuse of pregabalin (notified in 2009).

4. Activities

4.1 New psychoactive substances notified in 2013

Eighty-one new psychoactive substances were notified for the first time in 2013 (Table 1 and Annex). This continues the year on year increase in the number of new substances that have been notified since 2008 (Figure 1).

Technical profiles were created on the European Database on New Drugs (EDND) for each of the notified substances as well as five substances of interest. During the course of 2013, 444 reporting forms were submitted by the Early Warning System Network which were processed, analysed and added to the EDND; while 300 technical profiles on the EDND were updated with the information from these forms as well as from other sources including regular searches of the scientific and medical literature that is conducted by the EMCDDA and additional law enforcement information provided by Europol.

⁽⁹⁾ http://www.emcdda.europa.eu/attachements.cfm/att_185319_EN_EMA-EMCDDA-2012workingarrangement.pdf

Technical assistance, advice and feedback were provided to the Member States on a daily basis. Sixteen public health alerts or advisories were issued to the Early Warning System Network (section 4.4). Additional data collection and analysis took place on an *ad hoc* basis, including for the Joint Reports on 25I-NBOMe, AH-7921, MDPV and methoxetamine (section 4.2).

As part of a process that began in 2012, the EMCDDA has been reviewing its classification system for new psychoactive substances. In the main it is possible to group some substances by their chemical family or in the case of the synthetic cannabinoids by their mode of action. The former has long been the case with the phenethylamines, tryptamines, piperazines and cathinones. To take account of the increasing diversity of substances that have been notified in recent years, six new categories have been introduced during 2013: arylcyclohexylamines, aminoindanes, arylalkylamines, benzodiazepines, piperidines and pyrrolidines. The category of 'opioids' has also been introduced based on mode of action; this group contains eleven substances, ten of which have been notified since 2012. A category has also been created for plants and extracts of plants; no substances were reported in this group in 2013. Substances that do not conform to the groups described above were grouped separately, in an 'others' category.

Substance category	2013
Synthetic cannabinoids	29
Phenethylamines	14
Other substances	12
Arylalkylamines	7
Cathinones	7
Opioids	5
Benzodiazepines	2
Tryptamines	1
Aminoindanes	1
Arylcyclohexylamines	1
Piperazines	1
Piperidines & pyrrolidines	1
Plants & extracts	0

Table 1. Number of new psychoactive substances notified for the first time in 2013 by category.

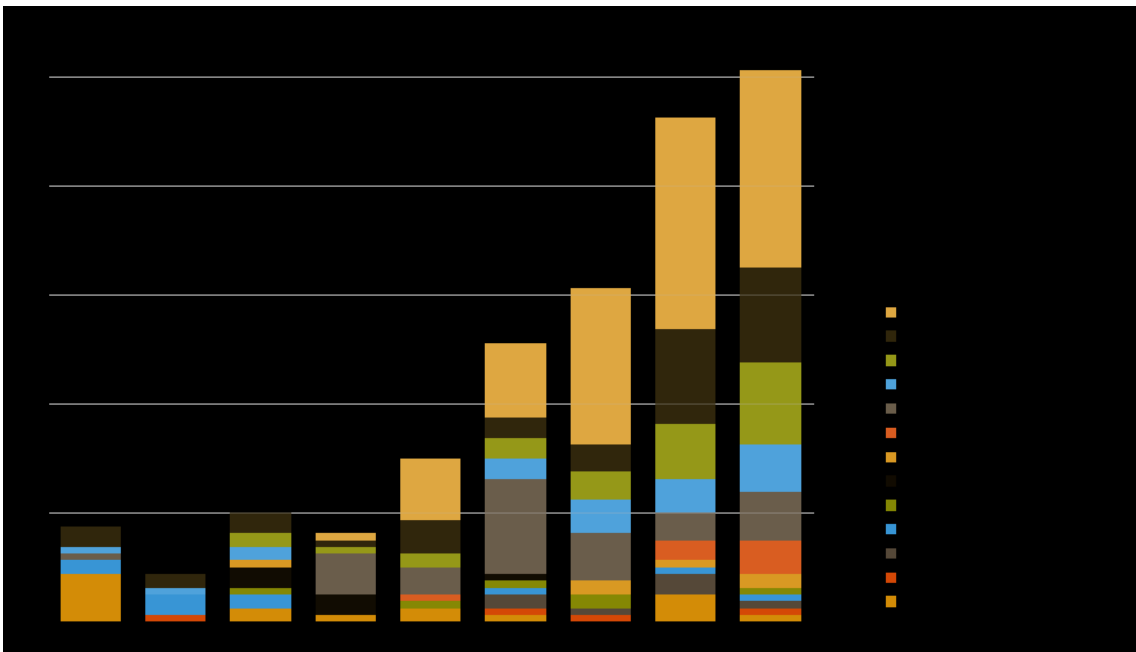


Figure 1. Number of new psychoactive substances notified for the first time to the Early Warning System since May 2005 (by year) ⁽¹⁰⁾

4.2 EMCDDA-Europol Joint Reports

In accordance with Article 5 of the Council Decision, after a review of the available information on the new psychoactive substances 25I-NBOMe, AH-7921, MDPV and methoxetamine, a formal procedure for the collection of information on these four new substances was launched by the EMCDDA and Europol on 7 October 2013. The Joint Reports were submitted to the Council, the Commission and the EMA on the 16 December 2013. A summary of the key findings for each of the four Joint Reports are provided below.

On the basis of the information provided therein, on the 29 January 2014 the Council requested that formal risk assessments be conducted on the substances. In accordance with Article 6 of the Council Decision, the risk assessments were conducted by the extended Scientific Committee of the EMCDDA on 1 and 2 April 2014. A Risk Assessment Report for each substance was submitted to the Council and the Commission on the 22 April 2014 ⁽¹¹⁾.

4.2.2 Joint Report on 25I-NBOMe

25I-NBOMe is a substituted phenethylamine. It is a potent full agonist of the serotonin 5-HT_{2A} receptor and appears to have hallucinogenic effects. It has been available on the European Union drug market since at least May 2012 and has been detected in 23 Member States and Norway. Severe toxicity associated with its use has been reported in four Member States and one death associated with 25I-NBOMe has been analytically confirmed. Seven countries have reported that it has been sold as LSD or as a 'legal' alternative to LSD. On this basis the potential impact from the further spread of 25I-NBOMe (and related 'NBOMe' compounds) on public health is a key concern ⁽¹²⁾.

4.2.3 Joint Report on AH-7921

AH-7921 is a synthetic opioid. It has been available in the EU since at least July 2012 and has been detected in seven Member States and Norway. In most cases it has been seized in small quantities as a powder. Over a short period of time it has been associated with fifteen deaths and six non-fatal intoxications in three countries. The similarity of AH-7921 to morphine in terms of

⁽¹⁰⁾ As noted the 2012 annual report listed 73 substances as notified through the Early Warning System in 2012; this figure should have been 74. The synthetic cannabinoid JWH-302 (1-pentyl-3-(3-methoxyphenylacetyl)indole), was identified by Germany in August 2012 but was not included in the 2012 annual report.

⁽¹¹⁾ The Risk Assessment Reports are available at: <http://www.emcdda.europa.eu/publications/risk-assessments>

⁽¹²⁾ EMCDDA and Europol (2014), *EMCDDA–Europol Joint Report on a new psychoactive substance: 25I-NBOMe (4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine)*, Lisbon, January 2014. Available at: <http://www.emcdda.europa.eu/publications/joint-report/25I-NBOMe>

pharmacology is a key concern. This may play an important role in the further spread of AH-7921 by opioid users, including the injecting population (¹³).

4.2.4 Joint Report on MDPV

MDPV is a synthetic cathinone derivative, which is closely related to pyrovalerone. MDPV has been present in the EU drug market since at least November 2008 and has been detected in 99 deaths and up to 107 non-fatal intoxications, particularly in Finland and the United Kingdom. There are some indications that it has been sold as a 'legal' or synthetic version of cocaine and it has also been found in tablets resembling 'ecstasy'. Large seizures have been made at borders and police operations have targeted its supply. Powder seizures have been reported including multi-kilogram quantities. Most, but not all the Member States have control measures at national level that cover MDPV, however, it continues to be available and this is concerning (¹⁴).

4.2.5 Joint Report on methoxetamine

Methoxetamine is an arylcyclohexylamine, closely related in many respects to ketamine. It has been available on the EU drug market since at least September 2010 and has been detected in 22 Member States, Turkey and Norway. Multi-kilogram quantities of the substance in powder form have been seized. Twenty deaths and 110 non-fatal intoxications associated with the substance have been reported. As methoxetamine is marketed as a legal and 'bladder-friendly' alternative to ketamine and at the same time being sold directly on the illicit drug market as ketamine, a key concern is that these may play a role in the further spread of the substance (¹⁵).

4.3 Risk assessments

4.3.1 Risk assessment of 5-IT

During 2012, a Joint Report on 5-IT (5-(2-aminopropyl)indole) was prepared by the EMCDDA and Europol and submitted to the Council, Commission and EMA on 12 December 2012 (¹⁶). This led to a request from the Council for a formal risk assessment on January 2013. The risk assessment was conducted, in accordance with Article 6 of the Council Decision, by the extended Scientific

(¹³) EMCDDA and Europol (2014), *EMCDDA–Europol Joint Report on a new psychoactive substance: AH-7921 (3,4-dichloro-N-[[1-(dimethylamino)cyclohexyl]methyl]benzamide)*, Lisbon, January 2014. Available at: <http://www.emcdda.europa.eu/publications/joint-report/AH-7921>

(¹⁴) EMCDDA and Europol (2014), *EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV (3,4-methylenedioxypyrovalerone)*, Lisbon, January 2014. Available at: <http://www.emcdda.europa.eu/publications/joint-report/MDPV>

(¹⁵) EMCDDA and Europol (2014), *EMCDDA–Europol Joint Report on a new psychoactive substance: methoxetamine (2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone)*, Lisbon, January 2014. Available at: <http://www.emcdda.europa.eu/publications/joint-report/methoxetamine>

(¹⁶) EMCDDA and Europol (2012), *EMCDDA–Europol Joint Report on a new psychoactive substance, 5-(2-aminopropyl)indole*, EMCDDA, Lisbon. Available at: <http://www.emcdda.europa.eu/publications/joint-reports/5-IT>

Committee of the EMCDDA on 16 April 2013, which included a representative from Europol, the EMA and Commission. Discussions during the risk assessment focused on the 24 deaths and 20 non-fatal intoxications associated with 5-IT that had been reported. The deaths occurred in four Member States over a period of five months in 2012, raising concern that if 5-IT were to become more widely available and used, the implications for public health could be significant. Full details are provided in the EMCDDA report on the risk assessment ⁽¹⁷⁾.

On 7 October 2013 the Council adopted a decision to subject 5-IT to control measures across the EU ⁽¹⁸⁾.

4.4 Public health alerts and advisories

One of the activities of the Early Warning System that provides added value to the Member States is public health alerts and advisories. Usually these concern deaths or other serious adverse events associated with new psychoactive substances; they can also include hazards that have the potential to cause serious harm ⁽¹⁹⁾. In addition, information is also exchanged on emerging trends in new uses of psychoactive substances that are controlled under the United Nations drug conventions and that may pose a potential risk to public health. Alerts and advisories may also provide information on possible public health related measures in accordance with the mandate and procedures of the EMCDDA.

Sixteen public health alerts and advisories were issued to the Early Warning System Network during 2013. A selection is provided below ⁽²⁰⁾.

Carfentanil

In February an alert was issued after the Latvian National Focal Point reported that the highly potent opioid and fentanyl derivative had been identified in a seizure of powder made by Latvian Police. The information also noted that this substance had been associated with a number of unconfirmed deaths in the country.

⁽¹⁷⁾ EMCDDA (2014), *Report on the risk assessment of 5-(2-aminopropyl)indole in the framework of the Council Decision on new psychoactive substances*, Publications Office of the European Union, Luxembourg. Available at: <http://www.emcdda.europa.eu/publications/risk-assessment/5-IT>

⁽¹⁸⁾ Council Decision of 7 October 2013 on subjecting 5-(2-aminopropyl)indole to control measures (2013/496/EU), OJ L 272, 12.10.2013, pp. 44-45.

⁽¹⁹⁾ Alerts and advisories issued by the Early Warning System are not legally binding and Member States are not obliged to act upon them.

⁽²⁰⁾ Note that the detection of new psychoactive substances in post-mortem biological samples does not necessarily imply a causal role in the death.

AH-7921

In February an alert was issued after the Norwegian National Focal Point reported that the opioid AH-7921 had been identified in a seizure of powder as well as in contents of a used syringe that was seized in connection with a death that was believed to be linked to the substance. Other alerts were issued during 2013 related to AH-7921 after reports of deaths associated with the substance were received from Sweden and Norway.

25I-NBOMe

In February an alert was issued after the United Kingdom National Focal Point reported 7 serious non-fatal intoxications associated with the use of the potent hallucinogen 25I-NBOMe that occurred in January 2013.

4,4-Dimethylaminorex (4,4'-DMAR)

In October an alert was issued after the Hungarian National Focal Point reported 8 deaths associated with the 4,4'-DMAR, which is believed to be a stimulant-type substance. This alert facilitated work by the United Kingdom national early warning system in identifying 18 deaths associated with 4,4'-DMAR which were subsequently reported to the Early Warning System in February 2014.

Ocfentanil

In September an alert was issued after the Netherlands National Focal Point reported the identification of the opioid and fentanyl derivative ocfentanil in a seizure made by Dutch police which may have been intended to be sold on the drug market as 'synthetic heroin'.

ADB-PINACA and 5F-ADBICA

In September an advisory was issued after information provided by law enforcement agencies in the United States, supplemented by information from the EMCDDA's monitoring of open source information, identified a series of non-fatal intoxications in the United States associated with ADB-PINACA and 5F-ADBICA. These substances are known to be present on the EU drug market and have been reported by several Member States.

In December an alert was issued after the Swedish National Focal Point reported a death associated with 5-EAPB, a substance which has a chemical structure very similar to the well-known ecstasy drug MDMA.

5. Conclusions

2013 saw the sustained growth of the market in new psychoactive substances within the EU. The new psychoactive substances reported this year unequivocally demonstrate a growing diversity in the types of substances being sold as 'legal' alternatives to controlled drugs. Of particular concern from a public health perspective are the new synthetic opioids that have been identified on the drug market in the past two years, such as AH-7921, MT-45, carfentanil and ocfentanil. These developments are compounded by the growing involvement of organised crime groups (OCGs) who appear to be drawn to the market by the potential large profits from this market. Europol's analysis of intelligence reports indicates that in the near future criminal groups based within the EU may expand their involvement in the trade, manufacture, trafficking and distribution of new psychoactive substances.

Despite these challenges, the Early Warning System, as well as the EMCDDA–Europol Joint Reports and the risk assessment conducted by the EMCDDA extended Scientific Committee continue to demonstrate the added value and strength of the EU system by ensuring robust data-driven analysis, assessment and response to the harms posed by new psychoactive substances.

The EMCDDA and Europol have devoted substantial internal resources to ensure that the current information exchange system setup under Council Decision 2005/387/JHA, and operationalised as the Early Warning System, has been successfully implemented on a continuous basis. Through the support of its partners, including the EMA, the Early Warning System provides added value to the Member States by playing an essential role as a sentinel network that ensures that they have access to the most up-to-date information on new psychoactive substances both from across Europe and beyond. The Early Warning System Network continues to grow, as does the amount and quality of the information that it collects. This continued development is underpinned by the Reitox National Focal Points and the Europol National Units who need to be adequately supported. There is little doubt that enhanced national monitoring systems are playing a key role in the early identification of harms by the Early Warning System. Such systems will require adequate resources if they are to continue to supply this essential data and scale-up to provide enhanced coverage. Resources will also be required in order to replicate these enhancements in other settings and regions. In addition there is a critical need for a strengthened data collection mechanism so that the Early Warning System can both effectively cope with the recent significant growth in the data and ensure that it can be monitored.

Monitoring new psychoactive substances is event-based. It is driven by the identification of new psychoactive substances in laboratory settings which are predominantly not research focused. These analytical and toxicological laboratories are the cornerstone of the Early Warning System.

They may be located at law enforcement, private sector, (public) health, academic establishments, etc. This is routine work for these laboratories and they urgently require both the enhanced provision of analytical data through a strengthened European Database on New Drugs (EDND) (see below) and a cost-effective mechanism to share reference standards easily and rapidly within the EU.

Given the growing role that organised crime groups (OCGs) are likely to play in the manufacture and supply of new psychoactive substances in the future it is essential that adequate resources and expertise are available to law enforcement agencies at both national and EU-level.

The toxicovigilance component of the Early Warning System is the mechanism that allows the early detection of an emerging toxicological problem—and an initial assessment of the potential scale of the problem—related to a new substance both at national and EU-level. This allows both public health warnings to be issued to the Early Warning System Network, and for the substance to be placed under intensive monitoring. In some cases this may also lead to formal action through a Joint Report, and, where necessary a risk assessment. In order for the EMCDDA to meet the increased needs and demands arising from the phenomenon, both at national and EU level, the identification, reporting and monitoring of serious adverse events requires strengthening.

For many years the European Database on New Drugs (EDND) has served the EU well by acting as a reference point on the available information on new psychoactive substances. However, adequate resources are not available to enable its development to keep pace with the amount and type of data arising from the increasing number of substances that are being identified and ensure effective monitoring. The EDND should be strengthened. A core part of this work will require the development of a new infrastructure that will allow secure electronic submission of data through standard web-based structured forms as well as facilitate the central analysis of data and production of reports. Alongside being able to provide real time information on a new drug (or a particular aspect of a new drug such as its detection in a particular 'legal high' product or reports of serious adverse events), the system should be able to provide an overview of the phenomenon as a whole to stakeholders. Resources are urgently required in order to ensure it can meet the needs of the EU in both in the near future and longer-term.

By its very nature the risk assessment process is completed in a short time-frame. As a result limited data is available, and the process is principally focused on the data related to acute harm. It is important to recognise here that the data provided and collected through the Early Warning System will be essential to this process, particularly in relation to serious adverse events. In addition, targeted non-clinical studies that characterise the pharmacological and toxicological properties of the new psychoactive substances will be required for the risk assessment process in order to understand the data reported through the Early Warning System. In order to provide these data sufficient resources must be made available.

It is hoped that the information and analysis provided by the EMCDDA and Europol in this report will provide greater insight in the growing complexity of the market in new psychoactive substances, and, as a result, the challenges that the Member States and the EU are likely to face in the near future. In addition, it is also hoped that the report can help inform the policy responses currently being discussed at EU-level.

Annex. New psychoactive substances notified to the Early Warning System for the first time in 2013 under the terms of Council Decision 2005/387/JHA.

1. 5-MAPB (1-(benzofuran-5-yl)-*N*-methylpropan-2-amine) – 3 January 2013, United Kingdom.
2. 4-Fluorocathinone (2-amino-1-(4-fluorophenyl)propan-1-one) – 10 January 2013, Finland.
3. JWH-methylcyclohexane-8quinolinol (Quinolin-8-yl 1-(cyclohexylmethyl)-1*H*-indole-3-carboxylate) – 29 January 2013, Spain.
4. A-834,735 ([1-(tetrahydropyran-4-ylmethyl)indol-3-yl]-(2,2,3,3-tetramethylcyclopropyl)methanone) - 29 January 2013, Poland.
5. JWH-368 ([5-(3-fluorophenyl)-1-pentyl-pyrrol-3-yl]-(1-naphthyl)methanone) – 7 February 2013, Latvia.
6. Carfentanil (methyl 1-(2-phenylethyl)-4-[phenyl(propionyl)amino]-4-piperidinecarboxylate) – 12 February 2013, Latvia.
7. EAM-2201 ((4-ethyl-1-naphthyl)-[1-(5-fluoropentyl)indol-3-yl]methanone) – 15 February 2013, Sweden
8. Flubromazepam (7-bromo-5-(2-fluorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one) – 7 March 2013, Germany.
9. 5F-PB22 (8-quinolyl 1-(5-fluoropentyl)indole-3-carboxylate) – 15 March 2013, Belgium.
10. JWH-307 brominated derivative ((5-(2-bromophenyl)-1-pentyl-1*H*-pyrrol-3-yl)(naphthalen-1-yl)methanone) – 4 April 2013, Germany.
11. JWH-030 (naphthalen-1-yl(1-pentyl-1*H*-pyrrol-3-yl)methanone) – 4 April 2013, Germany.
12. JWH-145 (naphthalen-1-yl(1-pentyl-5-phenyl-1*H*-pyrrol-3-yl)methanone) – 4 April 2013, Germany.
13. UR-144 heptyl derivative ((1-heptyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)-methanone) – 17 April 2013, Sweden.
14. 3,4-dichloromethylphenidate (methyl (2*R*)-2-(3,4-dichlorophenyl)-2-[(2*R*)-piperidin-2-yl]acetate) – 17 April 2013, Sweden.
15. 25H-NBOMe (2-(2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethanamine) – 24 April 2013, Sweden.

16. URB-597 ([3-(3-carbamoylphenyl)phenyl] *N*-cyclohexylcarbamate) – 24 April 2013, Poland.
17. *N*-ethyl-1-phenylbutan-2-amine – 2 May 2013, Sweden.
18. AB-PINACA (*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indazole-3-carboxamide) – 21 May 2013, Sweden.
19. α -PVT (2-(pyrrolidin-1-yl)-1-(thiophen-2-yl)pentan-1-one) – 21 May 2013, Hungary.
20. A-836,339 (*N*-[3-(2-methoxyethyl)-4,5-dimethyl-1,3-thiazol-2-ylidene]-2,2,3,3-tetramethylcyclopropane-carboxamide) – 3 June 2013, Hungary.
21. 4-methylbuphedrone, *N*-benzyl derivative (2-(benzylamino)-1-(4-methylphenyl)butan-1-one) – 5 June 2013, Finland.
22. 2-Me-DMT (*N,N*-dimethyl-2-(2-methyl-1*H*-indol-3-yl)ethanamine) – 5 June 2013, Finland.
23. 4-MeO- α -PVP (1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)pentan-1-one) – 12 June 2013, Finland.
24. NMP (1-methylpyrrolidin-2-one) – 13 June 2013, Italy.
25. Tropicamide (*N*-ethyl-3-hydroxy-2-phenyl-*N*-(pyridin-4-ylmethyl)propanamide) – 2 July 2013, Italy .
26. RH-34 (3-[2-(2-methoxybenzylamino)ethyl]-1*H*-quinazoline-2,4-dione) – 4 July 2013, France.
27. 2-(2,3-dimethoxyphenyl)-*N*-(3,4,5-trimethoxybenzyl)ethanamine – 4 July 2013, France.
28. JTE-907 (*N*-(benzo[1,3]dioxol-5-ylmethyl)-7-methoxy-2-oxo-8-pentyloxy-1,2-dihydroquinolin-3-carboxamide) – 4 July 2013, Germany.
29. AB-FUBINACA (*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide) – 4 July 2013, Belgium.
30. 5F-AB-PINACA (*N*-(1-carbamoyl-2-methyl-propyl)-1-(5-fluoropentyl)indazole-3-carboxamide) – 5 July 2013, Belgium.
31. Mebroqualone (3-(2-bromophenyl)-2-methylquinazolin-4(3*H*)-one) – 5 July 2013, United Kingdom.
32. Allylescaline (4-allyloxy-3,5-dimethoxy-phenethylamine) – 8 July 2013, Denmark.

33. α -PEP (1-phenyl-2-(1-pyrrolidinyl)heptan-1-one) – 8 July 2013, Sweden.
34. 5-EAPB (1-(1-benzofuran-5-yl)-*N*-ethylpropan-2-amine) – 11 July 2013, United Kingdom.
35. Mephtetramine (2-((methylamino)methyl)-3,4-dihydronaphthalen-1(2*H*)-one) – 11 July 2013, United Kingdom.
36. Escaline (3,5-dimethoxy-4-ethoxyphenethylamine) – 15 July 2013, Germany.
37. β k-PBDB (1-(1,3-benzodioxol-5-yl)-2-(propylamino)butan-1-one) – 17 July 2013, Czech Republic.
38. Proscaline (2-(3,5-dimethoxy-4-propoxyphenyl)ethanamine) – 7 August 2013, Netherlands.
39. W-15 ((*E*)-4-chloro-*N*-(1-phenethylpiperidin-2-ylidene)benzenesulfonamide) – 12 August 2013, Spain.
40. Nitracaine (3-(*N,N*-diethylamino)-2,2-dimethylpropyl-4-nitrobenzoate) – 13 August 2013, Sweden.
41. Diclazepam (7-chloro-5-(2-chlorophenyl)-1-methyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one) – 26 August 2013, Germany.
42. Methoxetamine brominated derivative (2-(2-bromo-5-methoxy-phenyl)-2-(ethylamino)cyclohexanone) – 28 August 2013, Poland.
43. 25iP-NBOMe (2-[2,5-dimethoxy-4-(propan-2-yl)phenyl]-*N*-(2-methoxybenzyl)ethanamine) – 6 September 2013, Finland.
44. 3C-P (1-(3,5-dimethoxy-4-propoxyphenyl)propan-2-amine) – 6 September 2013, Finland.
45. 3C-E (1-(4-ethoxy-3,5-dimethoxyphenyl)propan-2-amine) – 6 September 2013, Finland
46. 25I-NBMD (N-(1,3-benzodioxol-4-ylmethyl)-2-(4-iodo-2,5-dimethoxy-phenyl)ethanamine) – 6 September 2013, Poland.
47. 6-MAPB (1-(benzofuran-6-yl)-*N*-methylpropan-2-amine) – 10 September 2013, United Kingdom.
48. LY2183240 (*N,N*-dimethyl-5-[(4-biphenyl)methyl]tetrazole-1-carboxamide) – 10 September 2013, United Kingdom.

49. Methoxypiperamide ((4-methoxyphenyl)(4-methylpiperazine-1-yl)methanone) – 11 September 2013, United Kingdom.
50. bk-MPA (2-(methylamino)-1-(thiophenyl-2-yl)propan-1-one) – 12 September 2013, Hungary
51. AM-1248 azepane isomer ((adamant-1-yl)[1-(1-methylazepan-3-yl)-1*H*-indol-3-yl]methanone) – 26 September 2013, Hungary.
52. Methallylescaline (2-[3,5-dimethoxy-4-[(2-methyl-prop-2-en-1-yl)oxy]phenyl]ethanamine) – 11 October 2013, Sweden.
53. C30-NBOMe (2-(4-chloro-2,5-dimethoxy-phenyl)-*N*-[(3,4,5-trimethoxyphenyl)methyl]ethanamine) – 11 October 2013, Sweden .
54. ADBICA (*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indole-3-carboxamide), 11 October 2013, Sweden.
55. Gabapentin (2-[1-(aminomethyl)cyclohexyl]acetic acid) – 15 October 2013, Belgium.
56. Sibutramine (1-[1-(4-chlorophenyl)cyclobutyl]-*N,N*,3-trimethyl-1-butanamine) – 15 October 2013, United Kingdom.
57. Venlafaxine (1-[(2-dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol) – 15 October 2013, Austria.
58. 2-FMC (1-(2-fluorophenyl)-2-(methylamino)propan-1-one) – 23 October 2013, Hungary.
59. 25B-N(BOMe)₂ (2-(4-bromo-2,5-dimethoxyphenyl)-*N,N*-bis(2-methoxybenzyl)ethanamine) – 23 October 2013, Hungary.
60. Diphenhydramine (2-(diphenylmethoxy)-*N,N*-dimethylethanamine) – 23 October 2013, United Kingdom.
61. Atomoxetine ((3*R*)-*N*-methyl-3-(2-methylphenoxy)-3-phenylpropan-1-amine) – 24 October 2013, Denmark.
62. Ocfentanil (*N*-(2-fluorophenyl)-2-methoxy-*N*-[1-(2-phenylethyl)-4-piperidinyl]acetamide) – 24 October 2013, Netherlands.
63. 6-EAPB (1-(benzofuran-6-yl)-*N*-ethylpropan-2-amine) – 28 October 2013, Netherlands.

64. AM-6527 5-fluoropentyl derivative (1-(5-fluoropentyl)-*N*-(naphthalen-2-yl)-1*H*-indole-3-carboxamide) – 7 November 2013, Germany.
65. 4-MMA (*N*-methyl-1-(4-methylphenyl)propan-2-amine) – 13 November 2013, Poland.
66. AM-2201 indazole analogue ([1-(5-fluoropentyl)-1*H*-indazol-3-yl](naphthalen-1-yl)methanone) – 15 November 2013, Sweden.
67. *N*-methyl-2-aminoindane (*N*-methylindan-2-amine) – 20 November 2013, Denmark.
68. Embutramide (*N*-[2-ethyl-2-(3-methoxyphenyl)butyl]-4-hydroxy-butanamide) – 26 November 2013, Bulgaria.
69. ADB-FUBINACA (*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide) – 28 November 2013, Turkey and Germany.
70. ADB-PINACA (*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indazole-3-carboxamide) – 3 December 2013, United Kingdom.
71. β k-2C-B (2-amino-1-(4-bromo-2,5-dimethoxyphenyl)ethan-1-one) – 3 December 2013, United Kingdom.
73. Butorphanol (17-cyclobutylmethyl-morphinan-3,14-diol) – 3 December 2013, Denmark.
74. MT-45 (1-cyclohexyl-4-(1,2-diphenylethyl)-piperazine) – 5 December 2013, Sweden.
74. Lysergic acid 2,4-dimethylazetidide ('LSZ') ([*(2S,4S)*]-2,4-dimethylazetididin-1-yl)-[*(9R)*]-7-methyl-6,6a,8,9-tetrahydro-4*H*-indolo[4,3-*fg*]quinoline-9-yl]methanone) – 10 December 2013, Slovenia.
75. *N,N*-diethyl-2-(1-pentyl-1*H*-indol-3-yl)-4-thiazole-methanamine – 18 December 2013, Germany.
76. *N*-(2-methoxyethyl)-*N*-(1-methylethyl)-2-(1-pentyl-1*H*-indol-3-yl)-4-thiazole-methanamine – 18 December 2013, Germany.
77. 1-(Cyclohexylmethyl)-2-[(4-ethoxyphenyl)methyl]-*N,N*-diethyl-1*H*-benzimidazole-5-carboxamide – 18 December 2013, Germany.
78. A-796,260 isomer, ((*E*)-3,4,4-trimethyl-1-[1-(2-morpholinoethyl)indol-3-yl]pent-2-en-1-one) – 18 December 2013, Germany.
79. SDB-006 (*N*-benzyl-1-pentyl-1*H*-indole-3-carboxamide) – 19 December 2013, Finland.

80. 5F-SDB-006 (*N*-benzyl-1-(5-fluoropentyl)-1*H*-indole-3-carboxamide) – 19 December 2013, Finland.

81. FUB-PB-22 (8-quinolyl 1-[(4-fluorophenyl)methyl]-3*H*-indole-3-carboxylate) – 19 December 2013, Sweden.