PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga

Ministero della Salute

SISTEMA NAZIONALE DI ALLERTA PRECOCE
E RISPOSTA RAPIDA PER LE DROGHE
NATIONAL EARLY WARNING SYSTEM - N.E.W.S.

European Monitoring Centre
for Drugs and Drug Addiction

Reitox
Italian Focal Point

ACTIVITY REPORT AND RESULTS

National Early Warning System
N.E.W.S.

Year 2013 – Data base 2012

Coordination of bio - toxicological aspects

Istituto Superiore di Sanità
Dipartimento del Farmaco

General coordination and management

Regione del Veneto - Azienda ULSS 20
Dipartimento delle Dipendenze

Coordination of clinical - toxicological aspects

IRCCS - Fondazione S. Maugeri
Centro Antiveleni Pavia

National Early Warning System
National Early Warning System – N.E.W.S.
Anti-Drug Policy Department – President of the Council of Ministers

Presidency of the Council of Ministers

Presidency of the Council of Ministers
Department of Anti-Drug Policy
Head of Department: Dr Giovanni Serpelloni

Reitox Focal Point
Department of Anti-Drug Policy
Head: Dr Elisabetta Simeoni

National Monitoring Service
Department of Anti-Drug Policy
Coordinator: Dr Roberto Mollica

Ministry of Health
Department of public health and innovation
Department of scheduling and regulation of the National Health Service
Department of public veterinary health, food safety and the health protection boards – Head of Department *Dr Romano Marabelli*
General Prevention Executive – General Manager *Dr Giuseppe Ruocco*
Office VII - *Dr Giovan Battista Ascone, Dr Pietro Canuzzi*
Office IV - Director *Dr Liliana La Sala, Dr Aurelia Fonda*
General executive for medical devices, the pharmaceutical service and safety of care – General Manager *Dr Marcella Marletta*
Office VII - Director *Dr Paola D'alessandro*
Office VIII - Director *Dr Germana Apuzzo*
General executive for the hygiene and safety of foods and nutrition – General Manager *Dr Silvio Borrello*
Office IV - Director *Dr Bruno Scarpa*
Office VII - *Director Dr Monica Capasso*
Office VIII - *Director Dr Pietro Santo Noè*

National coordination centre
Coordination of bio-toxicology issues
Istituto Superiore di Sanità [Superior Health Institute], Drugs Department – *Dr Teodora Macchia*
Coordination of clinical-toxicological issues
Centro Antiveleni Pavia I.R.C.C.S. [Pavia Poison Centre] Salvatore Maugeri Foundation – *Dr Carlo Locatelli*
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Introduction

In accordance with relevant European provisions, the Anti-Drug Policy Department implemented the National Early Warning (N.E.W.S.) and Rapid Response System For Drugs in Italy at the end of 2008. The System, which has its offices at the National Monitoring Centre of the Department of Anti-Drug Policy, arose with a dual objective; firstly of early identification of situations potentially hazardous to public health associated with the appearance of new substances and new methods of consuming them; and secondly to make pre-Alert or Alert notifications which promptly involve the facilities assigned with the protection of public health and which are responsible for any implementation of emergency response measures.

As well as handling incoming notifications (input) and external communications (output), in the last four years the System has realised a series of activities which have significantly contributed to reducing the circulation of new psychoactive substances in Italy, therefore limiting episodes of intoxication, including fatal, among users.

The fruitful collaboration with the European Monitoring Centre, via the National Focal Point of the Department of Anti-Drug Policy, enabled extremely rapid exchanges of information between the European and the national levels and made other member states aware of the strategies and the products of the Italian Warning System.

This report summarises the activities and the primary results which the System has achieved over the course of these four years, especially thanks to the work and the collaboration of the collaborating centres, and in particular the internal coordination of the System – Superior Health Institute, Pavia Poison Centre, Department of Addiction of Verona Local Health Unit 20.

In light of the results that will be reported in the following, it is hoped that the System will continue its work in the coming years with the same energy the same efficacy demonstrated over these first four years of activity, demonstrating how collaboration and commitment can lead to beneficial results for the community.

Dr Giovanni Serpelloni
Head of the Department of Anti-Drug Policy
Presidency of the Council of Ministers
N.E.W.S. Management

1. Abstract

Consolidated collaboration with the Ministry of Health

During 2012 the National Early Warning System of the Department of Anti-Drug Policy of the Presidency of the Council of Ministers significantly strengthened its organisation and maintained a strict collaboration with the Ministry of Health via specific working methods aimed at including new psychoactive molecules in Table I of DPR [Decree of the President of the Republic] 309/90 and implementing other safety measures for public health protection (regulations on public health and safety, enabling the Carabinieri Force for public health safety protection, initiating the Consumer Code, implementing RASFF).

Inclusion in Table I of new cannabinoids and synthetic cathinones and phenethylamine

In 2012 three new decrees were signed to include new molecules in Table I of DPR 309/90 as described in the following.

- By the Decree of 11 June 2012 (Official Journal no 142 of 20/6/2012) the following monoester derivatives of morphine were made illegal: 6-monoacetylmorphine (6-MAM) and 3-monoacetylmorphine (3-MAM) and the chemical definition of analogues of the substance Butylone was replaced.
- Methoxetamine, analogue N-ethyl-derivative of ketamine; 4-methylamphetamine, analogue methylate of amphetamine; CP 47,497 and CP 47,497-C8-homologue with a chemical structure related to Delta-9-THC; 4-Flouroamphetamine analogue of amphetamine and 5,6-Methylenedioxy-2-aminoindane, a phenethylamine strictly related to MDMA (Ecstasy) were included in Table I by Decree of 24 October 2012 (OJ no 264 of 12 November 2012).
- Lastly, the molecule 5-IT or 5-(2-aminopropyl)indole, derivative of indole and positional isomer of methyltryptamine (α-MT) was included in Table I by Decree of 10 December 2012 (OJ no 303 of 31 December 2012).

The network

The number of the Warning System's Collaborating Centres increased from 64 in 2012 to 73 in 2013 (+14.1%), helping to increase the visibility and operations of the System nationally and increase the number of notifications by the input units.

The notifications +23.6%

In 2012 alone 157 notifications were recorded. The majority of these came from the European Monitoring Centre (42.0%) and the Police Forces (31.8%). Other notifications came from analysis laboratories (14.6%), Poison Centres (5.2%), the Ministry of Health (3.2%), Healthcare Facilities (1.3%) and from the Legal Offices (0.6%). In general an increase of 23.6% was recorded of notifications received compared to 2011, when there were 127 notifications and 48.1% compared to 2010, when there were 106.

Informatives and Alerts

In 2012, the National Early Warning System sent 34 communications to its output network. 19 were for Informatives purposes and 15 were Alerts. Of these Alerts 5 were second level and 10 were level 3. Compared to the previous year, Informatives were down (-12), and Alerts level 2 were down by 1.

New unknown substances

Since 2009 more than 200 molecules have been intercepted by the National Early Warning System, including:

- 70 synthetic cannabinoids
- 35 synthetic cathinones
- 51 phenetylamines
- 4 piperazine, 8 tryptamine, 5 ketamine and analogues, 5 natural substances, 10 active principles of drugs, 2 fentanyl, 7 oppioid, 2 other stimulants, 2 other anesthetics, 1 pesticide, 2 precursors, 6 azepane-like, 3 PCP derivatives, 3 tropane derivatives, 1 steroid and other 20 molecules of various kinds.

Cases of acute intoxication

There have been 41 acute intoxications associated with taking synthetic cannabinoids recorded since 2010, the majority being concentrated in northern Italy. Similarly, between 2010 and 2012, the National Early Warning System received 8 notifications of cases of acute intoxication associated with synthetic cathinones. All cases were recorded in the Regions of Lombardy, Veneto and Tuscany.
During 2012 numerous cases of methoxetamine intoxication have also been reported. In total 10 (1 case recorded in 2011) cases of methoxetamine intoxication were recorded by the System, the majority of which (6) were identified in northern Italy, while the remaining four in central Italy, in the Regions of Tuscany, Lazio and Emilia Romagna.

Web monitoring for preventing drugs supply: websites and rave parties

The web monitoring activity conducted from October 2010 to December 2012 also led to the identification of 116 illegal music events promoted online. 113 events were reported to the Police forces: 39 of these (33.6%) were stopped, i.e. closed before taking place; 25 were managed by intervention *in loco* by the Police forces (21.6%); 38 (32.8%) took place in spite of the notification, and 11 are pending a response from the Police forces. In total, 54 websites in the Italian language were identified with servers located within the national territory, and 426 web pages were reported. Of reports to the Police forces of sites which sell controlled substances, 63.4% resulted in the removal of the online marketing notice and in 21.8% of cases the web page was closed.

Variations in the method of consumption

Via the monitoring of the various routes of administration, the National Early Warning System, in collaboration with the National Epidemiological Monitoring Service of the Department of Anti-Drug Policy, was able to document changes in the methods of taking heroin, cocaine and other stimulants between 2008 and 2011 among users registered with the services. From the enquiry it emerged that the route of assumption most used for heroin was intravenous but on a downward trend (60.9% in 2008, this figure falls to 57.5% in 2011) in favour of inhaling (28.3% in 2008 against 31.2% in 2011) and insufflation (7.2% in 2008 versus 9.6% in 2011). For cocaine the method most used is insufflation, on a continual rise between 2008 (49.4%) and 2011 (59.9%); lastly, for the other stimulants the oral route is the one most used, with an increase from 57.5% in 2008 to 62.3% in 2011.

New cutting agents/adulterants

The notifications received by the System in the last year of operations illustrate that batches of heroin are in circulation in Europe contaminated, or cut, with *Bacillus anthracis*, the cause of the serious disease anthrax. In consideration of the speed with which narcotic substances can be marketed in Europe and, therefore, reach Italy, it was deemed appropriate to activate an Alert among facilities charged with public health protection and the laboratories of the Police forces. Moreover, the cutting agents/adulterants more frequently encountered for heroin in 2012 were paracetamol, caffeine and methorphan. Cocaine however was found to be cut/adulterated with tetramisole/levamisole, dipyrone, aminopyrine, benzocaine.

Conclusions

After 4 years of operations at the Department of Anti-Drug Policy, the National Early Warning System has achieved significant results which have made a solid contribution to countering the proliferation of new narcotic substances in Italy and to public health protection. The working method used thus far has been valid, reliable and, above all, effective. It is therefore deemed appropriate to maintain the operations of the National Early Warning System and to continue monitoring the areas described above in the coming year.

Main results

15 Alerts activated 2012
157 notifications received

2009-2012
237 new molecules recorded

73 collaborating Centres
(May 2013)

2010-2012
6 decrees for inclusion of new molecules in Table 1 DPR 309/90

Cases of acute intoxication 2010-2012

41 cases related to taking synthetic cannabinoids

8 cases related to taking synthetic cathinones

10 cases related to taking methoxetamine with emergency medical attendance

Internet monitoring 2010-2012

270 notices removed

38 websites blocked

93 webpages closed

64 illegal music events blocked or managed

2. Premises

Purposes of the National Early Warning System

In accordance with relevant European provisions, the Department of Anti-Drug Policy of the Presidency of the Council of Ministers implemented in Italy the National Early Warning (N.E.W.S.) and Rapid Response System For Drugs.
The System is tasked with identifying conditions potentially hazardous for public health, associated with the appearance of new drugs and new ways of consuming them, and with generating Alert notifications which promptly involve the facilities charged with health protection responsible for implementing adequate emergency response measures.

2.1 Organisational aspects

European level

The mechanism for the rapid exchange of information on new psychoactive substances involves all member states of the EU thanks to Decision 2005/387/GAI of the Council of Europe. Under this framework the Italian National Early Warning System forms the instrument which drives the exchange of information between Europe and the National Focal Point, the official interface with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). All notifications collected by the National Early Warning System via the national channels are conveyed to the National Focal Point of the Department of Anti-Drug Policy, which has the role of transferring the information to the EMCDDA which in turn circulates it between the various European countries. Similarly, when the Focal Point receives a notification from the EMCDDA, it transmits it to the National Early Warning System which informs its network or requests information on the matter, when needed. The interactions between the EMCDDA and the Warning System can also relate to technical-scientific information important for observing and monitoring new substances and new methods of consumption.

Figure 1 – Organisational structure of the National Early Warning System in Europe

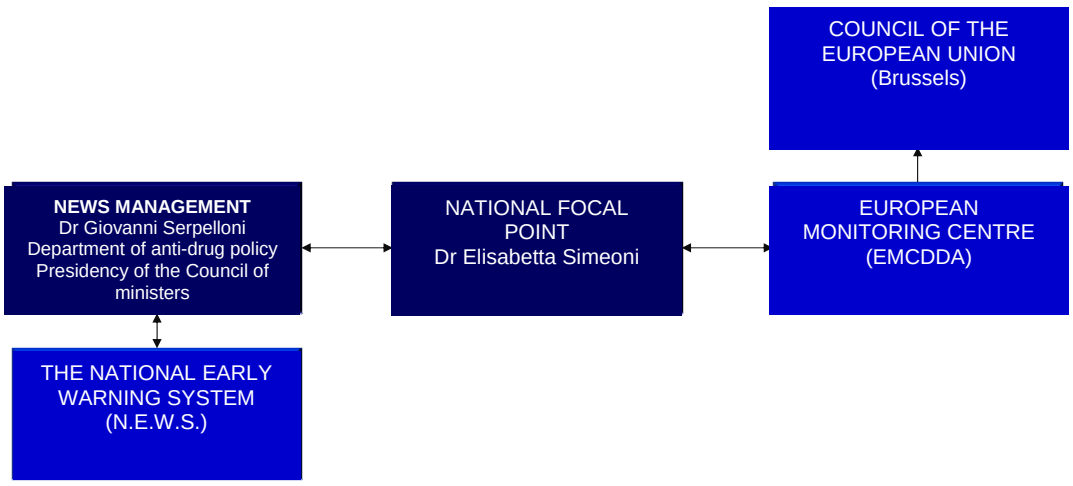


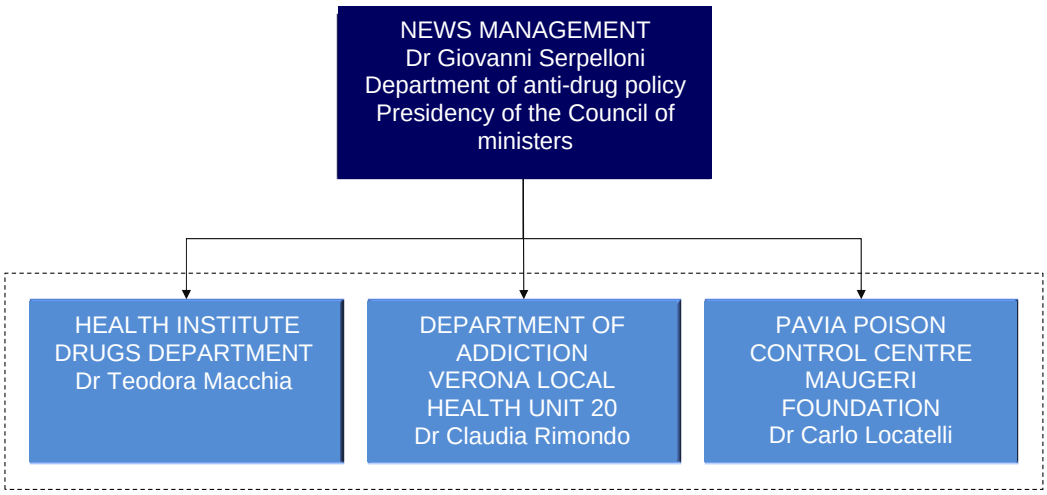
Figure 2 – Graphic representation of information flows between the National Early Warning System, European Monitoring Centre for Drugs and Drug Addiction and the Council of the European Union.

National level

Nationally, the System's Management sought the consultancy and operations of three facilities, each one competent and responsible for the coordination of a specific area:

- National coordination of bio-toxicology aspects: provided by the Superior Health Institute, provides opinions, consulting, supervision over documents and events which occur and which are subject to the activities of the System in terms of bio-toxicology;
- National coordination of clinical-toxicological aspects: provided by the Pavia Poison Centre, Salvatore Maugeri Foundation provides opinions, consulting, supervision of documents and events which occur and which are subject to the activities of the System in terms of bio-toxicology;
- National coordination of operating aspects: the Department of Addiction, Verona Local Health Unit 20, forms the centre for the collection of notifications, coordinates flows of information, prepares notifications and alerts for the supervision of other coordination and management, updates the network with input and output, coordinates the updating and technical operation of the software, manages the internal communication system, and coordinates field investigations.

Figure 3 – Organisational structure of the National Early Warning System.



Collaboration with the Ministry of Health and with the DCSA

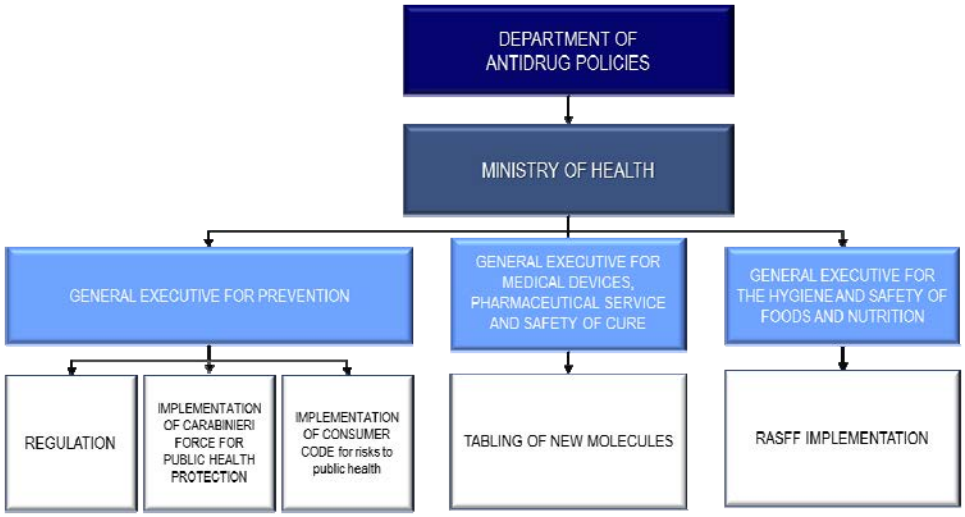
The System collaborates with the Ministry of Health and with the Central Executive for Anti-Drug Services (DCSA).
In particular, as regards the Ministry of Health, the collaboration operates especially with the Executives described below which have specific roles in relation to the operation of the Warning System:

- General executive for medical devices, the pharmaceutical service and safety of care
  - Assessment of the enquiry for inclusion in the Tables of DPR 309/90
  - Request for opinion to the Superior Health Council
  - Notification of opinion expressed by the Superior Health Council to the Department of Anti-Drug Policy
  - Preparation of the decree for updating the tables of D.P.R. 309/90
  - Transmission of the decree proposal to the Ministry by means of the Office of the Cabinet
  - Sending of the decree for publication in the Official Journal
  - Evaluation of the limitation of safety measures set out by Legislative Decree 713/86

- General Executive of Prevention
  - Alert activation
  - Activation of Consumer Code following the risk of a hazard to
  - public health
  - Activation of precautionary regulation for the withdrawal of commercial products containing the substance notified by the Alert – Carabinieri Force for health protection

- General executive for the hygiene and safety of foods and nutrition
  - Enactment of alerts of the National Early Warning System
  - Verification of any notification of the product
  - Activation of the RASFF

Figure 4 – Detail of collaborations of the National Early Warning System with the Ministry of Health.



2.1.1 Collaboration with the National Institute on Drug Abuse

Italy-USA Agreement

The second important international agreement for scientific collaboration between Italy and the United States was signed in Rome on 25 July 2011 between the Head of the Department of Anti-Drug Policy, Giovanni Serpelloni, and the director of the National Institute on Drug Abuse, Nora Volkow. The agreement promotes mutually beneficial research for improving the diagnosis, treatment of drug use and addiction, developing areas of particular interest which include: research, early diagnosis, screening, treatment and short-term interventions for addiction disorders, especially in adolescents and young adults. As part of prevention, the two bodies decided also to collaborate on the aspect of the National Early Warning System.

NEWS working group

During 2012 therefore the organisation, activities and results of the Italian Warning System were presented to a working group specifically appointed by professor Volkow to exchange information and knowledge both on the organisational aspects of the System, new narcotic substances and the new methods of use which were identified by its operations. The exchange of information took place via videoconference and face-to-face meetings at the 2012 NIDA International Forum held in June in Palm Springs (California). The collaboration continues today and above all takes the form of exchange of information and best practices and supervision by the NIDA of the development and realisation of the institutional database of the National Early Warning System.

2.1.2 Collaborating Centres of the System

Figure 6 illustrates the System's Collaborating Centres which are differentiated into collaborating centres for notification and response (level I) and Early Expert Network for rapid consultation (level II).
Among the first level (around 1500 centres) there are the Regions and Autonomous Provinces, the Departments of Addiction, therapeutic communities, mobile units, laboratories, facilities of the emergency system and the Police forces. These centres have the role of sending notifications to the System and implementing suitable response measures in the case of a alert.
Second level centres include the Central Executive for Anti-Drug Services, Scientific Police, Departments of Scientific Investigations of the Carabinieri, the Customs Agency, Forensic Toxicology, poison centres, university laboratories and some research centres. They have the role not only of sending notifications and implementing response measures, where necessary, but also of supporting the System in the operations for completing notifications and providing opinions and advice regarding the notifications and any alerts.

Figure 5 – Organisational structure of the National Early Warning System.

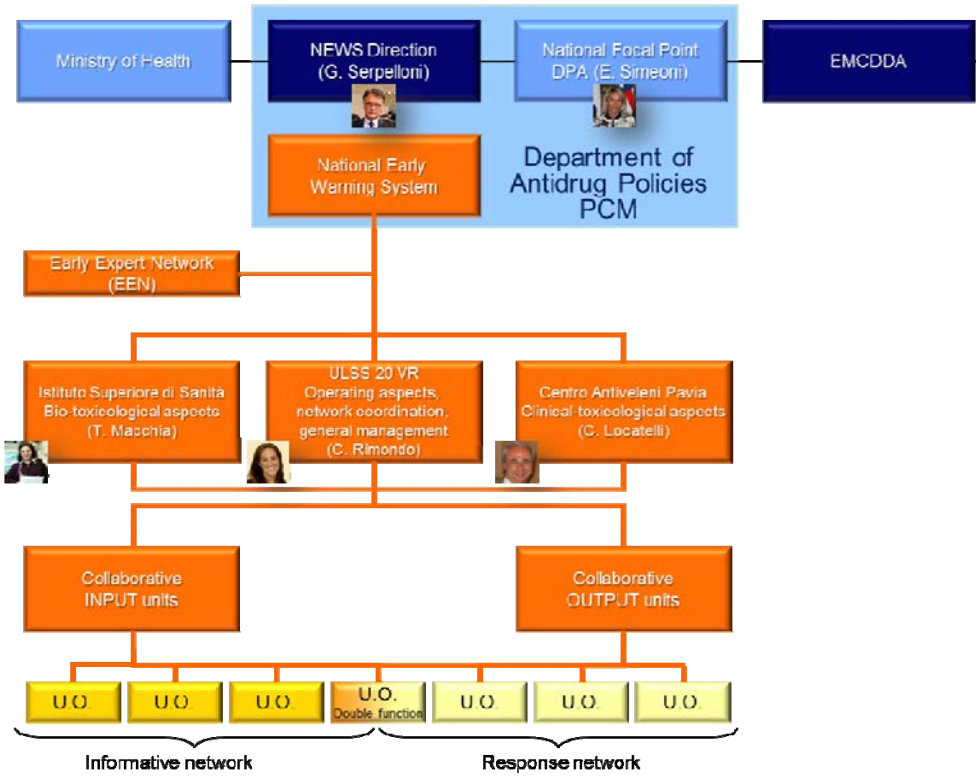
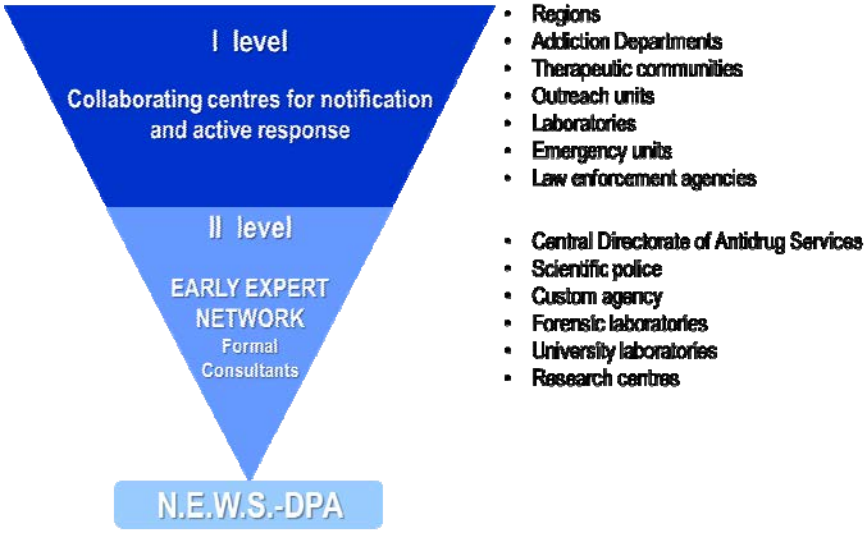


Figure 6 – Graphic of the organisation of Collaboration Centres of the National Early Warning System.



2.1.3 Collaboration with the Carabinieri

Agreement between DPA and the Carabinieri

In December 2012 an agreement was signed between the Presidency of the Council of Ministers – Department of Anti-Drug Policy and the Carabinieri Force. Via this accord, the Scientific Investigation Department (RIS) and Narcotic Substances Analysis Laboratories (LASS) of the Carabinieri Force coordinated by the Carabinieri Scientific Investigation Group (Ra.C.I.S.) of the Carabinieri Force were fully included within the network of Collaborating Centres of the National Early Warning System of the Department of Anti-Drug Policy (Presidency of the Council of Ministers), in order to collaborate and support this System in the identification of new drugs and new methods of use via analysis of confiscations by the Narcotic Substances Analysis Laboratories. Given the need to update specialist personnel on the analysis of new narcotic substances, the Department of anti-drug policy therefore promoted a specific project, known as "RIS – NEWS", with the general objective of supporting more efficient and prompt identification of new narcotic substances in Italy by facilitating the entry of the laboratories of the Carabinieri Force (RIS and LASS) into the National Early Warning System, their participation in the national data flow and the adoption of analytical methods appropriate for identifying new substances. In 2013 a training programme is under way for updating specialist personnel on issues concerning:

RIS-NEWS project for supporting the entry of the laboratories into NEWS

Training course

- Analytical protocols and good laboratory practices for chemical quality and quantitative analysis of samples of narcotic substances, regarding new psychoactive substances in particular;
- Participation in the National Early Warning System, for prompt detection of associated drug conditions potentially harmful for public health and the sending of notifications of alert and activation of response actions.

Figure 7 – Geographical distribution of the Collaborating Centres of the National Early Warning System (updated March 2013).

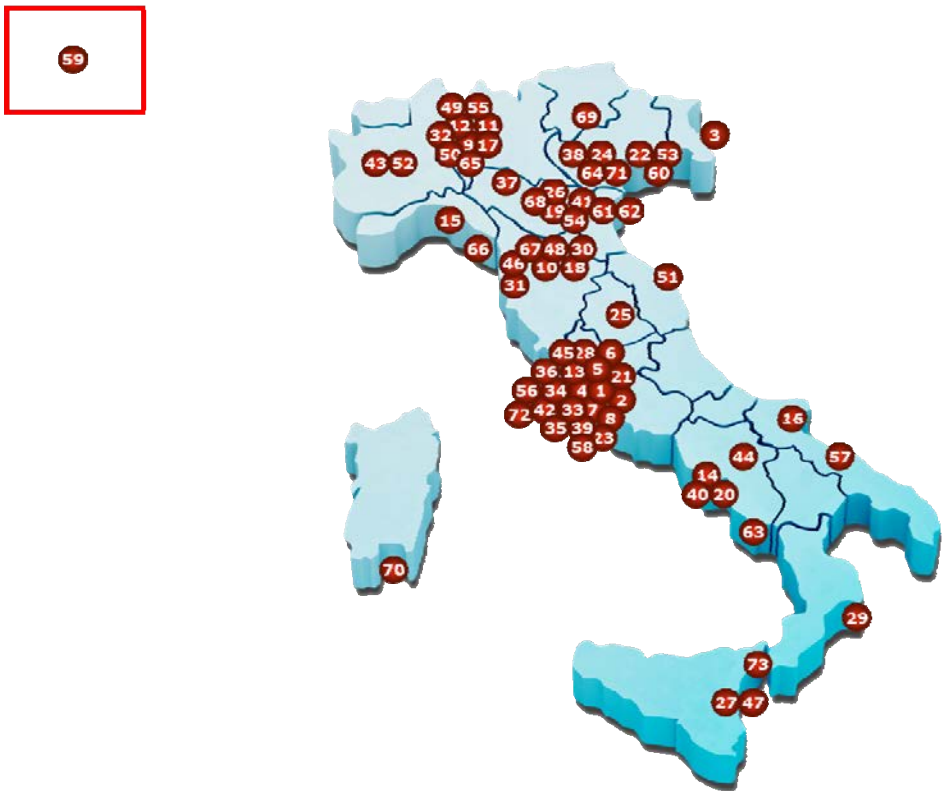


Table 1 – List of Italian Collaborating Centres of the National Early Warning System reported in Figure 7 (updated March 2013).

No	Name of Collaborating Centre	Contact
1	Istituto Superiore di Sanità - Dipartimento del Farmaco	Teodora Macchia
2	Istituto Superiore di Sanità - Dipartimento del Farmaco	Roberta Pacifici
3	Ministero Interno UTG Trieste - Nucleo Operativo Tossicodipendenze	Alma Biscaro
4	Ministero della salute - Direzione Generale della Prevenzione – Ufficio VII	Pietro Canuzzi
5	Ministero della salute - Direzione generale dei dispositivi medici, del servizio farmaceutico e della sicurezza delle cure - Ufficio VIII	Germana Apuzzo
6	Ministero della Salute - Ufficio IV - DG Prevenzione Sanitaria	Aurelia Fonda
7	Ministero della Salute - Direttore Ufficio IV - DG Prevenzione Sanitaria	Liliana La Sala
8	Osservatorio Italiano sulle Droghe - Dipartimento Politiche Antidroga	Roberto Mollica
9	Centro Antiveleni Pavia, Centro Nazionale di Informazione Tossicologica	Carlo Locatelli
10	Centro Antiveleni - Azienda Ospedaliera Universitaria Careggi, Firenze	Primo Botti
11	Centro Antiveleni Bergamo, Az. Ospedali Riuniti	Maria Luisa Farina
12	Centro Antiveleni Milano - Az. Osp. Ospedale Niguarda Cà Granda	Franca Davanzo
13	Centro Antiveleni Policlinico Gemelli - Roma	Alessandro Barelli
14	Centro Antiveleni, Ospedale Cardarelli - Napoli	Clara Volpe
15	Centro Antiveleni, Ospedale Gaslini - Genova	Mario Lattere
16	Centro Antiveleni, Ospedali Riuniti - Foggia	Anna Lepore
17	Laboratorio di Tossicologia Analitica - IRCCS Policlinico San Matteo - Pavia	Pietro Papa
18	Tossicologia forense Università degli studi di Firenze	Elisabetta Bertol
19	Tossicologia forense Università degli studi di Bologna	Elia Del Borrello
20	Tossicologia forense II Università degli studi di Napoli	Renata Borriello
21	Tossicologia forense Università Cattolica del Sacro Cuore - Roma	Marcello Chiarotti
22	Tossicologia forense Università degli studi di Padova	Santo Davide Ferrara
23	Tossicologia forense Università “La Sapienza” - Roma	Mauro Iacoppini
24	Tossicologia forense Università degli studi di Verona	Franco Tagliaro
25	Tossicologia Forense - Università degli studi di Perugia	Paola Melai
26	Tossicologia Forense - Università degli Studi di Modena e Reggio Emilia	Manuela Licata
27	Tossicologia Forense - Università degli Studi di Catania	Guido Romano

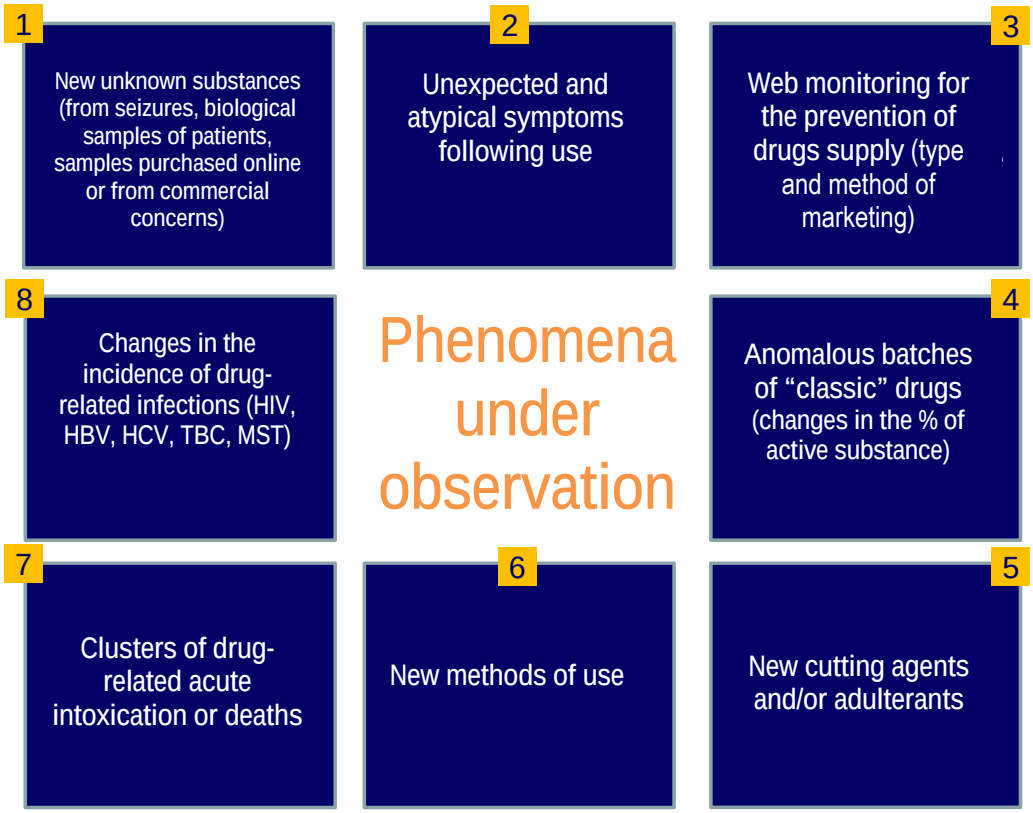
28	Tossicologia Forense - Istituto di Medicina Legale Università Cattolica del S. Cuore	Sabina Strano Rossi
29	Laboratorio di Tossicologia - Azienda Sanitaria Provinciale di Catanzaro	Loris Rivalta
30	Laboratorio Generale Azienda Ospedaliero Universitaria Careggi	Gianni Messeri
31	Dipartimento di Scienze Farmaceutiche - Università degli Studi di Pisa	Marco Macchia
32	Dipartimento di Scienze Farmaceutiche - Università degli Studi di Milano	Veniero Gambaro
33	Dip. di Scienze anatomiche, istologiche, medico-legali e dell'apparato locomotore - Università "La Sapienza", Roma	Federica Umani Ronchi
34	Direzione Centrale Anticrimine - Polizia di Stato - Servizio Polizia Scientifica	Egidio Lumaca
35	Servizio Polizia Scientifica - Sez. Indagini sulle droghe d'abuso - Polizia di Stato	Serena Detti
36	Arma dei Carabinieri - Reparto Investigazioni Scientifiche	Luigi Ripani
37	Reparto Carabinieri Investigazioni Scientifiche di Parma	Magg. Adolfo Gregori
38	Arma dei Carabinieri - Laboratorio Analisi Sostanze Stupefacenti Verona	Roberto Buonocore
39	Agenzia delle Dogane - Laboratorio chimico di Roma	Alessandro Proposito
40	Laboratorio e Servizi Chimici dell'Agenzia delle Dogane di Napoli	Francesco Parisi
41	Polizia di Stato - Squadra mobile di Bologna	Fabio Bernardi
42	Presidenza del Consiglio dei Ministri	Luigi D'Onofrio
43	Laboratorio Antidoping - Torino	Marco Vincenti
44	ARPAC - Dipartimento tecnico di Benevento	Caterina Martuccio
45	AIFA - Agenzia Italiana del Farmaco - Ufficio Valutazioni e Autorizzazioni	Lucio Covino
46	U.O. Biochimica clinica e tossicologia - Az. Sanitaria USL2 Lucca	Daniele Prucher
47	U.O.Chimica e Clinica Tossicologica ASP Catania - Regione Sicilia	Antonino Signorelli
48	Laboratorio di Sanità Pubblica - Area Vasta Toscana Centro - Azienda Sanitaria di Firenze	Roberto Baronti
49	Laboratorio Ospedale "S. Anna" - Como	Gianni Giana
50	Laboratori di Ricerche di appartenenza Analitiche e Tecnologiche su Alimenti e Ambiente - Università degli Studi di Milano	Fernando Tateo
51	Istituto di Medicina Legale -Dipartimento Neuroscienze Università Politecnica Marche	Raffaele Giorgetti
52	Procura della Repubblica - Torino	Raffaele Guariniello

53	Direzione Politiche Sociali Servizio promozione e inclusione sociale - Comune di Venezia	Alberto Favaretto
54	Libero professionista	Onelio Morselli
55	Libero professionista	Mario Franchini
56	Centro Antiveleni Policlinico Umberto I - Roma	Caterina Grassi
57	TF Università degli studi di Bari	Roberto Gagliano Candela
58	DCSA - III Servizio	Segreteria DCSA
59	University of Heartfordshire department of Pharmacy	Fabrizio Schifano
60	Laboratorio Igiene e Tossicologia Industriale Az. ULSS 12 Veneziana Dipartimento di Prevenzione	Frison-Gregio
61	Dipartimento di Scienze della Vita e Biotecnologie (SVeB)-Sezione di Farmacologia - Università di Ferrara	Matteo Marti
62	Università degli studi di Ferrara - Dipartimento di Scienze Farmaceutiche	Claudio Trapella
63	Tossicologia Clinica - SSD Area Critica	Nicola Maria Vitola
64	Struttura semplice Organizzativa Di Tossicologia Clinica C/O Pronto Soccorso	Giorgio Ricci
65	Laboratorio di Prevenzione - ASL Milano	Roberta Casa
66	Laboratorio di Tossicologia - ASL 5 Spezzino	Fabio Evangelisti
67	Laboratorio Analisi Sostanze Stupefacenti - Firenze	Giuseppe Dellasorte
68	AOSP di Bologna S. Orsola-Malpighi U.O Laboratorio Centralizzato - Motta	Edit Pierini
69	Laboratorio di Sanità Pubblica - Dipartimento di Prevenzione - Azienda Provinciale per i Servizi Sanitari di Trento	Fiorenza Svaizer
70	Arma Carabinieri - Reparto Carabinieri Investigazioni Scientifiche di Cagliari	Marco Palanca
71	Polizia di Stato - Squadra Mobile di Verona	Roberto Della Rocca
72	Arma Carabinieri - Reparto Carabinieri Investigazioni Scientifiche di Roma	Giuseppe Peluso
73	Arma Carabinieri - Reparto Carabinieri Investigazioni Scientifiche di Messina	Pietro Maida

2.2 Phenomena under the observation of the National Early Warning System

The National Early Warning System has defined 8 types of phenomena which are under observation and monitoring.

Figure 8 – Phenomena under the observation of the National Early Warning System.



1. *New unknown substances.* These are substances which appear for the first time on the market, found in seizures by the Police forces, biological samples of patients with acute intoxication or deceased, products purchased online or from smart shop type commercial operations.

New unknown substances

2. *Unanticipated and atypical symptoms after use.* The use of new substances has led to the appearance of unanticipated clinical conditions which are difficult to recognise and attribute to the effect of the narcotic substances. Specifically, unanticipated signs and symptoms can delay and complicate diagnosis of emergency medical personnel observing intoxication cases at the emergency Department. For this reason it is important to identify the clinical symptoms emerging associated with new drugs and therefore to share the information collected with the medical personnel of the health facilities involved, and in particular with the emergency services.

Unanticipated and atypical symptoms

3. *Web monitoring for the prevention of drugs* being on sale (type of products and marketing methods). One of the areas of monitoring of the Warning System is the worldwide web, where it is easily possible to sell and purchase illegal substances and products which contain them. As part of the System a specific Internet monitoring unit was established which, thanks to the

Web monitoring for preventing drugs supply

collaboration of the Central Executive for Anti-Drug Services, the Communications Police, the Carabinieri and Forensic Medicine Institute of the University of Verona Food Safety Unit, documented the characteristics of products marketed and allowed the Police force to notify numerous websites which market them. Lastly, monitoring the Internet has also focused on the identification and prevention of illegal music events (rave parties), events which generally carry a high risk of drug and alcohol related mortality and invalidity. As the majority of these events are promoted via the web, it has been possible to recognise the organisation of certain raves and notify them to the local authorities in order to implement safety measures aimed at preventing, or managing safely, the rave and therefore protecting the health of the participants.

4. *Anomalous batches of classic drugs (variations in the percentages of active substance),* where it is sought to find any changes in the percentages of active substance or the presence of additional components. Monitoring is carried out in collaboration with the Central Executive for Anti-Drug Services and information, referring to substances circulating in the national territory is recorded annually. Notifications from collaborating centres are also collated to detect potential clusters in geographic areas, and in a precise period of time, of anomalous batches of drugs with different percentages of active substances from normal and cutting agents which generate additional toxicity.

Anomalous batches of classic drugs

5. *New cutting agents/adulterants.* Classic drugs, especially heroin and cocaine, being cut or adulterated with particular substances is a known phenomenon. However, batches of heroin and cocaine cut/adulterated with new agents which can generate even more harmful consequences to users' health have appeared in recent years. It is therefore necessary to maintain continual monitoring of new cutting agents and adulterants in order to inform users of any increased hazard.

New cutting agents/adulterants

6. *New methods of use*, identifying changes in habits of users over the traditional methods of using substances. Changes in patterns of use can in fact increase the risk to the health of users and therefore require attention by the System.

New methods of use

7. *Clusters of acute intoxications and drug-related deaths.* It is important to record clusters of intoxication or overdose with a geographical reference, where possible, of the place and date of the event. Maps and graphs are used to represent the location and time of the phenomena.

Clusters of deaths or intoxication

8. *Variations of the incidence of drug related infections* (HIV, HBV, HCV, TBC, MST). The use of substances carries an elevated risk of contracting and transmitting serious diseases such as HIV and hepatitis for instance. These phenomena are highly relevant to public health and require the attention of the Warning System and constant epidemiological surveillance to prevent and contain the proliferation of these diseases, in collaboration with the Epidemiological Monitoring Service of the Department of Anti-Drug Policy.

Drug-related infections

3. Total activities

The following describes the activities and results of the National Early Warning System recorded during 2012 in terms of notifications received (input), and communications sent (output). Table 2 reports the number of activities carried out, distributed over the year.

Table 2 – Number of activities carried out by the National Early Warning System during 2012 by type of activity (input and output) and month of record.

	Input	Output				
Year 2012	Notification	Informative	Level 1 alert	Level 2 alert	Level 3 alert	Total
January	9	1	0	1	1	12
February	16	3	0	1	1	21
March	15	1	0	1	1	18
April	10	2	0	0	1	13
May	11	1	0	0	0	12
June	20	3	0	1	1	25
July	20	2	0	1	2	25
August	10	1	0	0	1	12
September	13	3	0	0	0	16
October	11	0	0	0	0	11
November	8	0	0	0	0	8
December	14	2	0	0	2	18
Total	157	19	0	5	10	191

3.1 Incoming notifications – input

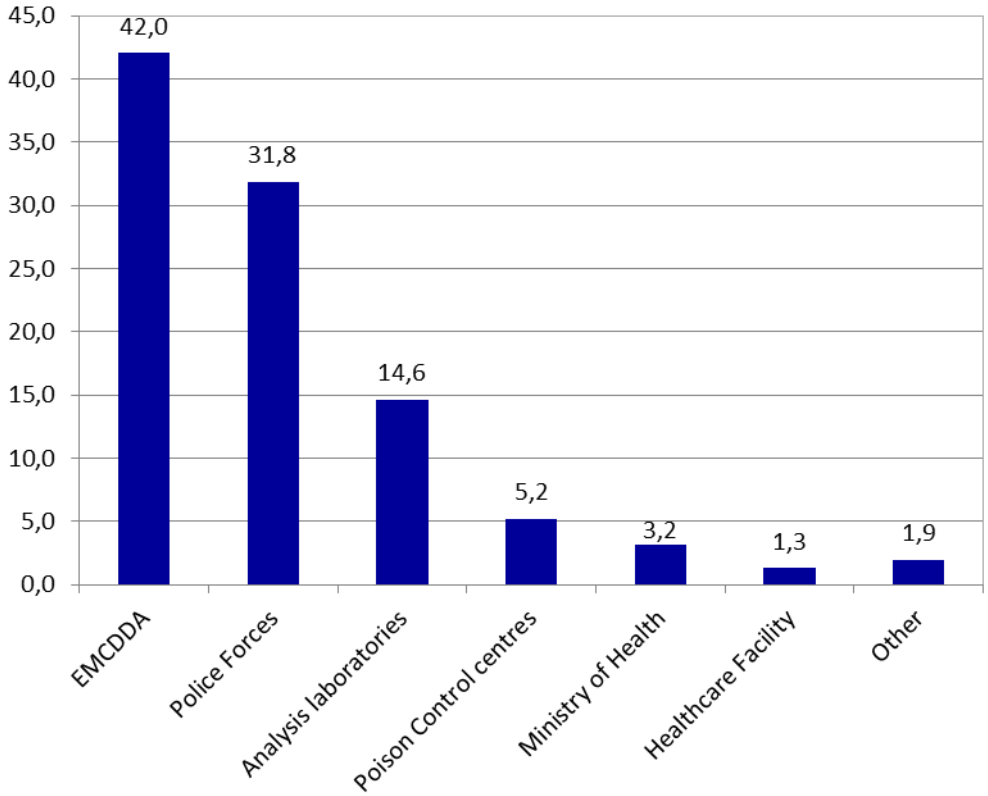
A total of 157 notifications were recorded by the System in 2012. The majority of these came from the European Monitoring Centre for Drugs and Drugs Addiction (42.0%) others from the Police forces (31.8%) and from analysis laboratories (14.6%). In 5.2% of cases, notifications came from Poison Centres, and 3.2% from the Ministry of Health. A lesser extent of notifications were sent to the System by Healthcare Facilities (ambulance service or Addiction Departments) (1.3%) and Legal Offices (0.6%).

42.0% of notifications from the EMCDDA, 31.8% from the Police forces and 14.6% from laboratories

Table 3 – Notifications sent to the National Early Warning System during 2012, according to type of notifying facility – number and percentage.

	No	%
EMCDDA	66	42.0
Police forces	50	31.8
Analysis laboratory	23	14.6
Poison Control centre	8	5.2
Ministry of Health	5	3.2
Healthcare Facility	2	1.3
Other	3	1.9
Total	157	100.0

Graph 1 – Notifications sent to the National Early Warning System during 2012, according to type of notifying facility – percentage.



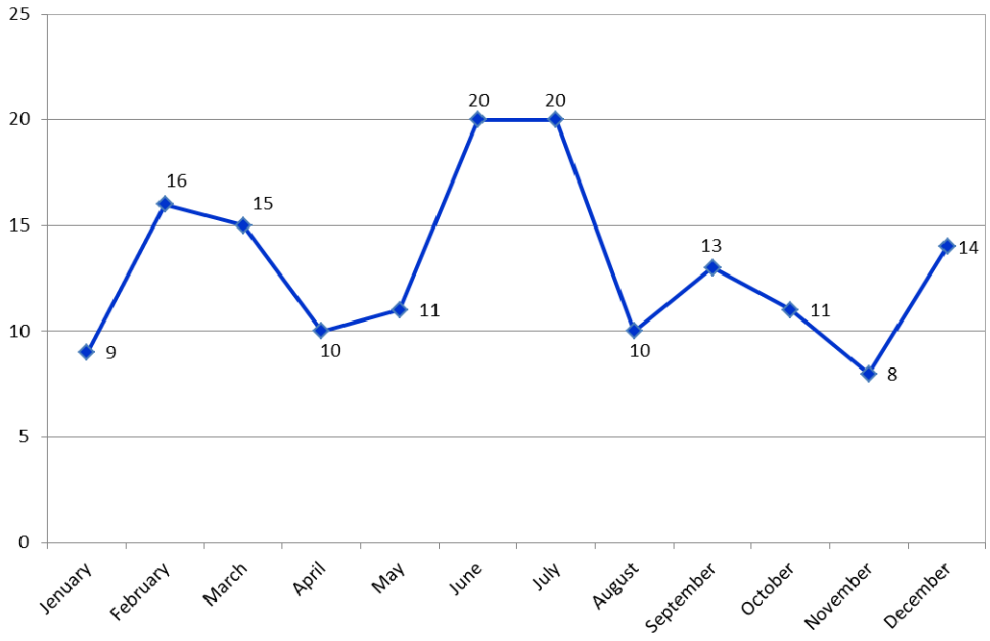
The majority of notifications was received in June and July

The majority of notifications was received in June and July (12.7% respectively), and in February and March (10.2% and 9.6% respectively); the lowest number of notifications received was in November (5.1%) and January (5.7%).
Considering the number of notifications received by the system since 2009, the first half of 2012 saw the maximum peak of notifications received (81) since the outset.

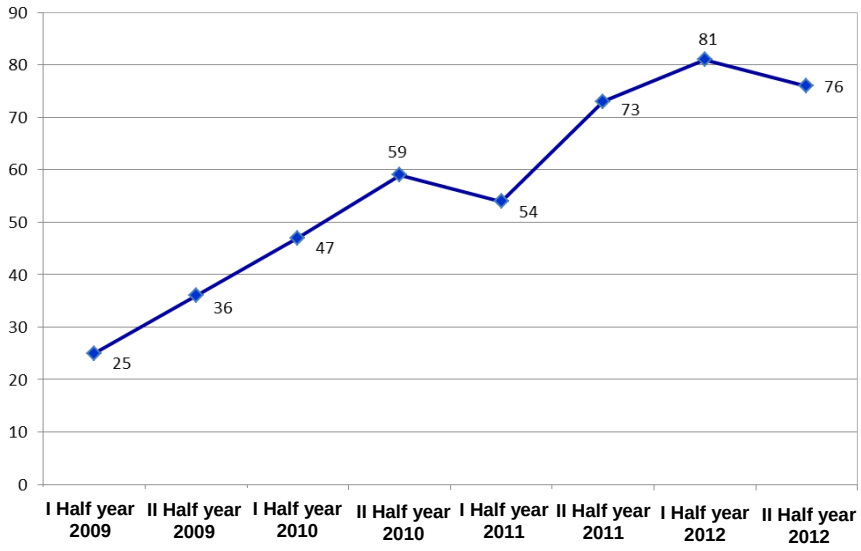
Table 4 – Notifications sent to the National Early Warning System during 2012, according to month – number and percentage.

	No	%
January	9	5.7
February	16	10.2
March	15	9.6
April	10	6.4
May	11	7.0
June	20	12.7
July	20	12.7
August	10	6.4
September	13	8.3
October	11	7.0
November	8	5.1
December	14	8.9
Total	157	100.0

Graph 2 – Notifications received by the National Early Warning System during 2012, according to month – number (Total notifications received = 157).



Graph 3 – Notifications received by the National Early Warning System from 2009 to 2012 – Number.



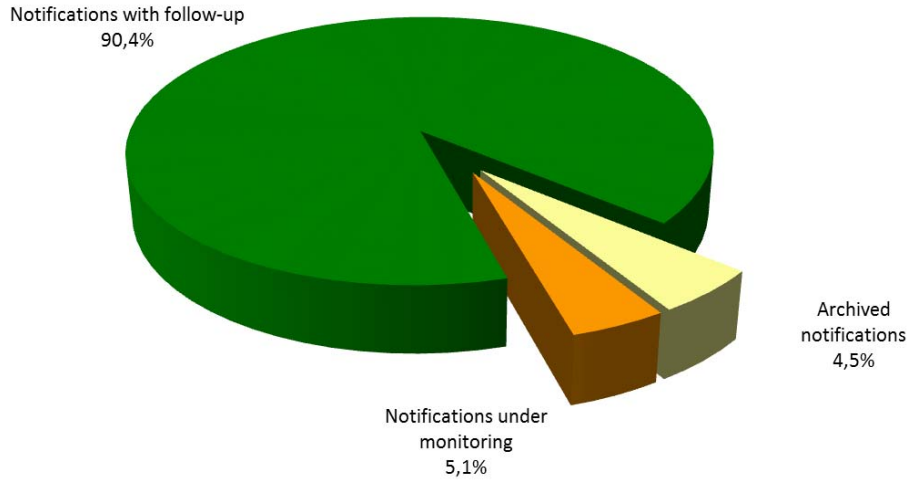
157.4% increase of notifications since 2009, 48.1% since 2010 and 23.6% since 2011

As illustrated by the trend illustrated in Graph 3, the number of notifications (157) received by the Warning System during 2012 increased 157.4% compared to 2009, when there were 61 notifications, +48.1% compared to 2010, when there were 106 notifications and 23.6% over 2011. This increase could be related to at least two factors. The first relates to the fact that since 2009 the visibility of the Warning System has increased nationally, therefore stimulating notification from the input units. Secondly, the activity to increase awareness by the System since February 2010 on the issue of cannabinoids and synthetic cathinones has increased involvement of the notifying units via the frequent sending of information useful for identifying new molecules and new clinical cases related to their use. Further to this, and the distribution to the network of laboratories of essential reference standards in 2010 and 2012 by the Superior Health Institute, the notifying units have been made able to identify new molecules and notify them to the System, thereby increasing the number of analytically defined rather than presumptive notifications.

90.4% of notifications had a follow-up

Of the 157 notifications received in 2012, 142 (90.4%) were subject to specific communications from the System to the output network, 8 (5.1%) are currently under monitoring (the System is collecting additional information to assess what outcome to attribute to them); 7 (4.5%) were archived because they did not require further communication or detail to the network.

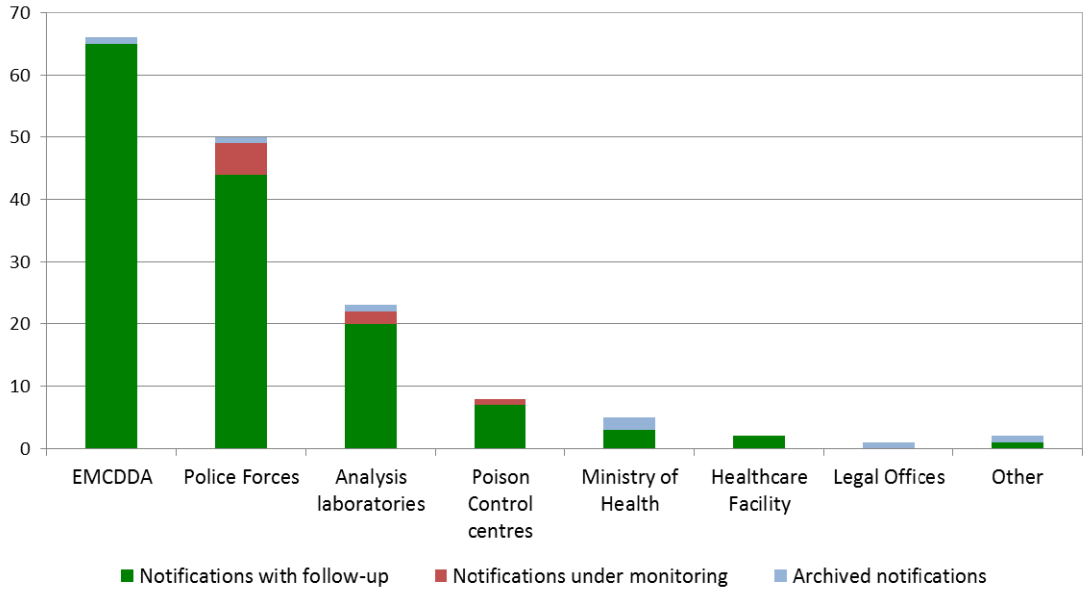
Graph 5 – Notifications received by the National Early Warning System in 2012 according to subsequent development – percentage.



83.1% of notifications from EMCDDA were sent to the network

A greater number of notifications with a continuation (65) were received from the EMCDDA. Of notifications having continuation sent from the EMCDDA, 83.1% were sent to the output network by the so-called EMCDDA Communications (see the following). 13.9% took the form of Alerts, while 3.1% were handled as other output documents.

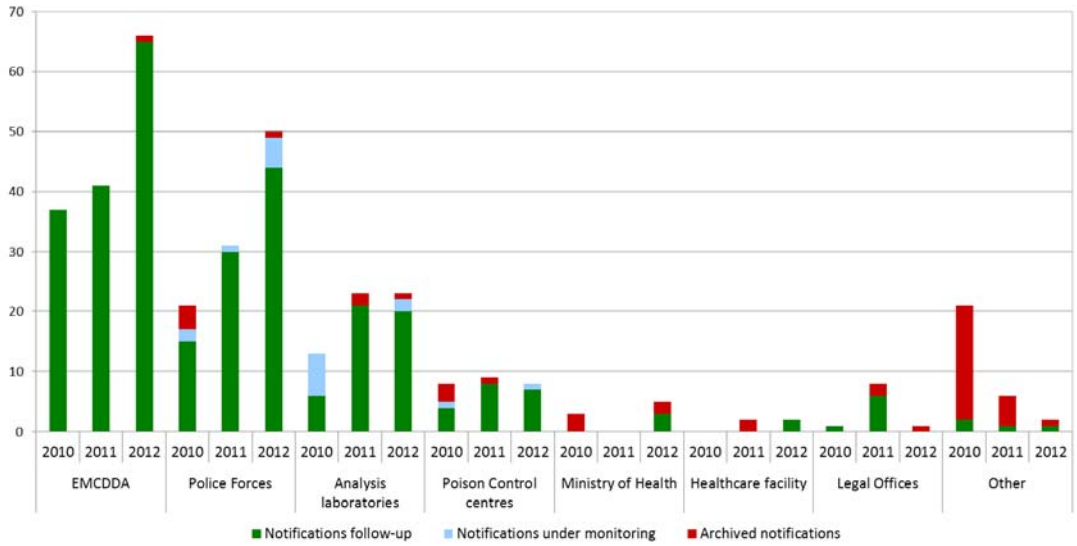
Graph 6 – Notifications received from National Early Warning System, according to sequel and type of notifying facility – number.



Reliability of notifications from EMCDDA and the Police forces

As illustrated in the graph below, as in the previous years the reliability and completeness of notifications sent by EMCDDA was confirmed in 2012; the number of notifications sent by analysis laboratories and the Police forces, processed and transmitted to the output network also increased.

Graph 7 – Notifications received from the National Early Warning System, according to sequel and type of notifying facility – number. Comparison between 2010-2011-2012.



3.2 Outgoing communications – output

During 2012, the National Early Warning System produced a series of outgoing communications (output) classified according to type of sequel reported:

- Informatives: material the System communicates to the output network and which is not urgent. This is aimed at informing the network units and is used to send notifications from the System's Collaborating Centres to the network of experts. The Information also has the objective of sharing analytical and clinical information in order to facilitate the identification of new molecules notified to the Warning System.

- Alerts: emergency notifications which imply action coordinated between the competent facilities for activating and implementing appropriate procedures in response to the issue notified. According to the severity of the alert and, therefore, the potential risk for the population, alerts can be Pre-alert, Level 1, 2, 3 Alerts:
  - Pre-alert: the appearance of a new psychoactive substance, a new method of use, a new cutting agent/adulterant in Europe or in Italy. No clinical cases recorded in Europe or in Italy. No deaths. Information pending confirmation. Potential for receiving additional information which could develop it into a Alert.
  - Level 1 alert: the appearance of a new psychoactive substance, a new method of use, a new cutting agent/adulterant in Europe or in Italy. Information confirmed by analysis. No clinical cases, neither in Europe nor in Italy. Risk of social disorder (social concerns, anxiety, alarm);
  - Level 2 alert: the appearance of a new psychoactive substance, a new method of use, a new cutting agent/adulterant in Europe or in Italy. Information confirmed by analysis. Clinical cases verified in Europe or in Italy. Risk of damage to health (temporary disorders, not potentially lethal) and risk of proliferation and use of toxic substances on the illegitimate market. No deaths;
  - Level 3 alert: the appearance of a new psychoactive substance, a new method of use, a new cutting agent/adulterant in Europe. Information confirmed by analysis. Clinical cases verified in Europe or in Italy. Risk of serious harm (disabling diseases, deaths).

Alerts can be the subject of updates according to additional information received by the System following activation. The updates can bring new related information from new communications to support those already communicated.

In 2012, 34 communications were sent from the National Early Warning System to the output network. For the majority Informatives notifications were sent (55.9%). Of the Alerts (44.1%), 5 Level 2 Alerts (33.3%) and 10 Level 3 (66.7%), no Pre-Alerts were sent in 2012.

19 Informatives notifications sent; 15 Alerts activated

Graph 8 – Output communications sent in 2012 by the National Early Warning System distributed according to type – percentage.

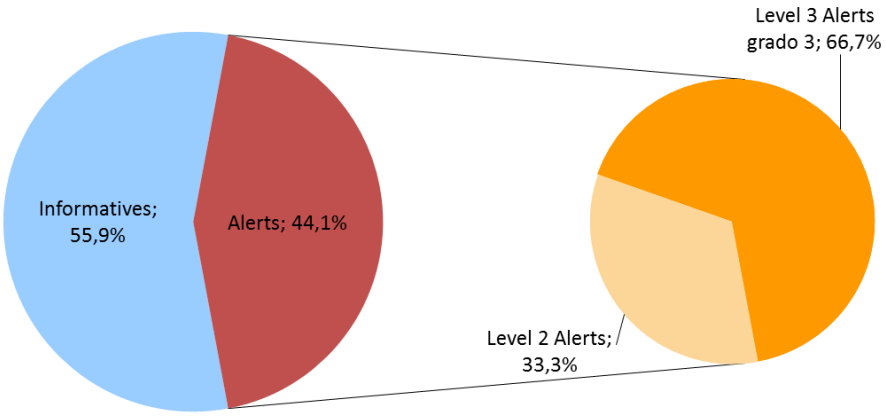


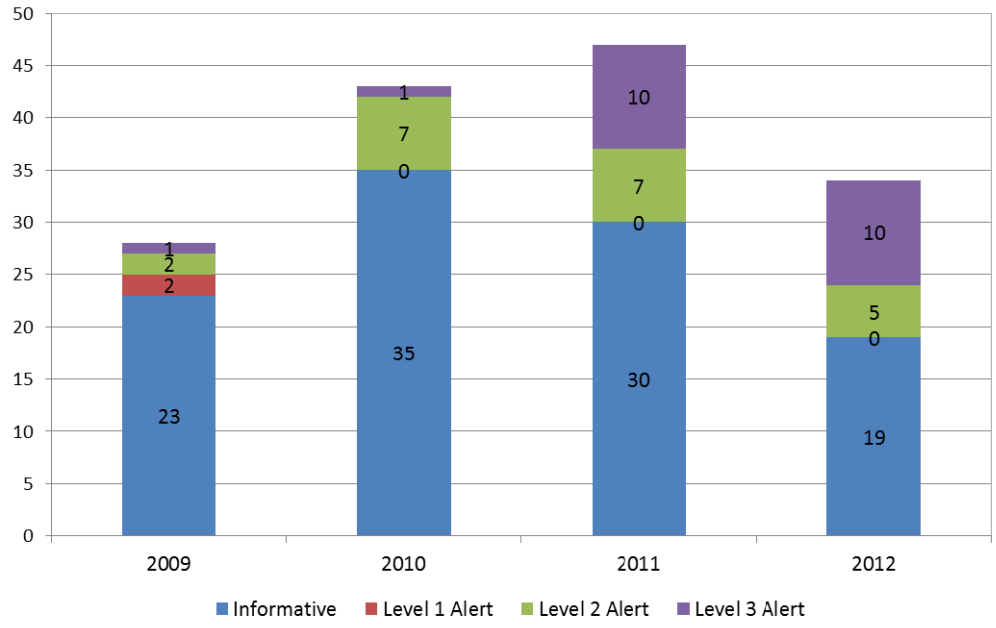
Table 5 – Output communications sent by the National Early Warning System 2009-2011 – number and percentage.

	2009		2010		2011		2012	
	No	%	No	%	No	%	No	%
Informative	23	82.2	35	81.4	30	63.8	19	55.9
Level 1 Alert	2	7.1	0	0.0	0	0.0	0	0.0
Level 2 Alert	2	7.1	7	16.3	7	14.9	5	14.7
Level 3 Alert	1	3.6	1	2.3	10	21.3	10	29.4
Total	28	100.0	43	100.0	47	100.0	34	100.0

Compared to 2011, Informatives notifications were down (-11), and Level 2 Alerts were down by 2.

Output communications: comparison 2009-2012

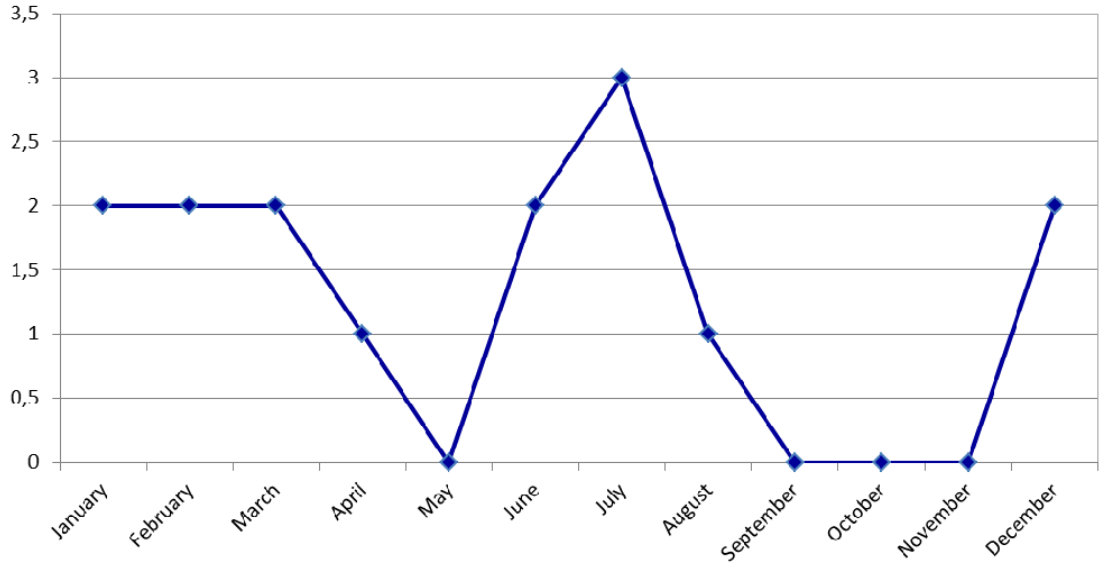
Graph 9 – Output communications sent by the National Early Warning System in 2009-2010-2011-2012 – number.



Main phenomena notified via Alerts

In 2012 ,15 Alerts were activated: 5 Level 2 Alerts and 10 Level 3 Alerts. No Level 1 Alerts were activated. The majority of Alerts (4) concerned acute intoxications and the identification of new molecules belonging to the class of synthetic cannabinoids; 3 Alerts concerned deaths and infections from *Bacillus anthracis*, among European heroin users; 2 Alerts included new intoxications in Italy and the identification of synthetic cathinones in seized materials; another 2 Alerts recorded deaths and acute intoxications following use of opiates. Lastly, 4 Alerts regarding: one case of acute intoxication in Rome after taking methoxetamine and identification of the molecule in seized material; one case of severe intoxication from 6-APB; numerous cases of death and acute intoxication recorded in Europe which can be related to the use of the molecule 5-IT and recordings in Europe of numerous deaths which can be related to the molecule 4-methamphetamine (4-MA).

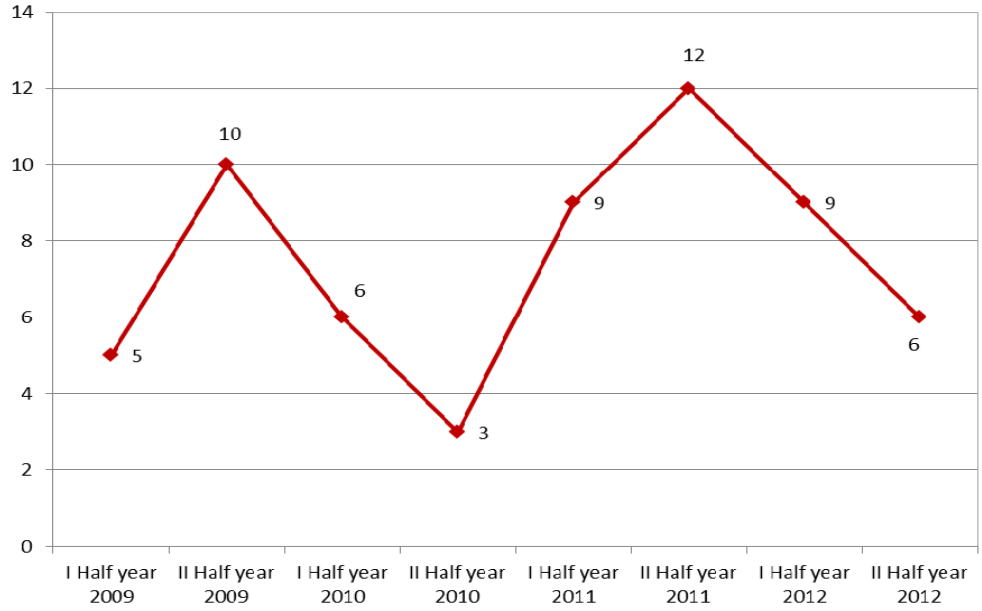
Graph 10 – ALERTS sent by the National Early Warning System during 2012, according to month – number.



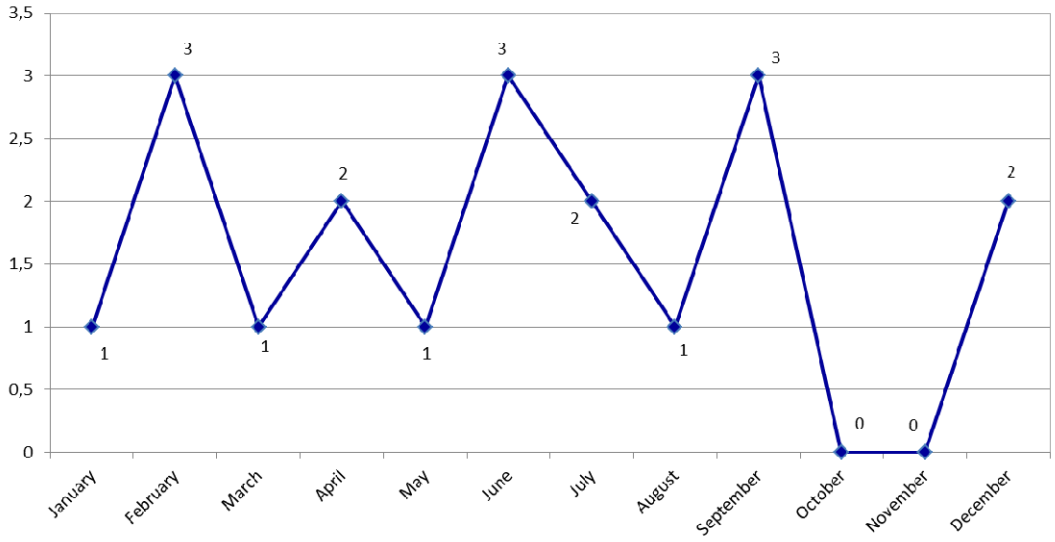
The following graph provides the trend of Alerts activated by month from 2009 to 2012.

Trend of Alerts 2009-2012

Graph 11 – Trend of Alerts activated for each month from 2009 to 2012 – number.



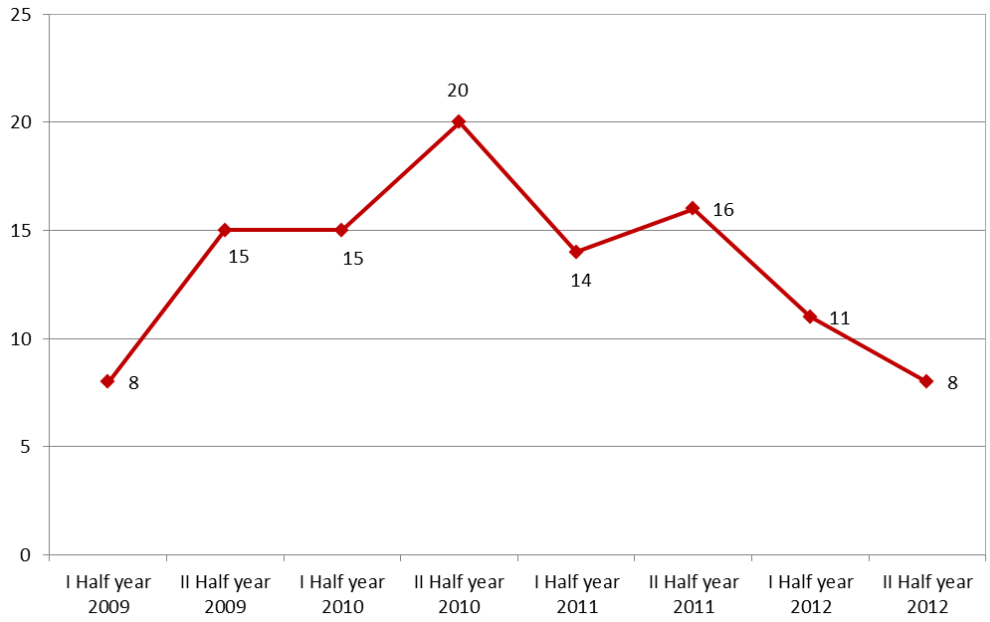
Graph 12 – INFORMATIVES communications sent by the National Early Warning System during 2012, according to month – number.



Trend of Informatives notices: 2009-2012

The comparison with previous years illustrates that in 2012 there were 4 fewer informatives communications than 2009 (23), 16 fewer than 2010 (35) and 11 fewer than 2011. The following graph provides the trend of Informatives notices activated by month from 2009 to 2012.

Graph 13 – Trend of Information notices activated for each month from 2009 to 2012 – number.



3.3 Reporting Form

Via Reporting Forms, and by means of the National Focal Point, the Warning System sends notifications to the European Monitoring Centre on the appearance of new molecules, identified for the first time in the Italian territory. In 2012 there were 17 notifications sent via Reporting Forms: 14 related to synthetic cannabinoids, 1 related to phenethylamine and 2 related to a case of acute intoxication following use of methoxetamine and its identification in a sample following a drugs seizure.

17 Reporting Forms sent to the EMCDDA

Figure 10a – Example of Reporting Form sent in 2012 by the National Early Warning System to the European Monitoring Centre regarding a synthetic cannabinoid JWH-307 – Page 1, Details.

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EUROPOL

REPORTING FORM FOR A NEW PSYCHOACTIVE DRUG

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

www.emcdda.eu.int

This section should be filled in by Europol or EMCDDA

Transmitted by Europol ☐ Transmitted by EMCDDA ☐

Ref. n°: Date of transmission:

The following sections should be filled by the Europol National Units (ENU) or REITOX National Focal Points (NFP) based on the information available and their respective competences

1. Member State: **ITALY**

Ref. n°: Date: **July 29th 2012**

Reporting authority: **NFP at the Department for Antidrug Policies**

ENU ☐ REITOX ☒

2. Chemical name: [5-(2-fluorophenyl)-1-pentylpyrrol-3-yl]-naphthalen-1-ylmethanone

Other name(s): **JWH-307**

Street name(s):

3. Source of information (fill one or more as appropriate)

Seizure(s) ☒ Specify amount (weight, number of tablets, etc.): **1 pack of a pot pourri labelled as "Blaze" and containing 3 g of herbal blend**

Seizing authority: **Carabinieri of Muggia (Trieste), Italy**

Date: **February 2012** Place: **Valico di Rabuiese, Muggia (Trieste)**

Biological sample(s)[1] ☐ Specify type:

Identifying authority:

Date: Place:

Collected sample(s)[2] ☐ Specify amount (weight, number of tablets, etc):

Collecting authority:

Date: Place:

Other substances present (if more than one case, specify for which one):

Psychoactive ingredients:
Other ingredients:

Figure 10b – Example of Reporting Form sent in 2012 by the National Early Warning System to the European Monitoring Centre regarding a synthetic cannabinoid JWH-307 – Page 2, Images.

4. Physical description (in case of seizure/collection)

Form: powder ☐ tablet ☐ capsule ☐ liquid ☐ other ☒
(specify): **herbal blend**

Colour:

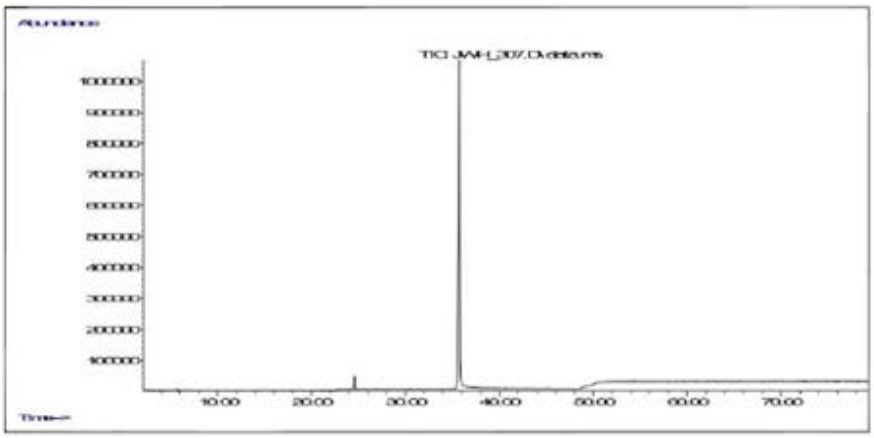
Dosage unit: weight: **3 g (reported on the label)** diameter: shape:
logo/markings: **see Figure 1**

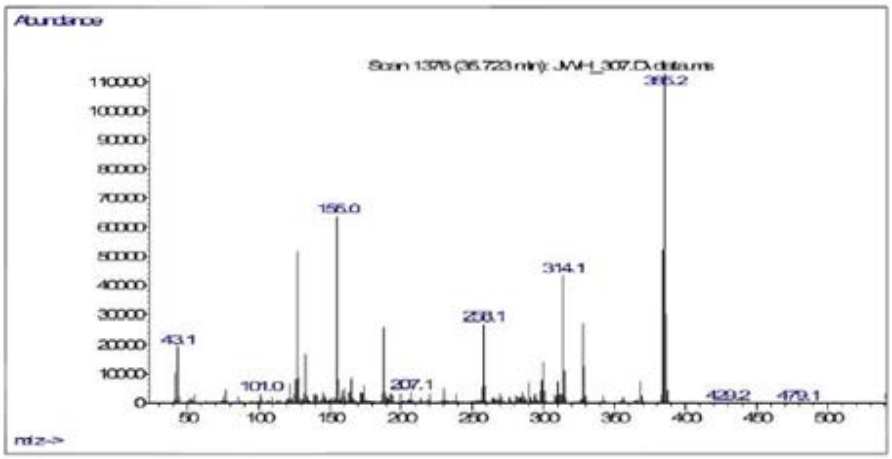
Figure 1 - Front and back of the pot pourri pack labelled as "Blaze" resulted to contain the synthetic cannabinoid JWH-307 (*Source: Scientific Investigation Group, Carabinieri of Parma*).

Figure 10c – Example of Reporting Form sent in 2012 by the National Early Warning System to the European Monitoring Centre regarding a synthetic cannabinoid JWH-307 – Page 3, Analytical information.

GC-MS analyses to identify JWH-307 have been performed by a Forensic Toxicology laboratory (Dipartimento di Prevenzione - A.S.S. n.1 Triestina) and results were confirmed by LC-HRMS by the Scientific Investigation Group, Carabinieri of Parma.

Below is reported the GC-MS analysis of the product:





Source: Scientific Investigation Group, Carabinieri of Parma.

Figure 10c – Example of Reporting Form sent in 2012 by the National Early Warning System to the European Monitoring Centre regarding methoxetamine – Page 3, Clinical information.

10. Effects in man

Objectively observed:

On February 2012, a 27 years old male was admitted to an emergency department in Rome.

At admission, the patient was tachycardic (HR 120 bpm), confused, hallucinated and severely agitated; diazepam was administered i.v.

By October 2011, he was treated with valproic acid, risperidone and quetiapine for a psychosis.

The day after admission, a treatment with midazolam 15 mg/day, delorazepam 7 mg/day and valproic acid 400 mg/day was started: subsequently, the delorazepam dosage was increased up to 20 mg/day and haloperidol was added.

The patient referred the consumption by snorting of half of a package. The package was labelled as methoxetamine (2-(3-Methoxyphenyl)-2-(ethylamino)cyclohexanone) purchased on Internet (Figure 1). He also referred the oral assumption of an undefined amount of dextromethorphan ("Aricodil tosse", dextromethorphan bromidrate).

Toxicological analyses performed by the Laboratory of Toxicology, "San Matteo" Hospital of Pavia, by means of GC-MS and LC-MS/MS on urine and serum samples and on a residue of the product consumed by the patient, resulted positive for methoxetamine. Urine resulted positive also for methorphan.

Methoxetamine analytical standard was not available. However, through the product consumed by the patient, it was possible to estimate a concentration of methoxetamine of 167 mcg/ml in urine and 0,2 mcg/ml in serum.

Subjective (described by users):

11. Context of use

User group(s):

Setting(s):

Availability at consumer level:

12. Indication on possible risks:

Health (individual):

Public health:

Social:

13. In case of production: large-scale ☐ small scale ☐ unknown ☐

Has any form of organised crime been detected: yes ☐ no ☐

3.4 Other activities

The network

Compared to 2011, the number of level II collaborating centres increased by 23.7%, from 59 to 73 centres (in 2009 there were 30 centres). This helped increase the visibility and effectiveness of the System nationally and helped increase the number of notifications by the input units.

23.7% increase of Level II Collaborating Centres over 2011

Reference materials

With collaboration of the Superior Health Institute and the Department of Addiction of Verona Local Health Unit 20, 36 analytical standards were sent to collaborating centre laboratories of the Warning System. Molecules for which analytical standards were provided were for 3-(1-naphtoyl)indole analogues: JWH-007, JWH-018, JWH-016, JWH-019, JWH-073, JWH-081, JWH-098, JWH-122, JWH-200, JWH-210, JWH-398 and AM-2201; for 3-phenylacetylindole analogues: JWH-203, JWH-250, JWH-251, JWH-302, RCS-8, WIN 48,098; for 3-benzoylindole analogues: AM-694, RCS-4, AM-2233; for 2-amino-1-phenyl-1-propanone analogues: Mephedrone, Methcathinone, Metamfepramone, N-Ethylcathinone, Methedrone (bk-PMMA), Flephedrone, 3,4-dimethylcathinone (3,4-DMMC), 4-methyl-N-ethylcathinone (4-MEC), Buphedrone, Pentedrone, Methylone (β-keto-MDMA), Ethylone (β-keto-MDEA), Butylone (β-keto-MBDB), Pentylone (β-keto-MBDP), Methylenedioxypyrovalerone (MDPV); others: CP 47,497, CP 47,497 C8-analogue, 4-Fluoroamphetamine, MDAI.

Distribution is by courier; the standards were fractionated in 100 ng/ml solutions (1 ml vials) and returned in kits together with the analysis certificates to the laboratories which requested relevant authorisations of the Ministry of Health for procuring the standards from the Superior Health Institute. Via the acquisition of the reference standards and the sharing of the analytical data, the capacity of the laboratories to identify new molecules has improved, with a corresponding increase of the specificity, sensitivity and promptness of the Warning System. As a consequence it has also been possible to reduce diagnosis times at clinical facilities as well as the time of inclusion in Table 1 of DPR 309/90 of new molecules found to be harmful to the health of the population of users.

Instruments for updating

In order to keep the input/output network and collaborations with Italian and overseas partners continually updated, the National Warning System has continued to use other instruments differentiated according to the purpose, target and specificity of the content. A summary description of such instruments as provided below.

- NE.W.S. Activity Report: NEWS The National Early Warning System Activity Report is an instrument of summary and proliferation for Collaborative Centres of the System, for keeping them continually informed on the most recent activities and acquisitions and to summarise the activities relating to the reference period. The initiative facilitates circulating information within the network periodically, giving the addressee the opportunity to connect to the original sources for any potential further detail. The Report is bimonthly.

A bimonthly review

Figure 11 – Examples of NEWS Activity Reports generated and sent by the National Early Warning System to the network of Collaborating Centres and, via the National Focal Point, to the European Monitoring Centre.

Participation on 5 international panels and in 10 national events for the promotion of the System

- Presentation at international congresses and events: during 2012 the management and operations and the activity data of the Warning System were presented at various national and international meetings, in order to share the information collected and promote awareness of the System. The following is a list of the European and international events where representative members of the System participated:

  - G. Serpelloni, C. Rimondo. Drugs online and web monitoring. Oral presentation. 16th National Congress of the Italian Toxicology Society – Toxicology in the globalisation era: safety of use and new markets 23 March 2012, Giardini Naxos (ME)
  - D Lonati, E Buscaglia, S Vecchio, A Giampreti, VM Petrolini, M Mazzoleni, F Chiara, M Aloise, L Manzo, A Valli, L Rocchi, P Papa, L Rolandi, C Rimondo, C Seri, G Serpelloni, CA Locatelli. Cannabinoids and synthetic cathinones: clinical issues. Oral presentation. 16th National Congress of the Italian Toxicology Society – Toxicology in the globalisation era: safety of use and new markets 23 March 2012, Giardini Naxos (ME)
  - CA Locatelli, D Lonati, E Buscaglia, S Vecchio, A Giampreti, VM Petrolini, M Mazzoleni, F Chiara, M Aloise, C Rognoni, L Manzo, A Valli, L Rocchi, L Rolandi, P Papa, C Rimondo, C Seri, G Serpelloni. New abused substances: clinical data in Italy. Oral presentation. 16th National Congress of the Italian Toxicology Society – Toxicology in the globalisation era: safety of use and new markets 23 March 2012, Giardini Naxos (ME)
  - G. Serpelloni, C. Rimondo. Best practice in drug prevention and the role of the National Early Warning System. Presentation at “The ever-changing world of psychoactive drugs”. 12-13 March 2012, Budapest, Hungary
  - G. Serpelloni, E. Simeoni, T. Macchia, C. Locatelli, C. Rimondo. Four oral presentations. Reitox workshop. Exchange on data collection challenges related to new psychoactive substances user. 19-20 April 2012, Budapest (Hungary)
  - G. Serpelloni, E. Simeoni, T. Macchia, C. Locatelli, C. Rimondo. Updates from the Italian Early Warning System. 12th Annual meeting of the Reitox Early-warning system network. 24–25 May 2012, Lisbon.
  - G. Serpelloni, C. Rimondo, C. Seri, T. Macchia, C. Locatelli, D. Lonati, Giampreti, V. Petrolini, S. Vecchio, C. Rognoni, E. Buscaglia, M. Mazzoleni, L. Manzo, P. Papa, A. Valli. Synthetic cannabinoids intoxication cases in Italy: analytical identification and clinical findings. Poster presented at the "2012 NIDA International Forum - New and Emerging Psychoactive Substances: Second Interdisciplinary Forum" 8-11 June 2012, Palm Springs (CA, USA) (Allegato 1).
  - G. Serpelloni, C. Locatelli, C. Rimondo, T. Macchia. The National Early Warning System. Presentation at Module 5 – Epidemiological monitoring and warning system, by The National School on Addiction, 13 April 2012, Rome.
  - Rimondo C. The National Early Warning System of the Department of Anti-Drug Policy – Organisational issues. SAR- NEUTRAVEL project. Workshop on the National Early Warning System Turin, Italy. 17 December 2012.
  - Locatelli C. Warnings, clinical cases and role of the emergency facilities. SAR-NEUTRAVEL project. Workshop on the National Early Warning System Turin, Italy. 17 December 2012.
  - Seri C. New drugs and new analytical frontiers. SAR-NEUTRAVEL project. Workshop on the National Early Warning System Turin, Italy. 17 December 2012.
  - Rimondo C. Integration of the Regional Warning System into the National Warning System. SAR- NEUTRAVEL project. Workshop on the National Early Warning System Turin, Italy. 17 December 2012.
  - Sistema Nazionale di Allerta Precoce per le Droghe - National Early Warning System for Drugs – N.E.W.S. (Poster) presented at the 3rd International Congress "ADDICTION: new evidences from Neuroimaging and Brain Stimulation”- Palazzo della Gran Guardia, 13

November 2012, Verona.

- Serpelloni G. National Early Warning System: operating functions, institutional collaboration and information flows. Presentation at Antidotes In Depth 2012 Clinical Toxicology, Substances Of Abuse And Chemical Emergencies - Continuing Education Course In Clinical Toxicology. Pavia, 19-21 September 2012.
- Rimondo C. The system activities: organization and coordination, data base, web monitoring and future developments. Presentation at Antidotes In Depth 2012 Clinical Toxicology, Substances Of Abuse And Chemical Emergencies - Continuing Education Course In Clinical Toxicology. Pavia, 19-21 September 2012.
- Macchia T. Unusual modalities and unawareness of assumption. Presentation at the conference, Antidotes In Depth 2012 Clinical Toxicology, Substances Of Abuse And Chemical Emergencies - Continuing Education Course In Clinical Toxicology. Pavia, 19-21 September 2012.
- Locatelli C, Papa P. Substances of abuse and the road code. Presentation at Antidotes In Depth 2012 Clinical Toxicology, Substances Of Abuse And Chemical Emergencies - Continuing Education Course In Clinical Toxicology. Pavia, 19-21 September 2012.
- Locatelli C. Drug internauts and the hazards of the network. Presentation at Addiction day. Lugano, 26 September 2012.
- Lonati D. Toxicology in emergency: clinical aspects Presented at SIMEL Regional Congress. Pavone Canavese (TO), 27 September 2012.
- Lonati D. Substance Abuse and the Rapid Warning System. Presented at SIMEL National Congress. Salerno, 02 October 2012.
- Locatelli C. Clinical-toxicological aspects of new abused substances. Presented at V Giornata Pesarese on the Study of affective disorders: from scientific basis to clinical practice Pesaro, 05 October 2012.
- Lonati D. Synthetic cannabinoids and cathinones: clinical aspects. Presented at SIMEU National Congress. Rimini, 20 October 2012.
- Locatelli C. Substance abuse in paediatric age: 15 years of experience of the Pavia Poison centre. Presented at SIMEU National Congress. Rimini, 20 October 2012.
- Lonati D. New abused substances: clinical data in Italy. Presented at SIMEU National Congress. Rimini, 20 October 2012.
- Lonati D. Emergency toxicology. Presented at SIMEUP National Congress X. Catania, 26 October 2012.
- Lonati D. New abused substances and the rapid warning system Presented at New drugs and behavioural addictions. Varese, 05 December 2012.

- Scientific publications: in 2012 were also made numerous scientific publications that highlight the activities and results of the System. The following are articles published on the subject.

12 scientific publications, 4 chapters of books and 4 abstracts

  - Gottardo R, Chiarini A, Dal Prà I, Seri C, Rimondo C, Serpelloni G, Armato U and Tagliaro F. Direct screening of herbal blends for new synthetic cannabinoids by MALDI-TOF MS. J. Mass. Spectrom. 2012, 47, 141–146.
  - Eloisa Liotta, Rossella Gottardo, Catia Seri, Claudia Rimondo, Ivan Miksik, Giovanni Serpelloni, Franco Tagliaro. Rapid analysis of caffeine in “smart drugs” and “energy drinks” by microemulsion electrokinetic chromatography (MEEKC). Forensic Science International. Available online 10 April 2012. In Press, Corrected Proof.
  - Giovanni Serpelloni, Elisabetta Simeoni, Silvia Zanone, Teodora Macchia, Carlo Locatelli, Claudia Rimondo and Catia Seri. Italy - early warning system. In Early Warning System - National Profiles, pages 79-84, EMCDDA, Lisbon, May 2012.
  - G. Serpelloni, C. Rimondo, C. Burgarella. Efficacy of monitoring and countering high-risk illegal rave parties via the Internet: strategies, methods and results of early prevention and identification of the National Warning System. Italian Journal on Addiction. Vol 2, n° 1-2 (2012).
  - L. Leone, G. Serpelloni, C. Rimondo, C. Seri. Bacillus anthracis infection in drug addicts. The use of narcotic substances and associated infectious diseases. Giovanni Serpelloni, Mario Cruciani. October 2012.
  - C. Seri, L. Leone, C. Rimondo, G. Serpelloni. New drugs and behaviour at risk. The Use of narcotic substances and associated infectious diseases. Giovanni Serpelloni, Mario Cruciani. October 2012.
  - Gottardo R, Bertaso A, Pascali J, Sorio D, Musile G, Trapani E, Seri C, Serpelloni G, Tagliaro F. Micellar electrokinetic chromatography: a new simple tool for the analysis of synthetic cannabinoids in herbal blends and for the rapid estimation of their logP values. J Chromatogr A. 2012 Dec 7;1267:198-205. doi: 10.1016/j.chroma.2012.08.085. Epub 2012 Sep 13.
  - Chap: IV.1.1. Warning System, 2011 activity. 2012 Annual report to the Parliament on the use of narcotic substances and drug addiction in Italy. Data relating to 2011 and the first half of 2012 – 2012 analysis. Anti-Drug Policy Department August 2012
  - Chap: IV.1.2. Sale of substances on the web Results of monitoring of the network. In 2012 Annual report to the Parliament on the use of narcotic substances and drug addiction in Italy. Data relating to 2011 and the first half of 2012 – 2012 analysis. Anti-Drug Policy Department August 2012
  - Chap: IV.1.3. Prevention of illegal rave parties. 2012 Annual report to the Parliament on the use of narcotic substances and drug addiction in Italy. Data relating to 2011 and the first half of 2012 – 2012 analysis. Anti-Drug Policy Department August 2012
  - Chap: IV.1.4. Joint methods of control and prevention. 2012 Annual report to the Parliament on the use of narcotic substances and drug addiction in Italy. Data relating to 2011 and the first half of 2012 – 2012 analysis. Anti-Drug Policy Department August 2012
  - VM Petrolini, E Keser, S Vecchio, A Giampreti, D Lonati, C Rognoni, S Bigi, L Manzo, CA Locatelli. GHB acute intoxication in Italy: recreational drug intoxication or medication overdose? Clinical Toxicology 2012; 50: 334
  - F Chiara, A Giampreti, S Vecchio, D Lonati, VM Petrolini, M Aloise, E Buscaglia, M Mazzoleni, S Siri, C Rognoni, L Manzo, C Locatelli. Drug abuse in paediatric age: increasing trend in the 15 years experience of Pavia Poison Centre. Clinical Toxicology 2012; 50: 295-296
  - D Lonati, E Buscaglia, P Papa, V Petrolini, S Vecchio, A Giampreti, L Rocchi, F Chiara, M Aloise, C Rognoni, L Manzo, G Serpelloni, C Rimondo, T Macchia, CA Locatelli. Prevalence of intoxication by new recreational drugs: preliminary data by the Italian network of emergency departments involved in the national early identification system.

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- B Brejcha, A Cunningham, H Donner, R Kasemäe, I Kipke, C Locatelli, L Okruhlica, J Perälä, C Spiliopoulou, B Stålenkrantz, A Talu, J Tuusov, M Vassilev. Fentanyl In Europe Emcdda Trendspotter Study. EMCDDA Expert meeting report; 2012 ,9-10 October pages: 3-10
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- D Lonati, E Buscaglia, P Papa, V Petrolini, S Vecchio, A Giampreti, L Rocchi, F Chiara, M Aloise, C Rognoni, L Manzo, G Serpelloni, C Rimondo, T Macchia, C Locatelli. Prevalence of intoxication by new recreational drugs: preliminary data by the Italian network of emergency departments involved in the national early identification system. 7th European Congress on Emergency Medicine (EuSEM 2012) Antalya, Turkey. October, 3-6 2012
- F Chiara, A Giampreti, S Vecchio, D Lonati, VM Petrolini, M Aloise, E Buscaglia, M Mazzoleni, C Rognoni, L Manzo, C Locatelli. Substance abuse in paediatric age: 15 years of experience of the Pavia Poison Centre. 16th National SITOX Congress. Toxicology in the era of globalisation: safety of use and new markets. Giardini Naxos (ME), Italy, 21-23 March 2012.
- C Locatelli, A Giampreti, M Mazzoleni, S Vecchio, D Lonati, V Petrolini, S Bigi, E Buscaglia, C Rognoni, L Manzo. Operating Guidelines for diagnosis, treatment and rehabilitation of cocaine addicts. Presidency of the Council of Ministers, Minister for international cooperation DPA, 2012 Chap 2.2 pages:128-135

Poster presented at the 2012 NIDA International Forum – New Emerging Psychoactive Substances: Second Interdisciplinary Forum – 8-11 June 2012, Palm Springs, California.

PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Ministro per la Cooperazione Internazionale e l'Integrazione
Dipartimento Politiche Antidroga
ITALIAN EARLY WARNING SYSTEM

Synthetic cannabinoids intoxication cases in Italy: analytical identification and clinical findings

2012 NIDA International Forum – New and Emerging Psychoactive Substances: Second Interdisciplinary Forum
June 8-11, 2012 Palm Springs, California, USA

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Background

According to EU directives, the Department for Antidrug Policies (DPA) of the Italian Presidency of the Council of Ministers actuated in 2006 the National Early Warning System (NEWS) aimed at detecting new psychoactive substances and at implementing actions to prevent health consequences related to their consumption (Figure 1-4). Since 2009, the NEWS detected several herbal blends sold as "incenses" in smart shops or via Internet. Numerous synthetic cannabinoids have been identified and some have been related to severe intoxications, as registered by the Pavia Poison Centre (PPC).

Figure 1 - Macrofunctioning of the Italian National Early Warning System

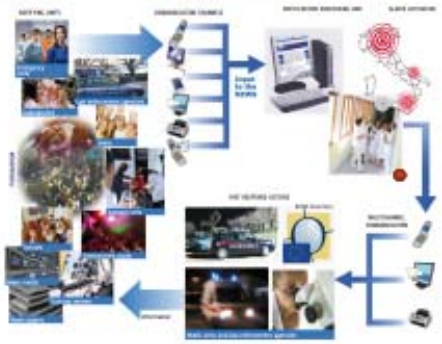


Figure 2 - Organizational structure of the Italian National Early Warning System

Figure 3 - Geolocation of the NEWS Collaborative Centres

Figure 4 - Output of the Italian National Early Warning System

Methods

Synthetic cannabinoids were identified in blood/serum samples of intoxicated patients registered by the PPC from January 2010 to October 2011, and in residues of consumed products using liquid chromatography-tandem mass spectrometry. Signs and symptoms of cases are described.

Results

29 cases of severe intoxications related to patients (14-55 years old) smoking herbal blends with different commercial names, have been registered (Figure 5). Main clinical manifestation observed are summarized in Graphic 1.

Figure 5 - 29 intoxications cases related to the consumption of synthetic cannabinoids with admission to emergency departments

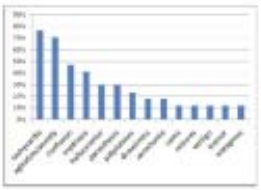
LC-MS/MS analysis detected the following synthetic cannabinoids:

Synthetic cannabinoid	N intoxications
JWH-018	11
JWH-122	9
JWH-081	2
JWH-250	3
JWH-018/JWH-073	1
N/A	3
Total	29

Patients received symptomatic treatment; no sequelae were observed.

Clinical manifestation	N
Tachycardia	16
Agitation	12
Confusion	11
Mydriasis	10
Coma	4
Seizures	2
Hallucinations	2

Graphic 1 - Main clinical manifestations for synthetic cannabinoids consumption



Conclusion

The identification of clinical cases and the analytical confirmation contributed to identify health risks related to synthetic cannabinoids consumption. That was crucial to ascertain the relationship between substances and clinical effects and to allow the DPA and the Ministry of Health to include these new molecules into the list of controlled substances and to adopt contrast measures to stop herbal blends sale in Italy.

Reference

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G. Serpelloni, C. Rimondo, Sistema di Allerta Precoce e Risposta Rapida per le Droghe. Drug early warning system, 2008.
G. Serpelloni, E. Simeoni, S. Zamboni, T. Macchia, C. Locatelli, C. Rimondo, C. Seri, Italy - Early warning system, in EMCDDA - Early warning system - National Profiles, 2012.

4. Results

The results of the National Early Warning System are presented according to the following key aspects under observation:

1. New unknown substances (in police seizures, biological samples of patients, samples purchased online or from commercial concerns)
2. Unanticipated and atypical symptoms after use
3. Web monitoring for preventing drugs being on offer
4. Anomalous batches of classic drugs (variations of the percentages of active substance)
5. New cutting agents/adulterants
6. New methods of use
7. Drug-related acute intoxication or clusters of deaths
8. Variations of the incidence of drug related infections (HIV, HBV, HCV, TBC, MST).

4.1. New unknown substances (in police seizures, biological samples of patients, samples purchased online or from commercial concerns)

Since 2009, 237 molecules have been intercepted by the National Early Warning System (Table 6), including:

- 70 synthetic cannabinoids
- 35 synthetic cathinones
- 51 phenetylamines
- 4 piperazine, 8 tryptamine, 5 ketamine and analogues, 5 natural substances, 10 active principles of drugs, 2 fentanyl, 7 oppioid, 2 other stimulants, 2 other anesthetics, 1 pesticide, 2 precursors, 6 azepane-like, 3 PCP derivatives, 3 tropane derivatives, 1 steroid and other 20 molecules of various kinds.

The notifications related to these molecules came from the European Monitoring Centre in Lisbon and from Italian laboratories and centres belonging to the National Early Warning System.

Table 6 – List of molecules notified to the National Early Warning System since 2009.

No	Name	Month/Year
1	Quetiapine	Dec-12
2	4-methyl-phendimetrazine	Dec-12
3	4-methylaminorex-4-methyl derivative	Dec-12
4	25N-NBOMe	Dec-12
5	25G-NBOMe	Dec-12
6	25E-NBOMe	Dec-12
7	2C-N	Dec-12
8	2C-G	Dec-12
9	UR-144 N-(5-chloropenthyl) derivative	Dec-12
10	25B-NBOMe	Dec-12
11	4-chloroamphetamine (4-CA)	Dec-12
12	Isobutanoylphentanyl	Dec-12
13	4-HTMPIPO	Nov-12
14	JWH-018 quinoline carboxamide	Nov-12
15	AB-005 azepan isomer	Nov-12
16	AB-005	Oct-12
17	AM-2201 Imidazolecarboxamide analogue	Oct-12
18	AKB-48F	Sep-12
19	AM-1248	Sep-12
20	N-Ethylketamine	Sep-12
21	5-(2-Aminopropyl)-2,3-dihydro-1H-indene	Sep-12
22	4-hydroxyamphetamine	Sep-12
23	3-methylmethcathinone (3-MMC)	Sep-12
24	2-MeO-Ketamine	Aug-12
25	Pyrazolam	Aug-12
26	4-AcO-DPT	Aug-12
27	AH-7921	Aug-12
28	JWH 018 N-(5-chloropentyl) derivative	Aug-12
29	JWH 018 N-(5-bromopentyl) derivative	Aug-12
30	1-(5-Fluoropentyl)-3-(2-ethylbenzyl)indole	Jul-12
31	1-(5-Fluoropentyl)-3-(2-methylbenzoyl)indole	Jul-12
32	JWH-122 pentenyl 2-methylindole derivative	Jul-12
33	JWH-122 pentenyl derivative	Jul-12
34	MAM-2201 chloropentyl analogue	Jul-12
35	3,4-Methylenedioxy-N,N-dimethylamphetamine	Jul-12
36	JWH-018 carboxamide derivative	Jul-12
37	APICA	Jul-12
38	25I-NBOMe	Jun-12
39	MPHP	Jun-12
40	STS-135	Jun-12
41	5-MeO-MET	Jun-12
42	4-HO-DPT	Jun-12
43	UR-144(-2H)	Jun-12
44	Zopiclone	Jun-12

45	5-(2-Aminopropyl)indole (5-IT)	Jun-12
46	APINACA	May-12
47	2,4,5-TMMC	May-12
48	1-Phenyl-2-(piperidin-1-yl)butan-1-one	May-12
49	4-AcO-DALT	Apr-12
50	LSD	Apr-12
51	A-796,260	Apr-12
52	25D-NBOMe	Apr-12
53	Benzocaine	Apr-12
54	5FUR-144	Mar-12
55	3-MeO-PCP	Mar-12
56	4-Fluoroephedrine	Mar-12
57	1-ethynyl-1-cyclohexanol (ECX)	Mar-12
58	4-Amino-3-phenylbutanoic acid (Phenibut)	Mar-12
59	MAM-2201	Mar-12
60	2-Fluoro-N-methyl-amphetamine - (2-FMA)	Mar-12
61	6-APDB	Mar-12
62	5-APDB	Mar-12
63	Alpha-methyltryptamine (AMT)	Mar-12
64	JWH-370	Feb-12
65	UR-144	Feb-12
66	MDMA	Feb-12
67	URB754	Feb-12
68	1-(Thyophen-2-yl)propan-2-amine	Feb-12
69	Clobenzorex (o-chlorobenzylamphetamine)	Feb-12
70	Phenylpropanolamine (PPA)	Feb-12
71	2-Fluoroamphetamine	Feb-12
72	1-(3-Methylbenzylpiperazine)	Feb-12
73	3-Fluoro-iso-methcathinone (3-FiMC)	Feb-12
74	Trans-CP 47,497-C8, homologue	Feb-12
75	1-Cyclohexyl-x-methoxybenzoyl	Feb-12
76	N-Propylamphetamine	Feb-12
77	3-(p-methoxybenzoyl)-N-methylindole	Feb-12
78	N-hydroxy MDA (MDOH)	Feb-12
79	Poppers (isopropyl nitrite)	Jan-12
80	HU-331	Jan-12
81	Scopolamine	Dec-11
82	Atropine	Dec-11
83	1-Phenyl-1-propanamine	Dec-11
84	AM-694 - chloro derivative	Dec-11
85	α-Pyrrolidinobutiophenone (α-PBP)	Dec-11
86	3-Amino-1-phenylbutane (3-APB)	Dec-11
87	AM-2232	Dec-11
88	Etizolam	Dec-11
89	Ethylphenidate	Nov-11
90	Camfetamine	Nov-11
91	JWH-022	Nov-11
92	4-methylbuphedrone(4-Me-MABP)	Nov-11

93	WIN 55,212-2	Nov-11
94	AM-679	Nov-11
95	CP 47,497-C8-homologue	Nov-11
96	Propoxyphene	Nov-11
97	Paracetamol	Oct-11
98	bk-MDDMA	Oct-11
99	Benzylpiperidine	Oct-11
100	4-EMC	Oct-11
101	Dexomorphine	Oct-11
102	4-BMC (Brephedrone)	Sep-11
103	Isopentedrone	Sep-11
104	WIN 48,098 (Pravadoline)	Sep-11
105	Pyrovalerone	Sep-11
106	Dipipanone	Sep-11
107	Sildenafil	Aug-11
108	Methylone (MDMCAT; MDMC; bk-MDMA)	Aug-11
109	4-fluoroamphetamine (4-FA)	Aug-11
110	Methamphetamine	Aug-11
111	N-Ethylbuphedrone	Aug-11
112	Org-29647	Aug-11
113	Org-27569	Aug-11
114	Org-27759	Aug-11
115	AM-2233	Aug-11
116	JWH-307	Aug-11
117	Caffeine (in heroin)	Aug-11
118	Benzoin isopropyl ether (BIE)	Jul-11
119	Pseudoephedrine	Jul-11
120	Nandrolone	Jul-11
121	JWH-412	Jul-11
122	JWH-387	Jul-11
123	Phenazepam	Jul-11
124	Ayahuasca (NN-DMT)	Jul-11
125	Ayahuasca (Harmine)	Jul-11
126	4-APB	Jun-11
127	6-APB	Jun-11
128	RCS-4(C4)	Jun-11
129	Ostarine	Jun-11
130	JWH-122 fluoropentyl derivative	Jun-11
131	2C-C-NBOMe	Jun-11
132	Rosin in hashish	Jun-11
133	OMMA	Jun-11
134	Methanandamide	May-11
135	AM-1220-azepane-derivative	May-11
136	AM-1220	May-11
137	5-HTTP	May-11
138	JWH-007	May-11
139	Tropicamide	May-11
140	Diazepam	Apr-11
141	(2-methoxyphenyl)(1-pentyl-1H-indol-3-yl)methanone	Apr-11

142	N-Ethylamphetamine	Apr-11
143	α-pyrrolidinopentiophenone (α-PVP)	Apr-11
144	DMMA	Apr-11
145	Methorphan	Mar-11
146	3-FMC	Mar-11
147	Derivative JWH-250	Mar-11
148	5-IAI	Mar-11
149	JWH-182	Mar-11
150	1-Pentyl-3-(1-adamantyl)indol	Feb-11
151	JWH-251	Feb-11
152	N,N-dimethylamphetamine	Feb-11
153	AM-2201	Jan-11
154	MPA	Jan-11
155	CRA-13	Jan-11
156	4-MeO-PCP	Jan-11
157	Desoxy-D2PM	Dec-10
158	5-APB	Dec-10
159	BMDB	Dec-10
160	BMDP	Dec-10
161	Arecoline	Nov-10
162	Dibutylone	Nov-10
163	MDPBP	Nov-10
164	3-MeO-PCE	Nov-10
165	3-(4-Hydroxymethylbenzoyl)-1-pentylindol	Nov-10
166	Methoxetamine	Nov-10
167	PMMA	Oct-10
168	JWH-019	Oct-10
169	JWH-203	Oct-10
170	3,4-DMMC	Oct-10
171	JWH-250	Oct-10
172	Desoxypipradrol	Oct-10
173	JWH-200	Sep-10
174	Buflomedil	Sep-10
175	Diltiazem	Sep-10
176	Etafedrine	Sep-10
177	JWH-210	Sep-10
178	Pentedrone (β-ethyl-methcathinone)	Sep-10
179	5-MeO-DPT	Sep-10
180	Pentylone	Sep-10
181	M-ALPHA	Sep-10
182	Naphyrone isomer	Aug-10
183	Variant C8 + C2 of CP-47,497	Aug-10
184	4MBC	Aug-10
185	MPPP	Aug-10
186	Butylone	Aug-10
187	MDPV	Aug-10
188	JWH-015	Jul-10
189	MPBP	Jul-10
190	JWH-122	Jul-10

191	AM-694	Jul-10
192	4-methylmethcathinone (4-MEC)	Jul-10
193	Buphedrone	Jul-10
194	JWH-073 methylderivative	Jul-10
195	Dimethocaine DMC	Jun-10
196	DMAA	Jun-10
197	iso-Ethcathinone	Jun-10
198	pFBT	Jun-10
199	Naphyrone	Jun-10
200	JWH-081	Jun-10
201	RCS-4 (JWH-018 analogue)	May-10
202	Fentanyl	May-10
203	4-FMA	Mar-10
204	Mephedrone (4-MMC)	Mar-10
205	Metamizole (Novalgin)	Mar-10
206	pFPP	Mar-10
207	MDAI	Mar-10
208	β-Me-PEA	Mar-10
209	N,N-dimethylpentylamine	Mar-10
210	N-benzyl-1-phenylethylamine	Mar-10
211	JWH-073	Feb-10
212	JWH-018	Feb-10
213	GHB	Jan-10
214	2C-B-BZP	Jan-10
215	Pregabalin	Dec-09
216	4-MA	Dec-09
217	JWH-200	Dec-09
218	3-FMA	Nov-09
219	Etaqualone	Nov-09
220	Metamfepramone	Nov-09
221	Flephedrone (4-FMC; 4-fluoromethcathinone)	Nov-09
222	Mitragynine (Mitragyna Speciosa)	Nov-09
223	Bromo-Dragonfly	Oct-09
224	Levamisole	Oct-09
225	Methedrone (bk-PMMA)	Oct-09
226	2-PEA	Oct-09
227	MDPV	Aug-09
228	DNP (2,4-dinitrophenol)	Aug-09
229	4-AcO-DMT	Aug-09
230	PMA	Jul-09
231	Pethidine/Demerol	Jul-09
232	Nortramadol (O-Desmethyltramadol)	Jun-09
233	Ketamine	Jun-09
234	mCPP	Jun-09
235	Piperonal	Jun-09
236	TMA-6	Jun-09
237	Carbaryl	May-09

From 2009 to today the National Early Warning System Collaborative Centres have notified the findings of analyses carried out on numerous samples of herbal blends marketed via the Internet or in the smart shops in the Italian territory and found to contain synthetic cannabinoids (Table 7).

Table 7 – List of commercial products and the synthetic cannabinoids identified in them between 2010 and 2012. Notifications to the National Early Warning System.

Commercial Name	Cannabinoid Identified	Commercial Name	Cannabinoid Identified	Commercial Name	Cannabinoid Identified
Genie	JWH-018	Blaze	JWH-018	Alesya Plus	JWH-081
N-Joy	JWH-018	Smoke	JWH-018	Orange Alesya New	JWH-081+AM-694
Spice Silver	JWH-018+JWH-073	Blaze	JWH-018	Lucy	JWH-081+JWH-019+AM-694
Spice Gold	JWH-018+JWH-073	Bonzai	JWH-018	Karma	JWH-210
Spice Gold Spirit	JWH-018+JWH-073	Bonzai Citrus	JWH-081	Orange Julia	JWH-081+AM-694
Spice Original Diamond	JWH-018+JWH-073	Creme Supreme Incense	JWH-250	Katy Plus	JWH-081
Spice Original Diamond Spirit	JWH-018+JWH-073	Gejnie	JWH-018	Orange Katy New	JWH-081+AM-694
Spice Tropical	JWH-018+JWH-073	Jamaica Spirit	JWH-081+JWH-250	Orange Darya New	JWH-081+AM-694
Spice Artic Synergy	JWH-018+JWH-073	King B	JWH-073+JWH-073 methyl derivative	Bonzai	JWH-122+JWH-018 (trace)
Amazonas	JWH-250	Original Diamond	JWH-073	Bonzai Summer Boost	unknown
Orange lilia	JWH-018+JWH-073	Original Diamond Spirit	JWH-073	Bonzai	JWH-122
Orange Oxana	JWH-073+delta-9-THC (trace)	Spice Artic Synergy	JWH-018+CP 47,497 (C8)	Blend Z	JWH-073; JWH-122; JWH-018; 1-butyl-3-(1-(4-methyl)naphtoyl)indole
Jamaican Gold	JWH-018	Spice Diamond	CP 47,497 (C8)	JWH-018 Powder	JWH-018
Jamaican Spirit	JWH-250+JWH-081	Spice Diamond Spirit	JWH-018	Unlabelled	JWH 250
Mojo	JWH-018	Spice Gold	CP 47,497 (C8)	Unlabelled	JWH 210
Infinity	JWH-073	Spice Tropical Synergy	JWH-018+CP 47,497 (C8)	Unlabelled	JWH 122
Bonzai	JWH-018	Yucatan Fire	JWH-018	Unlabelled	JWH 122
Sencation	JWH-073 methyl derivative	B 52 Plus Intensive Shot	JWH-250 + JWH-122	Smoked green powder	JWH-018 (in blood sample)
Bonzai Citrus	JWH-081	Ketama Gold	JWH-250	Atomic bomb	JWH-018 (in blood sample)
Afghan Incense	JWH-018	Jungle Mistic Incense	JWH-122	XXX Hurricane	RCS-4 (C4 homologue) RCS-4(o-isomer), JWH-073, JWH-018
Bonzai Winter Boost	JWH-250	Orange alesya new	JWH-122	Bonzai	JWH-122 (in blood sample)
New Jamaican Gold	JWH-081	Rasta Weed	JWH-073	Cannabis (reported)	JWH-122 (in blood sample)
Blaze	JWH-081	Katy Plus	JWH-081 and AM-694 (+trace of CBD; delta-9-THC <0.1%)	Test powder	AM-694
Blaze	JWH-250	Ketama Gold	JWH-122	Test powder	AM-679
Jamaican Spirit	JWH-200+JWH-081	Bonzai	JWH-081	Test powder	JWH-019
Forest Green	JWH-250+trace of JWH-122	Orange Darya New	JWH-081+JWH-073+AM-694	Test powder	JWH-081
Forest Green	JWH-122	Karma	JWH-210	Test powder	JWH-203
Intensive Shot	JWH-250	Katy Plus	JWH-081+AM-694	Test powder	JWH-250
Ketama Gold	JWH-250	Orange Alesya New	JWH-081+JWH-073	Test powder	WIN48098/ Pravadoline
Jungle Mistic Incense	JWH-122	Orange Julia	JWH-081	Test powder	WIN55212-2 mesylate
Jamaican Spirit	JWH-250	Orange Katy New	JWH-081+AM-694	Powder	CP47,497-(C8)
Start of Fire	JWH-250	Alesya Plus	JWH-081	Bonzai summer boost	JWH-210+AM-2201 + JWH-022

Bonzai	JWH-250	Lucy New	JWH-081	AM-HI-CO Oean Burst Red 2	JWH-073+JWH-018+JWH-122 (in serum)
Bonzai Citrus	JWH-018	Lucy	JWH-081+AM-694	Bonzai	JWH-122 (in serum)
Yucatan Fire	JWH-018+Vitamin E	Skunk mrk3 - Super strong fertiliser	JWH-073+JWH-250	Skunk mrk3 - Super strong fertiliser	RCS-4
Pineapple express - 1G - +18	RCS-4	Hurricane	RCS-4 (C4 homologue) RCS-4(o-isomer), JWH-073, JWH-018	Jamaican Gold Supreme	AM-2233
Blaze	JWH-307	Sintacaina	MAM-2201; benzocaine	Ocean burst	JWH-073+JWH-018+JWH-122 (in serum)
Ivory Wave	JWH-073+JWH-018+JWH-122 (in serum)				

4.2 The new drugs registered in Italy by the National Early Warning System

The new synthetic drugs

In recent years there has been a new phenomenon that has revolutionized youth trends, and not just with respect to the use of drugs. To traditional substances (cannabis, cocaine, heroin, etc..) the synthetic molecules, ie those prepared artificially in the laboratory have been added.
Some of these molecules are derived from the design of new potential products to therapeutic action, however, none has ever been progressed in phase of pharmaceutical development, while others are born specifically for use as drugs. Moreover, very often they are not available in literature toxicity data associated with the use of such substances. Therefore, the risk exists that not known and unexpected effects occur, including toxic effects, following their use, effects that, moreover, were actually found in many cases of poisoning caused to their consumption. The evolution of the phenomenon has led to the identification on the part of international organizations that play a regular monitoring of the supply of drugs, the appearance on the market of so-called synthetic cannabinoids and cathinones, as well as other substances that are found to be particularly dangerous for the health of consumers. Even the National Early Warning System, since 2009 has been monitoring the occurrence of these substances on the Italian territory.

Available in smart shops and on the Internet

Until 2011, almost all of the new synthetic drugs became available in smart shops located in various Italian cities. The rapid update of the tables of drugs, which made these substances illegal, and the diligent enforcement activities by the police currently have significantly reduced their presence in such places.
However, new drugs are still widely available on the Internet network through which their marketing takes place quickly and easily, due to the difficulty to monitor and combat environment in a continuous movement and development as the web. To counter this, the Department of Antidrug Policy, through its National Early Warning System, has activated a specific unit of monitoring for the detection of web sites selling new drugs and whose results are reported in the chapter on the Early Warning System.

The following describes the main features of the new drugs intercepted by the National Early Warning System in 2012, and cases of poisoning related to them.

4.2.1 Synthetic cannabinoids

What are they

In Europe, the first synthetic cannabinoids have been reported since 2008 in various herbal mixtures, also referred to as "herbal blends", which were sold as incense or air fresheners. The first cannabinoids to be identified were JWH-018 and JWH-073. The phenomenon of synthetic cannabinoids also begun to affect Italy in 2010. Analyzes of various "herbal mixture" type products, made by several international laboratories, showed the existence of many other synthetic cannabinoids in addition to those listed above, including JWH-122, JWH-200, JWH-250, JWH-251, JWH-081, JWH-398, JWH-019, HU-210 and CP 47,497 including its analogues with the alkyl chain C6, C8 and C9. These molecules act on CB1 receptors in mimicking the effects of cannabis.

Their power

The in vitro activity of JWH-018 and its analogs JWH-073 and JWH-019 appears to be superior to that of Δ9-THC. Similarly, the CP 47,497 shows the agonist activity on receptors CB1 from 3 to 28 times higher than that of Δ9-THC. For this reason, consumers often use them considering them natural alternative to cannabis, but with similar psychotropic activity. Furthermore, because of the ability of the synthetic cannabinoids identified to act as agonists on the CB1 receptors, it is possible to easily develop tolerance to these molecules.

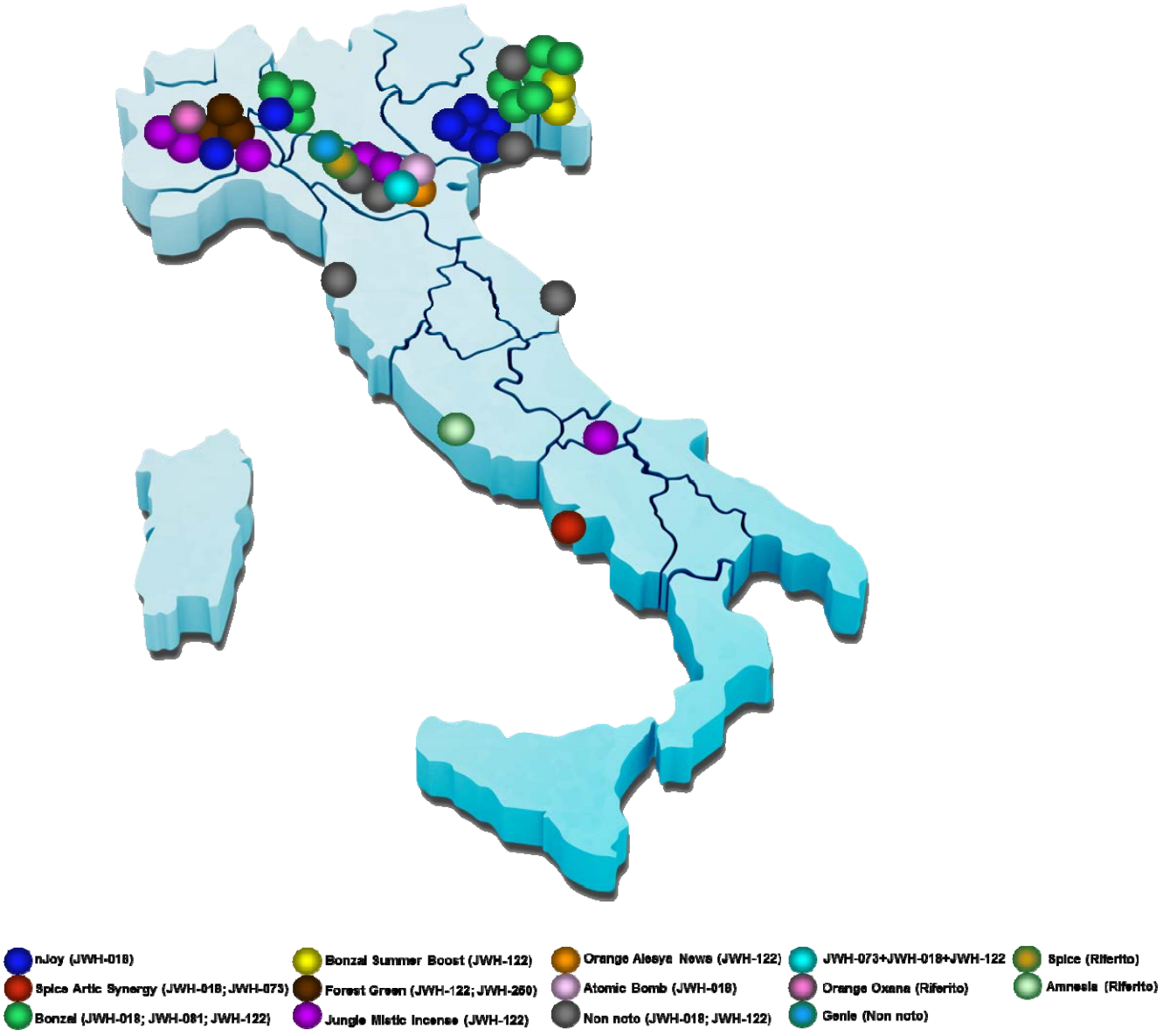
Use and effects

Synthetic cannabinoids are usually recruited by the respiratory route through the consumption of cigarettes containing herbal substance to the addition of these synthetic molecules. The effects of synthetic cannabinoids are similar, if not superior, to those that followed the consumption of cannabis. The intake of these products, in fact, generates, after ten minutes, conjunctivitis, increased heart rate, dry mouth and an alteration of perception and mood, effects that last for about six hours. In Germany, since 2009, there have been cases of people arriving in the emergency room after the consumption of "herbal mixture" with disorders of the cardiovascular system and of the nervous system, such as tachycardia and temporary loss of consciousness. In some cases, effects have been reported such as psychomotor agitation, panic attacks, and confusional states. Similar cases have been recorded in Sweden, Austria, Romania and Italy.

Acute poisoning in Italy by synthetic cannabinoids

Since 2010, in Italy, the National Early Warning System, through the reports of its collaborating centers, recorded 41 cases of acute poisoning related to the use of synthetic cannabinoids (of which 2 in 2012), for which it was necessary the admission to the emergency department. Figure 13 shows the geo-referencing of cases of poisoning by synthetic cannabinoids and the names of the products consumed by the patients intoxicated with indicated the synthetic cannabinoids found. The majority of cases were recorded in Northern Italy and involved subjects between 15 and 55 years old. In 2012.

Figure 13 – Location of cases of acute intoxication by synthetic cannabinoids which required access to the emergency services and which were recorded by the National Early Warning System since 2010, names of the products consumed by the patients and relative synthetic cannabinoids found in the samples analysed.



4.2.2 Synthetic cathinones

What are they

Another new drug registered by the National Early Warning System from 2010 is represented by synthetic cathinones.
The synthetic cathinones are structural analogues of cathinone plant (a molecule naturally present in the Khat plant) and are sold in tablets of various colors/shapes, in capsule, powder/crystal, are generally presented as "bath salts" or "fertilizer for plants. "In such products, often cathinones present are multiple and/or are associated with other psychoactive substances.
Those registered by the National Early Warning System from 2010 are: among the most frequent, mephedrone (14 reports), metilletcatinone 4-(4-MEC) (11), butylone (5), metylone (5), metylendiossipirovalerone (MDPV) (4), pentedrone (4), 3-fluorometcatinone (3) and bufedrone (2).

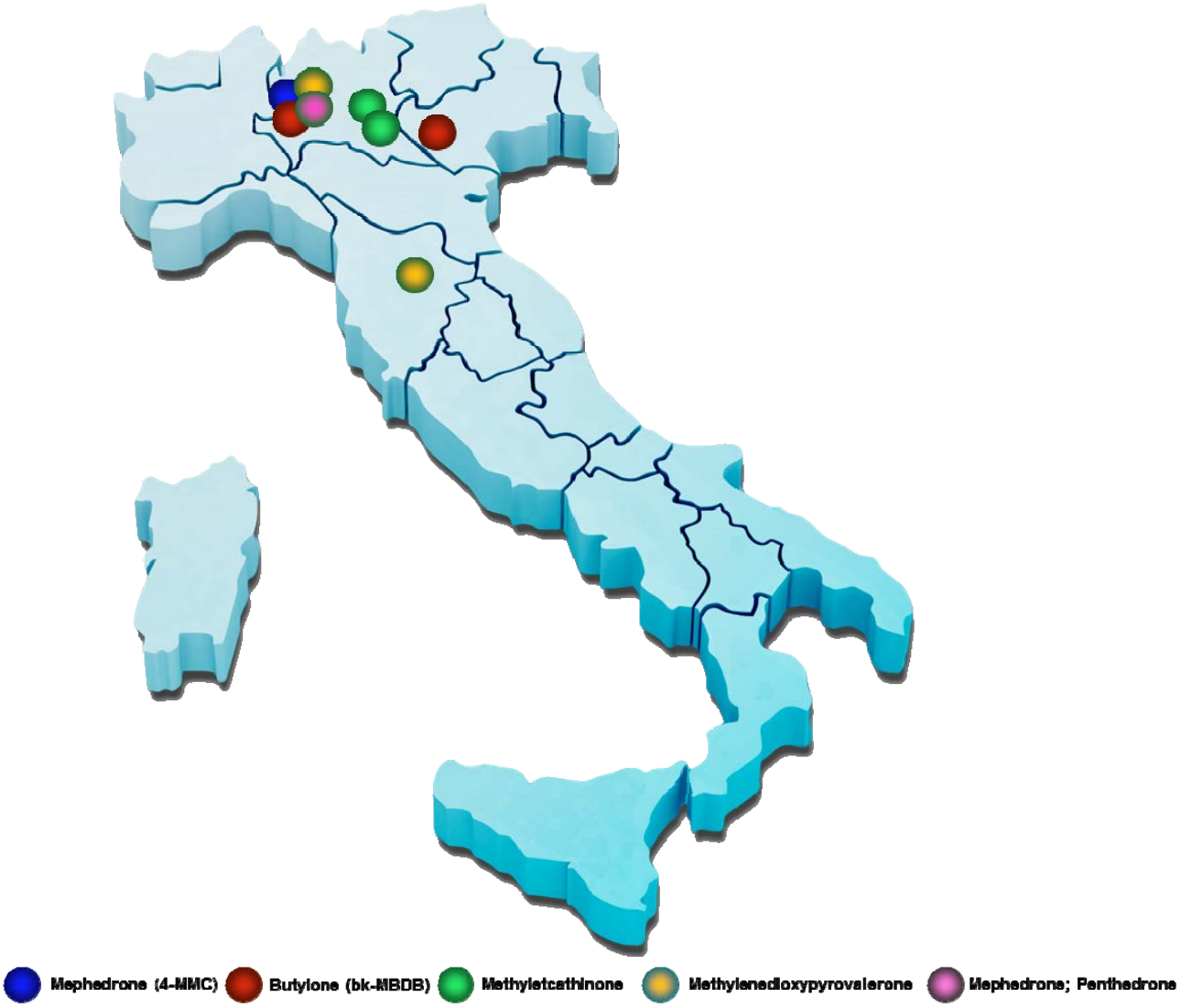
Use and effects

Because of their different modes of presentation, the cathinones can be ingested, snorted/smoked or taken by injection or rectally. Many synthetic cathinones are characterized by sympathomimetic activity, predominantly due to the release at pre-synaptic reuptake of catecholamines and inhibition of monoamine neurotransmitters. They are able to simulate the effects of cocaine. The clinical effects most commonly reported are: anxiety, impaired concentration and memory, short-term irritation of the nasal mucosa, headache, tachycardia, hypertension, hyperhidrosis, mydriasis, trismus, bruxism, hallucinations, severe agitation and aggression. For many of the synthetic cathinones also identified on the Italian territory are not available complete data regarding the pharmacological characteristics, the precise mechanism of action and possible toxic effects. However, the clinical presentation is indistinguishable from the acute effects of MDMA or from cocaine.

Acute intoxications in Italy by synthetic cathinones

Since 2010, in Italy, there have been 8 cases (aged 18 to 38 years) of acute intoxication by synthetic cathinones. The symptoms presented were: mydriasis, anxiety, panic attacks, visual and auditory hallucinations, agitation and violent behavior. In one case intake (ingestion/sniffing) of the product purchased in a smart-shop as fertilizer for plants has determined, in addition to systemic effects, even hyperemia of the oral cavity, edema of the glottis and uvula. All patients were treated symptomatically and discharged after 24-48 hours of observation. The cases were registered between the Region of Lombardy, the Veneto Region and the Region of Tuscany. Responsible for the poisonings were the synthetic cathinones butylone, Mephedrone, MDPV and metyletcathinone.

Figure 14 – Location of cases of acute intoxication by synthetic cathinones which required access to the emergency services and which were recorded by the National Early Warning System since 2010 and associated synthetic cathinones found in the samples analysed.



4.2.3 Methoxetamine

What it is

Methoxetamine is an analogue of ketamine from which it differs by the presence of a 3-methoxy substituent in place of the 2-chlorine on the aromatic ring and the 2-ethylamine instead of methylamine. Similarly to ketamine, methoxetamine is thought to act as non-competitive antagonist of NMDA receptors and as an inhibitor of dopamine reuptake. It would also act as an agonist of dopamine D2 receptors, serotonin 5HT2 receptors, muscarinic cholinergic, sigma-1, mu and kappa opioids.
Compared to the effects of ketamine, the presence of the N-ethyl group would result in an increased and prolonged toxicological effect, while the presence of the 3-methoxy group in place of 2-chloro lead to less anesthetic and analgesic effect, as well as a longer half-life.

Use and effects

Methoxetamine can be taken orally, intravenous, intramuscular, rectal and nasal. As reported online by some consumers, the effects can appear later (after 30-90 minutes) when taken for sniffing, with the risk of taking repeated doses within short distance; if the assumption is made instead by intramuscular injection effects can appear even after a few minutes. The duration of effect is highly variable (average 5-7 hours). To prolong the effects sought, it is often co-shouldered with hallucinogens (eg, LSD) or amphetamines /amphetamine-like.
The effects researched and reported after use of methoxetamine are euphoria, increased empathy, intensification of sensory experiences, distorted sense of reality, vivid and persistent visual hallucinations. Some consumers report having experienced nausea, vomiting, diarrhea, paranoia, anxiety, mental confusion, dizziness, distortion of time, aphasia, synaesthesia and severe psychomotor agitation. After taking methoxetamine are also reported, such effects "not wanted", sensory deprivation, derealization and dissociation (generically described as experiences "near-death").

Acute Intoxications acute in Italy by methoxetamine

During 2012, have been reported many cases of poisoning from methoxetamine. A total of 10 (one in 2011) cases of intoxication from methoxetamine recorded by the National Early Warning System, the majority of which (6) identified in Northern Italy, while the remaining 4 in central Italy, specifically in the regions of Tuscany, Lazio and Emilia Romagna.
The main symptoms recorded at the entrance to the emergency room were: severe psychomotor agitation associated with hallucinations, mydriasis, tachycardia, confusion, stupor.
Figure 15 shows the geo-referencing of cases of acute poisoning related to the intake of methoxetamine who required admission to the emergency department.

Figure 15 – Location of cases of acute intoxication by methoxetamine which required access to the emergency services and which were recorded by the National Early Warning System – 2011-2012.

4.3 Unanticipated and atypical symptoms after use.

Thanks to the distribution of analytical standards of synthetic cannabinoids and other new molecules to the laboratories of the network by the Superior Health Institute, it has been possible to facilitate the work of the laboratories, enabling them to identify these molecules in the materials analysed. Greater promptness of recognition has therefore speeded up the diagnoses of emergency medical staff, allowing them to implement the appropriate treatment of intoxicated patients more rapidly.

4.4 Web monitoring for the prevention of drugs supply – Substances available on the Internet (type of product and method of marketing)

In total, 54 websites in the Italian language were identified with servers located within the national territory, and 426 webpages were reported.

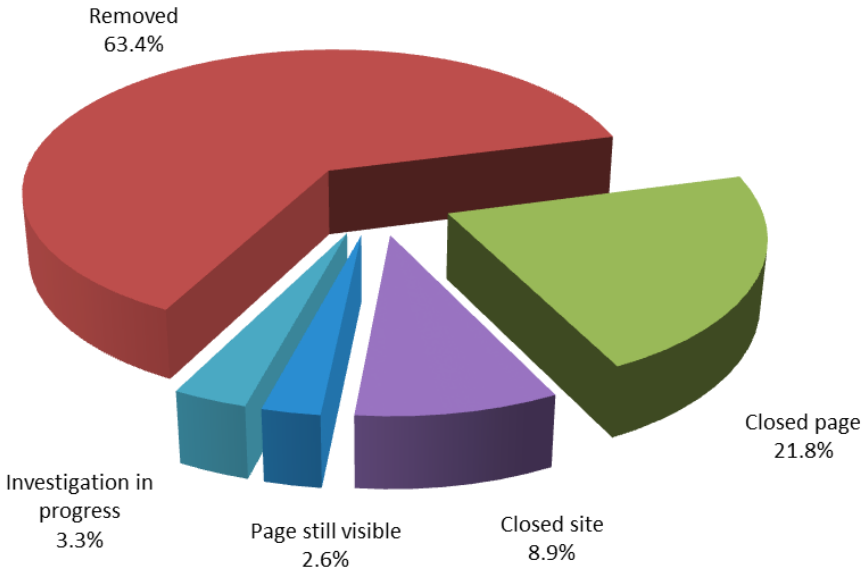
426 web pages notified

Of reports to the Police forces of sites which sell controlled substances, 63.4% resulted in the removal of the notice and in 21.8% of cases the web page was closed. The site notified was closed in 8.9% of cases. Only 2.6% of the pages notified are still visible on the web.

Table 8 – Outcome of notifications of sites which market illegal narcotic substances on the web.

Outcome of notification	No	%
Removed	270	63.4%
Closed page	93	21.8%
Closed site	38	8.9%
Page still visible	11	2.6%
Investigation in progress	14	3.3%
Total	426	100.0%

Graph 14 – Outcome of notifications of sites which market illegal narcotic substances on the web.



Thanks to the monitoring activities, a total of 34 different substances of been identified, of which controlled and scheduled (DPR 309/90) psychoactive substances and drugs sold without medical description.

Specifically, the following were found to be available:

- synthetic cathinones: mephedrone (4-methylmethcathinone), MDPV (3,4-methylenedioxypyrovalerone), butylone (bk-MBDB) and 4-MEC (4-methylcathinone);
- synthetic cannabinoids: JWH-018, JWH-019, JWH-073, JWH-081, JWH-122, JWH-203, JWH-210, JWH-250, RCS-4, AM-2201, AM-694, Eric-4.
- phenethylamines: 2C-B, 2C-I, 2C-T-2, 2C-T-7, 4-methylamphetamine.
- ketamine, cocaine, MDMA, LSD, marijuana, heroin;
- drugs which cannot be sold without medical prescription: Xanax, Valium, oxycodone, methadone, hydrocodone, morphine.

4.4.1 Online monitoring of rave parties

The monitoring activity conducted from October 2010 to December 2012 also led to the identification of 116 illegal music events promoted online. 113 of these were notified by the Prefecture, Police, municipality and referred to the Magistrate of the place where the event was to be held and the Central Executive for Anti-Drug Services, in order to verify the legitimacy of the organisation. 39 of these (33.6%) were prevented, i.e. closed before taking place; 25 were managed by intervention *in loco* of the Police forces (21.6%); 38 (32.8%) took place in spite of the notification (Graph 15 and Figure 16). 11 events (9.5%) are waiting for report ; 3 events indicated as not reported (2.5%) are events where insufficient advance information regarding the place has been collected and therefore they have not been notifiable to the Police forces and to the regional administrations.

Graph 15 – Rave parties identified via web monitoring and notified to DCSA, Prefecture, Police, municipality and magistrate of the relevant location.

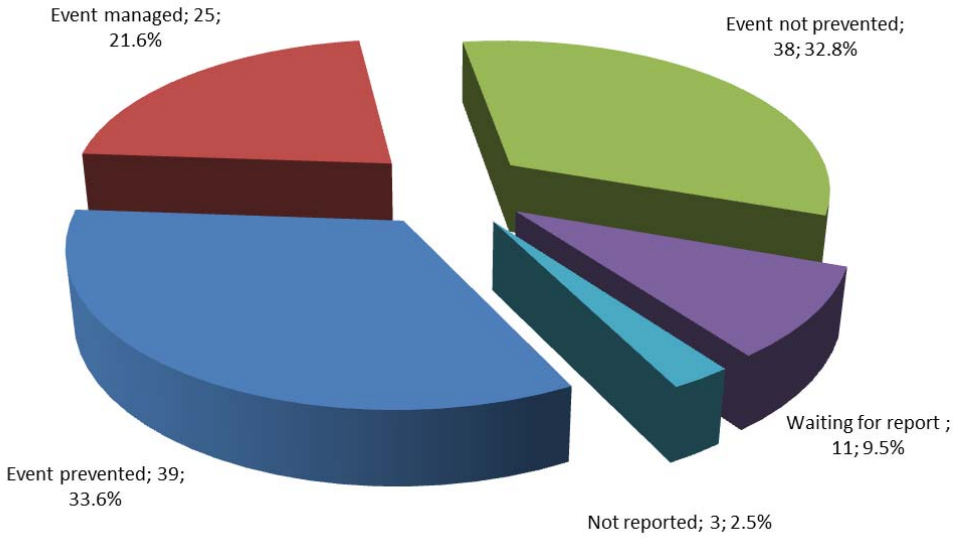
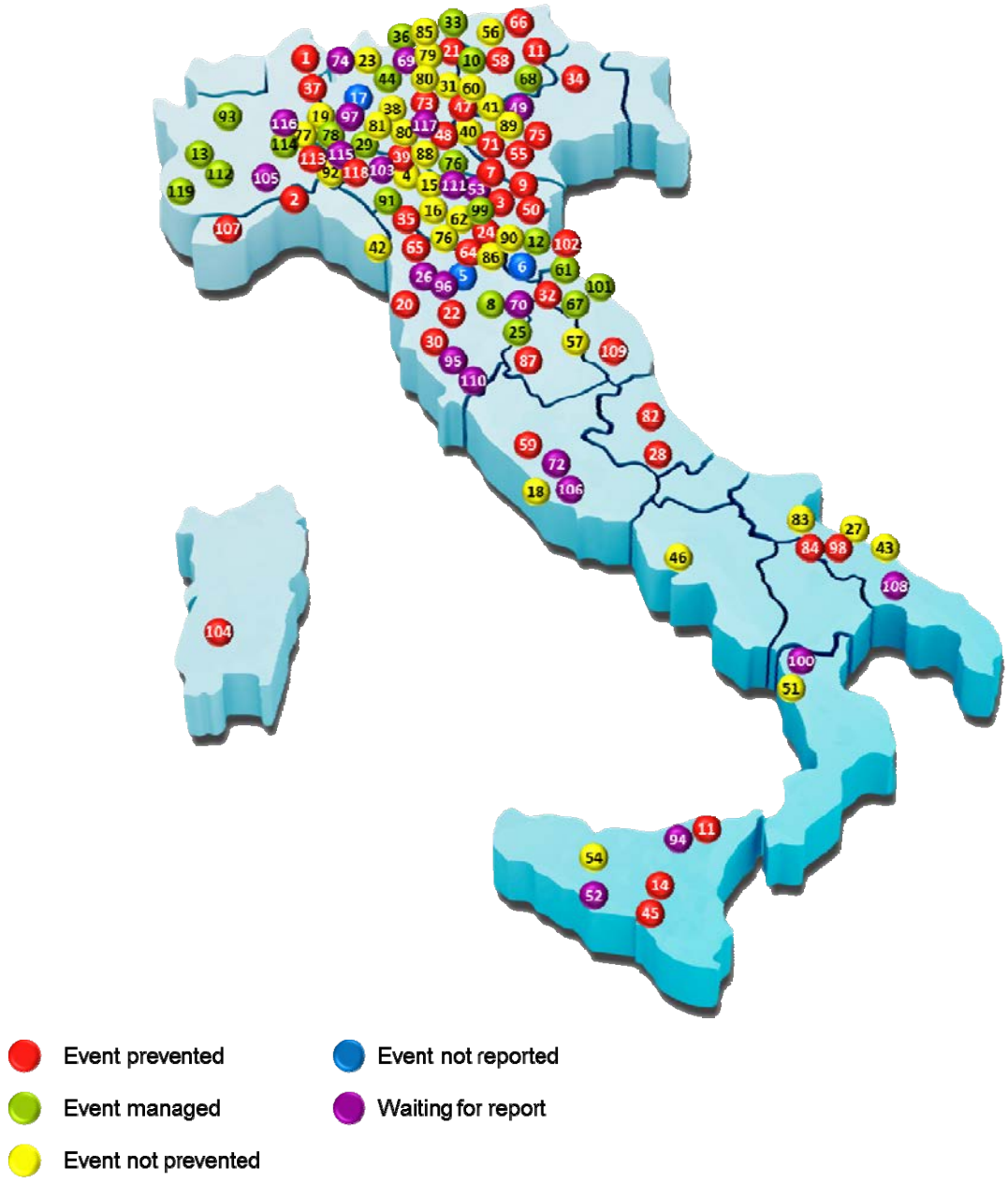


Figure 16 – Location of rave parties identified by web monitoring and notified to the Police forces and to the Local authorities.



4.5 Anomalous batches of classic drugs (variations of the percentages of active principle)

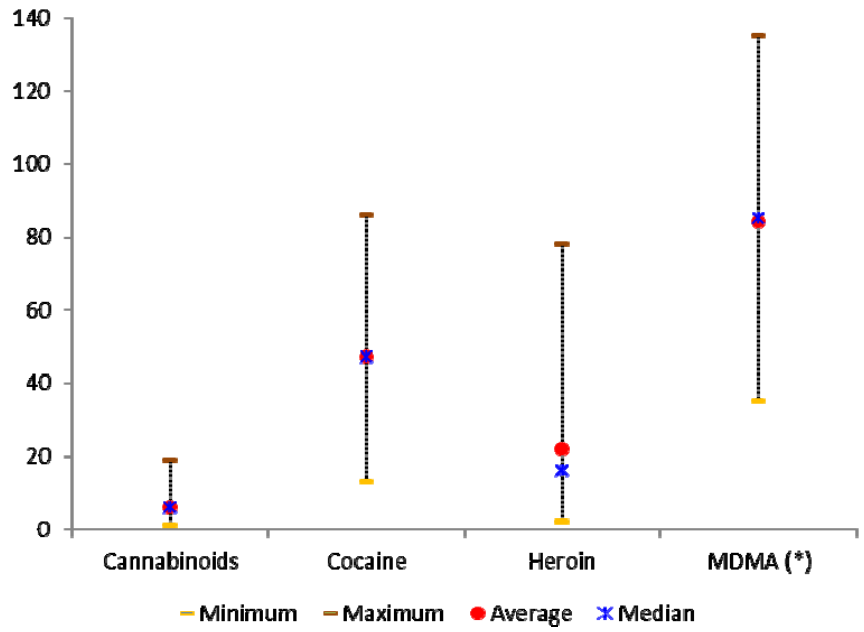
In collaboration with the Central Executive for Anti-Drug Services, it has been possible to monitor and bring to light variations of the active principle of the so-called classic drugs during 2011 as reported below.

Table 8 – Values of the active principle of cannabinoids, cocaine, heroin, MDMA recorded in 2011.

Year 2011	Cannabinoids	Cocaine	Heroin	MDMA (*)
Minimum	0.9	13	2	35
Average	6.0	47	21.9	84
Maximum	19.0	86	78	135
Median	6.0	47	16	85

(*) for MDMA the average weight is given in mg per tablet/unit

Graph 16 – Average, median, minimum and maximum of the active principle of cannabinoids, cocaine, heroin, MDMA recorded in 2011.



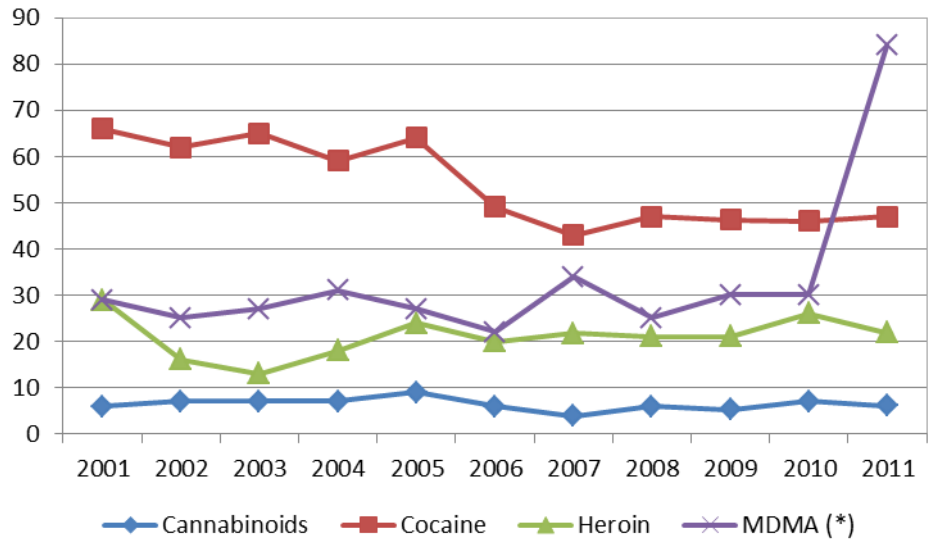
The following table indicates the percentage values of the active principle in cannabis, methylenedioxymethamphetamine, heroin and cocaine found between 2001 and 2011.

Table 9 – Values of the active principle of cannabinoids, cocaine, heroin, MDMA recorded from 2001 to 2011.

	Cannabinoids	Cocaine	Heroin	MDMA (*)
2001	6	66	29	29
2002	7	62	16	25
2003	7	65	13	27
2004	7	59	18	31
2005	9	64	24	27
2006	6	49	20	22
2007	4	43	22	34
2008	6	47	21	25
2009	5	46	21	30
2010	7	46	26	30
2011	6	47	22	84

(*) for MDMA the average weight is given in mg per tablet/unit

Graph 17 – Values of the active principle of cannabinoids, cocaine, heroin, MDMA recorded from 2001 to 2011 – percentage.



(*) for MDMA the average weight is given in mg per tablet/unit

Cannabis with high percentages of active principle

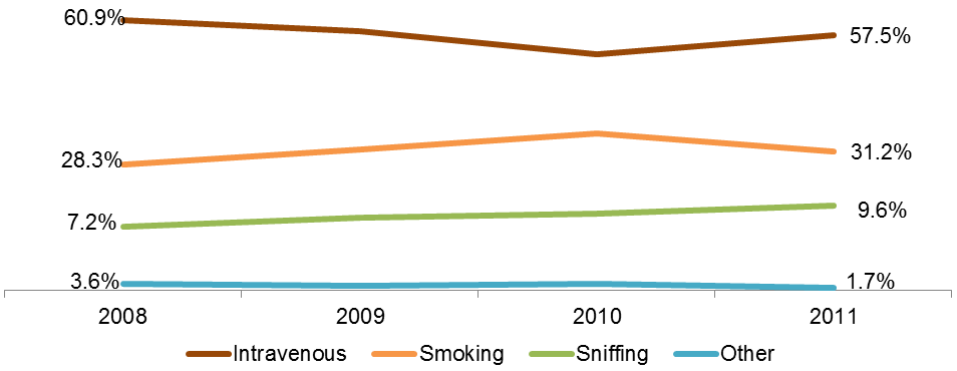
High percentages of THC in cannabis and its derivatives

During the year there were many notifications of reports of cannabis and derivatives seized by the Police forces. The analysis of which yielded a high percentage of the active principle Δ^9-Tetrahydrocannabinol (THC). More specifically, of 18 notifications from the various regions of Italy regarding finds of cannabis, inflorescence, hashish were found to contain percentages of THC varying between 15% and 35% with peaks of over 40% of active substance.

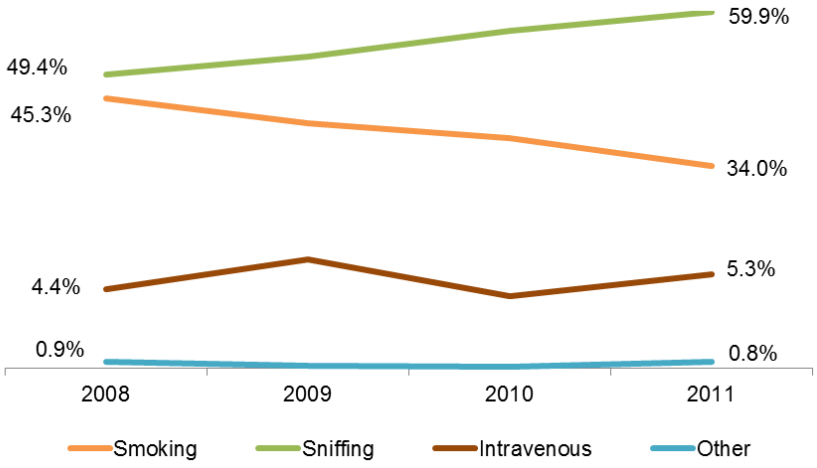
4.6 New patterns of heroin use: the national situation

Via the monitoring of the various methods of use, the National Early Warning System, in collaboration with the National Epidemiological Monitoring Service of the Department of Anti-Drug Policies, was able to document changes in the methods of taking heroin, cocaine and other stimulants between 2008 and 2011 among users registered with the services. From the investigation it emerged that the route of administration most used for heroin was intravenous but on a downward trend (60.9% in 2008, this figure falls to 57.5 in 2011) in favour of smoking (28.3% in 2008 versus 31.2% in 2011) and insufflation (7.2% in 2008 versus 9.6% in 2011). For cocaine the method most used is insufflation; on a continual rise between 2008 (49.4%) and 2011 (59.9%).

Graph 19 – Trend of the various routes of consumption of heroin – years 2008, 2009, 2010, 2011 – percentage.



Graph 20 – Trend of the various routes of consumption of cocaine – years 2008, 2009, 2010, 2011 – percentage.



4.7 New cutting agents/adulterants

The notifications received by the System in the last year of operations highlight that the cutting agents/adulterants more frequently encountered for heroin are paracetamol, caffeine and methorphan. Cocaine however was found to be cut/adulterated with tetramisole/levamisole, dipyrone, aminopyrine, benzocaine.

As regards heroin, notifications received by the System via the European Monitoring Centre in the last year show that batches of heroin contaminated with Bacillus anthracis are circulating in Europe.

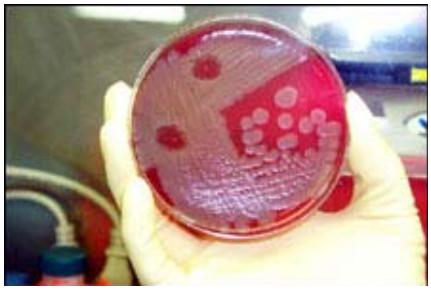
4.7.1 Heroin and Bacillus Anthracis

Cases of death by anthrax in Europe: Level 3 Alert in Italy

2012 featured a new wave of cases of sometimes lethal infections from *Bacillus anthracis*, recorded in Europe among intravenous heroin users. Anthrax is a serious disease caused by the bacterium *Bacillus anthracis*, which generates spores. The toxin secreted by *Bacillus anthracis* enables the bacterium to avoid the immune system and can kill the host during infection.
Following notification of the death of a *Bacillus anthracis* positive intravenous heroin user in Germany and given the speed with which narcotic substances can be marketed in Europe and therefore reach Italy, it was considered appropriate to implement a Level 3 Alert in June among the public health protection facilities and laboratories and Police forces. This alert was subsequently the subject of two updates during the year: the first in July, following the recording of 4 cases of infection, of which one death in Europe and the second in December relating to another 7 new cases of infection, of which two deaths, among heroin users.

To date no case of infection with *Bacillus anthracis* has been recorded among users in Italy and operators in contact with finds.

Figure 16 – Anthrax in culture



4.7.2 Heroin and Methorphan

The problem of the stereoisomer

To date, the National Early Warning System has recieved numerous notifications from the System's Collaborating Centres regarding finds from seizures of heroin adulterated with methorphan. Starting from the earliest notifications recorded by the System in July 2010, again in 2012 cases of identification of methorphan were recorded in samples of heroin from seizures, which brings total notifications to 33 at the end of 2012, listed in Table 12. As regards the stereoisomers of methorphan identified, dextro and levo, this information is critical given the different toxicological characteristics which led to the scheduling of solely the levorotatory form. Dextromethorphan is a sedative and, according to international literature, recreational use of dextromethorphan has also been associated with cases of death, while levomethorphan is a narcotic analgesic. Therefore during 2012, the Alert System deemed it appropriate to go into further detail on the issue by contacting the laboratories which transmitted these notifications. Specifically, the need emerged to understand the nature of the methorphan identified, dextro or levomethorphan, in consideration of the significant difference in the pharmacological effects generated by the two molecules. In just four cases it was possible to confirm that it was dextromethorphan.

Heroin taken in place of cocaine

A case where heroin containing methorphan was sold and used as cocaine leading to the use of heroin without the user being aware of it was recorded in 2012.

Table 12 – Notifications of finds of heroin found to be containing methorphan, which came to the attention of the Warning System (2010 – 2012).

No	Place (Province)	Date of notification to NEWS
1	Umbria	July 2010
2	Viareggio	March 2011
3	Bologna	April 2011
4	Bologna	July 2011
5	Imola	July 2011
6	Venice	August 2011
7	Benevento	October 2011
8	Benevento	October 2011
9	Benevento	October 2011
10	Benevento	October 2011
11	Benevento	October 2011
12	Benevento	October 2011
13	Benevento	October 2011
14	Benevento	October 2011
15	Benevento	October 2011
16	Benevento	October 2011
17	Benevento	October 2011
18	Benevento	October 2011
19	Olbia	December 2011
20	Olbia	December 2011
21	Cagliari	December 2011
22	Genoa	January 2012
23	Padua	February 2012

24	Verona	March 2012
25	Bologna	March 2012
26	Bologna	April 2012
27	Padua	April 2012
28	Bolzano	May 2012
29	Correggio-Carpi	July 2012
30	Reggio Calabria	July 2012
31	Cagliari	September 2012
32	Viterbo	November 2012
33	Fiuggi (FR)	November 2012

4.7.3 Cocaine and Benzocaine

Finds and biological samples

In June 2012 the results of analyses performed on a white crystalline, odourless and compacted powder seized in Lucca by the local mobile team were sent to the Warning System by the laboratory of the Biochemical Clinical-Toxicological Unit of Lucca hospital. Quantitative analysis showed that it was cocaine which also contained tetramisole, phenacetin and benzocaine.

A notification regarding the use of benzocaine in Italy was also received in July 2012 by the Pavia Poison Control Centre which recorded the case of acute intoxication of a 20-year-old man, who attended the emergency facility around six hours after having inhaled a product purchased on the Internet as legal cocaine called Sintacaine (Figure 23).

Figure 23 – Image of the white powder taken by the patient notified by the Pavia Poison Control Centre, contained in a plastic bag and having a weight of 650 mg. Source: Pavia Poison Control Centre.

Urine testing for abuse substances, carried out *in loco*, was positive for cocaine and negative for amphetamine, THC and MDMA, while toxicological analysis of the products and the biological samples, carried out at the Laboratory of Clinical Toxicological Analysis of the San Matteo General Hospital Foundation showed that the residue of the product was positive, as well as for sugars, for benzocaine and MAM-2201, a synthetic cannabinoid (analytical compatibility via comparison with the GCMS mass spectrometer). Cocaine and dimethocaine were absent.

Local anaesthetic as a cutting agent

Benzocaine or Ethyl 4-aminobenzoate, is a local anaesthetic often used for disorders or pain of the mouth, skin or mucosae. It is used as a cutting agent in cocaine as it can have an anaesthetic effect of the nose and mouth, thereby simulating a powder with a higher concentration of cocaine.

The presence of benzocaine (abnormal in the absence of cocaine) exposes the user to potential risks of methemoglobinanaemia (toxic effect documented after taking cocaine adulterated with benzocaine).

4.8 Drug-related acute intoxication or clusters of deaths

The Warning System also monitors for drug-related clusters of deaths and acute intoxications of multiple subjects over a short period of time. During 2012 no drug-related clusters of death were recorded in Italy.

However, in the previous years (2009-2010-2011), the System closely monitored the situation in Piedmont where various deaths by heroin overdose were notified over the three-year period, triggering a Level 3 Alert. The monitoring led to illustrating that the frequency of deaths recorded in the city of Turin from 2012 corresponded to the national average of almost 1 death per month (0.9). Following field investigations activated by the Department for Anti-Drug Policy to investigate further the causes of these deaths, it was found that the analysis carried out at the Alessandro Bertinaria Regional Anti-Doping Centre on the biological samples of the deceased individuals and on the evidence available on the scene of death (used syringes, powder, paper wraps, etc) showed no evidence for particularly high concentrations of active substance in the heroin taken, neither were there unresolved adulterants or cutting agents compared to those generally found in heroin in circulation.

In spite of this, it was shown how the majority of the deceased persons were not known to the territorial addiction services and were not therefore in treatment with replacement therapy. In light of the above, and also for avoiding clusters of overdose, such as those recorded in 2010 and in 2011 in Turin related to taking heroin containing high percentages of 6-monoacetylmorphine, it was recommended to:

a. increase and facilitate access to replacement and residential therapies for addicts especially those in poor conditions;
b. increase early outreach via the contact units on the street promoting additional early access to services;
c. provide information and training for patients already registered with the treatment services or held in prison while evaluating for those at a higher risk, the possibility of beginning therapy with Naltrexone before leaving the facility;
d. implement training by teaching the rules of first aid and for the use of Narcan for addicts already registered with the services;
e. advise users to avoid taking drugs in isolated places or alone where the rescue services may not be able to reach them or reach them late.

4.9 Variations of the incidence of drug related infections (HIV, HBV, HCV, TBC, MST).

Monitoring of the incidence of drug related infections (HIV, HBV, HCV, TBC, MST), conducted in collaboration with the Ministry of Health, the Superior Health Institute and the Epidemiological Monitoring Centre of the Department of Anti-Drug Policy, illustrated a general increase of the percentage of untested users within the services, both of new and registered users. This trend was previously found in 2010 and, unfortunately, was again confirmed in 2011 (2012 data not yet available). The autonomous province of Bolzano had the greatest percentage of tested users, followed by Tuscany, Abruzzo, Sicily and Sardinia. In December 2011 the National Early Warning System, based on the data available at the time (2010 Figures), had activated a Level 3 Alert addressed at the Regional Health Inspectorate, the Regional Inspectorate of Social Policy, the regional contact people for drug addiction and the Health Coordination of the Regions and Autonomous Provinces, highlighting the serious risks associated with the situation. The Alert also recommended incentivising testing for infectious diseases within the Department and the Addiction Services via specific and formal operating instructions.

Table 11 – Users registered with the Services, individuals tested and not tested for HIV. Years 2010 and 2011

Regions and Autonomous Provinces	Year 2010							Year 2011							
	Total Reg. Users	Users Tested				Untested		Total Reg. Users	Users Tested				Untested		
		N.U.	G.C.	Total		No	%		N.U.	G.C.	Total		No	%	Diff.
				No	%						No	%			
(1)Abruzzo	4,740	177	735	912	19.2	3,828	80.8	5,762	177	781	958	16.6	4,804	83.4	+2.6
(1)Basilicata	1,592	65	430	495	31.1	1,097	68.9	1,695	60	411	471	27.8	1,224	72.2	+3.3
(1)Calabria	4,145	304	1,330	1,634	39.4	2,511	60.6	3,651	189	1,097	1,286	35.2	2,365	64.8	+4.2
(1)Campania	17,878	1,762	6,602	8,364	46.8	9,514	53.2	18,764	1,915	6,951	8,866	47.3	9,898	52.7	-0.5
(2)Emilia Romagna	12,498	559	2,342	2,901	23.2	9,597	76.8	13,470	19	7,266	7,285	54.1	6,185	45.9	-30.9
(1)F.V.G.	3,671	335	1,399	1,734	47.2	1,937	52.8	3,371	175	1,208	1,383	41.0	1,988	59.0	+6.2
(3)Lazio	15,424	1,332	5,571	6,903	44.8	8,521	55.2	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.
(4)Liguria	7,262	134	1,001	1,135	15.6	6,127	84.4	n.p	n.p	n.p	n.p	n.p	n.p	n.p	n.p
(2)Lombardy	23,625	677	2,320	2,997	12.7	20,628	87.3	20,623	1,378	3,115	4,493	21.8	16,130	78.2	-9.1
(1)Marches	5,679	373	1,947	2,320	40.9	3,359	59.1	4,993	292	1,709	2,001	40.1	2,992	59.9	+0.8
(1)Molise	1,202	181	257	438	36.4	764	63.6	1,148	134	264	398	34.7	750	65.3	+1.7
(1)P.A. Bolzano	760	0	24	24	3.2	736	96.8	755	0	0	0	0.0	755	100	+3.2
(1)P.A. Trento	1,127	35	586	621	55.1	506	44.9	1,068	17	593	610	57.1	458	42.9	-2.0
(3)Piedmont	11,462	621	4,015	4,636	40.4	6,826	59.6	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.	n.c.
(1)Apulia	11,545	811	4,010	4,821	41.8	6,724	58.2	13,180	810	3,937	4,747	36.0	8,433	64.0	+5.8
(1)Sardinia	5,911	100	689	789	13.3	5,122	86.7	6,492	224	1,012	1,236	19.0	5,256	81.0	-5.7
(1)Sicily	13,416	1,024	2,776	3,800	28.3	9,616	71.7	14,555	750	1,999	2,749	18.9	11,806	81.1	+9.4
(1)Tuscany	13,965	377	1,777	2,154	15.4	11,811	84.6	14,314	305	1,617	1,922	13.4	12,392	86.6	+2.0
(2)Umbria	3,555	73	574	647	18.2	2,908	81.8	-	n.p	n.p	n.p	n.p	n.p	n.p	n.p
(1)Valle d'Aosta	366	15	121	136	37.2	230	62.8	358	22	112	134	37.4	224	62.6	-0.2
(1)Veneto	14,333	905	3,585	4,490	31.3	9,843	68.7	14,276	687	3,065	3,752	26.3	10,524	73.7	+5.0
Total	174,156	9,860	42,091	51,951	29.8	122.20	70.2	138,475	7,154	35,137	42,291	30.5	96,184	69.5	-0.7

n.p.= figure requested but not received
n.c.= not calculable
U.C.= Registered users
N.U.= New Users
G.C. = Previously registered

(1) Flow of information (Yrs 04 05 and 06)
(2) SIND flow (HIV monitoring)
(3) Partial SIND flow of information (indicator not calculable)
(4) Flows of information not transmitted (SIND and ANN)

Source: Processing of Ministry of Health data sent by the Regions and Autonomous Provinces

5. Inclusion of new molecules in Table I of the DPR 309/90 and regulations of the Ministry of Health

Inclusion in Table I of new cannabinoids and synthetic cathinones: 3 decrees in 2012

Following notifications received, as part of the operating procedure for the implementation of health safety measures relating to new narcotic and psychotropic substances identified via the operations of the National Early Warning System, agreed between the Department of Anti-Drug Policy (figure 22), in 2012, 3 decrees were signed to include new molecules in Table I of DPR 309/90.

Specifically:

- by the Decree of 16 June 2010 (OJ no 146 of 25 June 2010) declared illegal synthetic cannabinoids JWH-018, JWH-073 and the synthetic cathinone mephedrone.
- by the Decree of 16 May, 2011 (OJ no 112 of 16 May 2011) declared illegal synthetic cathinone 3,4-Methylendioxypyrovalerone (MDPV), synthetic cannabinoids JWH-250 and JWH-122, and all those with structures similar to 3-phenylacetylindole and 3-(1-naphtoyl)indole.
- Synthetic cathinone butilone (or bk-MBDB), certain analogs of the structure of 2-amino-1-phenyl-1-propanone, synthetic cannabinoid AM-694 and analogue structure resulting from 3-benzoylindole have been included in Table I with decree of 29 December 2011 (OJ no 3 of 4 January 2012).
- by the Decree of 11 June 2012 (Official Journal no 142 of 20 June 2012) monoester derivatives of morphine were made illegal: 6-monoacetylmorphine (6-MAM) and 3-monoacetylmorphine (3-MAM) and the chemical name of analogues of the substance Butylone was replaced;
- by Decree of 24 October 2012 (OJ no 264 of 12 November 2012) methoxetamine, analogue N-ethylderivative of ketamine; 4-methylamphetamine, methylate analogue of amphetamine; CP 47,497 and CP 47,497-C8-homologue structurally related to Delta-9-THC; 4-fluoroamphetamine, analogue of amphetamine; 5,6-methylenedioxy-2-aminoindane, phenethylamine strictly related to MDMA were made illegal;
- by the Decree of 10 December 2012 (OJ no 303 of 31 December 2012) the molecule 5-IT or 5-(2-aminopropyl)indole, a positional isomer of α-methyltryptamine (α-MT) was made illegal.

On publication of the decrees, thereby coming into effect, the Department of Anti-Drug Policy informed all the Magistrates, Prefectures and Police of their being updated in the Table and invited them to implement prompt appropriate control and verification actions throughout the national territory for identifying the molecules in question. These actions led to the control and seizure of numerous smart shop type commercial concerns and the seizure of numerous herbal blend type of products or bath salts containing the newly illegal substances. They also provided an opportunity for identifying new psychoactive molecules.

Implementation of other safety measures

Via the Competent offices, the Ministry of Health, informed of the urgency following the receipt of a communication of the Department for Anti-Drug Policy and the National Early Warning System, may:

Regulation

1 – To issue public health and hygiene regulation aimed at the immediate withdrawal of commercial products containing the substance identified throughout the national territory. Specifically a regulation may be issued to prohibit the manufacture, import, marketing, trading and use of the products containing the substance which gave rise to the alert. Simultaneously, the health and control authorities and the police and postal bodies can be activated to monitor compliance with the order (General Executive for Prevention).

Consumer Code

2 – Where the substance notified by the alert is not contained in products such as foods or medicine, the Ministry of Health – General Executive for Prevention, Office 4 – may activate the procedure prescribed

by Art 107 of the Consumer Code, based on Legislative Decree 206 of 6 September 2005 (General Executive for Prevention).

3 – In the case of narcotic substances being introduced and marketed, in Italy or in Europe, by means of non-food type products, where appropriate and necessary, activation of the RAPEX System (European Rapid Alert System for non-food consumer products) can also be evaluated. (General Executive for Prevention)

RAPEX Activation

4 – If the substance notified by the alert is presented as a food or is contained in food products, the Ministry of Health – General executive for the hygiene and safety of foods and nutrition, may examine the products notification and, if necessary, may activate RASFF (Rapid Alert System for Food and Feed), the European community warning system for notifying direct and indirect risks to public health associated with consuming food or feed (Regulation EC 178/2002 of the European Parliament and of the Council and Regulation EC 16/2011). RASFF is activated according to the procedures set out by the European Community, using the appropriate notification forms.

RASFF Activation

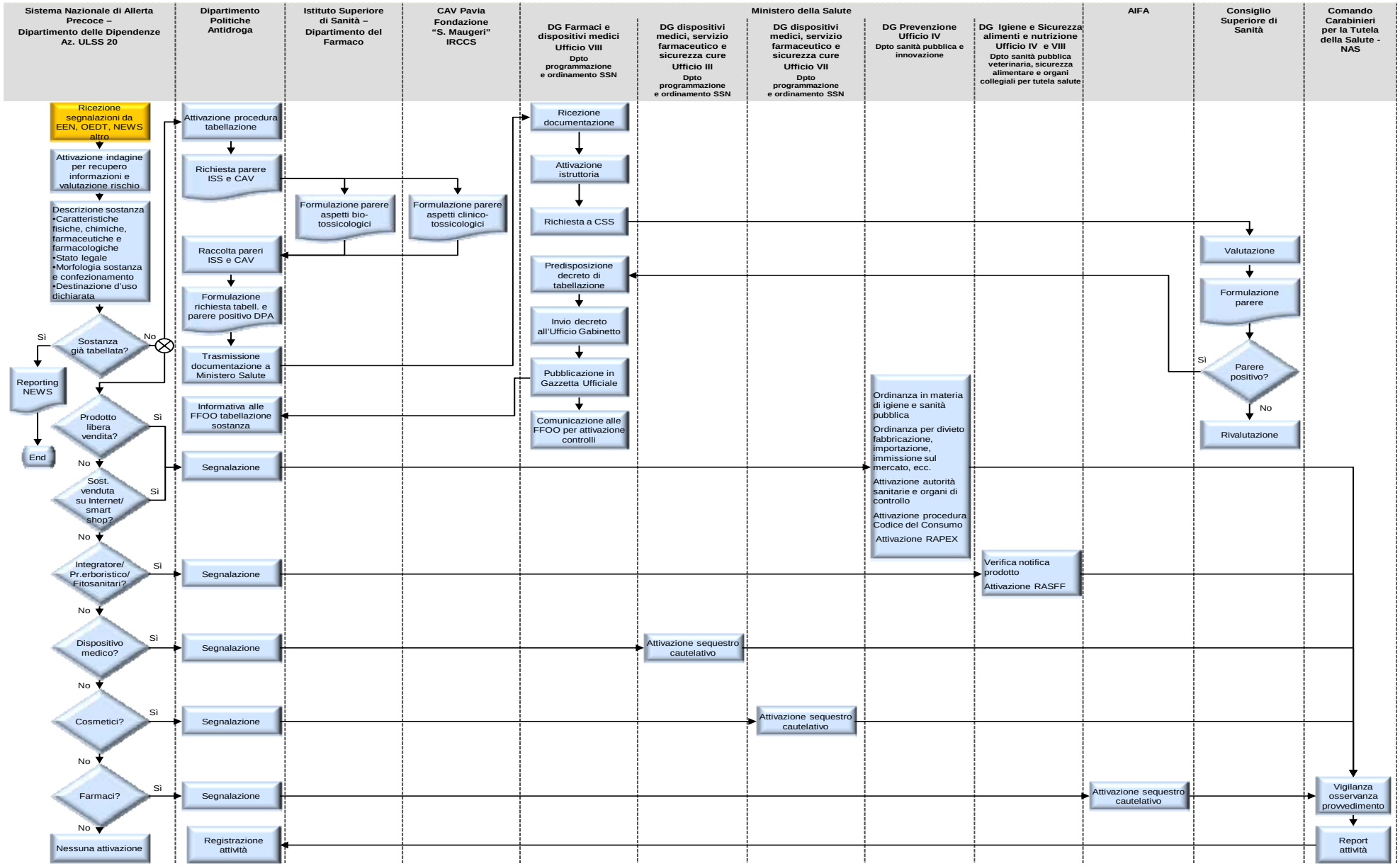
5 – Where narcotic substances are introduced and marketed in Italy or Europe, via cosmetic products, the Ministry of Health may evaluate the activation of precautionary seizures by the VII Office of the General executive for medical devices, the pharmaceutical service and safety of care.

Precautionary seizure

6 – Where narcotic substances are marketed illegally in Italy and they are active pharmacological ingredients (API), or drugs, activation of the precautionary seizure required by the AIFA may also be evaluated.

AIFA

Figure 22 – Procedure with responsibility and roles matrix for each entity involved in the activation of safety measures and in the inclusion in Table 1 of DPR 309/90 of new molecules.



6. Conclusions

After 4 years of operations at the Department of Anti-Drug Policy, the National Early Warning System has achieved significant results which have made a solid contribution to countering the proliferation of new narcotic substances in Italy.

The collaboration of a network of clinical services which identify cases of intoxication, together with the increased adhesion of Collaborating Centres and their increased capacity to identify new molecules thanks to the acquisition of reference standards and the sharing of analytical data, has increased the specificity, sensitivity and promptness of the System. As a result, it has been possible to reduce drastically the times of inclusion in the Tables of DPR 309/90 of new molecules found to be harmful to the health of the population and therefore to make the products which they contain, illegal.

The new illegal status of these products has enabled the Department of Anti-Drug Policy to activate the Police forces for controlled raids on smart shops which market them and therefore to remove from the market the reason behind numerous intoxications in Italy because of the consumption of products containing cannabinoids or synthetic cathinones.

These operations have been made possible thanks to coordination between the Department of Anti-Drug Policy, Ministry of Health, Collaborating Centres and Institutions in the flows of information which have been maintained during the period of operations.

The System has achieved significant visibility including overseas participation in European and international panels where the Italian strategy is particularly applauded both for its promptness and for its efficacy in the prevention of intoxications and the strong impact in terms of prevention and countering trafficking and dealing of narcotic substances.

It can therefore be concluded that the working method used thus far has been valid, reliable and, above all, effective. It is therefore believed that it should proceed according to the guidelines set out and continue the activity of the System in the areas described above. Any areas of monitoring and intervention may be opened based on the appearance of new needs or new conditions, which cannot today be foreseen.

PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga

Ministero della Salute

SISTEMA NAZIONALE DI ALLERTA PRECOCE
E RISPOSTA RAPIDA PER LE DROGHE
NATIONAL EARLY WARNING SYSTEM - N.E.W.S.

European Monitoring Centre
for Drugs and Drug Addiction

Reitox
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Coordination of bio - toxicological aspects

Istituto Superiore di Sanità
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General coordination and management

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