Monitoring illicit psychostimulants and related health issues

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Chapter 2

The Drug Information and Monitoring System (DIMS) in The Netherlands: implementation, results and international comparison

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Abstract

The Ministry of Health of The Netherlands has made illicit drug testing for drug users possible since the nineteen nineties, in order to prevent serious health hazards associated with unexpected dangerous substances. This system of illicit drug testing is called the Drug Information and Monitoring System (DIMS). In nearly two decades more than 100,000 drug samples have been handed in at the testing facilities that are part of the DIMS. This review describes the methodology of the DIMS and overviews results of the three main psychostimulant drug markets that have been monitored, i.e. ecstasy, amphetamine (speed) and cocaine. Additionally, monitoring results of hallucinogens are also described for the first time. For comparison, alternative international monitoring systems are described shortly and some of their results. Finally, drug monitoring is discussed from the perspectives of policy, prevention and the drug users themselves.

Introduction: Dutch drug policy

From a historical point of view, drug policy and legislation on drug use in The Netherlands is substantially different from that in many other countries. The aim of Dutch policy is to reduce both the demand for and the supply of drugs, and to limit the risks of drug use. One of the main features of Dutch policy on drugs is harm reduction, i.e. preventing drug use and limiting risks and harm to users and the people with whom they associate. This policy is based on recognition of the fact that, in an open society, drugs are quite simply available, and therefore (problematic) drug use is also unavoidable [Mensink & Spruit, 1999]. In The Netherlands it is an offence to produce, possess, sell and import or export drugs, although it is not considered an offence to use them. Preventive strategies are aimed to reduce the demand for drugs, while professional care limits the harm they cause to users and the people they associate with. To cut off supplies the authorities are cracking down on organized crime. Because in The Netherlands drugs are primarily regarded as a health issue, the minister of Health is responsible for the overall coordination of policy on drugs. The
central objective of the Dutch drug policy has already been formulated in the seventies of the past century. As in many Western countries, the drug problem in The Netherlands underwent a fundamental change at the end of the 80’s, beginning of the ninety nineties. In the slipstream of the increasingly popular rave scene the popularity of synthetic drugs such as ecstasy grew rapidly. Ecstasy became popular due to its non-addictive properties and euphoric effect.

The Dutch drug policy in the early nineties was characterized by great uncertainty about the substances being used, the user groups, and the risks [de Kort & Kramer, 1999; Spruit, 1999]. Use of the new synthetic drugs involved effects and risks that were different from those associated with the traditional substances of abuse. Instead of addiction, the most important risks became acute and chronic damage to the user's health. However, the risks that these new substances posed to health varied considerably, depending on their contents, the settings in which they were taken and individual factors. The characteristics of the new drug users were also very different from those of the traditional drug addicts [Parker et al., 1999]. Users of synthetic drugs were not marginalized, deviant young people who had adapted lifestyles revolving around drug use. The new psychotropic substances were consumed on an incidental, recreational basis by young people who did not differ from non-users in most respects. In fact, the only similarity with the previous decade was that the drugs being used were also psychoactive substances.

During the nineties and at present, besides using new synthetic drugs, the new generations of recreational drug users also started to embrace more traditionally abused drugs, like cocaine [Nabben, 2010]. Because of its psychostimulant properties, not that different from amphetamines, and it had an image of an associated successful and prosperous lifestyle. Because cocaine use poses its own unique array of health risks, especially when as casually used by the recreational users as synthetic drugs, and cocaine as traditionally adulterated substance with various pharmacological compounds, the widespread use of it has added an additional concern to the health authorities in The Netherlands.
The Ministry of Health developed information material aimed at discouraging young people from using ecstasy and other drugs associated with the nightlife settings [Spruit, 1999]. Specific measures were propagated to prevent or deal with problems caused by drug use at dance venues, raves and clubs, such as good ventilation, the presence of first aid teams and availability of free drinking water [Pijlman et al., 2003]. The scale in which they were used and the specific risks that the range of new recreational drugs brought about, such as the lack of certainty about their dosage and composition, made the government decide to monitor this market adequately [Spruit, 1999, 2001]. Illicit drug market monitoring was deemed necessary for surveillance, in order to detect acutely hazardous substances, dosages or situations at an early stage of appearance on the drug market.

The Drug Information and Monitoring System (DIMS)

From the viewpoint of harm reduction and prevention, it was essential to gain knowledge about the appearance of new risky substances on the drug market and to take decisive preventive action. To enable the monitoring of the rapid changes on the market for recreational drugs adequately, testing services were set up where users could have the composition and dosage of their XTC tablets and other drugs tested. These testing services, provided within the framework of the national Drug Information and Monitoring System (DIMS), offer valuable insights into the dynamic recreational drug market, particularly for policy makers. Additionally, it enables prevention activities to be expanded towards a group of drug users that would normally not be reached. The testing facilities of the DIMS network are usually embedded in the prevention departments of institutions for the care of addicts. Traditionally, these departments have much experience in prevention activities on the very problematic level of drug addicts, recreational drug users were not seen by these institutions. Since the foundation of the DIMS, users are frequently warned about the health risks associated with recreational substances. The authorities will act immediately when dangerous drugs are in circulation. Depending on the severity of circumstances, the network of testing facilities will be alerted,
flyers are distributed at clubs and rave venues and/ or warnings are published in the regional or national press [Spruit, 2001]. A nationwide network of test facilities at drug prevention institutions in different places in The Netherlands takes part in the DIMS. Drug users hand in ecstasy tablets or other preparations anonymously for a test. The personnel working at these testing facilities are health and prevention professionals, they communicate about the effects of the particular substances and their associated risks. A few of the participating institutions are merely receiving stations and directly send all the samples they receive to the DIMS Bureau at the Trimbos Institute and do not offer the opportunity for identifying any tablets at their own offices. However, most of the testing facilities are able to identify some of the tablets at the moment they are handed in by the drug user. This is referred to as 'office testing'.

“Office testing”

First the outward characteristics of tablets are registered, including diameter, thickness, weight, colour, presence of a groove, light or dark speckling (if present), and any logo visible (and its design). Second, a Marquis reagent test is performed to find out whether a tablet contains any ecstasy-like substances, amphetamine, a hallucinogenic compound, or none of these. The next step is to determine whether information is already available about the specific tablet based on these external characteristics and results of the Marquis test. This is done with the help of an online electronic database which is updated weekly by the DIMS Bureau. The database contains features of all (ecstasy) tablets that have recently been analyzed in a laboratory. Because of this weekly input of information on tablets and because of the fact that ecstasy tablets are usually produced in large batches, certain tablets can be determined and recognized through this specially developed and weekly updated database on the DIMS website, the 'recognition list'. The average MDMA (3,4-methylenedioxymetamphetamine) content and the variation of the tablet are then known, and the tablet does not have to be analysed necessarily in the laboratory. When the consumer decides to have the tablet analyzed in the laboratory anyway, its analysis results can be used for validation of the
recognition list. This has shown a 99% reliability of the recognition list. Therefore, this “office testing” recognition system provides the testing facilities throughout the country with a tool to give the drug consumer an immediate and accurate test result, without having to hand over the actual tablet. On average, 30% of tablets are determined this way.

Tablets that are not recognized by this on-line determination system and those about which doubt exist together with other drugs samples such as powders, capsules and liquids are forwarded to the DIMS Bureau at the Trimbos Institute. When possible, additional information, such as the place of purchase, the price that was paid and the consumer’s knowledge and opinion of the product is added. Finally, at the testing facility, a unique individual number is given to the drug consumer by which he or she is able to communicate the particular drug sample’s test result one week later. At the DIMS Bureau itself, all samples received are registered, and details are carefully re-examined for possible re-assessment of the determination that was done by the testing facilities. Basically, all samples received by the DIMS Bureau are then coded, packaged and transported to the laboratory for full chemical analysis (see Figure 1 for a scheme of the DIMS system).

![Figure 1. A schematic representation of the DIMS system.](image)

**Laboratory analyses**

Qualitative and quantitative analyses of the drugs samples that have been sent to the DIMS Bureau were performed in the laboratory of the Delta Psychiatric Hospital (Deltalab, Poortugaal, The Netherlands), which specializes in analyzing drug samples. A set of robust analytical methods was used to identify known and unknown components, to quantify and classify them. After crushing and homogenizing the sample, three separate analytical techniques were used. First, thin layer chromatography
(Toxilab® A) was performed for identification. Therefore, a small part of the sample (approximately 2 mg) was concentrated on a Toxidisc®, placed in the chromatogram and developed according to the Toxilab® A procedure. The analytes were identified by relating their position (RF) and colour to standards through four stages of detection: a colouring stage I (Marquis reagent), a washing stage II, an UV fluorescence stage III and finally a colouring stage IV with Dragendorff’s reagents. The Toxilab® methodology including three reference samples provides a robust identification [Goldschmidt, 2004]. An extensive library enables the chromatographer to check on correct location of spots as well as the identification of new substances.

Subsequently, the quantification of the main components (e.g. amphetamine, metamphetamine, 3,4-methylene-dioxyamphetamine (MDA), 3,4-methylene-dioxyethylamphetaamine (MDEA), N-methyl-a-(1,3-benzodioxol-5-yl)-2-butamine (MBDB), caffeine, cocaine and heroin) was performed with gas chromatography - nitrogen- phosphorous detection (GC-NPD). The samples were pretreated: after being crushed, 25 mg sample was ultrasonified in 0.01 M HCl. An internal standard was added (Chirald, Sigma-Aldrich, Zwijndrecht, The Netherlands); thereafter a liquid-liquid extraction was performed with Toxitube® A, a diluted sample of the extract was used for the cold-on-column injection on the GC-column (WCOT-CP-Sil-8-CB, length 25 m, id 0.32 mm df 0.25 μm). The total runtime was 12-28 minutes on a programmed time - temperature scale (75 - 280 °C) with nitrogen-phosphor-detector and helium as carrier gas. The two methods were running independently and were used as a mutual confirmation. In case of any discrepancies, or trace amounts requiring quantification, a gas chromatography-mass spectrometry (GC-MS) method was introduced as the tiebreaker. This generally needed to be done in approximately 10% of the samples. GC-MS (Varian Saturn 4D, Varian Medical Systems, Houten, The Netherlands) conditions were similar to GC-NPD and substances were identified full scan (EI) with the NIST-library. GC-MS was also used for quantification of certain uncommon substances (e.g. γ-hydroxybutyrate (GHB), γ-butyrolactone (GBL), para-methoxyamphetamine (PMA), para-methoxymethamphetamine (PMMA),
ephedrine, ketamine and lysergic acid diethylamide (LSD)). In exceptional cases, identification was performed using advanced GC-MS and nuclear magnetic resonance (NMR) spectroscopy structural analysis (e.g. 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-dimethoxy-4-bromoamphetamine (DOB) and 4-methylthioamphetamine (4-MTA)). Combining different routes for clarification and quantification leads to a growing list of identified compounds in illicit drugs found over the years (Fig. 2).

Figure 2. A flowchart representing the procedure of clarification of substances by the laboratory.

Drug users

An important difference between the DIMS and other ways of collecting toxicochemical data on drug samples, such as drug seizures by the police, is the fact that data are collected directly on the user’s level and there is contact with the users. With the DIMS, this means there is information exchange between the personnel at the testing facilities and the users.
Most important information, such as personal adverse effects, or adverse effects experienced by friends, with the drug sample in question is inputted and saved in the DIMS database. Other important inputs in the database are regional origin, date, source of purchase, price and reason for testing. Other relevant information may be added by the testing personnel, but anonymity of the drug user is always guaranteed, one of the main conditions to keep the DIMS system trustworthy for drug users. The information supplied by the users is often crucial in determining which substance is associated with unexpected risks and in which part of the country these risks may possibly occur. From the perspective of the institutions for addiction and mental health care that provide the testing facilities it is important to have one-on-one contact with young, recreational drug users as target for their prevention and harm reduction activities.

There have been at least two studies that attempted to describe the users that utilize the DIMS as a test facility for their drugs [Benschop et al., 2002; Korf et al., 2003]. These suggested that users utilizing testing systems are broadly similar to non-testing users. We can therefore consider the target group of the DIMS system as a reasonable reflection of all recreational drug users. The vast majority of drug users that visit the DIMS testing services are youths or men with an ethnic Dutch background who are engaged in paid employment or study. The group includes both experienced users who take ecstasy every week and less experienced ones who just take it occasionally. As well as taking ecstasy, they report considerable experience with alcohol, tobacco and cannabis, and to a lesser extent also with cocaine and other drugs. Most of them have no experience with heroin or basecokie. The most common lifetime pattern of ecstasy use involves increasing amounts taken up to a peak of use, followed by a decline to a somewhat lower level. The average dose is two tablets per occasion. If ecstasy is taken in combination with another substance, it is usually alcohol, and, to a lesser extent, cannabis. Tablets are usually bought from a friend or a known dealer some time before a night out. Buying ecstasy, knowing the dealer is considered far more important than obtaining tablets with a familiar logo or colour. Visitors of the test facilities were also asked about the main reason why they have their
drugs tested. The majority answered curiosity about the results, followed by health concern and circulating warnings about dangerous drugs. With regard to the attitude towards prevention and harm reduction, the testing systems were seen as a very reliable source of information and users also appreciated this way of contact with prevention organizations [Benschop et al., 2002; Korf et al., 2003].

The DIMS results are not, by definition, an exact representation of the ecstasy market in The Netherlands. The DIMS monitoring system depends on drug samples handed in by users, and will therefore not be an exact reflection of the use and availability of drugs on the market. However, the DIMS is a qualitative monitor that does not focus on the precise number (quantity) of specific tablets or other drugs on the market, but on the contents (quality, chemically and toxicologically) of drug samples. However, a study comparing drug samples as delivered at the DIMS with those obtained from police seizures at dance venues and rave parties, showed that the DIMS results in fact provide a fairly accurate picture of the total Dutch ecstasy market at consumer level [Vogels et al., 2009].

**Monitoring results**

Since the DIMS was set up in 1992, the Dutch illicit drug market has now been monitored for almost two decades. In particular DIMS follows movements of ecstasy, amphetamine and cocaine and to a lesser extent, of synthetic hallucinogens on the market. Cannabis products, hallucinogenic mushrooms and doping-related substances such as anabolic steroids are not systematically monitored. For cannabis-related products, DIMS has a different monitoring system [Pijlman et al., 2005]. Here we will discuss the DIMS results of the contents of ecstasy, amphetamine, cocaine and LSD drug samples over the past 18 years. More specific details for ecstasy may be found in Spruit, 2001 and Vogels et al., 2009 and for amphetamine and cocaine in Brunt et al., 2009, 2010.
Figure 3. Number of drug samples per year delivered at DIMS between 1993 and 2010. Data reflect pharmaceutical appearance.

Figure 4. Relative contribution of tablets, amphetamine, cocaine, XTC-powders and other drugs delivered at DIMS between 1993 and 2010 that have been analyzed in the laboratory.
It is well-known that The Netherlands has been an important country for the illegal production of amphetamine and ecstasy for many years [UNODC, 2008], and it seems reasonable to assume that most ecstasy and amphetamine on the Dutch consumer market comes directly from this illegal production. This contrasts with cocaine, which is exclusively obtained through illegal imports. Large changes in the composition of amphetamine and ecstasy are therefore often a direct reflection of changes in production processes, such as shortages of precursors or other chemicals. In contrast, changes in the composition of cocaine could be explained by law enforcement activities affecting export and import.

As for the overall results of the monitor, a combined total of more than 100,000 drug samples have been handed in at the DIMS since 1992 until July 2010. The vast majority of these samples were tablets, falling into the categories "recognized" or "analyzed by the laboratory" (Fig. 3). Figure 4 shows the proportion of tablets, powders and other drugs (liquids, capsules, papertrips) that have been analyzed in the laboratory between 1993 and 2010. Powders make up the largest part of the rest of the drug samples, these comprise mainly MDMA-, speed- or cocaine powders. Liquids, capsules or miscellaneous forms of drug samples only make up for a very small percentage of the total.

Ecstasy

There is a difference between what in pharmacological literature is defined as ecstasy and what is called ecstasy by drug users. Pharmacological and chemical scientific literature defines ecstasy as 3,4-methylenedioxy-N-methylamphetamine (MDMA) [Segen, 2002]. When epidemiological or socio-scientific research refers to ecstasy, preparations are meant that are known to the interviewees by that name. By no means everything that is sold as ecstasy is MDMA [Vogels et al., 2009; Parrott, 2004]. In the beginning of the nineties, MDMA, MDEA and MDA were the substances most frequently found in tablets bought as ecstasy (Fig. 5). MDMA, MDEA and MDA, often referred to as ecstasy-like substances, are substituted methylenedioxyphenethylamines, a chemical class of
derivatives of the phenethylamine group, to which group also amphetamine belongs. Apart from MDMA, MDEA and MDA, MBDB, or "Eden", also belongs to the group of methylenedioxyphenethylamines (see Fig. 6 for chemical structure formulas).

The use of MDMA in The Netherlands was first reported in 1985 [Konijn et al., 1997]. MDMA induces the so-called entactogenic effect [Nichols, 1986]. MDMA and MDA hardly exert any hallucinogenic effects and MDA causes nothing more than light illusory perceptions and distorted images. MDEA has a stronger stimulating effect than MDA and MDMA, but a weaker entactogenic effect.

The most common form of MDMA incorporated in ecstasy tablets is the hydrochloride salt. It is a white powder that is easily soluble in water. Ecstasy products on the market are seen typically as tablets with a characteristic logo, less commonly as powders, capsules, liquids or crystals. A typical ecstasy tablet contains between 80 and 100 mg of MDMA. From the literature, it may be concluded that people take anything from half a tablet to several tablets per evening or weekend [Gouzoulis-Mayfrank et al., 2000; El-Mallakh et al., 2007]. If these figures are used as a reference mark, the recreational doses taken by users amount to 0.5-4 mg/kg, distributed over many hours and sometimes several days. In some cases, peak use can be as high as 10 mg/kg. What people take and how much they take depends, however, on factors such as the effects they want to achieve, their degree of experience and the actual, often unknown, composition of the tablets.
Figure 5. Composition of tablets sold and bought as ecstasy handed in at DIMS per year, a number of novel substances found are given at the top of the figure, in order of appearance through time.
Figure 6. Chemical structures of the methylenedioxyphenethylamines: MDMA, MDA, MBDB and MDEA.

Figure 5 summarizes the composition of tablets sold as ecstasy as analyzed by DIMS in the laboratory throughout 1993-2010. The picture shows that there have been two periods during which many tablets contained other substances in addition to or instead of MDMA. In and around 1997, many ecstasy tablets contained amphetamine and in and around 2009 many tablets contained *meta*-chlorophenylpiperazine (mCPP) instead of or in addition to MDMA. At the peak of the shortage of MDMA, in October 1997, only 30% of the ecstasy tablets handed in at the DIMS contained MDMA or a MDMA-like substance. The peak of shortage of MDMA in 2009 was in March, with only 40% of all ecstasy tablets containing MDMA.

MDEA and MDA, which were present in about 30% of the ecstasy tablets before 1997, have virtually disappeared from the ecstasy market; MDEA and MDA were never present in substantial amounts, since 1997. Sporadically, nowadays, only small amounts of MDEA and MDA are found in combination with MDMA in tablets. Apart from the marked decline in the number of tablets containing MDMA-like substances, the periods around
1997 and 2009 are characterized by the appearance of other psychoactive substances in tablets sold as ecstasy, e.g. MBDB, 2C-B, atropine, 4-MTA, PMA around 1997 and mCPP and mephedrone around 2009 (Fig. 5). The appearance of PMA was accompanied with a national warning campaign in The Netherlands, since this is a much more hazardous substance as any MDMA-like substance, with a steep dose-response curve [Jaehne et al., 2007]. In the late 1990s, PMA appeared in ecstasy tablets all over the world and caused numerous emergencies and even deaths [Kraner et al., 2001; Schifano et al., 2003a; Dams et al., 2003; Refstad, 2003]. Between 1996 and 2001 less than 50% of the ecstasy tablets contained more than 70 mg MDMA; the same applies for 2009, when only 42% of the tablets sold as ecstasy contained more than 70 mg MDMA per tablet. Before 1997 and between 2000 and 2009, more than 50% of the ecstasy tablets contained more than 70 mg MDMA per tablet.

Speed

In the nineteen thirties amphetamine was marketed as a nasal inhaler to shrink mucous membranes under the trade name Benzedrine™. Early users of the Benzedrine inhaler discovered that it had a euphoric stimulant effect, which resulted in becoming one of the earliest synthetic stimulants widely used for non-medical (recreational) purposes [Rasmussen, 2009]. Speed and pep are the street names for amphetamine, like XTC and ecstasy are street names for MDMA. In The Netherlands, amphetamine is a controlled substance since 1976 [Buisman, 2000]. The proportion of the people in The Netherlands that recently used amphetamine, as well as the lifetime prevalence of the general population of twelve years and older, is quite low and relatively stable, in 2005 0.3 and 2.1 percent respectively [van Laar et al., 2010]. In the mid-nineties of the last century there has been a temporary increase of amphetamine abuse. In that period, speed became especially popular among certain subgroups of partygoers. They often distinguished themselves from others by music preference (hardcore) and dress [ter Bogt, 1997; Doekhie et al., 2009]. Because amphetamine (speed) is much cheaper than cocaine (coke), it was previously also known as "coke for the poor". Methamphetamine is closely related to
amphetamine. In Thailand, tablets containing methamphetamine are sold as Yaba [APAIC, 2010]. Yaba is much stronger and is much longer acting than amphetamine. In The Netherlands, recreational use of amphetamine is much more common than abuse of methamphetamine; in fact, methamphetamine use is very uncommon.

Unlike MDMA, amphetamine has no entactogenic properties. The recreational user of amphetamine seeks the mental and physical stimulation which it produces. The desired effects usually last up to four hours and as the effects begin to wear off may be succeeded by a period of restlessness, anxiety, fatigue, disinterest or tiredness [Rasmussen, 2009]. Some users seek the stimulating properties of amphetamine for other purposes. Those in monotonous occupations may abuse amphetamine in the workplace and students may use the drug to decrease tiredness, enabling studying for long periods of time [Rasmussen, 2009].

Amphetamine is a member of the phenethylamine family. As an illicit drug, amphetamine is mostly found as a sulfate salt, which is a white powder, easily soluble in water. Although amphetamine appears in tablets with logos similar to ecstasy, on the street amphetamine is mostly sold in powder form and like cocaine, it is often snorted [van Laar et al., 2010]. When snorted or ingested, a dose may vary from several tens to several hundreds of milligrams depending on the purity and the individual tolerance for the drug.

Between 1992 and July 2010, 8,239 powder samples bought as speed have been handed in at the DIMS. In about 85% of these samples, the amount of amphetamine was high enough for quantification. Thus, over the years, 15% of the speed powders did not contain a quantifiable amount of amphetamine. Between 1997 and 2001, the percentage of samples that did not contain quantifiable amounts of amphetamine was over 20 percent, reaching a peak of over 40% in 1999. Until 1996, the number of speed samples delivered to the DIMS was hardly high enough to describe the speed market. Since 1996, the number of samples increased to over 10 samples per month from 1996 until 1999, and since 2000 on average more than twenty samples per month were handed in. In 2008 and 2009, more than sixty samples per month were received at the DIMS.
The analyzed speed powders that were handed in between 1995 and 2010, with detectable amounts of amphetamine, contained on average 30% pure amphetamine (30.2 ± 0.2%; mean ± SEM). Between July 1998 and April 2001, the mean amount of amphetamine decreased to less than 20% with an absolute low in January 2000 of less than 5%. Simultaneously with the decrease in amphetamine concentration, the amount of caffeine in speed powders increased (Fig. 7). The purity of speed, expressed as the mean percentage of amphetamine, seems to follow an inverse relationship with the percentage of caffeine over time, with the mean percentage of amphetamine in a powder being high, the percentage of caffeine being low and vice versa.

**Figure 7.** Mean percentage of amphetamine and caffeine in speed powders per year (quartiles indicated by scaling lines on axis). Only powders containing quantifiable amounts of amphetamine (>1%) have been included.
A similar phenomenon as in 1999 occurred in 2008/2009, with declining amphetamine percentages and increasing caffeine percentages. This time, an absolute low was reached in December 2008, with a mean percentage of amphetamine of 18% and a mean percentage of caffeine of 60%. The amount of samples handed in did not drop, and neither did the percentage of samples not containing quantifiable amounts of amphetamine. The most common route of synthesis for amphetamine is by the Leuckart method [Rasmussen, 2009]. This method uses benzylmethylketone (BMK, 1-phenyl-propanone) as a precursor. Around 1999 and in 2008 and 2009, there were shortages of this amphetamine precursor in the illegal drug production circuit. Therefore, it became extremely difficult to produce amphetamine. The available speed powders hardly contained amphetamine and were much more cut with caffeine. Caffeine is often added to amphetamine at the production source, whereas other cutting agents, such as glucose and other sugars are usually added elsewhere [UNODC, 2008]. Unlike MDMA, a shortage of amphetamine on the illegal drug market does not seem to cause the appearance of “new” psychoactive compounds in speed powders. However, the transient shortage of amphetamine in 2008/2009 caused the appearance (and disappearance) of two psychoactive substances: 4-fluoroamphetamine and 4-methylamphetamine (not to be confused with methylamphetamine), substances that had not been seen in speed powders before (see Fig. 8 for chemical structure formulas).
Figure 8. Chemical structures of amphetamine, methamphetamine, p-fluoroamphetamine and p-methylamphetamine.

Cocaine

Cocaine is a natural product extracted from the leaves of Erythroxylon coca. Cocaine has a psychomotor stimulant effect similar to that of amphetamine. Cocaine base and the hydrochloride salt are white powders [King, 2009]. In recreational use, cocaine is typically snorted whereby it is absorbed through the nasal mucosa. Since 1993 DIMS received cocaine powders; in the early nineties, on average between 5 and 10 samples per month, but in subsequent years this number quickly increased. Since 2004, more than 50 samples per month were handed in. Of the powders that were sold as cocaine averagely 10% did not contain quantifiable amounts of cocaine. The remaining powders contained 56 ± 0.3% (mean ± SEM) pure cocaine. In the nineties (1993-1999), the average purity was higher than in the past decade (2000-2010), 66.3 ± 0.7% (mean ± SEM) versus 54.9 ± 0.8% (mean ± SEM) respectively. Often adulterants are added to increase weight, and sometimes other, mainly less costly substances are added to make up for lost potency [Fry & Levy, 2009]. Alternatively, adulterants are added to camouflage the decrease in potency of the cut up cocaine,
usually other local anesthetics, which produce the same numbness to the gums as cocaine, thereby creating the false impression to the consumer of high purity. The cocaine powders that were handed in at DIMS were cut with a variety of substances: inert compounds (mannitol, maltose, inositol, flour, starch), synthetic local anesthetics (lidocaine, benzocaine, procaine, tetracaine) and other pharmacologically active substances (caffeine, phenacetine, levamisole, hydroxyzine, diltiazem) [Brunt et al., 2009].

![Graph showing mean percentage of cocaine purity in samples with and without pharmacologically active substances](image)

**Figure 9.** Mean percentage of cocaine (purity) in cocaine powders containing pharmacologically active adulterants and samples not containing pharmacological adulterants. Only powders containing quantifiable amounts of cocaine have been included.

Approximately 10% of all cocaine samples contained a synthetic local anesthetic. The average amount of pure cocaine in these samples (44.6 ± 0.9%; mean ± SEM) was significantly lower than in the samples not containing a synthetic local anesthetics (57.0 ± 0.3%; mean ± SEM).
Similarly, cocaine cut with other pharmacologically active substances also contained less pure cocaine (38.8 ± 0.4%; mean ± SEM) than cocaine powders that did not contain these substances (62.1 ± 0.3%; mean ± SEM) (see Fig. 9). Apparently, all of these adulterants were added for compensatory purposes as mentioned above. Table 1 summarizes the major pharmacologically active substances found in DIMS cocaine powders during the last five years (2005-2009). Atropine was found in 2005, and again in 2007. The presence of atropine in cocaine was accompanied by several hospitalizations and even fatalities in both occasions, in The Netherlands and across the border (Italy, France, Germany, Belgium) [EMCDDA, 2007; Braida et al., 2008]. In situations as these, it is a vital part of the surveillance function of the DIMS to immediately orchestrate a national mass media warning to warn the (potential) users and furthermore, to alert the international network of early warning systems throughout the EU.

Table 1  Psychoactive compounds most commonly found in DIMS cocaine powders (2005-2009).

<table>
<thead>
<tr>
<th></th>
<th>Present in % of samples</th>
<th>Mean ± S.E.M.</th>
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<tbody>
<tr>
<td>Phenacetin</td>
<td>38</td>
<td>25.5 ± 1.3 (n=956)</td>
</tr>
<tr>
<td>Levamisole</td>
<td>21</td>
<td>7.4 ± 0.3 (n=338)</td>
</tr>
<tr>
<td>Caffeine</td>
<td>15</td>
<td>9.0 ± 2.6 (n=502)</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>8</td>
<td>n.q.</td>
</tr>
<tr>
<td>Procaine</td>
<td>7</td>
<td>n.q.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>6</td>
<td>n.q.</td>
</tr>
<tr>
<td>Hydroxyzaine</td>
<td>3</td>
<td>n.q.</td>
</tr>
<tr>
<td>Benzocaine</td>
<td>0.4</td>
<td>n.q.</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>0.1</td>
<td>n.q.</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>0</td>
<td>n.q.</td>
</tr>
<tr>
<td>Atropine</td>
<td>0</td>
<td>2.0 ± 3.0 (n=5)</td>
</tr>
</tbody>
</table>

N.q., not quantified; n, number of samples quantified; ¹ Data from 2010.
LSD and other hallucinogens

Of all hallucinogens, lysergic acid diethylamide (LSD or “acid”) is the most prevalent handed in at the DIMS. LSD samples are usually papertrips, taken from greater formats of colourfully decorated paper. The LSD is impregnated into the paper at a certain concentration, which does not have to be equally spread among individual papertrips taken from one original sheet of paper. The other form in which LSD is handed in at the DIMS is as microdot. This is a minute tablet, usually weighing less than 10 mg, without logo or much other specific characteristics. Most microdots are coloured uniformly black.

In The Netherlands, LSD is used by small subpopulations of users and in other settings as the mainstream clubs or events where ecstasy or cocaine are used. One subpopulation is often referred to as the “psychonauts”; the experimental drug users that are interested in exploring new psychological avenues in the brain as well as going out and listening to dance music [Schifano et al., 2003b]. This dance music is often another style (e.g. psytrance, a psychedelic type of dance music) than the more mainstream dance music played at big clubs or events [Nabben, 2010]. Because LSD is used in the busy and noisy setting of a dance party, the dosages used nowadays tend to be considerably lower (20 – 125 μg) than the dosages that were reported in the 1960s and 1970s (300 – 2000 μg; [Henderson & Glass, 1994]). This reduces the risk of a negative mental experience or “bad trip”, while undergoing LSD’s specific effects.

At the DIMS, first numbers of LSD samples were handed in around 1999. In that year, only 6 samples were handed in that were sold as LSD. This increased to 10 samples in 2000 and 12 in 2001. From 2002 and onwards the amount of LSD samples handed in at the DIMS became more and more substantial, with a peak of 99 samples in 2003 and a 66 samples for the first half year of 2010. Based on these numbers, something can be said about the LSD market, at least on an annual basis. Around 80% of the samples that were sold as LSD contained the hallucinogenic substance (Fig. 10). An exception was 2002, when only 26% of all LSD samples contained the hallucinogen, in the rest of the samples the concentration
was either not quantifiable or traces of other compounds were found, such as methamphetamine or DOB. In 2007, some papertrips were handed in containing fentanyl, a very potent synthetic opioid, which led to a special warning campaign, directed at the small target group of LSD users. The average concentration LSD ranged from 20 µg to 96 µg/unit (unit meaning either papertrip or a microdot) (Fig. 10). However, the variation in LSD concentration was substantial: from 1 – 500 µg/unit. This wide spread in concentration between units probably represents two extremes of the market: the low dosages, probably being used at nightlife settings, such as dance parties and raves, whereas the higher dosages might come from the more experienced users that take LSD in a more secluded, private setting [Erowid, 2010a].

![Figure 10. Percentage of samples containing LSD of all samples that were sold as LSD and the average concentration of LSD per trip (papertrip or microdot), 3 substances found in samples sold as LSD are given at the top of the figure, in order of appearance through time.](image)

There were only a few other hallucinogens handed in at the DIMS with 2C-B being the most prevalent one after LSD. Initially 2C-B was sold as small tablets, with concentrations between 1-15 mg 2C-B per tablet. During the
second half of the 2000s, 2C-B was frequently found in tablets sold as ecstasy and these tablets highly resembled ecstasy tablets, with different logo’s, shapes and colours. Recently, 2C-B was also encountered in LSD papertrips (Fig. 10). Concentrations 2C-B rarely exceeded 5 mg per sample (tablet or papertrip). Other hallucinogens that have been found by the DIMS were on sporadic basis and comprised 2,5-dimethoxy-4-ethylthiophenethylamine (2C-T-2 and 2C-T-7), N,N-Dimethyltryptamine (DMT), 5-methoxy-diisopropyltryptamine (5-MeO-DiPT) and Dextromethorfan (DXM), among others.

Other drug markets and monitors

Illicit drug testing in order to gain insight in certain drug markets for health or even law enforcement purposes is nothing new. Usually, information concerning the contents of illicit street drugs comes from the various national forensic institutes that are situated in most countries. These forensic institutes often receive parties of drugs that have been seized by the police, either at customs, clandestine production facilities or directly from consumers at local events. Actually, this is no different in The Netherlands, were the National Forensic Institute provides important information about the drug market in addition to the DIMS system. The presence of two independent systems offering quantitative and qualitative information about the state of the illicit drug market makes for an ideal situation to compare and validate results. It also adds to a more complete picture of the illicit drug market and allows to specify which parties of drugs were distributed domestically and which were probably meant for export. Regardless the advantages, most countries do not have an additional direct costumer-derived information source of the illicit drug market, besides the seized samples.

However, besides The Netherlands, there are other nations assembling illicit drug market data from additional sources than the forensic institutes, like the French National Identification System for Drugs and Other Substances (SINTES) in France, a combination of police and customs’ seizures and samples obtained directly from the consumers by social field workers [Giraudon et al., 2007]. TICTAC in the United Kingdom, which
utilizes amnesty bins from large clubs and venues in some major British cities to describe the chemo-analytical contents of the drugs in these bins [Ramsey et al., 2001; Kenyon et al., 2005]. There is the “on-the-spot” dancefloor High Performance Liquid Chromatography (HPLC) analysis by the Check-It team from Vienna, Austria, and in Switzerland there is the Safer Party© initiative, collecting samples from the users directly through fieldwork contacts [EMCDDA, 2009; Helmlin, 2010]. Their analysis procedure is based on an automated HPLC for the separation process [Helmlin, 2010]. These HPLC systems are equipped with DAD/UV-Vis Spectrometers (DAD=Diode Array Detector) and autosamplers and analysis results can be obtained within 20 minutes, making it useful for testing on the dancefloor. In the United States there is the DanceSafe website, they test drugs and make the test results public to the potential consumer audience [Tanner-Smith, 2006; Dancesafe, 2010]. It more or less seems to work according to the way the DIMS recognition list works (see paragraph "office testing" of this review), with the exception that the drug consumer has to do the colouring test him-/herself and combine the result of this test with the tablet characteristics given on the website. Finally, the National Drug and Alcohol Research Centre in Australia provides a very elaborate system of monitoring the illicit drug markets, and besides using the laboratory analysis information provided by the Australian Crime Commission they use a wide network of drug users for information on “perceived drug purity” for instance, collectively referred to as the Illicit Drug Reporting System (IDRS) and the Ecstasy and Related Drugs Reporting System (EDRS) [Matthews et al., 2009; Topp et al., 2004]. Whereas these initiatives have all contributed to the knowledge of the composition of the illicit drug markets throughout the world, by far, most international chemo-analytical data were reported by the different national forensic institutes [Cole et al., 2002; Simonsen et al., 2003; Camilleri & Caldicott, 2005; Sharma et al., 2005; Teng et al., 2006]. Because of the large differences in types of drug sample monitoring methodologies between the various countries around the world it is virtually impossible to make an one-on-one comparison between countries on market variables, such as purity, price or contents. Large institutes, such
as the EMCDDA and the UNODC, provide some insight into the variety of the different global illicit drug markets [UNODC, 2010; EMCDDA, 2009], but the quantity and extent of coverage still differs considerably between countries. Nonetheless, figures 13-16 aim to provide some insight into international comparison between the three main illicit drug markets previously discussed in this review, i.e. ecstasy, cocaine and amphetamine. Important to bear in mind is that not all countries provided information on every substance, for instance amphetamine is barely monitored outside of Western-Europe, but methamphetamine instead. Also, the analytical methods of the different international laboratories might differ considerably, which of course impacts on the results as well. Therefore, the results are more indicative of global trends than they are exact comparisons.

Comparing the different monitoring results in recent years to those of the DIMS, it is evident that every country shows its own unique drug market composition and dynamic (Figure 11). Roughly, and not surprisingly, the different Western European ecstasy markets show more resemblance to each other as to Eastern Europe or Western Australia for instance (Fig 11). The different Western European “speed” markets also show resemblance, but the amphetamine purity in all of them is considerably lower than it is in The Netherlands (Fig 11). In contrast to the ecstasy markets, the different cocaine markets show a less clear pattern of resemblance between Western European countries. The markets in the US and Western Australia are in fact very comparable with many European markets (Fig 11). This makes sense, since the source of cocaine (Latin America) is the same in all considered countries.

Additionally, new psychoactive additives are also reported by many countries, providing an alternative source of comparison between drug markets (Table 2). To keep matters simple, only the cocaine and ecstasy markets are compared, since these two markets are most known for emerging new substances/adulterations anyway. The United States are compared to two major Western-European countries, France and Germany, to provide some degree of cross-Atlantic comparison. As is shown, the ecstasy markets show a lot of similarities between these countries divided by the Atlantic. However, the United States seems to have its own specific compounds appearing in ecstasy tablets, such as dextromethorphan (DXM) or phentermine for instance. On the other hand, phenethylamines like MBDB or MDHOET were not seen in the United States ecstasy market. As for cocaine adulterants, there is once again a more uniformous spread among all three countries, confirming cocaine as the import product it is to all these countries [UNODC, 2010]. Interesting
from a global diversion point of view, however, are the different time-points that the adulterants arose in the different countries. As with the purity data, it is important to bear in mind that the drug testing systems between these countries might probably differ in a number of aspects.
Table 2. New psychoactive substances detected on the ecstasy- and cocaine markets in 2004 – 2009 in Germany, United States and France

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Germany</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecstasy market</td>
<td>2C-I, MBDB</td>
<td>Ephedrine, MBDB</td>
<td>BZP</td>
<td>mCPP</td>
<td>mCPP, BZP</td>
<td>Mephedrone, PMA</td>
</tr>
<tr>
<td>Cocaine market</td>
<td>Lidocaine, phenacetin, caffeine, procaine</td>
<td>Phenacetin, lidocaine, caffeine, diltiazem, procaine, levamisole, hydroxyzine, bezocaine</td>
<td>Phenacetin, lidocaine, diltiazem, caffeine, procaine, hydroxyzine, Levamisole, benzocaine, amphetamine</td>
<td>Phenacetin, lidocaine, caffeine, procaine, hydroxyzine, levamisole</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>United States</strong></td>
<td>Ephedrine, DXM, BZP, TFPMP, creatine</td>
<td>Ephedrine, DXM, fentanyl, mCPP, 5-Meo-MiPT</td>
<td>Ephedrine, DXM, ketamine, MDDMA, procaine</td>
<td>mCPP, modafinil, ketamine, provitamin amide, BZP</td>
<td>mCPP, BZP, ketamine, phentermine, 2C-I, 5-Meo-DMT, TFPMP, procaine</td>
<td>mCPP, 2C-B, BZP, ketamine, DXM, FPP, mephedrone, 5-Meo-DMT, TFPMP, diphenhydramine, procaine</td>
</tr>
<tr>
<td>Ecstasy market</td>
<td>Diltiazem, Hydroxyzine, methyl-ephedrine</td>
<td>Procaine, caffeine,</td>
<td>Diltiazem, procaine, caffeine, hydroxyzine, benzocaine, caffeine</td>
<td>Diltiazem, procaine, caffeine, levamisole, nicotinamide</td>
<td>Caffeine, levamisole, lidocaine</td>
<td></td>
</tr>
<tr>
<td>Cocaine market</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>MBDB, 5-Meo-Dipt</td>
<td>mCPP, MDHOET</td>
<td>4-MTA, ketamine, mCPP, TFPMP, BZP</td>
<td>BZP, ketamine, TFPMP, 2C-B, mCPP</td>
<td>mCPP, BZP</td>
<td>4-fluoro amphetamine, mephedrone</td>
</tr>
<tr>
<td>Ecstasy market</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine</td>
<td>Phenacetin</td>
<td>Phenacetin</td>
<td>Levamisole</td>
<td>Levamisole</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
market, lidocaine, procaine, Atropine*, lidocaine, procaine, caffeine, isole, phenacetin, diltiazem, caffeine, hydroxyzine, lidocaine, procaine

MBDB, N-Methyl-1-(1,3-Benzodioxol-5-yl)-2-Butanamine; TFMPP, 1-(3-trifluoromethylphenyl)-piperazine; BZP, benzylpiperazine; MDDMA, 3,4-methylenedioxymethylamphetamine; DXM, dextromorphan; MDHOET, 3,4-methylenedioxy-N-(2-hydroxyethyl)amphetamine; 4-MTA, 4-methylthioamphetamine; 2C-I, 2,5-dimethoxy-4-iodophenethylamine.

*Detected in drugs obtained from intoxicated hospitalized patients.

Sources USA: [Dancesafe, 2010; United States Drug Enforcement Administration: Microgram Bulletins, 2010].

Sources France & Germany: [EMCDDA: National reports, 2010; EMCDDA: EWS final reports, 2010].
Discussion

Illicit drug market monitoring is recognized as a surveillance tool for the benefit of public health [Ritter, 2010; Katz et al., 2010], somewhat analogous to agencies concerned with inspecting product quality of foods or medicines, that are well-spread throughout all countries over the world. Similar to warnings about food poisonings, drug monitors try to keep track of acutely hazardous substances found in illicit drugs and issue warnings to take a rapid course of action. The monitoring results of the DIMS have provided valuable qualitative information on changes in the content of drug samples in The Netherlands throughout the years. The DIMS results were used for national and international risk assessments and major warning and prevention activities. In this capacity it functions almost directly at the level of the potential drug consumers and this ensures quick delivery of the prevention message. Secondly, it attempts to accurately follow drug market processes in time. This is in contrast to the forensic institutes which do not usually aim at public health related matters, nor strive to monitor processes through time.

During nearly two decades of monitoring street drugs, the DIMS has shown that the different psychostimulant markets are very dynamic and new psychoactive substances and additives are emerging frequently. Interestingly, the rise of new substances often co-occurs with the shortage of a specific illicit drug of abuse. This applied to amphetamine, 4-MTA and PMA, found in ecstasy tablets, during the 1990s or mephedrone and mCPP during the last couple of years. Mephedrone, actually, is rather a special case as recent literature has made clear [Winstock et al., 2011; Measham et al., 2010; Brandt et al., 2010a; Brandt et al., 2010b; Brunt et al., 2010]. It was sold through various websites, as plant fertilizer, especially in the UK [BBC, 2009]. Although in The Netherlands it was found as a replacement for MDMA in ecstasy tablets, mephedrone seems to be a part of a far more greater whole: “legal highs”, referring to drugs sold through the internet that mostly do not have a legally controlled status. This phenomenon seems to be persistent, because, after the ban of mephedrone in a number of countries, a new generation of post-
mephedrone products were already signalled [Brandt et al., 2010a]. These products can be produced in laboratories anywhere around the world and their sale via the internet will make legislation more complex, thereby changing the face of drug trade radically. Besides these new psychoactive substances, also novel adulterants, such as levamisole, could provide new challenges for health care and policymaking [Chang et al., 2010; Zhu et al., 2009; Buchanan et al., 2010; Bradford et al., 2010].

In the UK, massive use of mephedrone among youth caused such a stir, that it was banned earlier in 2010 [Morris, 2010]. It has been banned in many other EU member states at the moment and a risk assessment procedure has already been conducted by the EMCDDA and the European Medicines Agency (EMA), on the basis of a EMCDDA-Europol report [EMCDDA, 2010], which may possibly lead to a ban in the remainder of the EU member states. Following the continuing rise of new psychoactive substances on the drug markets, described in this review, such collective European efforts to ban substances seem to have increased in frequency over time. Other substances that underwent the same fate and got banned were BZP, 4-MTA, PMA, MBDB, among others [EMCDDA, 2009; EMCDDA Risk assessments, 2010]. But it is the monitoring systems that are at the core of these Pan-European policy initiatives.

Whereas the special drug policy of The Netherlands makes a system like the DIMS possible, other countries have made great efforts of their own to create intelligible insights into their drug markets. Some of these efforts resulted in similar systems like the DIMS, whereas others derive drug market information in a different way [Giraudon et al., 2007; Ramsey et al., 2001; Kenyon et al., 2005; Tanner-Smith, 2006; Matthews et al., 2009; Schifano et al., 2006a; Mounteney & Haugland, 2009; Legleye et al., 2008]. As suggested in this review, it is apparent that analytical testing procedures for drug samples probably differ between many countries, reflecting on the results. Several factors could be of importance: ways of extraction, measuring to the base or salt form, purity definitions, quantification method used, etc. Nevertheless, on various drugs of abuse, very similar results over time were reported by different countries [UNODC, 2010; EMCDDA, 2009]. This provides interesting avenues of investigation,
like import, export, routes of dispersion or sources of adulteration for example. Recently, perhaps one of the most striking new chemo-analytical methods of measuring drug market information that has been reported by several research groups is the detection of drugs of abuse, their metabolites and adulterants in public wastewater by HPLC-tandem mass spectrometry [Huerta-Fontela et al., 2007; Kaspryk-Hordern et al., 2009; van Nuijs et al., 2009; Shao et al., 2009; Zuccato et al., 2008; Chiaia et al., 2008]. In this way, drug markets can be monitored without the involvement of anyone participating in the illicit drug circuit, from users to producers. But this method rather measures consumption itself and is better developed for large, non-specified, bulk analyses from certain areas. User-specific or sample-specific data are impossible to gain by this method. These methods might be useful in assessing the scale of temporal and spatial illicit drug use in the future.

Finally, there is the question of the benefit of a monitoring system for the drug users themselves. Despite the fact that most recreational drug users are relatively well-informed about the risks, they are often willing to accept them nonetheless [Gamma et al., 2005; Murphy et al., 2006; Morgan et al., 2010]. So how could a system like DIMS possibly aid in prevention or harm reduction? There are at least two arguments to be made in favour of a drug analysis and testing system in this context. Firstly, it has been suggested that individual directed harm-reduction advice serves the needs of existing users better than simply promoting abstention [Gamma et al., 2005]. In this sense, the one-on-one contacts the users have with the personnel at the DIMS testing offices, combined with factual information concerning their drug purchase and other drugs circulating the streets largely meets the information needs of drug users. Additionally, young drug users often dismiss government messages as tendentious and untrustworthy and more persuaded by personal contact with well-informed peers or professionals [Gamma et al., 2005; Murphy et al., 2006; Falck et al., 2004; Allott et al., 1999; Toumbourou et al., 2007]. It has to be noted, however, that the reach of a drug testing system such as the DIMS is limited to a fraction of all (potential) drug users.
Conclusion

Monitoring the market of illicit drugs creates a platform on which to base policymaking and public health preventive activities, as well as for research purposes. This review of the DIMS system and other drug testing systems has made clear that the market for psychoactive substances of abuse is continuously moving, underlining the necessity to continue the systematic monitoring of this market. Future challenges for the DIMS could lie in developing ways to monitor the internet- and doping drug markets, as these seem to be developing rapidly and good insights into these markets are lacking.