

# Analysis of drugs in sewage: an approach to assess substance use, applied to a prison setting

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Reported levels of illicit drug use and diffusion are determined using data from law enforcement agencies (customs, police, national *Gendarmerie*), health sources (reports, statements, etc.) and epidemiological surveys. In addition to the potential biases of these sources (under- or over-estimation of substance use trends), estimating illicit drug use also involves considerable time and monetary costs with respect to conducting surveys, performing analyses and generating reports.

In the 2000s, a new method to estimate psychoactive substance use was developed: testing drug residues in sewage. Analysis of effluent samples from sewage treatment plants (STP) initially made it possible to measure the quantities of drugs and metabolites originating from a specific population (in urine and faeces) (Daughton 2011). Then, in 2005, a formula was proposed which enabled the quantities measured to estimate the quantities used in the area demarcated by the sewage network connected to the sampling point (Zuccato et

al. 2005). Ten or so years later, this innovative method usually named "sewage epidemiology", is now applied in numerous countries.

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In 2011, a group of researchers in this field came together to propose a European study aiming to carry out a simultaneous week long sampling campaign in all of the cities involved. The first comparative study on substance use levels in Europe, based on this method, brought together 19 major European cities, including Paris (Thomas et al. 2012). This study currently involves more than 25 cities, including non-EU cities. In 2013, the first international convention, Testing the Water, was organised by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), based in

Lisbon. This provided an opportunity to review all research on the subject, which had developed considerably both in terms of method and representativeness. Internationally renowned, this approach leads to an objective estimation of illicit drug use in a given population area, varying in size depending on the chosen sampling point. This method evidently has some biases, and the results obtained are merely a reflection of the situation at a specific moment in time and does not provide data on the prevalence of use or user profile. However, it has the advantage of allowing illicit substance use to be mapped, in terms of the quantities used and type of substance, according to different geographical sectors. Comparing these findings with the economic and social data in the regions studied, together with the possibility for monitoring use over time appear to be relevant applications of this approach, to help manage prevention action and harm reduction measures related to illicit drug use.

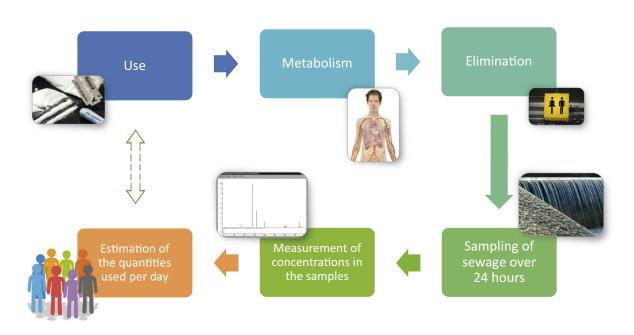
The objective of this report is to present the method and its application in the specific context of a university research project initiated in 2015 in a prison setting. An initial feasibility study was conducted in three prisons in France. The first results, together with the difficulties encountered, the limitations and ethical considerations will be developed in order to generate all of the aspects necessary to understanding and interpreting these types of analyses.

# **METHOD**

In order to understand this method in detail, it is essential to note that a drug, for instance, cocaine or heroin, is made up of several active molecules, cocaine or heroin, respectively, and other active molecules, either manufacturing or degradation residues, or added cutting agents.

Once absorbed, the cocaine or heroin molecules are metabolised before or after reaching the receptors. Metabolism transforms all or part of the molecules consumed into metabolites. Hence, these metabolites, along with the active molecules if metabolism is not complete, are eliminated in urine and/or faeces found in sewage (Figure 1). Briefly, this method involves sampling, analysing, quantifying, calculating and estimating the quantity of metabolites and active molecules present in a volume of sewage over a defined period. However, at each step, numerous parameters should be taken into account to reduce errors in the final estimation of the quantities of drugs used, as far as possible.

Figure 1 - Illustration of the method used to estimate the quantities used based on the sewage analysis



# **S**ELECTION OF THE SAMPLING POINT

The sampling point should be located at a site where the origin of sewage is well-defined, since it is essential to clearly identify the pipes in an establishment or local sewage network to shed light on the population connected to this network. Although a number of chemical and biological markers are present in sewage which enable the number of individuals connected to the network to be estimated, this does not enable the scope of the network to be evaluated. This information is nonetheless essential in order to then utilize other demographic data and interpret the results obtained. Once this prerequisite has been met, the sampling method then needs to be chosen.

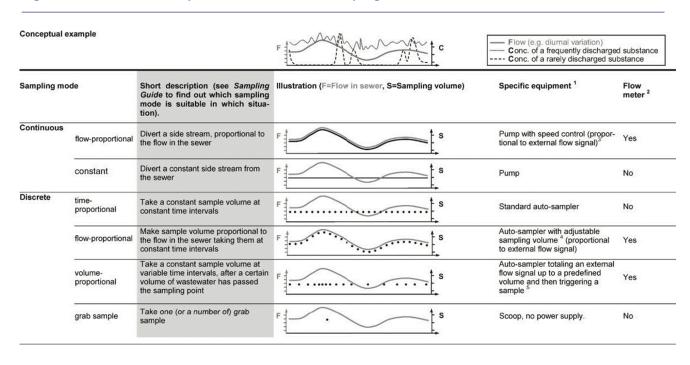
# **S**AMPLING METHOD

The essential characteristic of a sample is its representativeness: this parameter is all the more important since the analyses are carried out in order to evaluate the efficacy of purification systems or to evaluate illicit substance use. In this context, spot sampling is not at all representative of molecule circulation and should be avoided.

In the majority of studies, sampling takes place at the inlet and/or outlet of sewage treatment plants (STP), in the form of average samples over a 24-hour period. This type of sampling requires the use of automatic samplers which can be programmed to taking discrete time-proportional samples (Boleda *et al.* 2009; Castiglioni *et al.* 2006; Huerta-Fontela *et al.* 2008; Postigo *et al.* 2010; Zuccato *et al.* 2005), flow-proportional samples (Berset *et al.* 2010; Chiaia *et al.* 2008; Irvine *et al.* 2011; Karolak *et al.* 2010; Lai *et al.* 2011; Terzic *et al.* 2010; van Nuijs *et al.* 2009), or volume-proportional samples, for example, a 100-mL sample every 1000 m³ (van Nuijs *et al.* 2011). However, the sampling method is not always specified (Boleda *et al.* 2007; Mari *et al.* 2009; Pedrouzo *et al.* 2011) and certain authors use spot sampling, despite its lack of representativeness (Bones *et al.* 2007; Hummel *et al.* 2006; Kasprzyk-Hordern *et al.* 2010; Loganathan *et al.* 2009).

Intermittent, average and time-proportional samples do not take into account fluctuations in flow rate and do not reflect the increase in the quantities of molecules discharged at the highest points in circulation. Samples proportional to volume will be taken closer together the faster the flow rate, and vice versa, with the risk of insufficient sampling at slower flow rates and when substance discharge is at a high level. It has been established that the most representative model corresponds to a protocol able to sample a volume proportional to flow rate at a constant time interval, with estimated uncertainty of 5% (Figure 2).

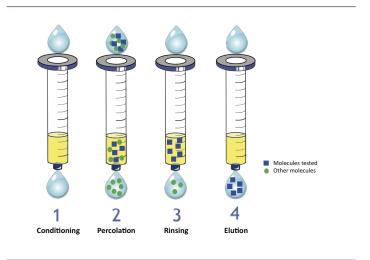
Figure 2 - Outline and description of different water sampling methods (from Ort et al. 2010)



# **A**NALYTICAL METHOD

The samples are initially filtered to eliminate as much suspended solid matter as possible. The extraction and concentration phase takes place after filtration. The elements tested, drugs and metabolites, are extremely diluted in sewage and are therefore present in very small quantities, in the region of nanograms per litre (equivalent to a sugar cube in an Olympic swimming pool). Although highly sensitive, the equipment used for testing is unable to detect such small quantities. The sample extraction and concentration phase passes a specific volume of the sewage sample through a cartridge consisting of a solid phase which captures the molecules of interest, i.e. solid-phase extraction (Figure 3). The molecules captured by the cartridge are separated from the solid phase by passing a solvent volume smaller than the sample volume, i.e. elution. The fraction obtained, the eluate, is then evaporated and the dried extract is diluted in an even smaller volume. Hence, the final sample contains the same quantity of drugs or metabolites, but in a smaller volume. As the concentration is much higher, this facilitates analysis.

Figure 3 - Principle of solid-phase extraction



The assays are generally carried out by liquid chromatography coupled to mass spectrometry (MS) in tandem (HPLC-MS/MS or UPLC-MS/MS).

- Liquid chromatography is a separation method. In the test sample, the molecules investigated are part of a matrix which makes identification of the molecules more complex. Owing to this technique, the molecules present in the sample are separated, thus facilitating identification by the detection system.
- Detection and quantitation are generally carried out using a mass spectrometer. This highly specific and highly sensitive technique is able to detect and quantify molecules present in very small quantities.

## **CALCULATION OF QUANTITIES USED**

Drug use is estimated based on the residue concentrations measured in sewage, taking several parameters into account: metabolism and rate of elimination of the drug or its metabolite, the daily volume of water passing through the sampling point and the number of inhabitants connected to the network.

Use is estimated by means of "reverse" calculation as per the following equation (Zuccato et al. 2008b):

$$Q_{used} = \frac{C_{24h} \times V_{24h}}{U_{ex}} \times M_{ratio} \times 1000 / N_{inhabitants}$$

#### where:

- Q<sub>used</sub>: quantity used in 24 hours,
- $\blacksquare V_{24h}^{2...}$ : volume of water flowing through the sampling point over the 24-hour sampling period,
- U<sub>ex</sub>: percentage tracer excretion,
- M<sub>ratio</sub>: drug and tracer molecular mass ratio (equal to 1 when calculation is based on the drug),
- N<sub>inhabitants</sub>: number of inhabitants (inhab.) connected to the STP.

As regards synthetic stimulants, MDMA, amphetamine, methamphetamine, the tracers are the drugs themselves, with 65%, 30% and 43% elimination, respectively.

The tracer used for cocaine is its main metabolite, benzoylecgonine with 45% elimination.

The active molecule of cannabis, tetrahydrocannabinol (THC), and its metabolite, carboxy-THC, are eliminated in trace amounts (<1 %); however, the latter is normally used to calculate cannabis use, with elimination of 0.6% (Terzic *et al.* 2010; Zuccato *et al.* 2008b) or 2.5% (Postigo *et al.* 2011).

As regards opiates, heroin is metabolised and eliminated mainly in the form of morphine; however, it is difficult to evaluate heroin use based on measured concentrations of morphine given its therapeutic use. An intermediate metabolite, 6-monoacetylmorphine, exists which may be used as a tracer for heroin use; however, this metabolite is eliminated at a very low level of 1.3% in urine (Baselt 2004). The other method involves using morphine concentrations, with 42% excretion, and then subtracting the estimated fraction corresponding to therapeutic use, based on therapeutic morphine use (Zuccato *et al.* 2008a).

Several approaches are described for methadone: either the use of methadone (Postigo et al. 2011) with 27.5% excretion, or the use of its main metabolite, EDDP (2-ethylidine-1,5-dimethyl-3,3-diphenylpyrrolidine), with excretion of 23% (van Nuijs et al. 2011) or 31% (Terzic et al. 2010).

Table 1 - Examples of drugs and their selected tracer for calculation of use.  $U_{ex}$  = urinary elimination percentage,  $M_{ratio}$  = molecular mass ratio (drug/metabolic tracer) (Zuccato et al. 2008a)

Substance	Metabolic tracer (MT) for calculation of use	U <sub>ex</sub> (%)	M <sub>ratio</sub> (drug/MT)
Cocaine	Benzoylecgonine (BZE)	45	1.05
MDMA	MDMA	65	1.0
Amphetamine	Amphetamine	30	1.0
THC	THC-COOH	0.6	0.91
Methadone	EDDP	23	0.82
Buprenorphine	Buprenorphine	95	1.0

As a general rule, use is expressed as the quantity per day relative to 1,000 inhabitants. However, some authors (Bijlsma *et al.* 2012; Boleda *et al.* 2009; Castiglioni *et al.* 2011; Huerta-Fontela *et al.* 2008; Irvine *et al.* 2011; Kasprzyk-Hordern and Baker 2012; Mari *et al.* 2009; Thomas *et al.* 2012; van Nuijs *et al.* 2012; Zuccato *et al.* 2008b) prefer to calculate daily drug or metabolite circulation in sewage, expressed as g/day or mg/day/1,000 inhab., without reference to the quantities used. In contrast, some authors have attempted to estimate the number of doses used based on mean purity percentages and mean quantities for each dose.

Furthermore, the results are sometimes expressed relative to the total population or relative to a defined fraction of the population according to age group, based on the presentation of statistics in EMCDDA reports (Zuccato *et al.* 2005).

Hence, in order to connect drug use to the population, and compare different studied sites, it is essential to determine, with optimum precision, the size of the population covered by the sewage network connected to the sampling point.

# **U**NCERTAINTY AND LIMITATIONS

Each magnitude used to calculate substance use comprises an error which is more or less easy to quantify in the calculation of uncertainty.

# Sampling methods

The uncertainty depends on the representativeness of the sampling method and sampling frequency. The frequency required in order to minimise error mainly depends on the extent of the short-term variations in the concentrations of the compounds in sewage, and sewage flow rate at the sampling point. Sampling uncertainty was estimated at between 5% and 10%, and the preferred sampling method, mentioned above, is average samples taken over 24 hours and subject to flow rate, with approximately 5% uncertainty (Castiglioni *et al.* 2013).

# Degradation of target molecules

Uncertainty due to degradation of the molecules in sewage depends on the degradation rates before and after sampling. Most of the target molecules used to estimate drug use are fairly stable in sewage conditions (pH approximately 6.5 and temperatures between 15 and 20° C). However, stability after sampling will depend on the storage conditions, and these parameters may vary from one study to another. It has been established that the optimum storage method was to acidify the sample at pH 2 and store it at -20° C, or to store the extraction cartridges at 4° C before elution. If this storage protocol is applied, the calculated uncertainty is less than 10% (Castiglioni *et al.* 2013). Under these conditions, the uncertainty related to storage of the compounds may be estimated at 10%; however, if these storage measures are not followed, uncertainty increases in relation to the stability of the molecules.

# Molecule quantification

The uncertainty of the quantification of the compounds within the sewage matrix, taking into account extraction of the molecules and all errors related to the analytical method, was estimated at 15%.

#### Data on metabolism

The uncertainty for estimation of use obtained based on the equation should take into account the percentage absorption for drugs depending on the routes of administration (oral, snorting, injecting, etc.), the percentages for metabolism and elimination in urine and, lastly, frequency of use. In addition, uncertainty may also vary according to the target molecules chosen to estimate use since, depending on the molecules, interindividual variations on the stated parameters may be more or less considerable. This uncertainty is very difficult to evaluate given the number of variables and deviations which may exist between individuals. Castiglioni *et al.* (2013) established this uncertainty at 26% when estimating cocaine use based on measured BZE (its main metabolite) concentrations.

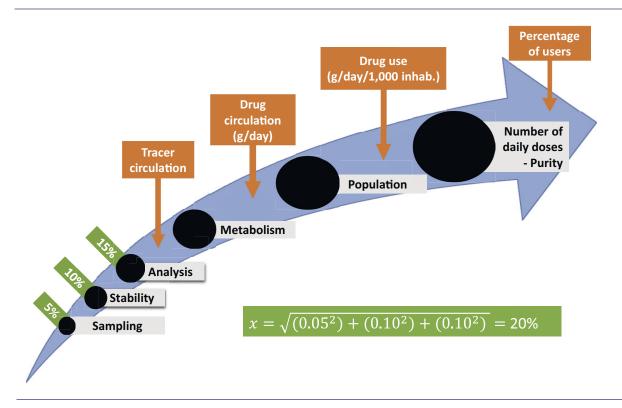
# Estimation of the population

The size of the population connected to the STP where the samples are taken may be estimated according to several methods: by census, nominal STP capacity, biochemical parameters, and chemical or biological markers. Although census is the most reliable method, it is often difficult to obtain the most recent data, and it is not always straightforward to define the urban areas corresponding to a STP with accuracy. The method recommended by Castiglioni *et al.* (2013) is to use hydrochemical parameters; however, these vary according to sewage type and proportions (household, industrial, hospital, etc.). This entails thorough knowledge of both networks and waste. The uncertainty concerning estimation of the population varies between 7% and 55% according to the estimation method applied, the hydrochemical parameters used, and knowledge of the network (Castiglioni *et al.* 2013).

# Summary of uncertainty

Figure 4 shows the changes in uncertainty as the method progresses, and in the method used to express the chosen result. The first step, with results expressed in the form of daily tracer circulation, is mainly marred by sampling and analytical errors. Taking into account 5% uncertainty for sampling, 10% uncertainty for the stability of the molecules and 15% analytical uncertainty, by applying the propagation of uncertainty law, uncertainty in terms of tracer circulation may be estimated at 20%.

Figure 4 - Outline of the changes in uncertainty as the method progresses, and in the method used to express the chosen result



# Limitations of the method

The use of sewage analysis to estimate the quantities of drugs used is not therefore devoid of uncertainty. Determining the number of users adds uncertainty in terms of the estimation of the number of inhabitants in the area covered by the sewage network from the sampling point, the elimination percentages which can vary from one individual to another, the purity of the substances in circulation in the region, together with the mean number of doses used per person.

Hence, although authors such as Zuccato et al. (2008b) have attempted to determine the number of doses used based on the quantities used estimated by taking into account the quantity of drug per dose and percentage purity, this method cannot yield any information on prevalence in terms of use. It simply serves to evaluate the quantity of drugs eliminated in the urine and faeces of a specific population, over a given period. If samples are taken regularly, it is then possible to monitor the circulation of these molecules and thus identify trends in use over time. This, moreover, represents the most worthwhile and relevant use of this method which is not intended to replace declaration-based surveys which allow prevalence in terms of use to be estimated. These are therefore two different but complementary methods for monitoring use.

Furthermore, other limitations also exist. Firstly, those related to the conditions of the network in which the samples are taken. The sewage network may not be completely intact and a substantial fraction of the sewage may leak into the soil without reaching the STP (Devault *et al.* 2014). Weather conditions may also affect the concentrations of the molecules in the sewage matrix. Heavy rain results in dilution, with a risk of under-estimating the quantities of drugs eliminated. High temperatures accelerate the degradation of the molecules, also giving rise to a risk of under-estimation (Devault *et al.* 2014). Thus, it is advisable to take samples during temperate climatic periods, avoiding rain.

Lastly, as sewage is a matrix with very high organic and inorganic content, it would seem very difficult to screen for all drugs possibly present in the sample, even after filtration, purification and concentration. Hence, only preselected molecules included in the analytical method are investigated. In view of this bias, it is thus possible that certain drugs may not be identified despite being used and present in the sewage.

# STATE OF THE ART

Initially conducted in a few European urban areas, and testing a small number of molecules and metabolites, these studies have now been developed with a view to being conducted on a large scale in numerous cities worldwide, and to estimate the use of a large number of substances.

The first study in France was conducted in 2009, in the Paris region, by the *Laboratoire de Santé publique - Environnement, Université Paris Sud* (Karolak *et al.* 2010). This study, conducted for a year, notably enabled an initial evaluation of illicit drug use in Paris and its suburbs. Sewage samples were taken from five STP in the Paris region, to assay the levels of cocaine, MDMA, amphetamine and their metabolites. Although amphetamine has never been detected, the quantities measured for the other molecules made it possible to estimate cocaine and MDMA use, which corresponded to 385 mg/day/1,000 inhabitants and 6.4 mg/day/1,000 inhabitants on average, respectively (Karolak *et al.* 2010). Lastly, daily samples were taken over several full weeks, at intervals over time. Variations in the eliminated quantities of certain substances were evidenced in the course of the week and referred to as a "weekend effect". This phenomenon, mainly observed for stimulants, corresponds to an increase in the levels measured during the weekend or in the following days (up to Tuesday for MDMA) compared with other days of the week. This phenomenon reflects the recreational use of these substances in the festive setting, predominantly observed during the weekend. This trend is also observed for party events, such as the 2009 *Fête de la musique* in Paris (Karolak *et al.* 2010).

The team from *Université Paris Sud* then extended the scope of its study to 25 urban areas in mainland France and tested for new substances, namely buprenorphine and methadone, both of which are dispensed as opioid substitution treatments and may also be used in a non-therapeutic context (Néfau *et al.* 2013). The results obtained offer a snapshot of the quantities of illicit drugs used at the studied sites at a given time. Significant differences between the sites along with variations over time were also observed. However, a higher number of repeated samples from each site over a longer period would have been necessary in order to obtain consolidated data on the quantities used and thus compare these findings with data on the prevalence of use obtained in general population surveys.

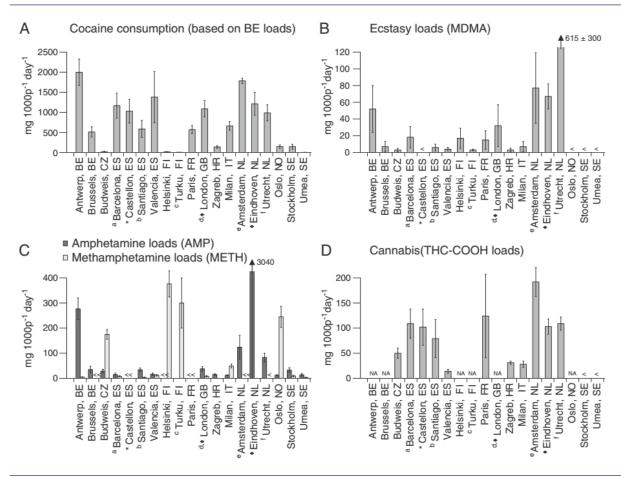
This is the purpose of a European study, conducted by the SCORE group which has been coordinating samples in several major EU cities since 2011 (Thomas *et al.* 2012). During the first sampling campaign in 2011, marked differences were already observed between different countries, notably concerning cannabis, cocaine, amphetamine and methamphetamine use. Hence, the highest quantities of THC-COOH in sewage, reflecting cannabis use, were measured in Spain and France (Figure 5), among the European countries with the highest prevalence of use, and also in the Netherlands where this could be attributed both to use by inhabitants of the urban area concerned and also the many tourists who go there to use cannabis. As regards stimulant use, the methamphetamine levels measured were below the limit of detection in countries where the estimated quantities of cocaine used and amphetamine levels measured in sewage were high, in Belgium and the Netherlands. Conversely, in countries with high quantities of methamphetamine, Czech Republic and Finland, the amphetamine levels or quantities of cocaine used were very low or even non-existent (Figure 5). These findings are consistent with the data of the epidemiological surveys which show that Western European countries are among those with the highest cocaine use while methamphetamine is particularly present in the Czech Republic (EMCDDA 2016).

France's participation in this European project allowed samples to be taken in the Paris region from 2009 to 2016. All of the results of this study, together with the data originating from other participating European cities are available on the EMCDDA site<sup>1</sup>. In order to describe the French data in detail, an interpretation of the results for 2009 to 2013 is shown in Figure 6.

Estimated mean weekly cocaine use increased from 368 mg/day/1,000 inhab. in 2009 to 568 mg/day/1,000 inhab. in 2013, this change being particularly pronounced between 2012 and 2013.

<sup>1.</sup> http://www.emcdda.europa.eu/topics/pods/waste-water-analysis#panel2

Figure 5 – SCORE study (Thomas et al. 2012)



Average estimates of cocaine (COC) consumption (back-calculated from benzoylecgonine (BE) loads, the main metabolite of COC) and population-normalized loads of amphetamine (AMP), methamphetamine (METH) in 19 selected European cities and cannabis (THC-COOH, all in mg/1000 inhabitants/day) in 13 of them between the 9th and 15th March 2011 (mean±SD from all sampling days, n=7).

aSampling one week later (16th–22th March 2011). b n=6, sample of Monday 14th March missing. n=6, sample of Sunday 13th March missing. n=6, sample of Saturday 12th March missing. n=6, sample of Monday 14th and Tuesday 15th March missing. Sampling started one day later (10th–16th March 2011). Sampling uncertainty estimated to be larger than variation of interlaboratory comparison of chemical analysis. Exfiltration of sewerage larger than 20%. Na Not analyzed. All measured concentrations were below the limit of quantification.

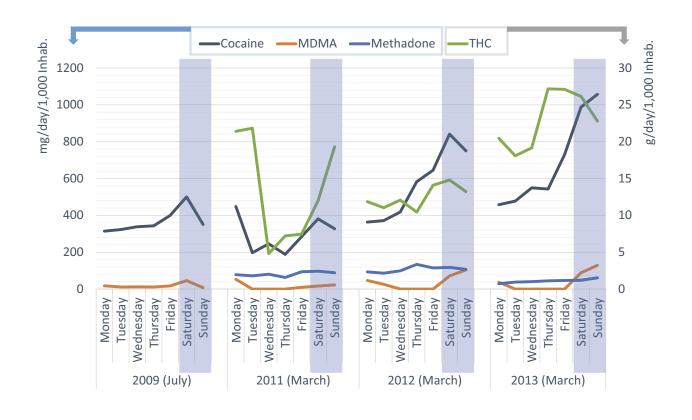
Estimated mean weekly MDMA use, much lower than for cocaine, also shows an increase of 4 mg/day/1,000 inhab. in 2009 to 35 mg/day/1,000 inhab. in 2013, this increase mainly resulting from higher weekend use, this compound not being detected on 3 consecutive weekdays (Wednesday, Thursday, Friday) both in 2012 and 2013. MDMA is increasingly used in a recreational setting, which was described simultaneously based on the ethnographic observations of the OFDT Emerging Trends and New Drugs (TREND) scheme, back in 2012 (Cadet-Taïrou et al. 2014), indicating renewed popularity of MDMA in recreational settings and among a younger and well-integrated population. General population surveys, among 18-64 year-olds (Baromètre Santé) and among 17 year-olds (ESCAPAD), also demonstrated higher MDMA use between 2010 and 2014.

Estimated cannabis use appeared stable in the first 2 years of the sampling campaign (2010 and 2011), between 10 and 20 g/day/1,000 inhab. on average, increasing to 27 g/day/1,000 inhab. in 2013.

Methadone use, only estimated in the last two years of the campaign, has remained stable in the region of 100 mg/day/1,000 inhab. on average over the week.

The samples for 2009 were taken in the week of the 14<sup>th</sup> July, thus including the party events organised for the French national holiday, resulting in 100% higher cocaine and MDMA use (Karolak *et al.* 2010). The values obtained that week are thus higher than the average for the year, consolidating the idea that cocaine and MDMA use in the Île-de-France region has indeed increased since 2009.

Figure 6 - Estimated quantities of drugs used in Paris and its suburbs between 2009 and 2013. THC and methadone use has only been estimated since 2011 and 2012, respectively



Due to its rapid and objective characteristics, this analytical approach has proved to be a valuable addition to the different evaluation schemes already in existence. Based on the data collected, illicit drug use can now be mapped region by region with the aim of pointing out the different patterns of use according to users' geographical and socio-economic environment. Although several uncertainty factors exist (uncertainty in terms of assay of trace amounts in loaded matrices, stability of the molecules, census of study populations, etc.), sewage analysis is an effective instrument for monitoring and estimating psychoactive substance use. This approach may allow associations and public organisations in the prevention field to adapt their public health and drug use harm reduction campaigns, to target their interventions and ultimately distribute their workforce more effectively. This method moreover has the advantage of making it easier to monitor changes in use, particularly the possibility for detecting the emergence of new drugs in the different areas concerned.

# **CASE STUDY: PRISON, CLOSED ZONES**

The scope of the areas monitored by sewage analysis is determined by the sampling point, the site at which samples are taken; it is therefore possible to take samples closer to certain populations higher up the sewage network. More restricted urban areas, housing estates, institutions or even buildings may be targeted. Several studies have already been conducted on housing estates in certain large cities, or at specific sites such as schools or prisons (Brewer *et al.* 2016; Postigo *et al.* 2011; van Dyken *et al.* 2014).

# SEWAGE ANALYSIS IN A PRISON SETTING (LITERATURE REVIEW)

There are few studies on sewage analysis in a prison setting, which help to determine the presence of illicit substances and medications; some of these have already been published. The first of these studies was conducted in 2008 and 2009 in Catalonia (Postigo *et al.* 2011). The analytical results demonstrated the presence of cocaine, THC-COOH (the main metabolite of THC, the psychoactive molecule of cannabis), methadone, morphine, ephedrine, a decongestant with stimulant properties, and alprazolam, a benzodiazepine, in 100% of samples (n=42). The concentrations measured vary from one substance to another, the highest corresponding to methadone, ephedrine and morphine. The number of doses used daily was calculated based on the concentrations measured and an average quantity of substance per dose. Hence, the maximum estimated use corresponded to 9 cocaine doses, 48 cannabis doses, 185 methadone doses, 120 heroin doses, 129 alprazolam doses and, lastly, 1.4 MDMA doses per day, per 1,000 inmates. Furthermore, comparisons with the estimated quantities used based on the sewage analysis method applied to the city of Barcelona, close to the prison, show that cannabis and ephedrine use may be up to 17 times higher in the prison setting compared to the general population (Postigo *et al.* 2011).

The other studies on sewage analysis in a prison setting were conducted in Australia. Thanks to the analytical results, cannabis use was estimated to reach between 20 and 45 doses per day for the whole establishment comprising approximately 500 individuals, including prison guards, along with codeine use (50 to 90 doses per day) and methamphetamine use (1 to 4 doses per day). The substances present in the sewage thus differ between these first two studies. However, these correspond to the findings based on samples taken from the general population. For example, cocaine is present in Spain but not methamphetamine, whereas the opposite was observed in Australia. In the Australian study (van Dyken *et al.* 2014), methadone was also detected and quantified in the samples. Moreover, the authors obtained methadone dispensing data for the establishment, and were thus able to compare the quantities administered with those estimated based on the measurements in sewage. The numbers of estimated doses according to the two methods are equivalent, to within roughly 2 doses depending on the sampling days; this tends to prove that the estimated use of other substances, based on the sewage analysis, is close to the actual situation.

The other studies conducted in Australian prisons (Brewer *et al.* 2016; van Dyken *et al.* 2016) also enabled the detection of cannabis, methamphetamine, codeine and methadone. The team led by van Dyken (2016) also tested for buprenorphine and, as was the case for methadone in their first study (van Dyken *et al.* 2014), the estimated doses used based on the sewage analysis were compared with the doses dispensed as part of the substitution programme. In contrast to the findings for methadone, major differences emerged between estimated use and buprenorphine dispensing data. According to the authors, this difference can be explained by the higher misuse of this substitution medication compared to methadone. The "tablet" form of buprenorphine is much easier to hide and traffic than methadone syrup bottles. Tablets are not always therefore taken when they are dispensed, but may be kept by inmates enrolled on the substitution programme to be sold, traded or used at a later date.

During this study (van Dyken *et al.* 2016), methylone was also identified in some samples. This is a new psychoactive substance (NPS) belonging to the cathinones class, which has stimulant properties. This method also therefore proves valuable in rapidly evidencing the use of new substances.

#### Value of this approach in a French prison setting

Psychoactive substance use among inmates is poorly documented in France. This is estimated from declaration-based surveys, some of which are conducted among new inmates, reflecting their substance use prior to imprisonment: DREES institutional surveys (Mouquet 2005) or conducted by OPPIDUM drug abuse and dependence monitoring centres (Pauly *et al.* 2010), or based on interviews with a sample of inmates (Falissard *et al.* 2006). Qualitative studies have enabled patterns of use to be described, via the Coquelicot study (Jauffret-Roustide *et al.* 2006). Only one local study described inmate drug use while in custody (Sannier *et al.* 2012).

In all cases, these reflect the high prevalence of dependence on psychoactive substances: 10 to 60% of the population interviewed regularly used a drug, mainly cannabis. Less than 10% reported cocaine, heroin or other drug use (MDMA, LSD, glue, etc.). Alcohol use while in custody was also described, along with misuse of psychoactive medications.

Nevertheless, declaration-based surveys are relatively difficult to implement in a prison setting, and the declaration bias is higher than in general population.

No simple drug tests or screens are organised in the prison setting, modelled on what was carried out in British establishments for instance. Furthermore, prison authorities do not draw up reports on the nature of substances seized in a prison setting.

Hence, no objective data are currently available in France to evaluate inmate drug use. The available treatments currently organised for drug-using inmates, and the actions for promoting health and harm reduction measures cannot be fully adapted in practical terms.

In this context, regular sampling of sewage could easily provide this missing information on drug use in a prison setting. Ideally, combining sewage analyses with declaration-based surveys would resolve some of the biases inherent to each of these methods.

Furthermore, a comparison of results from Spanish and Australian studies shows variations in prison settings in each of the countries, from a qualitative (different molecules detected) and quantitative (divergent levels of use for a given molecule) perspective. Thus, using this approach would help rapidly detect the molecules used in French prisons and perhaps reveal specific characteristics according to geographical location.

# **ETHICAL CONSIDERATIONS**

Using this sewage analysis method to monitor substance use bypasses the need to intervene among general population, as required for declaration-based surveys. As a result, sewage analysis might be perceived as pernicious by those concerned, given that they are not approached directly and inclusion in molecular analyses occurs without their consent. However, when samples originate from an environmental source in which it is impossible to identify specific individuals, confidentiality and anonymity are protected (Hall *et al.* 2012). That being said, when a study site is a restricted, closed area, such as public or private buildings, schools or prisons, and has a relatively small population, individuals at these sites may perceive a sewage analysis to be intrusive as well as a breach of their privacy.

Caution should therefore be exercised when designing the study protocol, presenting the study to the study population and particularly when communicating the results to the general public in light of resulting interpretations and reactions. Using this method to monitor drug use in certain housing estates, buildings and specific sites inevitably creates the risk of the study being perceived and/or used as a means of comparing these sites with each other. This difficulty is emphasised when the results are taken up by non-specialists, particularly the media, without measuring the limitations of this type of study. Hence, alarmist media coverage and associated comments could cause the areas concerned to be stigmatised in some respects (Prichard *et al.* 2014).

Some sites, such as prisons, call for even greater caution with regards to the use of sewage results. Although anonymity is protected, provided that samples are not taken from a specific cell and take into account the entire prison, other issues specific to this type of establishment should be taken into account. The results of the sewage analysis may be used to evaluate the effectiveness of the control measures on drug possession and use within the prison setting and to guide management decisions (Prichard *et al.* 2010). Improved access to health care and the development of harm reduction programmes could be the result of this analysis once disclosed, which seems beneficial for inmates. Conversely, depending on the results, the management may opt for the repressive approach and, for instance, increase the frequency of searches, or temporarily suspend visits, etc.

Thus, implementing sewage analysis studies requires prior consideration and agreement between survey administrators and the management of the establishments studied so that all parties agree on the final aim, in compliance with the rights of both inmates and prison staff. It should be noted that prison sewage system samples may also include waste from buildings frequented by administrative staff and include any substance use among personnel. Although this can be prevented based on knowledge of the network, thereby preventing collection of sewage from these buildings, it is more complicated for prison guards whose toilets can be located in the same buildings as inmates.

Prison authorities contribute to the implementation of drug use-related harm reduction measures. They take part in health promotion actions intended for inmates, and guarantee their safety. With the French Ministry of Health, in charge of organising inmate health care in compliance with Law no. 94-43 of 18 January 1994 relative to public health and social protection, it contributes to organising access to care.

Sewage analysis is establishing itself as a possible and efficient means of improving these actions. Their results need to be analysed in complete transparency with all partners concerned so that the programmes developed or envisaged can benefit from the knowledge provided.

# SEWAGE ANALYSIS IN FRENCH PRISONS: A PRELIMINARY STUDY

In 2015, a study initiated by the Prisons Administration Directorate, funded by the *Mission interministérielle de lutte contre les drogues et les conduites addictives* (French Interministerial Mission for Combating Drugs and Addictive Behaviours, MILDECA), supported by the French monitoring centre for drugs and drug addiction (OFDT) was conducted in several prisons by the *Laboratoire de Santé Publique – Environnement (UMR 8079), Université Paris Sud.* 

Although several foreign studies had already shown that this method could be used in a prison setting, the specific characteristics of each country, and also each establishment, could not guarantee the success of any sampling campaigns essential in order to obtain significant results. Hence, the feasibility of the most representative sample possible was initially evaluated. A sample over a 24-hour period and according to flow rate (See Sampling methods p. 3) was taken from each selected prison using a refrigerated automatic sampler.

#### **Establishments**

For confidentiality purposes, we will use codes instead of the names of establishments. Two establishments in the Île-de-France region (IDF1 and IDF2) and one establishment in the Centre Val de Loire region (CVL) were selected, with the authorisation of interregional prison authority departments.

Meetings that brought management and technical teams, along with healthcare providers, were scheduled at each prison long before sampling was initiated. These meetings provided an opportunity to present the study objectives and methodology to key stakeholders, while also defining practical arrangements to perform sampling.

# Choice of molecules

The molecules were selected for the study based on several decisive criteria; the most important is the available data on the prevalence of illicit drug use in France. The main illicit psychoactive substances used in the population are cannabis, cocaine, MDMA/ecstasy and heroin, together with new psychoactive substances (OFDT 2015). Psychoactive medications falling within the scope of misuse may also be included in this list.

The pharmacokinetic profile is the second determining factor in defining the list of molecules to be investigated, more specifically the metabolism and elimination phases. Knowledge thereof helps to identify the substances eliminated in the urine (known as metabolites) and thus liable to be detected in sewage networks (Table I).

Other factors also play a role in the selection of molecules, such as the data available in the literature on sewage analysis, together with the experience acquired by the laboratory.

In the light of the different information collected, the molecules tested for during this study corresponded to:

- heroin and its main metabolites (6-monoacetylmorphine, morphine),
- cocaine and its main metabolites (benzoylecgonine, ecgonine methylester, cocaethylene),
- the main metabolite of THC: THC-COOH,
- MDMA,
- new psychoactive substances belonging to the cathinones class (mephedrone, 4-MEC),
- biological markers for the use of opioid substitution treatments:
  - methadone and its main metabolite (EDDP),
  - buprenorphine,
- a biological marker for benzodiazepine use: oxazepam.

#### Results

Since technical issues prevented samples from being taken at the CVL establishment (See Difficulties encountered p. 16), only results for the Île-de-France establishments will be presented. Samples were taken from two different buildings at the IDF2 site, named IDF2A and IDF2B.

Among the molecules investigated, indicating drug use or substitution treatment, only four showed levels higher than the limits of quantitation in one or more samples. THC-COOH (marker for cannabis use) was present in all samples, and cocaine together with its main metabolite (BZE) in a large majority of samples. Lower levels of MDMA/ecstasy use were also evidenced at one of the sites. Traces of morphine were detected in some samples originating from the IDF1 site, but at insufficient levels for quantitation.

#### ■ Cannabis

THC-COOH was detected at quantifiable levels in all samples. The concentrations ranged from 347 to 3,152 ng/L for the IDF1 site, 1,021 to 8,900 ng/L for the IDF2A site and 640 to 6,240 ng/L for the IDF2B site, corresponding respectively to quantities discharged in sewage of approximately 709 mg, 119 mg and 562 mg. According to the formula shown above (Zuccato et al. 2008b), approximately 7 g to 107 g of pure THC were used per day.

As mentioned in the section on uncertainties, the number of doses used cannot be reliably estimated. However, to provide a clear summary and interpretation of the results, we have chosen to present an indicator of number of doses per day. For this purpose, only the number of inmates present in the buildings concerned at the time of sampling were taken into consideration. Hence, prison staff present at the same time, in the same buildings, were not included in the calculations. Substance use per person may therefore be over-estimated.

The results in terms of the number of doses per day, per 1,000 individuals, are very similar according to the sites. Overall, and taking into account the average THC dose of 34 mg per dose, cannabis use among inmates at the two prisons in which sewage samples were taken may be estimated at between 0.5 and 3 joints per person, per day.

Table 2 - Estimated cannabis use

	IDF1 site		IDF2A site		IDF2B site	
	Min	Max	Min	Max	Min	Max
Quantities discharged in sewage (mg THC-COOH/day)	709		119		562	
Quantities discharged in sewage (mg THC-COOH/day/1,000 ind.)*	545		397		618	
Quantities used (g THC/day)	43	107	7	18	34	85
Quantities used (g THC/day/1,000 ind.)*	33	83	24	60	38	94
Number of doses/day/1,000 ind.*	973	2,432	711	1,777	1,103	2,758

<sup>\*</sup>Results only take into account the number of inmates present in the buildings concerned on the day each sample was collected.

#### ■ Cocaine

Cocaine use was estimated based on assay of BZE, its main metabolite. BZE was detected in sewage from the three sites studied, at concentrations ranging from detectable but non-quantifiable levels of 970, 1,083 and 492 ng/L, respectively, for the IDF1, IDF2A and IDF2B sites. Taking the flow rate values into account, the quantities of BZE discharged over the 24-hour sampling period therefore corresponded to 105 mg, 12 mg and 50 mg, respectively, for the IDF1, IDF2A and IDF2B sites.

These results are consistent with estimated quantities of pure cocaine used ranging from approximately 27 mg to approximately 367 mg per day.

Table 3 - Estimated cocaine use

	IDF1 site		IDF2A site		IDF2B site	
	Min	Max	Min	Max	Min	Max
Quantities discharged in sewage (mg BZE/day)	105		12		50	
Quantities discharged in sewage (mg BZE/day/1,000 ind.)*	81		40		55	
Quantities used (mg COC/day)	244	367	27	40	116	175
Quantities used (mg COC/day/1,000 ind.)*	188	282	90	135	128	192
Number of doses/day/1,000 ind.*	2	4	1	2	2	2

<sup>\*</sup>Results only take into account the number of inmates present in the buildings concerned on the day each sample was collected.

For cocaine also, the results in terms of the number of doses per day, per 1,000 individuals, are very similar according to the sites.

## ■ Opiates

The presence of morphine in the samples is difficult to interpret. This may result from the metabolism of a dose of heroin or direct use of morphine. Regardless of the origin of traces detected in 3 samples from the IDF1 site, the concentrations are below the quantitation limits of the method and it is therefore impossible to draw any conclusions regarding possible opiate use among the inmate population.

# ■ MDMA/ecstasy

Traces of MDMA were detected at the two sampling sites of the IDF2 prison. For building IDF2B, these are below the quantitation limit. However, at the IDF2A site, traces of MDMA were quantified in 4 samples, ranging from 21 to 226 ng/L, which corresponds to an eliminated quantity of approximately 1.27 mg/day. Taking into account urinary elimination levels, the quantity of MDMA used at the IDF2A site is therefore estimated at between 2 to 8 mg/day.

#### ■ New psychoactive substances (NPS)

No traces of the new psychoactive substances investigated (mephedrone and 4-MEC) could be found in sewage from the three prisons studied.

As the metabolic pathways of these new substances have not yet been clearly established, it is also possible that these molecules are not (or only slightly) eliminated in the unchanged form and were not consequently detected by the analytical method used.

## ■ Benzodiazepines

Traces of oxazepam are present in all of the samples at quantifiable levels (132 to 3,104 ng/L); however, as oxazepam is a metabolite of several different benzodiazepines, it is difficult to determine which ones were used. The results obtained simply enable benzodiazepine use to be observed in all buildings at the prisons studied. This result was expected in view of the prescribing data provided by the pharmacies at the particular establishments.

#### **■** Buprenorphine

Traces of buprenorphine were detected at the 3 sites, but in 2 cases (IDF1 and IDF2B), these were below the quantitation limits of the method. The absence of buprenorphine (or its presence in very small quantities) at the IDF1 site was expected as it is not included in the list of the 50 medications most prescribed by the prison health department.

However, at the IDF2A site, a discharged quantity of buprenorphine in the region of 5 mg/day was reported, corresponding to approximately 24 mg/day used, i.e. 3 tablets per day. Based on the premise that use is identical in each building, the results obtained when analysing sewage show that approximately 10,750 tablets of buprenorphine are used over 10 months, as opposed to 53,280 tablets actually prescribed over the same period.

#### ■ Methadone

Methadone use was estimated based on assay of EDDP, its main metabolite. EDDP was detected in all sewage samples, at the three sites studied. The concentration levels range from 51 to 353 ng/L for the IDF1 site, 313 to 8,507 ng/L for IDF2 and 51 to 605 ng/L for IDF2B. Taking into account the sewage flow rate values, the quantities of EDDP eliminated over the 24-hour sampling period are 91 mg, 59 mg and 66 mg, respectively.

Hence, the estimated quantities of methadone used range from 215 mg to 787 mg per day.

Table 4 - Estimated methadone use

	IDF1 site		IDF2A site		IDF2B site	
	Min	Max	Min	Max	Min	Max
Quantities discharged in sewage (mg EDDP/day)	91		59		66	
Quantities discharged in sewage (mg EDDP/day/1,000 ind.)*	70		197		73	
Quantities used (mg MTD/day)	331	787	215	512	238	567
Quantities used (mg MTD/day/1,000 ind.)*	255	606	718	1,707	262	623
Number of doses/day	8	20	5	13	6	14
Number of doses/day/1,000 ind.*	6	15	18	43	7	16

<sup>\*</sup>Results only take into account the number of inmates present in the buildings concerned on the day each sample was collected.

The results in terms of the number of methadone tablets taken per day, per 1,000 individuals, are very similar in sites IDF1 and IDF2B. However, use is significantly higher in building IDF2A. According to the information received from the medical department at this establishment, building IDF2A effectively houses more inmates on methadone substitution treatment.

Based on sewage analysis, the quantity of methadone used at IDF1 are estimated at 2,900 to 7,300 units. Methadone is not included in the list of the 50 most prescribed medications at the time of sampling, and 9,380 units of the last medication on the list were distributed. The estimated number of methadone doses used based on the sewage analysis is therefore consistent with the data provided by the health department at this establishment.

This is also the case for prison IDF2, where 9,834 doses of methadone were prescribed from 1 January to 27 October 2015, i.e. approximately 33 doses per day, and for which the calculations based on the sewage analysis results estimated between 11 and 27 doses of methadone distributed. Hence, for this establishment also, there is a satisfactory correlation between the quantities prescribed and the quantities detected. This makes it possible to validate the methodology for estimating drug use.

#### Difficulties encountered

The major difficulty we faced was of a logistical nature. We needed an access to the sewage discharge pipe to install the sampler. This was possible in all of the prisons concerned by the feasibility study. However, in one prison (CVL), as the discharge pipe was narrower than usual, it was often blocked when sampling was scheduled. The samples could not therefore be taken over the planned period. Hence, the results could not be presented in this report.

The other difficulty involved measurement of flow rate. A flow meter needs to be fitted at the sampling point, for this purpose. At the IDF1 site, the flow meter was installed and the results show a reduction in flow rate between 21:00 and 07:00 in the morning, corresponding to an expected decline in prison activity at night. Recovery seems to be a two-stage process, with an initial peak around 07:30, then a second peak around 09:30. However, a reduction in flow rate was observed between 14:00 and 15:00, although there is no explanation for this, based on the available information.

At the IDF2A site, the flow meter was installed, but the sensor could only record water height due to the configuration of the pipe. No values were therefore available as the flow rate could not be measured. In order to estimate substance use based on the concentrations measured in sewage, flow rate therefore had to be estimated, using the water height tracing and the monthly municipal water consumption recorded in 2015. For the IDF2B site, these calculations were performed by extrapolation from the water heights measured at the IDF2A site.

# **DISCUSSION/CONCLUSION**

# THERE APPEARS TO BE MASSIVE OR, INDEED, ENDEMIC CANNABIS USE IN THE PRISON SETTING

These initial results are not fully in keeping with the declaration-based data available until now.

Despite the limitations in terms of the interpretation of the results arising from technical constraints, failure to take into account the total number of individuals present at the establishment at the time of sampling, and the initial objectives of this feasibility study, these initial results evidence cannabis use in a prison setting, which can be qualified as endemic compared to other illicit drugs. Very large quantities of cannabis metabolites were routinely detected in all of the establishments included in the study.

The declaration-based surveys conducted in France until now describe regular cannabis use prior to imprisonment evaluated in 29.8%, 36.8% and 38.6% of new inmates (Mouquet 2005; Sannier *et al.* 2012; Zerkly *et al.* 2015).

In the 2011 survey on the Liancourt prison, bordering the Île-de-France region, 38.6% of questionnaire respondents reported cannabis use while in custody, and 16.3% of these reported daily use.

Even though new samples should be taken to corroborate the initial study results, the levels of cannabis use, at the three sites undergoing sampling, were similar, ranging from 711 to 2,758 doses per day, per 1,000 individuals. As a reminder, this considerable variability in the estimates is explained by the accumulative inaccuracies in the parameters in the process for estimating the quantities used. However, despite these uncertainties, this points to high cannabis use.

Hence, cannabis use could affect all inmates if each person smoked 0.7 to 2.8 cannabis joints daily.

If we exclusively refer to the percentage of daily cannabis smokers described in the survey conducted at Liancourt, the quantities detected in sewage correspond to 4.4 to 17.2 daily doses per person.

Lastly, if all inmates reporting prior use at the time of imprisonment continue these practices while in custody, the quantity per user would range from 1.4 to 5.5 doses per day.

#### HEROIN AND COCAINE USE IN A PRISON SETTING APPEAR TO BE MARGINAL

No opiates were detected in the samples. This does not mean that no opiates are used in the prison setting. These results only show that none were detected at the time of sampling.

Nevertheless, the metabolites of methadone and high-dose buprenorphine were indeed detected in proportions consistent with the volumes dispensed by the health unit pharmacy which provides care within the establishment.

These results do not agree with findings from French declaration-based studies, which report levels of heroin use among new inmates prior to imprisonment ranging from 6.5% (Mouquet 2005), to 10% (Zerkly et al. 2015) or even, 20% (Sannier et al. 2012). Furthermore, they are not consistent with the results of the study conducted at Liancourt prison, which reported declaration of heroin use while in custody among 8.1% of inmates interviewed (i.e. 31 inmates). However, we still need to tread carefully as the samples were not taken at the same establishments as those in which the declaration-based surveys were carried out. Furthermore, only one sample was taken per establishment, over a single day, which does not necessarily reflect use within the establishments.

Similarly, small quantities of cocaine were found in each sample taken, corresponding to 1-4 doses per 1,000 inmates at the establishments analysed.

These quantities also seem marginal in relation to the regular use reported by new inmates, around 7% (Mouquet 2005; Zerkly et al. 2015). These could match the study conducted at Liancourt where 3 individuals claimed to use cocaine daily, and 19 more occasionally. However, this reported use seems higher than the estimates based on the quantities of metabolites detected in sewage during the study.

Moreover, this use only appears to concern 1 to 4 individuals at the establishments studied. Inmates, prison staff and outside contributors use the sewage network. Substance use among the latter cannot be ruled out given that 1.1% of 18-65 year-olds in the general population used cocaine in 2014 (OFDT 2015).

# SEWAGE ANALYSIS SHOULD BE EXPANDED SO AS TO PROVIDE THE NECESSARY EVIDENCE FOR HEALTH PROMOTION AND PREVENTION ACTIONS

In view of the limitations inherent in this method for estimating drug use, together with the difficulties encountered during this feasibility study, it is essential for these results to be expanded so that they can be taken into account with a view to adapting the action undertaken by the prison authorities and health workers aiming to control addictive behaviours.

Hence, the current study demonstrated the feasibility and benefit of this monitoring process, providing technical and methodological precautions are applied. This will be repeated at new sites in 2017.

In order to improve the interpretation of the sample results and discussion of substance use in the prison setting, the molecules analysed and the sampling methods will be adjusted. The procedures for taking into account all individuals within the prison setting at the time of sampling will be discussed. Furthermore, other prison and health data will be collected (seizures of narcotic substances by the prison authorities, volume of all medicinal treatments dispensed within the establishment, etc.). Lastly, other types of surveys on addictive behaviours will be conducted simultaneously within the establishments studied. The next national survey on "circulation, use, and trading of psychoactive substances in a prison setting (CIRCE)" should notably document these behaviours.

Application of harm reduction measures intended for drug users defined in Article L3411-8 of the French Public Health Code, particularly adaptation of its procedures to the prison setting, should take these new data into account.

Harm related to cannabis use has now been fully documented (Costes 2007). However, harm related to the use of other illicit drugs and patterns of use such as intravenous use or nasal use (snorting) is still under reported.

The implementation of future action intended for inmates, defined as part of the latest MILDECA governmental action plan for 2016-2017 (MILDECA 2016) is now able to take these data into consideration. Actions intended for cannabis smokers in these populations should be envisaged. These must be combined with actions to control tobacco smoking in a prison setting, which is authorised in cells, as both types of dependence are extremely closely linked (Schwitzer *et al.* 2016) and their prevalence in the prison setting is evidently high.

Drug use in prisons, hence particularly cannabis use, requires specifically documented strategies for prevention, identification and management in this setting. These bring together both health workers (health units and specialised drug treatment centres) and the prison authorities, along with various contributors such as associations and mutual aid groups.

Moreover, these actions should not overshadow the fact that cannabis use in the general population in France is still particularly high (3% of regular users among 18-64 year-olds). Promotion of health in the prison setting should also allow for a paradigm shift and not exclusively focus on inmate health.

Prisons are a closed environment. The actions undertaken must include prison staff who are the first points of contact with inmates. Hence, the prison authorities are increasing their actions aiming to train and provide prison staff with information on drug use. In collaboration with the Ministry of Health and MILDECA, they are currently promoting actions to improve the coordination of measures taken by prison staff and health workers to identify individuals displaying addictive or risk behaviour. They are encouraging the development of early interventions intended for inmates.

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