Supplementary Information

Monitoring psychoactive substance use at six European festivals through wastewater and pooled urine analysis

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Chemicals and reagents

HPLC-grade water was obtained by purifying demineralized water in a Mili-Q plus system from Millipore (Bedford, MA, USA). LC-MS grade acetonitrile (ACN), methanol (MeOH), ammonium acetate (NH_4Ac) and formic acid (HCOOH, 98 - 100 %) were acquired from Scharlab S.L. (Barcelona, Spain). β-glucuronidase from E.Coli K12 (140 Units / mL at 37 °C) was purchased from Roche Diagnostics GmbH (Mannheim, Germany) and Leucine-enkephalin was purchased from Sigma-Aldrich (Augsburg, Germany). SPE cartridges, generic Oasis HLB (3 cm^3; 60 mg) built of hydrophilic and lipophilic monomers, and Oasis MCX (3 cm^3; 60 mg) with strong cation-exchange properties, were purchased from Waters (Milford, MA, USA).

Psychoactive substances selected for quantitative analysis.

In total 35 drugs and NPS and 17 isotopically labelled analogues were purchased from Cerilliant (Round Rock, TX, USA) and Cayman Chemical Co. (An Arbor, MI, USA). The compounds selected were: amphetamine, benzoylecgonine (the main metabolite of cocaine), buphedrone, butylone, cocaine, ethylone, ketamine, mephedrone, methamphetamine, methcathinone, methedrone, methoxetamine, methylenedioxypyrovalerone (MDPV), methylone, N-ethylcathinone, naphyrone, ephenidine (NEDPA), 3,4-methylenedioxymethamphetamine (MDMA), 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THC-COOH, the main metabolite of cannabis) 3,4-methylenedioxy-N,N-dimethylcathinone (bk-MDDMA), 4-bromo-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine (25-B-NBOMe), 4-chloro-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine (25-C-NBOMe), 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine (25-I-NBOMe), 4-isopropyl-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine (25-iP-NBOMe), 4-methyl-α-pyrrolydinopropiophenone (4-MePPP), α-pyrrolidinopentiophenone (α-PVP), dimethylpentylone (bk-DMBDP), ρ-methoxymethamphetamine (PMMA), 2-phenethylamine, 3,4-dimethoxy-α-pyrrolidinopentiophenone (3,4-DiMeO-α-PVP), 3,4-dimethylmethcathinone (3,4-DMMC), 4,4'-dimethylaminorex (4-4'-DMAR), 4-chloro-α-pyrrolydinopropiophenone (4-chloro-α-PPP), 4-fluoromethcathinone (4-FMC) and 4-methylethcathinone (4-MEC). Isotopically labelled analogues used were: amphetamine-d_6, benzoylecgonine-d_3, butylone-d_3, cocaine-d_3, ketamine-d_4, mephedrone-d_3, methamphetamine-d_5, methoxetamine-d_3, MDPV-d_8, methylone-

d_3, MDMA-d_5, naphryone-d_5, 25-B-NBOMe-d_3, 25-C-NBOMe-d_3, 25-I-NBOMe-d_3, α-PVP-d_8 and PMMA-d_3.

Database for screening

In total, 197 NPS were screened using an *in-house* database (**Table S1**). Information was collected by reviewing the EWS reports most recently published from EMCDDA, the United Nations Office on Drugs and Crime (UNODC), and the scientific literatur. The complete database is available on the NPS-Euronet website (Priority NPS Database; http://www.npseuronet.eu/results/2018) and include information on chemical family, communication source, metabolism (when available) information necessary to perform the chemical analysis (molecular formula, exact mass, chemical structure, mass spectrometric fragmentation data, and availability of reference standards) and the references consulted (see also special reference section in this SI).

Instrumentation qualitative suspect screening

A Waters Acquity I-Class UPLC system (Waters, Milford, MA, USA) was interfaced to a VION IMS-QTOF mass spectrometer, using an electrospray ionization (ESI) interface operating in positive mode.

The chromatographic separation was performed using a CORTECS® C18 2.1 x 100 mm, 2.7 µm fused core column (Waters) at a flow rate of 300 µL/min. Gradient elution was performed using mobile phases of A = H_2O and B = MeOH, both with 0.01% HCOOH. The initial percentage of B was 10%, which was immediately linearly increased to 90% for 14 min, followed by a 2 min isocratic period, then, returned to initial conditions (at 16.1 min) with 2 min equilibration of the column. The total run time was 18 min. Nitrogen was used as the drying gas and nebulizing gas. The injected volume was 3 µL for both pooled urine and wastewater extracts.

A capillary voltage of 0.8 kV and cone voltage of 20 V were used. The desolvation temperature was set to 550 °C, and the source temperature to 120 °C. The cone gas flow was 250 L/h and desolvation gas flow of 1000 L/h. The column temperature was set to 40 °C and sample temperature at 10 °C. MS data was acquired using the VION in HDMS^e mode, in the range 50-1000 m/z, with N_2 as the drift gas, an IMS wave velocity of 250 m/s and wave height ramp of 20-

50 V. Leucine enkephalin (*m/z* 556.27765) was used for mass correction. Two independent scans with different collision energies were acquired during the run: a collision energy of 6 eV for low energy (LE) and a ramp of 28-56 eV for high energy (HE). The LE and HE functions settings were for both a scan time of 0.3 s. Nitrogen (≥99.999%) was used as collision-induced dissociation (CID) gas. All data was examined using an in-house built accurate mass screening workflow within UNIFI informatics platform from Waters Corporation.

In addition, an Agilent HP-1200 Series LC system (Agilent Technologies, Santa Clara, CA) was coupled to a Q-ExactiveTM Hybrid Quadrupole-OrbitrapTM mass spectrometer (Thermo Scientific, Bremen, Germany) equipped with an ESI source. The chromatographic separation was performed at a flow rate of 200 µL min-1 using a XBrigde® C18 (2.1x100mm, 3.5 µm) column (Waters) and a mobile phase consisting of (A) 0.1 % formic acid in MilliQ water and (B) ACN. The gradient was as follows: 0 min (10 % B), 20 min (60 % B), 25 min (99 % B), 30 min (99 % B) and 31 min (10 % B); the initial conditions were finally kept for 6 min in order to re-equilibrate the column (total run time 38 min). The volume of injection was 8 µL both for pooled urine and wastewater extracts.

HRMS analyses were done in positive mode under the following working conditions: sheath gas pressure 45 bar, auxiliary gas pressure 5 bar, ion spray voltage 3.5 kV, heated capillary temperature 320 °C, S-lens RF 60. MS2 experiments were carried out using the collision-induced dissociation (CID) mode and applying two fixed collision energy (CE) 35 and 50 V in the quadrupole to a precursor ion selected with an isolation window of 3 m/z. Data processing was done with the Thermo XcaliburTM 2.3 software (Thermo Scientific).

Analytical strategy and identification criteria

Current analytical instruments provide the sensitivity, selectivity, and identification requirements to determine drugs, NPS and their metabolites in pooled urine and wastewater at low concentration levels. Accurate-mass full-spectrum measurements from HRMS are of great value for elucidation purposes and allow searching for a large number of compounds without the immediate need for reference standards. This is important since reference standards of NPS and their metabolites are not always commercially available. Moreover, purchasing of NPS reference

standards is time-consuming and expensive, not only the initial acquisition also its maintenance (e.g. considering stability and expiration of standards). Furthermore, the presence of newly reported NPS and metabolites, initially not considered in the suspect list, could be investigated at any time from data acquired in a retrospective way without the need for additional analysis (Bijlsma et al., 2013; Hernandez et al., 2018). Finally, ion mobility spectrometry in QTOF instruments adds a new dimension to the chromatographic and HRMS separations, which notably facilitates the identification process, which is particularly important in complex-matrix samples.

We reported compounds based on the identification levels for small molecules described by Schymanski *et al.* 2014 (Schymanski et al., 2014). A mass accuracy of < 5 ppm and at least 1 matched fragment was utilized in order to tentatively identify a suspect analyte. Obviously, reference standards are required for unambiguous confirmation, by matching MS and MS/MS spectra, retention time (and Collisional cross section (CCS) in ion mobility systems), but they need to be acquired only in a final stage, when well-founded evidence exists on the presence of the substance in the sample (Ibáñez et al., 2014). Hence, we endeavoured to purchase (if available) or synthesize reference standards of the substances tentatively identified. As was the case for α-methyltryptamine (AMT), which was synthetized and subsequently characterized using NMR and UHPLC-HRMS.

After screening pooled urine extracts and wastewater extracts (for wastewater, after SPE with HLB and MCX) by LC-HRMS, samples were also analysed for quantification and additional confirmation of the substances using a more sensitive target method based on LC-MS/MS. Quantification and confirmation was feasible by selecting three transitions for each compound. Furthermore, isotope-labelled internal standards were used for all drugs and most NPS detected to correct for potential losses during sample treatment and to compensate for matrix effects. Specific information on analytical methods can be found elsewhere (Bade et al., 2017; Bijlsma et al., 2014; González-Mariño et al., 2016; Zuccato et al., 2016).

Table S1: 197 NPS and metabolites included in the *in-house* database, together with the IUPAC name and chemical family

Compound	IUPAC NAME	Chemical family
25B-NBOMe	(2-(4-bromo-2,5-dimethoxyphenyl)-N,N-bis(2-methoxybenzyl)ethanamine)	phenethylamine
25C-NBOMe (2C-C-NBOMe)	2-(4-chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine	phenethylamine
25E-NBOMe	2-(4-Ethyl-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine	phenethylamine
25H-NBOMe	2-(2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine	phenethylamine
25I-NB34MD	(N-(1,3-Benzodioxol-5-ylmethyl)-2-(4-iodo-2,5-dimethoxyphenyl)ethan-1-amine)	phenethylamine
25I-NBMD	2-(4-iodo-2,5-dimethoxyphenyl)-N-[(2,3-methyldioxyphenyl)methyl]ethanamine	phenethylamine
25I-NBOMe	4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine	phenethylamine
25iP-NBOMe	2-[2,5-Dimethoxy-4-(propan-2-yl)phenyl]-N-(2-methoxybenzyl)ethanamine	phenethylamine
2C-B	4-bromo-2,5-dimethoxyphenethylamine	phenethylamine
2C-E	2,5-dimethoxy-4-ethylphenethylamine	phenethylamine
2-Cloro-4,5-MDMA	1-(6-chloro-1,3-benzodioxol-5-yl)-N-methylpropan-2-amine	phenethylamine
2-methoxyamphetamine	1-(2-methoxyphenyl)propan-2-amine	phenethylamine
2-PEA (phenetylamine)	2-phenethylamine	phenethylamine
3,4-DMA-NBOMe	1-(3,4-Dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]propan-2-amine	phenethylamine
3,4-MDPA	1-(1,3-benzodioxol-5-yl)-N-propylpropan-2-amine	phenethylamine
4-EA-NBOMe	1-(4-Ethylphenyl)-N-[(2-methoxyphenyl)methyl]propan-2-amine	phenethylamine
4-FA (4-fluoroamphetamine)	1-(4-Fluorophenyl)propan-2-amine	phenethylamine
4-FMA (4-fluorometamphetamine)	1-(4-Fluorophenyl)-N-methylpropan-2-amine	phenethylamine
4-MMA (4-methylmethamphetamine)	(N-methyl-1-(4-methylphenyl)propan-2-amine)	phenethylamine
4-MMA-NBOMe	N-[(2-Methoxyphenyl)methyl]-N-methyl-1-(p-tolyl)propan-2-amine	phenethylamine
5-APB-NBOMe	1-(Benzofuran-5-yl)-N-[(2-methoxyphenyl)methyl]propan-2-amine	phenethylamine
5-EAPB	1-(1-benzofuran-5-yl)-N-ethylpropan-2-amine	phenethylamine
6-APB [6-(2-Aminopropil)benzofurano]	1-(1-Benzofuran-6-yl)propan-2-amine	phenethylamine
6-APDB	1-(2,3-Dihydro-1-benzofuran-6-yl)propan-2-amine	phenethylamine
6-Bromo-MDMA	6-bromo-3,4-methylenedioxy-N-methylamphetamine	phenethylamine
6-EAPB	(1-(1-benzofuran-6-il)-N-etilpropan-2-amina)	phenethylamine
bk-2C-B	(2-amino-1-(4-bromo-2,5-dimethoxyphenyl)ethanone)	phenethylamine

DOC	1-(4-Chloro-2,5-dimethoxyphenyl)propan-2-amine	phenethylamine
DOIP	1-[2,5-Dimethoxy-4-(propan-2-yl)phenyl]propan-2-amine	phenethylamine
DOM	1-(2,5-Dimethoxy-4-methylphenyl)propan-2-amine	phenethylamine
MDAI	6,7-Dihydro-5H-cyclopenta[f][1,3]benzodioxol-6-amine	phenethylamine
MPA (Methylthienylpropamine)	N-methyl-1-(thiophen-2-yl)propan-2-amine	phenethylamine
NEDPA	(N-iso-propil-1,2-difeniletilamina)	phenethylamine
N-methyl-2AI	(N-methyl-2,3-dihydro-1H-inden-2-amine)	phenethylamine
N-methyl-2C-B	2-(4-Bromo-2,5-dimethoxyphenyl)-N-methylethanamine	phenethylamine
PMA	para-Methoxyamphetamine	phenethylamine
PMMA	para-Methoxy-N-methylamphetamine	phenethylamine
Deschloroketamine	(2-(Methylamino)-2-phenyl-cyclohexan-1-one)	arilcicloexilamine - ketamine anal.
Methoxetamine bromo derivative	2-(2-bromo,5-methoxyphenyl)-2-(ethylamino)cyclohexanone	arilcicloexilamine - ketamine anal.
Methoxethamine (MXE / 3-MeO-2'-Oxo-PCE)	2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone	arilcicloexilamine - ketamine anal.
2-MeO-diphenidine (MXP / 2-MXP)	1-(1-(2-methoxyphenyl)-2-phenylethyl)piperidine	piperidine
3-MeO-PCP	1-[1-(3-methoxyphenyl)cyclohexyl]-piperidine	piperidine
Diphenidine	1-(1,2-diphenylethyl)piperidine	piperidine
Isopropylphenidate	(Propan-2-yl 2-phenyl-2-piperidin-2-yl acetate)	piperidine
HDEP-28 (Ethylnaphthidate)	(Ethyl 2-(naphthalen-2-yl)-2-(piperidin-2-yl)acetate)	piperidine
HDMP-28 (methylnaphthidate)	(Methyl (2R)-2-naphthyl[(2R)-2-piperidinyl]acetate	piperidine
5-MeO-DALT	N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-prop-2-enylprop-2-en-1-amine	tryptamine
5-MeO-EIPT	N-ethyl-N-(2-(5-methoxy-1H-indol-3-yl)ethyl)propan-2-amine	tryptamine
5-MeO-MIPT	N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-methylpropan-2-amine	tryptamine
5-MeO-NiPT	N-[2-(5-methoxy-1H-indol-3-yl)ethyl]propan-2-amine	tryptamine
AMT (α-methyltryptamine)	1-(1H-Indol-3-yl)propan-2-amine	tryptamine
DALT	N-[2-(1H-indol-3-yl)ethyl]-N-prop-2-enylprop-2-en-1-amine	tryptamine
MET (N-methyl-N-ethyltryptamine)	N-Ethyl-2-(1H-indol-3-yl)-N-methylethanamine	tryptamine
2-FMC (2-fluoromethcathinone)	(1-(2-fluorophenyl)-2-(methylamino)propan-1-one)	cathinone
2-methylmethcathinone	(1-(2-methylphenyl)-2-(methylamino)propane-1-one)	cathinone
3,4-dimethoxy-alpha-PHP (3,4-DMeO-α-PHP)	1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)octan-1-one	cathinone
3,4-Dimethylethcathinone (3,4-DMEC)	1-(3,4-dimethylphenyl)-2-(ethylamino)propan-1-one	cathinone

3,4-DMeO-α-PVP	1-(3,4-dimethoxyphenyl)-2-(pyrrolidin-1-yl)pentan-1-one	cathinone
3-CMC	1-(3-Chlorophenyl)-2-(methylamino)propan-1-one	cathinone
3-methoxymethcathinone	1-(3-methoxyphenyl)-2-(methylamino)propane-1-one	cathinone
3-methylmethcathinone (3-MMC)	2-(Methylamino)-1-(3-methylphenyl)-1-propanone	cathinone
3-methylethcathinone (3-MEC)	2-(ethylamino)-1-(3-methylphenyl)propan-1-one	cathinone
3,4-dimethylmethcathinone (3,4-DMMC)	1-(3,4-dimethylphenyl)-2-(methylamino)propan-1-one	cathinone
4'-chloro-α-PPP	1-(4-chlorophenyl)-2-pyrrolidin-1-ylpropan-1-one	cathinone
4-bromoamphetamine (4-BA)	(1-(4-Bromophenyl)propan-2-amine)	cathinone
4-Bromoethcathinone (4-BEC)	1-(4-bromophenyl)-2-(ethylamino)propan-1-one	cathinone
4Br-α-PVP	(1-(4-Bromophenyl)-2-(1-pyrrolidinyl)-1-pentanone)	cathinone
4-EEC (Ethylethcathinone)	2-(Ethylamino)-1-(4-ethylphenyl)propan-1-one	cathinone
4-FEC	(2-(Ethylamino)-1-(4-fluorophenyl)propan-1-one)	cathinone
4-fluoromethcathinone (4-FMC)	RS)-1-(4-Fluorophenyl)-2-methylaminopropan-1-one	cathinone
4-fluoro-N-isopropilnorpentedrone	1-(4-fluorophenyl)-2-(1-methylethylamino)pentan-1-one	cathinone
4-fluoropentedrone	(1-(4-fluorofenil)-2-(metilamino)pentan-1-one)	cathinone
4F-PBP	(1-(4-Fluorophenyl)-2-(1-pyrrolidinyl)-1-butanone)	cathinone
4F-PE	1-(4-Fluorophenyl)-2-(pyrrolidin-1-yl)heptan-1-one	cathinone
4F-α-POP	1-(4-fluorophenyl)-2-(pyrrolidin-1-yl)octan-1-one	cathinone
4F-α-PVP	(1-(4-fluorofenil)-2-(pirrolidin-1-il)pentan-1-one)	cathinone
4-MEC (4-Methylethcathinone)	2-(ethylamino)-1-(4-methylphenyl)propan-1-one	cathinone
4-MeO-α-PBP	1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)butan-1-one	cathinone
4-MeO-α-PEP or 4-MeO-α-PV8	1-(4-methoxyphenyl)-2-pyrrolidin-1-yl-heptan-1-one	cathinone
4-MeO-α-PV9	Methyl 2-{[1-(cyclohexylmethyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate	cathinone
4-methyl-N-ethylpentedrone	2-(Ethylamino)-1-(4-methylphenyl)pentan-1-one	cathinone
4-methylpentedrone	(2-(metilamino)-1-(p-tolil)pentan-1-one (4-metilpentedrone)	cathinone
4-Methyl-N,N-diethylcathinone	2-Diethylamino-1-(4-methylphenyl)propan-1-one	cathinone
5-BPDi	1-(2,3-Dihydro-1H-inden-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one	cathinone
5-DBFPV	(1-(2,3-dihydro-1-benzofuran-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one)	cathinone
Bk-IVP	1-(2,3-dihydro-1H-inden-5-yl)-2-(ethylamino)pentan-1-one	cathinone

bk-MDMA (3,4-methylenedioxy-N-methylcathinone/ Methylone)	1-(1,3-benzodioxol-5-yl)-2-(methylamino)propan-1-one	cathinone
bk-PMMA (Methedrone)	1-(4-methoxyphenyl)-2-(methylamino)propan-1-one	cathinone
Clephedrone	1-(4-chlorophenyl)-2-(methylamino)propan-1-one	cathinone
bk-DMDBP (Dipentylone)	1-(1,3-benzodioxol-5-yl)-2-(dimethylamino)-pentan-1-one	cathinone
Eutylone	1-(1,3-benzodioxol-5-yl)-2-(ethylamino)butan-1-one	cathinone
MDPHP	1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one	cathinone
MDPV (3,4-Methylenedioxypyrovalerone)	1-(Benzo[*d*] [1,3]dioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one	cathinone
Mephedrone (4-MMC)	(RS)-2-methylamino-1-(4-methylphenyl)propan-1-one	cathinone
MTTA (mephtetramine)	2-((metilamino)metil)-3,4-diidronaftalen-1(2H)-one)	cathinone
N-Methyl-bk-MMDA-2	1-(6-methoxy-1,3-benzodioxol-5-yl)-2-(methylamino)propan-1-one	cathinone
Nor-mephedrone	(2-Amino-1-(4-methylphenyl)propan-1-one)	cathinone
NPDPA	(1-(1,3-benzodiossol-5-il)-2-(dimetilamino)-pentan-1-one)	cathinone
α-ethylaminopentiophenone	2-(ethylamino)-1-phenylpentan-1-one	cathinone
α-PBT	2-(Pyrrolidin-1-yl)-1-(thiophen-2-yl)butan-1-one	cathinone
Pentedrone (α-methylamino-valerophenone/ β-ethyl-methcathinone)	1-phenyl-2-(methylamino)pentan-1-one	cathinone
α-PVP (α-Pyrrolidinopentiophenone / α-pyrrolidinovalerophenone)	1-Phenyl-2-(1-pyrrolidinyl)-1-pentanone	cathinone
α-PVT (α-Pyrrolidinopentiothiophenone)	2-(pyrrolidin-1-yl)-1-(thiophen-2-yl)pentan-1-one	cathinone
α-PHP (α-pyrrolidinohexanophenone)	2-(pyrrolidin-1-yl)-1-(phenyl)hexan-1-one	cathinone
α-POP (α-Pyrrolidinooctanophenone)	1-Phenyl-2-(pyrrolidin-1-yl)octan-1-one	cathinone
β-propylmethcathinone (Hexedrone / "hexa")	2-(methylamine)-1-(phenyl)hexan-1-one	cathinone
2NE1 (APICA/ JWH-018 adamantil carbossammide/ SDB-001)	N-[(3s,5s,7s)-Adamantan-1-iy]-1-pentyl-1H-indole-3-carboxamide	Synthetic cannabinoid
5F-APICA (STS-135)	N-(Adamantan-1-yl)-1-(5-fluoropentyl)-1H-indole-3-carboxamide	Synthetic cannabinoid
5C-AKB48	(N-(Adamantyl)-1-(5-chloropentyl)-1H-indazole-3-carboxamide)	Synthetic cannabinoid
5F-AB-FUPPYCA	(N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-5-(4-fluorophenyl)-1H-pyrazole-3-carboxamide)	Synthetic cannabinoid
5F-ADBICA/ 5F-ADBICA-144/ 5F-AMBICA / 5-FADB/ 5F-ADBINACA	N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1Hindol-3-carboxamide	Synthetic cannabinoid
5F-ADB-PINACA	(N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide)	Synthetic cannabinoid

5F-AMB-PICA / AMB-PICA / MMB2201 / MMB-2201 / I-AMB	Methyl 2-({[1-(3-fluoropropyl)-1H-indol-3-yl]carbonyl}amino)-3-methylbutanoate	Synthetic cannabinoid
5F-AMB	Methyl (2S)-2-{[1-(5-fluoropentyl)-1H-indazol-3-yl]formamido}-3-methylbutanoate	Synthetic cannabinoid
5F-APINACA / AKB-48F / 5F-AKB48	N-(1-adamantyl)-1-(5-fluoropentyl)-1Hindazole-3-carboxamide	Synthetic cannabinoid
5F-APP-PICA	N-(2-amino-1-benzyl-2-oxo-ethyl)-1-(5-fluoropentyl)indazole-3-carboxamide	Synthetic cannabinoid
AB-PINACA	N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-pentyl-1H-indazole-3-carboxamide	Synthetic cannabinoid
5F-AB-PINACA	N-[(2S)-1-amino-3-methyl-1-oxobutan-2-yl]-1-(5-fluoropentyl)indazole-3-carboxamide	Synthetic cannabinoid
5F-APP-PINACA / PX-2 / PX 2 / 5-fluoro APP PINACA / FU-PX	N-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-(5-fluoropentyl)-1H-indole-3-carboxamide	Synthetic cannabinoid
5F-EMB-PINACA / 5F-AEB	(Ethyl 2-(1-[5-fluoropentyl]-1H-indazole-3-carboxamido)-3-methylbutanoate)	Synthetic cannabinoid
5-Fluoropentyl-3-pyridinoylindole	(1-(5-Fluoropentyl)-1H-indol-3-yl](3-pyridinyl)methanone)	Synthetic cannabinoid
5F-MDMB-PINACA / 5F-Methyl-AMB / 5-fluor-MAMB / 5-fluor ADB / 5F-ADB	Methyl (S)-2-[1-(5-fluoropentyl)-1H-indazole-3-carboxamido]-3,3-dimethylbutanoate	Synthetic cannabinoid
PB-22	1-Pentyl-1H-indole-3-carboxylic acid 8-quinolinyl ester	Synthetic cannabinoid
5F-PB-22	8-quinolinyl ester-1-(5-fluoropentyl)-1H-indole-3-carboxylic acid	Synthetic cannabinoid
5F-NPB-22	1-(5-Fluoropentyl)-8-quinolinyl ester-1H-indazole-3-carboxylic acid	Synthetic cannabinoid
5F-PB-22 indazole analogue	Quinolin-8-yl 1-(5-fluoropentyl)-1H-indazole-3-carboxylate	Synthetic cannabinoid
5F-PY-PICA	(1-(5-Fluoropentyl)-3-(pyrrolidine-1carbonyl)-1-H-indole)	Synthetic cannabinoid
5F-PY-PINACA	((1-(5-Fluoropentyl)-1H-indazole-3-yl)(pyrrolidine-1-yl)methanone)	Synthetic cannabinoid
AB-CHMINACA	N-[(2S)-1-amino-3-methyl-1-oxo-2-butanyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
AB-FUBINACA	(S)-N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
ADAMANTYL-THPINACA	N-(1-adamantyl)-1-(tetrahydropyran-4-ylmethyl)indazole-3-carboxamide	Synthetic cannabinoid
ADB-CHMINACA / MAB-CHMINACA	N-[1-(Aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
ADB-FUBINACA	(N-[(1S)-1-(amminocarbonil)-2-metilpropil]-1-[(4-fluorofenil)metil]-1H-indazolo-3-carbossamide)	Synthetic cannabinoid
ADB-PINACA	(N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1H-indazole-3-carboxamide)	Synthetic cannabinoid
AKB-48 (APINACA)	N-(adamantan-1-yl)-1-pentyl-1H-indazole-3-carboxamide	Synthetic cannabinoid
AM-2201	[1-(5-Fluoropentyl)-1H-indol-3-yl](naphthalen-1-yl)methanone	Synthetic cannabinoid
AM-6527 5-fluoropentyl derivative / 5-Fluor-NNEI / 5F-NNEI / 5F-MN24	(1-(5-fluoropentil)-N-(naftalen-2-il)-1H-indolo-3-cabossamide)	Synthetic cannabinoid
AMB-CHMINACA / MA-CHMINACA	2-(1-(cicloesilmetil)-1H-indazolo-3-carbossammide)-3-metilbutanoato	Synthetic cannabinoid

AMB-FUBINACA	Methyl 2-({[1-(4-fluorobenzyl)-1H-indazol-3-yl]carbonyl}amino)-3-methylbutanoate	Synthetic cannabinoid
APP-FUBINACA	N-(1-amino-3-phenyl-1-oxopropan-2-yl)-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide	Synthetic cannabinoid
BB-22	8-Quinolinyl 1-(cyclohexylmethyl)-1H-indole-3-carboxylate	Synthetic cannabinoid
CBL-018	(Naphthalen-1-yl-1-pentyl-1H-indole-3-carboxylate)	Synthetic cannabinoid
CUMYL-5FPICA	1-(5-Fluoropentyl)-N-(2-phenylpropan-2-yl)-1H-indole-3-carboxamide	Synthetic cannabinoid
CUMYL-5F-PINACA (SGT-25)	1-(5-Fluoropentyl)-N-(1-methyl-1-phenylethyl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
CUMYL-BICA (SGT-55)	1-Butyl-N-(2-phenylpropan-2-yl)-1H-indole-3-carboxamide	Synthetic cannabinoid
CUMYL-PICA (SGT-56)	1-Pentyl-N-(2-phenylpropan-2-yl)-1H-indole-3-carboxamide	Synthetic cannabinoid
CUMYL-PINACA	1-Pentyl-N-(2-phenylpropan-2-yl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
CUMYL-THPINACA (SGT-42)	N-(2-phenylpropan-2-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1-H-indazole-3-carboxamide	Synthetic cannabinoid
DB-MDBP	(1-((2,2-difluorbenzo [D] [1,3] dioxol-5-yl) methyl) piperazine)	Synthetic cannabinoid
EMB-FUBINACA	(Ethyl 2-(1-[4-fluorobenzyl]-1H-indazole-3-carboxamido)-3-methylbutanoate)	Synthetic cannabinoid
FDU-PB-22	Naphthalen-1-yl-1-(4-fluorobenzyl)-1H-indole-3-carboxylate	Synthetic cannabinoid
FUB-144 / FUB-UR-144	([1-(4-Fluorobenzyl)-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone)	Synthetic cannabinoid
FUB-AKB48 / AKB48 N-(4-fluorobenzyl) analogue	N-((3s,5s,7s)-adamantan-1-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide	Synthetic cannabinoid
FUB-JWH-018	(1-(4-Fluorobenzyl)-1H-indol-3-yl)(naphthalen-1-yl)methanone)	Synthetic cannabinoid
FUB-PB-22	(Quinolin-8-yl-1-(4-fluorobenzyl)-1H-indole-3-carboxylate)	Synthetic cannabinoid
JWH-018 indazole analogue (THJ-018)	Naphthalen-1-yl(1-pentyl-1H-indazol-3-yl)methanone	Synthetic cannabinoid
THJ-2201	[1-(5-Fluoropentyl)-1H-indazol-3-yl](1-naphthyl)methanone	Synthetic cannabinoid
EG-018	1-Naphthyl(9-pentyl-9H-carbazol-3-yl)methanone	Synthetic cannabinoid
BZ-2201	(1-(5-fluoropentyl)-1H-benzo[d]imidazol-2-yl)(naphthalen-1-yl)methanone	Synthetic cannabinoid
JWH-071	(1-etil-1H-indol-3-il)-1-naftalenil-metanone	Synthetic cannabinoid
JWH-122 (1-pentyl-3-(1-(4-methyl)naphthoyl)indol)	(4-methylnaphthalen-1-yl)-(1-pentylindol-3-yl)methanone	Synthetic cannabinoid
JWH-210	1-Pentyl-3-(4-ethyl-1-naphthoyl)indole	Synthetic cannabinoid
JWH-412 5-fluoropentyl derivative	(4-fluoronaphthalen-1-yl)[1-(5-fluoropentyl)-1H-indol-3-yl]methanone	Synthetic cannabinoid
M-CHMIC	(Methyl-1-(cyclohexylmethyl)-1H-indole-3-carboxylate)	Synthetic cannabinoid
MDMB(N)BZ-F' / MDMB-FUBINACA	metil-2-[1-(4-fluorobenzil)-1-H-indazol-3-carbossamide]-3,3-dimetilbutanoato	Synthetic cannabinoid
MDMB-CHMICA	Methyl 3,3-dimethyl-2-{[(1-(cyclohexylmethyl)-1H-indol-3-yl)carbonyl]amino}butanoate	Synthetic cannabinoid

MDMB-CHMICA /MMB-CHMINACA	(metil-2-(1-(cicloesilmetil)-1-H-indol-3-ilcarbonilamino)-3,3-dimetilbutanoato)	Synthetic cannabinoid
MDMB-FUBICA	Methyl 2-(1-(4-fluorobenzil)-1H-indol-3-carbossammide)-3,3- dimetilbutanoate	Synthetic cannabinoid
MDMB-CHMCZCA	methyl 2-(9-(cyclohexylmethyl)-9H-carbazole-3-carboxamido)-3,3-dimethylbutanoate	Synthetic cannabinoid
Mepirapim	(4-methylpiperazin-1-yl)(1-pentyl-1H-indol-3-yl)methanone	Synthetic cannabinoid
MN-18	N-(naphthalen-1-yl)-1-pentyl-1H-indazole-3-carboxamide	Synthetic cannabinoid
5F-MN18	1-(5-fluoropentyl-N-1-naphtalenyl-1H-indazole-3-carboxamide	Synthetic cannabinoid
NM-2201 / CBL-2201	Naphthalen-1-yl-1-(5-fluoropentyl)-1H-indol-3-carboxylate	Synthetic cannabinoid
PB-22 indazole analogue	Quinolin-8-yl 1-pentyl-1H-indazole-3-carboxylate	Synthetic cannabinoid
RCS-4	4-methoxyphenyl-(1-pentyl-1H-indol-3-yl)methanone	Synthtic cannabinoid
RH-34	(3-[2-[(2-methoxyphenyl)methylamino]ethyl]-1H-quinazoline-2,4-dione)	Synthtic cannabinoid
SDB-005	(Naphthalen-1-yl-1-pentyl-1H-indazole-3-carboxylate)	Synthetic cannabinoid
SDB-006	(N-benzyl-1-pentyl-1H-indole-3-carboxamide)	Synthetic cannabinoid
4-fluoro-butyrfentanyl	N-(4-fluorophenyl)-N-[(1-(2-phenylethyl)-4-piperidinyl)]butanamide	Synthetic oppioid
Acetylfentanyl	N-Phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]acetamide	Synthetic oppioid
AH-7921	3,4-dichloro-N-[(1-(dimethylamino)cyclohexyl)methyl]benzamide	Synthetic opioid
Butyrfentanyl	N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]-butanamide	Synthetic opioid
Despropionyl-2-fluoro fentanyl	(N-(2-Fluorophenyl)-1-(2-phenylethyl)piperidin-4-amine)	Synthetic opioid
MT-45	1-cyclohexyl-4-(1,2-diphenylethyl)-piperazine	Synthetic opioid
Ocfentanyl (A-3217)	(N-(2-fluorophenyl)-2-methoxy-N-[1-(2-phenylethyl)piperidin-4-yl]acetamide)	synthetic opioid
U-47700	Trans 3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide	synthetic opioid
W-18	4-Chloro-N-(1-[2-(4-nitrophenyl)ethyl]-piperidin-2-ylidene)benzenesulfonamide	Synthtic opioid
Para methyl-4-methylaminorex (4-4'-DMAR)	4-Methyl-5-(4-methylphenyl)-4,5-dihydro-1,3-oxazol-2-amine	aminorex derivate
4-Methylmethylphenidate	Methyl 2-(1-(4-fluorobenzyl)-1H-indol-3-carboxamido)-3,3-dimethylbutanoate	aminorex derivate
N-Methyl aminorex	(3-Methyl-5-phenyl-1,3-oxazolidin-2-imine)	aminorex derivate
Ibogaine	(-)-12-Methoxyibogamine	natural substance
Methallylescaline	(2-[3,5-dimethoxy-4-(2-methylprop-2-enoxy)phenyl]ethanamine)	natural substance
Mitragyna (kratom)	(αE,2S,3S,7aS,12bS)-3-ethyl-1,2,3,4,6,7,7a,12b-octahydro-7a-hydroxy-8-methoxy-α-(methoxymethylene)-indolo[2,3-a]quinolizine-2-acetic acid methyl ester	natural substance
Mesembrine	(3aS,7aS)-3a-(3,4-dimethoxyphenyl)-1-methyl-2,3,4,5,7,7a-hexahydroindol-6-one	natural substance
Clonazolam	6-(2-chlorophenyl)-1-methyl-8-nitro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine	benzodiazepine

Phenazepam	7-Bromo-5-(2-chlorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one	benzodiazepine
Deschloroetizolam / ETZ-2 / Etizolam-2	2-ethyl-9-methyl-4-phenyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine	benzodiazepine
Pyrazolam	8-Bromo-1-methyl-6-pyridin-2-yl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine	benzodiazepine

Table S2: Limits of detection (LOD) and limits of quantification (LOQ) for quantitative analysis of wastewater and pooled urine.

	Influent WW		Pooled Urine	
	LOD (ng L^{-1})	LOQ (ng L^{-1})	LOD (µg L^{-1})	LOQ (µg L^{-1})
Amphetamine	30	100	1.06	3.54
Benzoylecgonine	0.6	2	0.02	0.07
Buphedrone	0.2	0.7	0.31	1.02
Butylone	1.5	5	0.21	0.71
Cocaine	1.5	5	0.05	0.18
Ethylone	50	167	0.25	0.84
Ketamine	6	19	0.20	0.67
Mephedrone	1.5	5	0.21	0.71
Methamphetamine	25	82	0.87	2.90
Methcathinone	8	27	0.28	0.95
Methedrone	1.5	5	0.21	0.71
Methoxetamine	2	5	0.05	0.18
MDPV	0.1	1	0.04	0.14
Methylone	1.5	5	0.21	0.71
N-ethylcathinone	1.5	5	0.21	0.71
Naphyrone	0.3	1	0.04	0.14
Ephenidine (NEDPA)	0.1	0.2	0.10	0.34
MDMA	9	30	0.32	1.06
THC-COOH	18	60	0.64	2.12
bk-MDDMA	6	20	0.21	0.71
25-B-NBOMe	0.3	1	0.04	0.14
25-C-NBOMe	1.5	5	0.21	0.71
25-I-NBOMe	1.5	5	0.21	0.71
25-iP-NBOMe	0.1	0.3	0.11	0.35
4-methyl-α-pyrrolydinopropiophenone (4-MePPP)	5	18	0.19	0.64
α-pyrrolidinopentiophenone (α-PVP)	13	43	0.46	1.52
Dimethylpentylone (bk-DMBDP)	2	6	0.06	0.21
ρ-methoxymethamphetamine (PMMA)	3	10	0.11	0.35
2-phenethylamine	36	120	1.27	4.25
3,4-DiMeO-α-PVP	3	9	0.10	0.32

3,4-dimethylmethcathinone (3,4-DMMC)	25	83	0.14	0.45
4,4'-dimethylaminorex (4-4'-DMAR)	0.1	0.2	0.08	0.27
4-chloro-α-PPP	5	17	0.18	0.60
4-fluoromethcathinone (4-FMC)	25	83	0.27	0.89
4-methylethcathinone (4-MEC)	8	27	0.27	0.91

Table S3: Concentration (µg/L) of drugs and NPS measured in pooled urine samples of UK 2015.

	Day 1										Day 2									
Location	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Amphetamine	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d
Methamphetamine	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d
MDMA	519	504	389	594	692	629	619	578	227	196	792	415	247	925	419	579	1166	1068	802	1044
Cocaine	10	35	3.9	207	203	43	218	216	0.8	d	24	1.1	0.7	1.8	0.9	2.1	329	254	7.4	94
Benzoylecgonine [a]	166	134	104	188	197	131	209	197	135	84	176	146	94	136	152	120	352	243	158	230
THC-COOH [b]	60	478	89	54	43	39	43	42	23	31	48	43	25	44	72	71	74	64	51	93
4-FMC	-	-	-	-	1.3	-	1.5	23	-	-	-	-	-	-	-	-	-	-	-	2.1
4-MEC	-	25	-	0.3	-	-	0.7	1.4	-	-	2.6	-	-	0.6	-	-	0.7	57	-	13
α-PVP	2.5	2.3	1.8	9.5	4.1	1.6	26	12	1.9	d	10	63	36	65	5.9	4.8	20	29	1.1	16
Butylone	-	-	-	-	-	-	-	-	-	-	-	0.7	0.5	-	-	-	-	-	-	-
Ethylone [c]	d	d	-	d	d	d	d	d	-	-	d	-	-	-	-	d	d	d	d	d
Ketamine	28	14	14	13	38	1.9	45	32	4.4	1.1	23	24	17	37	2.8	11	28	54	30	27
MDPV	d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mephedrone	-	-	-	4.6	-	-	4.0	-	-	-	4.5	-	-	-	-	-	4.3	13	-	-
Methylone	-	-	-	1.7	0.4	-	-	-	-	-	-	-	-	-	-	-	0.7	1.0	-	-
SUM TOTAL NPS	31	41	16	29	44	3.5	77	68	6.3	1.1	40	88	54	103	8.7	16	54	154	31	58

d = detected, concentrations below limit of quantification (< LOQ)

[a] Benzoylecgonine is the main metabolite of cocaine

[b] 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THC-COOH) is the main metabolite of cannabis

[c] Ethylone was retrospectively detected by UHPLC-IMS -QTOF. It could be confirmed, but not quantified as at the time of analysis the quantitative method was not fully validated for this compound

Table S4: Concentration (µg/L) of drugs and NPS measured in pooled urine samples of UK 2016.

	Day 1												Day 2											
Location	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Amphetamine	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d
Methamphetamine	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d	d
MDMA	350	253	478	760	706	532	428	800	421	362	497	539	610	467	569	710	760	688	833	1965	401	497	487	689
Cocaine	2.6	0.9	3.9	1.7	1.4	d	3.2	0.8	1.3	1.2	5.5	1.2	0.7	-	1.8	3.3	d	1.0	0.9	d	d	1.0	1.7	0.9
Benzoylecgonine	213	124	333	181	185	199	308	174	126	107	179	126	126	171	157	178	174	162	177	132	176	169	166	173
THC-COOH	5.9	26	7.1	6.9	8.5	12	2.6	14	6.3	18	4.6	7.2	8.4	6.8	7.7	15	9.9	19	13	11	12	5.2	14	14
α-PVP	1.4	1.7	2.3	1.0	d	d	d	1.1	2.4	1.8	d	d	1.0	-	2.2	1.7	2.6	1.1	4.7	3.5	1.1	1.7	6.4	2.3
Butylone	-	-	-	-	-	-	-	-	-	-	-	-	d	-	-	-	-	-	-	-	-	-	-	-
Ketamine	35	28	55	83	89	70	86	61	36	27	60	18	29	51	63	54	118	70	130	178	18	8.2	41	84
Mephedrone	-	-	-	-	d	-	-	-	-	-	-	-	-	d	-	d	-	-	-	-	-	-	-	d
Methoxetamine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	2.8	-	-	-	1.7
Methylone	-	-	-	-	-	-	-	d	-	-	-	-	-	-	-	-	-	-	-	2.1	-	-	-	-
SUM TOTAL NPS	36	30	57	84	89	70	86	62	38	29	60	18	30	51	65	56	121	71	135	186	19	9.9	47	88

d = detected, concentrations below limit of quantification (< LOQ)

Table S5: Concentration (µg/L) of drugs and NPS measured in pooled urine samples of Belgium.

	Day 1			Day 2			Day 3		
Hour (h)	**16**	**20**	**24**	**16**	**20**	**24**	**16**	**20**	**24**
Amphetamine	d	d	d	d	d	d	d	d	d
Methamphetamine	d	d	d	d	d	d	d	d	d
MDMA	232	281	683	344	518	949	529	516	955
Cocaine	15	30	75	210	59	62	28	98	69
Benzoylecgonine	78	58	126	189	110	122	97	87	119
THC-COOH	43	78	50	34	27	41	34	32	32
Ketamine	0.5	0.5	7.3	d	2.1	6.2	d	6.9	8.0
Mephedrone	-	1.5	-	-	-	-	-	-	-
Methylone	1.6	-	-	0.4	1.0	-	-	0.8	0.7
SUM TOTAL NPS	2.1	2	7.3	0.4	3.1	6.2	d	7.7	8.7

d = detected, concentrations below limit of quantification (< LOQ)

Table S6: Concentration (µg/L) of drugs and NPS measured in pooled urine samples of Norway.

Day	**1**	**2**	**3**
Amphetamine	11	4.9	4.5
Methamphetamine	1.4	3.8	1.9
MDMA	27	29	8.7
Cocaine	15	46	17
Benzoylecgonine	6.6	13	11
THC-COOH	1.4	1.3	0.9
2-Phenethylamine	-	d	d
4-chloro-α-PPP	d	d	-
Ketamine	0.05	0.07	-
Methcathinone	0.3	0.3	0.3
Methoxetamine	d	-	-
SUM TOTAL NPS	0.35	0.37	0.3

d = detected, concentrations below limit of quantification (< LOQ)

Table S7: Loads (g/day) of drugs and NPS measured in wastewater samples of Portugal (2017) during one week, which coincided with a festival.

Day	1* THU	2* FRI	3* SAT	4 SUN	5 MON	6 TUE	7 WED
Amphetamine	-	-	-	-	-	-	-
Methamphetamine	-	d	d	d	d	-	-
MDMA	8.5	15.9	26.3	30.0	20.8	21.6	8.0
Cocaine	4.9	29.4	32.3	25.2	30.8	18.6	11.6
Benzoylecgonine	264	251	290	288	258	223	222
THC-COOH	65	305	353	362	413	340	338
2-Phenethylamine	d	d	d	d	d	d	d
25-E-NBoMe	d	-	-	-	-	-	-
3,4-DMMC	-	-	-	0.3	-	-	-
4-chloro-α-PPP	d	d	d	d	d	-	-
α-methyltryptamine	d	-	-	-	-	-	-
Buphedrone	-	-	0.5	0.3	0.2	-	0.2
DOiP	-	-	d	-	-	-	-
Ketamine	-	-	d	d	d	d	-
Methcathinone	-	0.2	0.1	0.1	0.1	-	-
Mephedrone	0.2	1.6	1.4	0.9	0.5	0.3	0.2
SUM TOTAL NPS	0.2	1.8	2.0	1.6	0.8	0.3	0.4

*Festival days; d = detected, concentrations below limit of quantification (< LOQ)

Table S8: Loads (g/day) of drugs and NPS measured in wastewater samples of Portugal (2017) during six consecutive days, which did not coincide with a festival or special event.

Day	1 WED	2 THU	3 FRI	4 SAT	5 SUN	6 MON
Amphetamine	-	-	-	-	-	-
Methamphetamine	-	-	-	-	-	-
MDMA	7.7	7.1	5.6	20.8	47.6	16.5
Cocaine	20.4	24.5	27.2	38.3	30.2	13.3
Benzoylecgonine	114	129	127	238	247	162
THC-COOH	56	35	42	39	28	34
SUM TOTAL NPS	-	-	-	-	-	-

d = detected, concentrations below limit of quantification (< LOQ)

Table S9: Loads (g/day) of drugs and NPS measured in wastewater samples of Serbia (2017) during one week, which coincided with a festival.

Day	1 MON	2 TUE	3* WED	4* THU	5* FRI	6 SAT	7 SUN
Amphetamine	4.7	3.6	6.5	6.2	8.7	11.9	11.8
Methamphetamine	-	-	d	d	0.1	0.2	0.1
MDMA	6.2	4.4	9.9	41.9	93.3	120	175
MDA	-	-	0.7	3.0	7.4	8.2	12.9
Cocaine	2.5	1.9	2.9	2.9	3.9	4.9	5.0
Benzoylecgonine	14.8	10.7	13.9	15.7	18.8	30.3	27.2
THC-COOH	na	na	na	na	na	na	na
25-iP-NBoMe	-	0.3	-	-	-	-	-
4,4-DMAR	-	-	0.08	0.03	-	-	-
α-methyltryptamine	-	-	-	-	d	-	-
Methcathinone	-	-	-	0.04	0.04	0.05	0.04
NEDPA	-	0.3	-	-	-	-	-
SUM TOTAL NPS	-	0.6	0.08	0.07	0.04	0.05	0.04

*Festival days; d = detected, concentrations below limit of quantification (< LOQ); na = not analysed. These samples were analysed using the methodology developed by Zuccato et al. 2016 for drugs and González-Mariño et al., 2016 for NPS.

Table S10: Loads (g/day) of drugs and NPS measured in pooled wastewater samples (week and weekend) of Serbia (2017), which did not coincide with a festival or special event.

	1	**2**
Day	**Week days**	**Weekend days**
Amphetamine	5.8	7.8
Methamphetamine	-	-
MDMA	3.2	9.2
MDA	-	0.8
Cocaine	3.1	3.4
Benzoylecgonine	14.2	17.3
THC-COOH	na	na
4,4-DMAR	-	0.11
α-methyltryptamine	-	d
Methcathinone	0.05	0.05
SUM TOTAL NPS	0.05	0.16

d = detected, concentrations below limit of quantification (< LOQ); na = not analysed. These samples were analysed using the methodology developed by Zuccato et al. 2016 for drugs and González-Mariño et al., 2016 for NPS.

Table S11: Loads (g/day) of drugs and NPS measured in wastewater samples of Spain (2018) during seven consecutive days, which coincided with a festival.

	1	2	3*	4*	5*	6*	7
Day	**TUE**	**WED**	**THU**	**FRI**	**SAT**	**SUN**	**MON**
Amphetamine	-	d	1.1	2.8	12.7	11.4	5.6
Methamphetamine	-	-	-	d	d	0.5	d
MDMA	0.5	0.7	1.8	17.8	123	106	39.7
Cocaine	3.0	4.5	6.0	5.7	20.0	17.4	10.4
Benzoylecgonine	12.3	17.5	24.2	27.9	76.9	66.8	31.9
THC-COOH	1.4	1.3	2.8	2.4	3.6	3.4	3.5
Ketamine	1.1	d	d	1.2	12.6	5.6	2.9
Methylone	-	-	-	-	-	d	d
SUM TOTAL NPS	1.1	d	d	1.2	12.6	5.6	2.9

*Festival days; d = detected, concentrations below limit of quantification (< LOQ)

Table S12: Loads (g/day) of drugs and NPS measured in wastewater samples of Spain (2018) during seven consecutive days, which did not coincide with a festival or special event.

	1	2	3	4	5	6	7
Day	**MON**	**TUE**	**WED**	**THU**	**FRI**	**SAT**	**SUN**
Amphetamine	-	-	-	-	-	-	-
Methamphetamine	-	-	-	-	-	-	-
MDMA	d	d	d	d	d	0.2	0.3
Cocaine	4.3	5.4	3.5	3.2	4.9	5.2	4.4
Benzoylecgonine	11.0	11.3	8.0	7.7	10.3	13.5	10.5
THC-COOH	0.7	0.9	0.8	0.7	0.9	1.2	0.6
Ketamine	-	-	d	-	-	d	d
Methylone	-	-	-	-	-	-	-
SUM TOTAL NPS	-	-	d	-	-	d	d

d = detected, concentrations below limit of quantification (< LOQ)

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