WP2 - Qualitative and quantitative analysis of new psychoactive substances (NPS) in Europe, with focus on synthetic opioids and prescriptions opioids

Deliverable 6

Analytical procedure for qualitative analysis of NPS

Qualitative analysis of new psycoactive substances (NPS) in urban wastewater (WW) and pooled urine samples was performed by solid-phase extraction (SPE) followed by liquid-chromatography-high resolution-mass spectrometry (LC-HRMS). A new "suspect" screening approach has been developed for the qualitative analysis of 253 priority NPS, adopting a workflow previously validated in our lab (Salgueiro-González, 2019). The activities to perform the qualitative analysis of NPS are described in detail below.

Selection of "priority NPS"

The Early Warning Systems (EWS) of different organizations (i.e. United Nation Office on Drugs and Crime (UNODC), the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the National EWS of Italy) reported more than 550 NPS between 2018 and 2019. At the beginning of the EuSeME project, we created a database of these 550 NPS (Deliverable 1), collecting information on their chemical properties, the first alert of intoxication/seizure (date and place) and additional information (e.g. poly-drug use, human metabolism). Among them, a list of "priority NPS" was selected considering the NPS most frequently and recently recorded in the

market or during seizures. This list of "priority NPS" has been updated every 6-months within the project (last update in September 2021), considering all reports published by the EWS of EMCDDA and Italy. The final list of 253 "priority NPS" used for the screening analysis is shown in Annex 1 of this Deliverable.

Sample preparation

Sample (pre)treatment protocols for urban WW and pooled urine have been adapted from previous works (Castiglioni et al, 2021; Gjerde et al, 2019) and applied both for qualitative (present deliverable) and quantitative NPS analysis (Deliverable 7).

Urban wastewater. WW samples were vacuum-filtered and pooled for analyses. Pooled weekend and weekday samples (50 mL) were prepared mixing fixed aliquots from each day, as follows: Saturday, Sunday and Monday are pooled for "weekend" composite sample and Tuesday to Friday for "week" composite sample.

WW samples (50 mL) were acidified to pH~2 with HCl (37 %), spiked with internal standards (2 ng of each compound), and extracted by SPE using Oasis® MCX cartridges (150 mg, 6 cc). Before the extraction, MCX cartridges were conditioned with 10 mL methanol (MeOH), 5 mL Milli-Q water, and 5 mL water acidified to pH 2. Samples were manually loaded at a flow rate of about 5 mL min^{-1}. MCX cartridges were vacuum-dried for 10 min and eluted with 2 mL of MeOH and 2 mL of a 2% ammonia solution in MeOH. Eluates were dried under a gentle nitrogen stream, reconstituted in 80 µL of a mixture of Milli-Q water:MeOH (90:10), centrifuged for 2 min at 2500 rpm, and transferred into glass vials for LC-HRMS analysis.

Urine. One mL of pooled urine sample was spiked with internal standard (2 ng of each compound) and hydrolysed with β-glucuronidase at 55ºC for 2 h (pH=4.5-5, buffer acetic acid/ammonium acetate). Then, urine extracts were acidified to pH~2 with HCl (9 %) and extracted by SPE using Oasis® MCX cartridges (60 mg, 3 cc). Before the extraction, MCX cartridges were conditioned with 6 mL MeOH, 3 mL Milli-Q water and 3 mL of Milli-Q water acidified to pH 2. After sample loading, MCX cartridges were vacuum-dried for 5 min and eluted with 1 mL of MeOH and 1 mL of a 2% ammonia solution in MeOH. Eluates were dried under a gentle nitrogen stream, reconstituted in 200 µL of a mixture of Milli-Q water:MeOH (90:10), centrifuged for 2 min at 2500 rpm, and transferred into glass vials for LC-HRMS analysis.

HRMS analysis

LC-HRMS analysis was done with an Agilent 1200 series HPLC coupled to a Q-Exactive™ Hybrid Quadrupole-Orbitrap™ (Thermo Scientific, Bremen, Germany) mass spectrometer equipped with a heated electrospray ionization (HESI) source. LC separation was performed at room temperature using an XBridge® C_{18} column (2.1x100 mm, 3.5 µm) from Waters Corporation (Milford, MA, USA) and a dual eluent system consisting of (A) 0.1 % formic acid (FA) in MilliQ water and (B) acetonitrile (ACN), at a constant flow rate of 200 µL min^{-1}. The gradient was: 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 37 min). The column temperature was set at 30°C and the volume of injection was 8 µL. HRMS analyses were carried out in positive mode, under the following working conditions: sheath gas pressure 45 bar, auxiliary gas pressure 5 bar, auxiliary gas temperature 160°C, ion spray voltage 3.5 kV, heated capillary temperature 320°C, S-lens RF 60. Data were acquired using Thermo Xcalibur™ 4.0

software (Thermo Scientific, Bremen, Germany). More details about MS and MS^2 parameters can be found in a previous work (Salgueiro-González, 2019).

Identification criteria and workflow for screening analysis

The identification of "suspect NPS" was performed according to the criteria proposed by different guidelines (WADA, 2010; SANTE, 2019). It includes key parameters like the accurate mass of the most abundant ion (normally protonated molecule) with delta mass < 5 ppm, the isotope pattern, and at least one product ion identified with a delta mass lower than 5 ppm. When reference standards are available, the retention time (RT) is also considered for identification with an acceptable variability of ± 2% min.

The screening workflow comprises three main steps (Figure 1) (Salgueiro-González, 2019):

(i) *Full-scan analysis* (70,000 resolution), looking for molecules with a mass-to-charge ratio (m/z) between 60 and 900. HRMS chromatograms are screened using the software Trace Finder™ 3.1 (Thermo Scientific, Bremen, Germany) and "preliminary suspects NPS" are identifying considering the accurate mass ion of the "priority NPS" (m/z of the protonated molecule with delta mass < 5 ppm) and their expected RT.

(ii) *MS^2 analysis*. "Preliminary suspects NPS" are fragmented in a second step, and accurate mass product ions are considered for identification. MS^2 experiments (35,000 resolution) were done with the collision-induced dissociation (CID) mode by applying normal collision energy (NCE) values of 35 and 50 V and with a precursor ion isolation window of ± 3.0 m/z that ensures a good sensitivity avoiding interferences. Firstly, a data-dependent analysis mode (FullMS-ddMS^2) is applied, in which the first data event

is a full-scan MS (scan range 60–900 m/z), and the next *n* events were MS^2 scans of the *n* most intense m/z recorded in the first event among the specific list of "preliminary suspect NPS". If fragmentation is not obtained, a data-independent analysis (DIA) mode will be employed, indicating the accurate masses of "suspect NPS" to be confirmed as targets for the acquisition of MS^2 scans during the selected retention time window.

(iii) *(Tentative) identification of "suspect NPS".* Finally, different confidence levels of identification are established according to the scheme proposed by Schymanski et al for the chemical identification by HRMS (Schymanski, 2014): *Level 1*, assigned when reference standards are available and confirmation is possible by matching RT, MS and MS^2 spectra. *Level 2*, assigned when no reference standard is available, but the detection is still possible, as the chemical structure can be elucidated from diagnostic evidence or with matching spectra data (library/database or literature). *Level 3*, assigned to a tentative identification when the information is not enough to confirm the chemical structure of NPS, but the accurate mass ion is found and some product ions are identified with the potential chemical structure. In levels 2-3, references standards are mandatory for confirmation purposes.

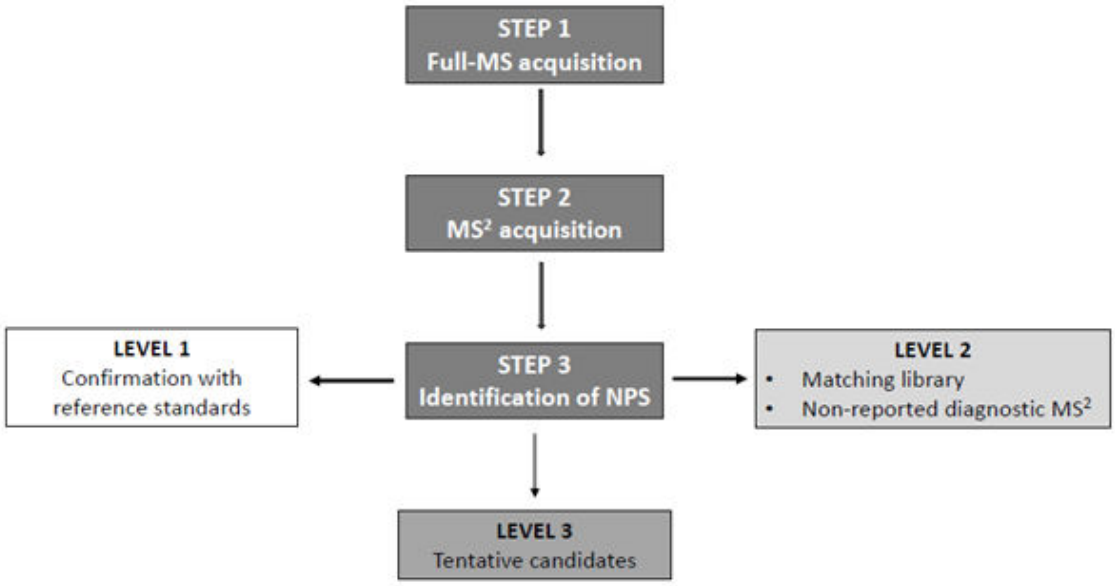

Figure 1. Scheme of suspect screening workflow and confidence levels of identification (1-3) using a Q-Exactive mass analyzer.

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ANNEX 1. Database of "priority NPS" selected for screening analysis.

Number	NPS Categories	Compound	Formula
1	Phenethylamines	**1-PEA/1-Phenethylamine**	C8H11N
2		**2C-B-FLY**	C12H14BrNO2
3		**2C-C**	C10H14ClNO2
4		**2C-D**	C11H17NO2
5		**2C-E**	C12H19NO2
6		**2C-H**	C10H15NO2
7		**2C-I**	C10H14INO2
8		**2C-P**	C13H21NO2
9		**2-FA/2-Fluoroamphetamine**	C9H12FN
10		**2-FEA/2-fluoroethylamphetamine**	C11H16FN
11		**2-FMA/ 2-Fluoromethamphetamine**	C10H14FN
12		**2-PEA/PEA/2-Phenethylamine**	C8H11N
13		**3-FEA / 3-fluoroethylamphetamine**	C11H16FN
14		**3-FMA/3-Fluoromethamphetamine**	C10H14FN
15		**4-FA/4-Fluoroamphetamine**	C9H12FN
16		**4-FEA/ 4-fluoroethylamphetamine**	C11H16FN
17		**4-FMA/ 4-Fluoromethamphetamine**	C10H14FN
18		**4-MA/4-Methylamphetamine**	C10H15N
19		**5-APB/ 5-(2-Aminopropyl)benzofuran**	C11H13NO
20		**5-EAPB/5-(2-ethylaminopropyl) benzofuran**	C13H17NO
21		**5-MAPB/N-Methyl-5-APB**	C12H15NO
22		**25D-NBOMe**	C19H25NO3
23		**25E-NBOH**	C19H25NO3
24		**25I-NBOH**	C17H20INO3
25		**bk-2C-B**	C10H12BrNO3
26		**DOC/2,5-Dimethoxy-4-chloroamphetamine**	C11H16ClNO2
27		**DOI/2,5-Dimethoxy-4-iodoamphetamine**	C11H16INO2
28		**M-alpha**	C11H15NO2
29		**MPA/Methiopropamine**	C8H13NS
30		**N,N-dimethylphenethylamine**	C10H15N
31	Synthetic cathinones	**3-CMC/3-chloromethcathinone**	C10H12ClNO
32		**3-CEC/3-chloroethcathinone**	C11H14ClNO
33		**3F-α-PVP/3F-α-Pyrrolidinovalerophenone**	C15H20FNO
34		**3-FMC/3-Fluoromethcathinone**	C10H12FNO
35		**3-MEC/3-methylethcathinone**	C12H17NO
36		**4-BMC/4-Bromomethcathinone/ Brephedrone**	C10H12BrNO

37		**4-CBC/4-chlorobutylcathinone**	C13H18ClNO
38		**4-CDMC/4-chloro-N,N-dimethylcathinone**	C11H14ClNO
39		**4-CEC/4-chloroethcathinone**	C11H14ClNO
40		**4-CMC/ 4-chloromethcathinone/Clephedrone**	C10H12ClNO
41		**4-CPD/4-Chloropentedrone**	C12H16ClNO
42		**4-Cl-α-PVP/4-chloro-α-pyrrolidinopentiophenone**	C15H20ClNO
43		**4-EMC/4-Ethylmethcathinone**	C12H17NO
44		**4-FPD/ 4-Fluoropentedrone**	C12H16FNO
45		**4-F-α-PHP/4-fluoro-alpha-pyrrolidinohexanophenone**	C16H23FNO
46		**4F-α-PVP/4-fluoro-alpha-pyrrolidinovalerophenone**	C15H20FNO
47		**4-MDMC/4-methyl-N,N-dimethylcathinone**	C12H17NO
48		**4-MEAPP/ 4-Methyl-alpha-ethylaminopentiophenone**	C14H21NO
49		**4-MeO-alpha-POP/4-MeO-α-PV9/4-methoxy-alpha-pyrolidinooctanophenone**	C19H29NO2
50		**4-MPD/4-Methylpentedrone**	C13H19NO
51		**5-DBFPV/5-dihydrobenzofuranpyrovalerone**	C17H23NO2
52		**Benzylone /BMDP**	C17H17NO3
53		**Dibutylone/ bk-DMBDB**	C13H17NO3
54		**Dimethylone/bk-MDDMA**	C12H15NO3
55		**Dipentylone/bk-DMBDP/N,N-dimethylpentylone**	C10H13NO
56		**Ephylone/ N-ethylpentylone**	C14H19NO3
57		**Eutylone/bK-MDEA**	C13H17NO3
58		**IsoPentedrone**	C12H17NO
59		**MDBVP/N-butyl pentylone**	C16H23NO3
60		**MDPBP/3,4-Methylenedioxy-α-pyrrolidinobutyrophenone**	C15H19NO3
61		**MDPHP/3,4-methylendioxy-α-pyrrolidinhexaphenone**	C17H23NO3
62		**Mexedrone**	C12H17NO2
63		**MPHP/4-Methyl-α-pyrrolidinohexiophenone**	C17H25NO
64		**MPPP/MePPP/4-Methyl-α-pyrrolidinopropiophenone**	C14H19NO
65		**NBH/N-butyl hexedrone**	C16H25NO
66		**NEH/ N-ethyl hexedrone**	C14H21NO
67		**N-ethyl pentedrone/α-EAPP/alpha-ethylaminopentiophenone**	C13H19NO
68		**N-methylbenzedrone/N-methyl-4-MBC**	C18H21NO
69		**N,N-diethylpentylone**	C16H23NO3
70		**Nor-mephedrone/4-methylcathinone**	C10H13NO
71		**Thiothinone/bk-MPA**	C8H11NOS
72		**TH-PVP/3,4-tetramethylene-α-PVP**	C19H27NO
73		**α-PEP/α-pyrrolidinoheptaphenone**	C17H25NO
74		**α-PiHP/α-Pyrrolidinoisohexanophenone**	C16H23NO

75		**α-PHP/ α-pyrrolidinohexanophenone**	C16H23NO
76		**α-PPP/alpha-pyrrolidinovalerophenone**	C13H17NO
77		**α-PVT/α-Pyrrolidinopentiothiophenone**	C13H19NOS
78	Synthetic cannabinoids	**4F-MDMB-BICA**	C20H27FN2O3
79		**4F-MDMB-BINACA/4F-MDMB-BUTINACA**	C19H26FN3O3
80		**5Cl-AB-PINACA/ 5Cl-ABP**	C18H25ClN4O2
81		**5Cl-AKB48/ 5Cl-APINACA**	C23H30ClN3O
82		**5F-AB-PINACA**	C18H25FN4O2
83		**5F-ADBICA/5F-ADB-PICA**	C20H28FN3O2
84		**5F-ADB/ 5F-MDMD-PINACA**	C20H28FN3O3
85		**5F-ADB-PINACA**	C19H27FN4O2
86		**5F-AKB57/ 5F-APINAC**	C23H29FN2O2
87		**5F-AMB-PINACA/5F-AMB/5F-MMB-PINACA/5F-AMP**	C19H26FN3O3
88		**5F-APINACA / 5F-AKB-48**	C23H30FN3O
89		**5F-CUMYL-P7AICA/CUMYL-5F-P7AICA/SGT-263**	C22H26FN3O
90		**5F-CUMYL-PeGaClone**	C25H27FN2O
91		**5F-CUMYL-PICA/SGT-67**	C23H27FN2O
92		**5F-CUMYL-PINACA/CUMYL-5F-PINACA/SGT-25**	C22H26FN3O
93		**5F-EDMB-PINACA**	C21H30FN3O3
94		**5F-EMB-PINACA/5F-AEB**	C20H28FN3O3
95		**5F-INPB-22/5F-PB-22 indazole/5F-NPB-22**	C22H20FN3O2
96		**5F-MDMB-PICA/ 5F-MDMB-2201**	C21H29FN2O3
97		**5F-MMB-PICA/5F-AMB-PICA/I-AMB/ MMB-2201**	C20H27FN2O3
98		**5F-MPP-PICA/ MPHP-2201/5F-MPhP-PICA**	C24H27FN2O3
99		**5F-PB-22/5F-QUPIC**	C23H21FN2O2
100		**AB-FUBINACA**	C20H21FN4O2

101		**AB-PINACA**	C18H26N4O2
102		**ADB-CHMINACA/ MAB-CHMINACA**	C21H30N4O2
103		**AM-694**	C20H19FINO
104		**AM-2201**	C24H22FNO
105		**AMB-CHMINACA/MA-CHMINACA**	C21H29N3O3
106		**APINACA / AKB-48**	C23H31N3O
107		**CUMYL-4CN-BINACA/4-CN-BINACA-ADB/CUMYL-CB-PINACA/CUMYL-CYBINACA/ SGT-78**	C22H24N4O
108		**DMBA-CHMINACA**	C21H29N3O3
109		**EMB-FUBINACA/AEB-FUBINACA/FU-AEB/ FUB-AEB**	C22H24FN3O3
110		**FDU-PB-22**	C26H18FNO2
111		**FUB-144/ FUB-UR-144**	C23H24FNO
112		**FUB-PB-22**	C25H17FN2O2
113		**JWH-018 / AM678**	C24H23NO
114		**JWH-073**	C23H21NO
115		**JWH-210**	C26H27NO
116		**JWH-250**	C22H25NO2
117		**MAM-2201/JWH-122 (5-fluoropentyl)/AM-2201 4-methylnaphthyl analog**	C25H24FNO
118		**MBA-CHMINACA/ AMB-CHMINACA/MAB-AB-CHMINACA/ MMB-CHMINACA**	C20H27N3O3
119		**MDMB-4en-PINACA/ 5-CL-ADB-A**	C20H27N3O3
120		**MDMB-CHMCZCA/EGMB-CHMINACA**	C27H34N2O3
121		**MDMB-CHMINACA**	C22H31N3O3
122		**MMB-022/AMB-4en-PICA/ AMB-P4EICA**	C20H26N2O3

123		**MMB-CHMICA/AMB-CHMICA**	C22H30N2O3
124		**MMB-FUBINACA/FUB-MMB/AMB-FUBINACA/FUB-AMB**	C21H22FN3O3
125		**NM-2201 / CBL-2201**	C24H22FNO2
126		**RCS-4**	C21H23NO2
127		**THJ-018/ JWH-018 indazole analogue**	C23H22N2O
128		**THJ-2201/ AM-2201 indazole**	C23H21FN2O
129		**UR-144 /KM-X1**	C21H29NO
130		**XLR-11 /5-Fluoro UR-144**	C21H28FNO
131	Tryptamines	**4-AcO-DET/4-Acetoxy-N,N-diethyltryptamine**	C16H22N2O2
132		**4-AcO-MET/4-acetoxy-N-methyl-N-ethyltryptamine**	C15H20N2O2
133		**4-HO-DET/4-Hydroxy-N,N-diethyltryptamine**	C14H20N2O
134		**4-HO-MET/4-Hydroxy-N-methyl-N-ethyltryptamine**	C13H18N2O
135		**4-HO-MiPT/4-hydroxy-N-isopropyl-N-methyltryptamine**	C14H20N2O
136		**5-HO-DMT/Bufotenin/5-Hydroxy-N,N-dimethyltryptamine**	C12H16N2O
137		**5-MeO-DALT/ 5-Methoxy-N,N-diallyltryptamine**	C12H16N2O
138		**AMT/alpha-Methyltryptamine**	C11H14N2
139		**DPT/N,N-dipropyltryptamine**	C16H24N2
140	**Fentanyl analogs and other synthetic opioids**	**2-Furanylbenzylfentanyl**	C23H24N2O2
141		**2-methylacetylfentanyl**	C22H28N2O
142		**3-Furanylfentanyl**	C24H26N2O2
143		**3-Fluoromethoxyacetylfentanyl**	C22H27FN2O2
144		**3-methylcrotonylfentanyl**	C24H30N2O
145		**4-Fluorocyclopropylbenzylfentanyl**	C22H25FN2O
146		**4-FBF/4-Fluorobutyrfentanyl**	C23H29FN2O
147		**4-FiBF/4-fluoroisobutyrfentanyl**	C23H29FN2O
148		**4-Fluorofuranylfentanyl/4-F-FuF**	C24H25FN2O2
149		**4-hydroxybutyrfentanyl/4-HO-BP**	C23H30N2O2
150		**Acetylbenzylfentanyl**	C20H24N2O
151		**Acrylfentanyl**	C22H26N2O
152		**Benzodioxolefentanyl**	C27H28N2O3
153		**Benzoyloylbenzylfentanyl**	C25H26N2O
154		**Benzylfentanyl**	C21H26N2O
155		**Benzylfuranylfentanyl**	C23H24N2O2
156		**Crotonylfentanyl**	C23H28N2O
157		**Cyclohexylfentanyl**	C26H34N2O

158		**Cyclopentylfentanyl**	C25H32N2O
159		**Despropionyl 2-fluorofentanyl**	C19H23FN2
160		**iBF/Isobutyrylfentanyl**	C23H30N2O
161		**Phenylfentanyl/Benzoylfentanyl**	C26H28N2O
162		**THF-F/Tetrahydrofuranylfentanyl**	C24H30N2O2
163		**Thienylfentanyl**	C19H24N2OS
164		**Thiophene fentanyl/2-Thiofuranylfentanyl**	C24H26N2OS
165		**2F-viminol**	C21H31FN2O
166		**2-methyl-AP-237**	C18H26N2O
167		**3,4-methylenedioxy-U-47700**	C17H24N2O3
168		**AH-7921**	C16H22Cl2N2O
169		**AP-237**	C17H24N2O
170		**AP-238**	C18H26N2O
171		**Bromadoline / U-47931E**	C15H21BrN2O
172		**Brorphine**	C20H22BrN3O
173		**Etazene/Etodesnitazene**	C22H29N3O
174		**etonitazepine/N-pyrrolidinetonitazene**	C22H26N4O3
175		**Furanyl UF-17**	C19H24N2O2
176		**Isopropyl-U-47700**	C18H26Cl2N2O
177		**Isotonitazene**	C23H30N4O3
178		**Metazene/Metodesnitazene**	C21H27N3O
179		**N-methyl bromadoline/N-Methyl U-47931E**	C16H23BrN2O
180		**nortilidine**	C16H21NO2
181		**O-AMKD**	C16H21NO3
182		**O-DT/O-desmethyltramadol**	C15H23NO2
183		**Piperidylthiambutene/Piperidinohton**	C17H21NS2
184		**Tianeptine**	C21H25ClN2O4S
185		**U-47700**	C16H22Cl2N2O
186		**U-48800**	C17H24Cl2N2O
187		**U-50488**	C19H26Cl2N2O
188		**U-51754**	C17H24Cl2N2O
189		**W-15**	C19H21ClN2O2S
190	Piperazine	**BZP/N-Benzylpiperazine**	C11H16N2
191		**MBZP**	C12H18N2
192		**mCPP**	C10H13ClN2
193		**TFMPP/ mTFMPP**	C11H13F3N2
194	Benzodiazepine	**Bromazolam**	C17H13BrN4
195		**Clonazolam**	C17H12ClN5O2
196		**Diclazepam**	C16H12Cl2N2O
197		**Etizolam**	C17H16N4S
198		**Flualprazolam**	C17H12ClFN4

199		**Flubromazepam**	C15H10BrFN2O
200		**Flubromazolam**	C15H10BrClN2O
201		**Fluclotizolam**	C15H10ClFN4S
202		**Flunitrazolam**	C17H12FN5O2
203		**Fonazepam/Desmethylflunitrazepam**	C15H10FN3O3
204		**Nitrazolam**	C17H13N5O2
205		**Norfludiazepam**	C15H10ClFN2O
206		**Phenazepam**	C15H10BrClO
207	Arylcyclohexylamine ketamine analogue	**2-FDCK/Fluoroketamine**	C13H16FNO
208		**3-HO-PCE/3-hydroxyeticyclidine**	C14H21NO
209		**3-HO-PCP/ 3-Hydroxyphencyclidine**	C17H25NO
210		**3-MeO-PCE/3-methoxyeticyclidine**	C15H23NO
211		**3-MeO-PCP/ 3-Methoxyphencyclidine**	C18H27NO
212		**Deschloroketamine**	C13H17NO
213		**Hydroxetamine/HXE**	C14H19NO2
214		**MXiPr/methoxisopropamine**	C16H23NO2
215		**MXPr/methoxpropamine**	C16H23NO2
216		**O-PCE/Deschloro-N-ethyl-ketamine/Eticyclodone**	C14H19NO
217	Aminorex derivative	**4Cl-MAR/4-chloromethylaminorex**	C10H11ClN2O
218		**4Br-MAR/4-bromomethylaminorex**	C10H11BrN2O
219	piperidine and pyrrolidine	**1-(1,3-diphenylpropan-2-yl)pyrrolidine**	C19H23N
220		**4F-EPH/4-fluoroethylphenidate**	C15H20FNO2
221		**4F-MPH/4-fluoromethylphenidate**	C14H18FNO2
222		**DCMP/3,4-Dichloromethylphenidate**	C14H17Cl2NO2
223		**DEP/diphenidine**	C19H23N
224		**Isopropylphenidate**	C16H23NO2
225		**MXP/2-MeO-diphenidine**	C20H25NO
226	Aminoindane	**2-AI/2-aminoindane**	C9H11N
227		**MDAI/5,6-Methylenedioxy-2-aminoindane**	C10H11NO2
228		**NM-2AI/N-methyl-2-aminoindane**	C10H13N
229	Plant-based NPS/Natural NPS	**Ergine/LSA/Lysergic acid amine**	C16H17N3O
230		**Harmaline**	C13H14N2O

231		**Harmine**	C13H12N2O
232		**Ibogaine/12-Methoxyibogamine**	C20H26N2O
233		**Mesembrine**	C17H23NO3
234		**Mitragynine (Kratom)**	C23H30N2O4
235		**Salvinorin A (Salvia)**	C23H28O8
236	Other NPS	**1,3-DMAA / Dimethylamylamine/Methylhexanamine**	C7H17N
237		**1cP-LSD**	C24H29N3O2
238		**1p-LSD/1-propionyl LSD**	C23H29N3O2
239		**3-FPM/3F-Phenmetrazine**	C11H14FNO
240		**AL-LAD/6-allyl-6-nor-LSD**	C22H27N3O
241		**ALD-52/1-acetyl-LSD**	C22H27N3O2
242		**Amantadine**	C10H17N
243		**CRL-40,028/Adrafinil**	C15H15NO3S
244		**CRL-40,941/Fladrafinil**	C15H13F2NO3S
245		**Dichloropane/RTI-111**	C16H19Cl2NO2
246		**DMC/Dimethocaine**	C16H26N2O2
247		**DMBA/N,N-Dimethylbutylamine**	C6H15N
248		**ETH-LAD/6-ethyl-6-nor-lysergic acid diethylamide**	C21H27N3O
249		**GHB/γ-hydroxybutyric acid**	C4H7O3
250		**Phenibut**	C10H13NO2
251		**Scopolamine**	C17H21NO4
252		**Sibutramine**	C17H27Cl2N
253		**Troparil**	C16H21NO2