GC-MS – Still standing for clinical and forensic analysis: validation of a multi-drug method to detect and quantify illicit drugs

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ABSTRACT

An SPE-GC-MS analytical method using whole blood samples has been developed and validated to detect and quantify nineteen compounds belonging to the Drugs of Abuse (DA) groups of cocaine and metabolites, opiates and new psychoactive substances (NPS) The method detailed here is necessary because the recreational consumption of these DA has increased considerably in recent years and poly-drug-consumption is now very common.

The method developed was both specific and selective. Three different working ranges have been defined due to the differences between therapeutic, toxic and lethal concentrations of DA. Linearity was confirmed for the defined working ranges of all DA, except pseudoephedrine, ephedrine, norephedrine, and TFMPP. Since the remaining nineteen substances showed heteroscedasticity, six ponderation factors were studied to find the best fit for each compound.

Limits of Detection and Lower Limits of Quantification have been studied and defined. No carryover was noted, with acceptable extraction recoveries.

The achievement of all validation criteria according to international guidelines allows the application of the proposed method in routine forensic analysis. Using this method can also significantly reduce response times and GC-MS analysis costs.

Key-words: Forensic toxicology, multi-drug method, cocaine, opiates, new psychoactive substances, GC-MS, solid-phase extraction

1 - Introduction

The need for analytical methods allowing the interpretation of toxicity-related death situations and the assessment of an influenced state has fostered the development of sophisticated techniques for the detection and quantification of drugs of abuse (DA) in biological samples. In addition, in recent years the development of new multi-drug analysis methods has increased in forensic toxicology, with laboratories continually seeking to increase their methodological and analytical capacities. The application of multi-substance methods has several objectives, namely to reduce the response time of the laboratory, since the detection of several substances from different groups is carried out in a single analysis, the use of smaller amounts of sample and reduction of costs in terms of material, without compromising the sensitivity and fit-for-purpose of the method.

There are several reviews available that elucidate the most appropriate detection and quantification techniques and methods for several groups of drugs, such as cocaine and its metabolites[1,2], opiates/opioids[3] and new psychoactive substances (NPS)[4]. Gas chromatography coupled with mass spectrometry (GC-MS) remains the most widely used technique in clinical and forensic toxicology laboratories[5] because GC systems are less expensive and require less maintenance than alternative systems (such as liquid chromatography)[6]. Because GC-MS exhibits good sensitivity and robustness, the development of methods that include this technique continues to be pursued, although in smaller numbers than the other techniques.

Despite the increasing development of multi-drug methodologies using less conventional matrices, such as hair, sweat or vitreous humour[7–9], blood and blood products remain the most commonly used matrices to detect, quantify and interpret drug

concentrations and metabolites. This is especially true for analytes belonging to the three DA groups mentioned, as this preference is evident in recently published multi-drug GC-MS methods which use whole blood, serum or plasma as samples5,10–14. Although serum or plasma are cleaner matrices, it is not always possible to obtain them in forensic toxicology samples[15,16]. Besides its homogeneity and the possibility of detecting and quantifying not only the drug metabolites but also the original drug, one of the main advantages of using a whole blood matrix is the possibility of obtaining samples *in vivo* or *post-mortem*, which is extremely relevant in forensic toxicology[17].

The main objective of the present work was to develop and validate an SPE-GC-MS analytical method to detect and quantify 23 compounds belonging to the DA groups of cocaine and metabolites, opiates/opioids and NPS, both *in vivo* and *post mortem* whole blood samples.

The DA groups and the selection of analytes were based both on the casuistry of the Chemistry and Forensic Toxicology Service of the National Institute of Legal Medicine and Forensic Sciences North Branch (SQTF-N), as well as on information from the competent authorities monitoring consumption[18]. In Europe, cocaine is, along with ecstasy and amphetamines, the most widely used stimulant drug[18]. As for opiates/opioids, the misuse of prescription opioids, the increase in heroin use, the rise of fentanyl derivatives on the market and the presence of opioids in 85% of fatal overdoses in 2018 reinforce the need to unequivocally detect and identify these substances in biological samples[18,19] The increase in internet sales has encouraged the consumption of NPS[18]. Known as “legal highs”, the variety of existing NPSs seriously affects the development of methodologies robust enough to be used in routine analysis situations[18,20] and the European Union has created an Early-Warning System, to share NPS’ information among authorities in member countries. At the end of 2017, more than 700 compounds were

monitored by the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) and this number continues to increase, albeit at a slower pace, compared to previous years[18]. In addition, the simultaneous consumption of several psychotropic substances is also increasing[18], making it imperative to develop methodologies to determine the analytes of several classes of DA.

2 - Material and Methods

2.1. Materials, standards, and chemicals

Pure standards of the target compounds and deuterated internal standards (IS) were provided by Cerilliant Corporation (Texas, USA) and Lipomed (Arlesheim, Switzerland). Stock standard solutions (1 mg/mL) and working solutions were prepared in methanol. A mixture of all IS with a final concentration of 5000 ng/mL was prepared, as well as three mixtures of analytes (Table 1): Set 1 with tramadol and ketamine at 10000 ng/mL, Set 2 with cocaethylene, 6-mono-acethyl-morphine (6-MAM), fentanyl, phencyclidine (PCP) and buprenorphine at 500 ng/mL and Set 3 with ephedrine, pseudoephedrine, norephedrine, ecgonine methylester (EME), 3-Trifluoromethylphenylpiperazine (TFMPP), d-propoxyphene, pethidine, N-desmethyltramadol (N-DT), O-desmethyltramadol (O-DT), 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), 3-Methoxyphencyclidine (3-MeO-PCP), methadone, cocaine, benzoylecgonine, codeine and morphine at 5000 ng/mL. All standard solutions were stored at -20ºC.

Methanol, n-hexane, dichloromethane, propan-2-ol, ammonia and ethyl acetate were purchased from Merck (Darmstadt, Germany). Stock sodium carbonate buffer from Thermo Fisher Scientific (Waltham, USA) was used to prepare sodium carbonate 0.15 M pH 9.5 buffer. Similarly, phosphate buffer saline (PBS) solution was prepared with a

dilution of 50 mL of Phosphate Buffered Saline PBS 20X pH 7.5, from AMRESCO (Solon, USA) in 950 mL of deionized water. Solid-phase extraction was performed using OASIS MCX® columns from WATERS™ (Massachusetts, USA). The derivatization reagent [BSTFA (N,O-bis(trimethylsilyl) trifluoroacetamide) + 1% TMCS (trimethylchlorosilane)] was obtained from Supelco (Madrid, Spain).

2.2. Biological samples collection

Analytical validation was developed from whole blood samples (previously tested for positivity) and obtained from the Portuguese blood bank.

Selectivity was tested using 10 pooled samples, consisting of 4 different sub-samples (*in vivo* and post-mortem). The samples were collected in vivo (at General Hospitals' Emergency Rooms), according to the procedures described in Portuguese legislation concerning driving under the influence of drugs, and also collected post-mortem according to the routine procedures in force in the Forensic Pathology Department of the Portuguese National Institute of Legal Medicine and Forensic Sciences, North Branch.

2.3. Sample preparation, Solid Phase Extraction and derivatization procedure

Four millilitres of PBS buffer were spiked with IS solution and working solutions (Set 1, 2 and 3). A 500 µL aliquot of whole blood, previously shaken in a roller mixer for 15 minutes, was added to this mixture. Then the mixture was vortexed and centrifuged at 4000 rpm for 30 minutes. The supernatant solution was used for SPE, which was performed using OASIS MCX® columns. Cartridge condition and equilibration were achieved by adding 2 mL of methanol and 2 mL of deionised water to the cartridge. The sample was loaded onto the conditioned cartridge and allowed to drain by gravity. For

the washing step, 2 mL of sodium carbonate 0.15 M pH 9.5 buffer, followed by 2 mL of deionised water and 3 mL of hexane were added to the column. After that, vacuum drying was carried out for half an hour. The samples were then eluted with 2 mL of dichloromethane/propan-2-ol/ammonia (78:20:2, v/v/v) mixture and evaporated to dryness at 45ºC, for 60 minutes, in a rotary evaporator. Finally, the dry eluates were silylated with 60 µL of BSTFA:TMCS (99:1) by heating at 65ºC, for 30 minutes, followed by instrumental analysis using GC-MS.

2.4. GC-MS analysis

GC-MS analysis was performed using an Agilent 6890N gas chromatograph (Agilent, Santa Clara, USA), with a J&W HP-5MS Capillary Column (30 m - 0.25 mm i.d. - 0.25 µm film thickness) (Agilent, Santa Clara, USA), coupled to an Agilent 5973N simple quadrupole (Agilent, Santa Clara, USA). The temperature of the GC oven was initially set to run at 100ºC for 4 minutes, increased to 290ºC at 15ºC/min, and held at this temperature for six minutes, with a total run time of 27 minutes. The temperatures of the injector, transfer line and source were set at 300ºC, 280ºC and 230ºC, respectively. Helium (GASIN, Barcelona, Spain) was used as carrier gas with a flow rate of 1 mL/min for 18.5 min and 1.3 mL/min until the end of the run. The splitless mode was used to inject 2 µL of sample and the MS detector was operated in SIM mode. The retention time (in minutes) and monitored ions (*m/z*) for all the analytes are described in Table 2. GC-MS control, data acquisition and processing were achieved with Enhanced ChemStation Software (Agilent, Santa Clara, USA).

2.5. Validation studies

To assess and choose the three diagnostic ions to monitor each standard and IS compound (at a concentration of 10 mg/L) was derivatized and injected in SCAN mode. After that, standards were injected in SIM mode to optimize GC-MS conditions.

The developed method was validated according to the guidelines suggested by Peters *et al* [6,21]. The acceptance analytical criteria, internally established and based on WADA guidelines[22] were applied.

To assess specificity and selectivity, 10 sample pools of 4 different whole blood samples were used. The analytes and IS were added at a concentration of 300 ng/mL for the substances of Set 1, 10 ng/mL for the compounds belonging to Set 2 and 100 ng/mL for the analytes of Set 3 and IS Set. At the same time, pools of the equivalent non-fortified sample were also tested.

In this work, three working ranges were proposed (Table 1), according to the relevant forensic concentrations for each drug considered. The calibration linearity was studied using a calibration curve, of ten standard concentrations, with the concentration ranges between the different standards being as equal as possible (Figure 1 shows an example for 6-MAM). After evaluation of the coefficient of correlation (r^2) and origin interception, aliquots of the lower and higher limits of each calibration curve were injected five times. To assess the homoscedasticity, the variance (s^2) of each concentration level (Set 1: 50 and 4000 ng/mL; Set 2: 5 and 100 ng/mL; Set 3: 25 and 1000 ng/mL) was calculated and an F-test was applied. The tested value (F_{calc}) was compared to the reference value (F_{crit}) of the F-test table (4 degrees of freedom).

To determine the limits of detection (LOD) and quantification (LOQ), calibration curves close to the estimated LOD for each set (Set 1 with LOD = 25 ng/mL, Set 2 with LOD = 2 ng/mL and Set 3 with LOD = 10 ng/mL) were prepared. The parameters of the generated calibration curves, namely the standard deviation of the response ($S_{y/x}$) and the

slope of the linear regression (b), were used to estimate the limits of detection and quantitation using the following equations: LOD = $(3.3S_{y/x})/b$ and LOQ = $(10S_{y/x})/b$. After calculation, the LOD and LOQ were tested, as well as the maximum concentration level of each working range, using five replicates for the chosen concentrations. LOQ was also studied for accuracy and precision.

Carryover studies were performed by injecting extracted blank samples between samples spiked at high concentrations (6000 ng/mL for psychotropic drugs included in Set 1, 200 ng/mL for compounds in Set 2 and 2000 ng/mL for DA in Set 3) and the presence of the target substances in the blank samples was verified. For each DA, five whole blood samples were used.

Although not considered a mandatory parameter of the validation process[21], extraction recovery was also tested, as some authors understand that recoveries need to be optimized[23]. For this, IS and analyte sets were added to the blank samples, at two distinct concentrations, representative of the low (50 ng/mL for Set 1, 10 ng/mL for Set 2 and 100 ng/mL for Set 3) and high ranges (3500 ng/mL for Set 1, 75 ng/mL for Set 2 and 700 ng/mL for Set 3), before and after the extraction procedure. The IS Set was added to all the samples at 100 ng/mL before the SPE step. Each concentration level was tested in triplicate (n=12). Recovery percentage was determined by calculating the ratio between the area ratios before and after extraction.

The precision was assessed by calculating the intermediate precision, repeatability, and limit of repeatability, using an ANOVA test, at three different concentration levels for each set (Set 1: 500, 1500 and 3000 ng/mL; Set 2: 5, 10 and 70 ng/mL; Set 3: 100, 400 and 700 ng/mL). Along with these quality controls (QC), calibration curves for all analytes were prepared and the respective *weighting factor,* selected for each DA, was applied. This procedure was repeated eight times, with

intermediate precision conditions. The coefficient variation (CV) obtained for each concentration level was also determined.

The data obtained in the precision study were used for the estimation of uncertainty in this work. For the uncertainty associated with accuracy (u ($\bar{R}$m)) evaluation, a t-student test was applied and the values of t_{exp} obtained for each substance at each CQ level were compared to $t_{crit} = 2.131$, considering 15 degrees of freedom for a confidence interval of 95%. If the condition $t_{exp.} < t_{crit.}$ was verified, no correction of the results in terms of accuracy was needed. Otherwise, calculation of the relative standard uncertainty (u'($\bar{R}$m)) was required. Concerning the uncertainty associated with the precision (u'precision), its value was considered to be equal to the Relative Standard Deviation (in %) obtained for the intermediate precision. The uncertainties associated with accuracy and precision were used to determine the combined uncertainty (u(y)) and the expanded combined uncertainty (U(y)).

3. Results and discussion

3.1. Selectivity/Specificity

The target compounds were unequivocally identified, using the three diagnostic ions established for each DA (supplementary data S1), as well as their retention time and the relative retention time of the internal standard. The results obtained from the selectivity/specificity evaluation generally showed an absence of possible interferences. Thus, the method was considered to be selective and specific for the 23 compounds.

3.2. Working range, linearity and calibration model

Calibration curves within working ranges for all considered DA were prepared and linearity was studied. By applying the least-squares model, r^2 and origin interception

were determined (Table 3). Since pseudoephedrine, ephedrine, norephedrine and TFMPP did not comply with the defined criteria for linearity ($r^2 > 0.98$), working range studies ended at this point for these four substances.

The evaluation of the homoscedasticity variances was carried out using an F-test, considering a critical F (F_{crit}) value equal to 6.388. All 23 substances showed $F_{calculated} > F_{crit}$ (Supplemental data S2), and so were considered heteroscedastic. These results were expected, due to the wide working ranges proposed in this method, which exceed an order of magnitude[6,21]. In forensic toxicology, the need to use wide working ranges makes it difficult to adjust them until homoscedasticity is verified. As such, Peters *et al*[21] proposed a mathematical transformation of the data or the application of a weighted least squares model.

For this work, six weight factors (*w*) were evaluated for each drug ($1/x^{1/2}$, $1/x$, $1/x^2$, $1/y^{1/2}$, $1/y$, $1/y^2$). The sum of the relative errors (Σ %RE) is mentioned as a sensitive indicator to assess the adjustment of a *weighting factor* to a calibration curve[24]. However, some authors suggest independent studies of quality control and accuracy [25]. As such, we determined the limits of repeatability and expanded uncertainties for each level of CQ (Supplemental Data S3). In addition, r^2 and Σ %RE were calculated for each of the eight calibration curves, generated in intermediate precision conditions, for the target analytes with confirmed linearity(Table 4). The *w* which revealed a mean $r^2 < 0.98$ weren't evaluated for the remaining parameters (Σ %RE, the limit of repeatability and expanded uncertainty).

A rank classification was assigned to the three parameters evaluated for each *w*, shown in Tables 4, 5 and 6. The weight factors providing the lowest percentage result for each parameter and therefore those which best fitted to each substance data were assigned with the lowest score. Therefore, the *w* with the lowest sum of ranks, or the final rank,

was chosen for each of the 19 quantifiable psychotropic drugs (Table 7). The data confirm that ketamine, fentanyl, cocaethylene, d-propoxyphene, pethidine, N-DT and codeine have at least one *w* with a mean $r^2 < 0.99$. As this is an essential criterion for the acceptance of the calibration curves, those w were no longer studied for the indicated DA and no classification was given. It´s also worth mentioning that, for methadone, 2 *w* obtained the same rank score, meaning both *w*'s had an equal adjustment to the defined working range. Thus, the choice *of w* for methadone was based only on the *w* fitting to most of the compounds in Set 3. The weighted least squares models chosen for the analytes in this method are summarized in Table 8.

3.3. LOD/LLOQ

As mentioned previously, the calibration curves close to the pre-defined LOD were used to determine the LOD and LLOQ for the DA present in each Set. For pseudoephedrine, ephedrine, norephedrine and TFMPP, due to poor signal-to-noise ratio at low concentrations or imprecise or non-linear calibration curves ($r^2 < 0.98$), the positivity criteria were verified at 25 ng/mL for pseudoephedrine and ephedrine and at 50 ng/mL for norephedrine and TFMPP. From this moment, the presented method was considered as qualitative for these four DA.

The LOD values, determined for the remaining DA, were as follows: for the compounds of Set 1, the calculated LOD was less than 3 ng/mL, for the analytes of Set 2, the obtained LOD was between 1.0 and 1.6 ng/mL and the DA present in Set 3 showed LOD values between 1.6 and 3.4 ng/mL, except for N-DT, which LOD was 7.8 ng/mL. As for the LLOQ, the substances of set 1 showed an LLOQ ≥ 9 ng/mL. The DA in Set 2 and Set 3 had an LLOQ between 3.1 and 4.7 ng/mL and 4.7 and 24 ng/mL, respectively.

Despite the LOD and LLOQ presented, and according to the literature[21], it is acceptable to establish a higher LLOQ as long as it remains appropriate for the toxicological interpretation. As such, these LLOQ were established for the presented method: 50 ng/mL for Set 1, 2.5 ng/mL for Set 2 and 25 ng/mL for Set 3. These defined LLOQs and the upper points of each working range were tested for their variation coefficients (CV%). The results obtained confirmed a CV% less than or equal to 20% satisfying the laboratory acceptance criteria.

3.4. Carryover and Extraction Recovery

Carryover evaluation did not reveal any false positives, proving the absence of carryover phenomena for the 23 analytes.

Extraction recovery data demonstrates a good per cent recovery for the majority of DA, with values ranging from 62.07% to 97.14% (Table 9). However, there were two substances with lower recovery percentages – EDDP and buprenorphine. Despite these results, it was still possible to perform the identification and quantification in the working range. On the other hand, the detection of metabolites, such as EDDP, is much more valuable than the quantitation value itself, being that aim properly verified in LOD validation procedure, with proper identification of the compound, even with a low recovery value as this.

The compounds d-propoxyphene, 3-MeO-PCP and N-DT are distinguished by recoveries greater than 100%. The recovery percentages of d-propoxyphene and 3-MeO-PCP remain within the laboratory acceptance criteria (100 ± 20%). As for N-DT, several reasons may help to justify the recovery value obtained, since the instability of compounds with N-amines has already been reported[26,27]. One possible explanation is the presence of enzymes in blood samples, due to the putrefaction process, which can increase

the pH value, allowing the formation of N-DT. In addition, the physicochemical properties of N-DT and the pH variations resulting from the SPE extraction process can be based on the high recovery rates obtained[26].

Even if the recovery percentages make it possible to detect and quantify all DA in the working ranges tested, they can be considered suitable for the methods presented.

3.5. Precision

The precision results are shown in Table 10. The CV % determined for the high-level concentration QCs of the quantifiable analytes were less than 10%, except for ketamine, pethidine and N-DT, and less than 20% for the low concentration level QCs of the 19 substances considered. The CV percentages obtained for an intermediate level concentration were also evaluated and considered in compliance, since they were equal to or less than the maximum value established for high concentration levels, 10%, except for EME and pethidine, which were below the percentage defined for low concentration levels.

3.6. Accuracy/Uncertainty

As occurred for precision, accuracy was assessed only for the 19 quantifiable compounds (Supplemental Data S3), taking into account the selected weight factors. For validation and routine application purposes, this method is assumed to be exact, with the highest percentage of U(y) for each DA being considered as the uncertainty associated with the method. The method uncertainty values range from 24.76% to 76.66%. However, these results are compatible with the use of the method in a routine forensic laboratory setting, giving the complexity of the samples used.

3.7. Application to Real samples

Actual clinical samples were obtained from DUID (Driving Under the Influence of Drugs) police actions. Postmortem samples were obtained through routine sampling procedures applied at the Portuguese National Institute of Legal Medicine and Forensic Sciences. All samples were selected after previous analysis according to routine laboratory procedures. A summary of the results obtained is shown in Table 11. The results were all consistent with previous results reported in the routine procedure.

4. Conclusions

In this work, we have developed a method that detects and quantifies nineteen compounds belonging to the Drugs of Abuse (DA) groups of cocaine and metabolites, opiates and new psychoactive substances (NPS). All results presented complied with the acceptance criteria for quantitative laboratory analysis, being possible to consider the presented GC-MS method is suitable for identification and quantitation of 19 analytes. In addition, this method can be used as a qualitative technique to detect ephedrine, pseudoephedrine, norephedrine and TFMPP. The working ranges and limits of detection and quantification are suitable for the toxic and lethal concentrations of the target analytes. Furthermore, the presented methodology is found to be precise and accurate for the main objective, without carryover and excellent recoveries for 17 out of 19 compounds, considering the small amount of sample, the SPE extraction procedure and the derivatization method.

Combining the detection and quantification of multiple target compounds in a single multi-drug method is very useful in laboratory routine as it reduces the laboratory response times, as well as solvent and sample consumption.

Although different techniques can be used to detect DA and metabolites in biological samples, GC-MS remains a robust and reliable technique, easy to use and maintain, with contained costs and meets all the major requirements for DA forensic analysis. Thus, the proposed method could present itself as a reliable method, applicable to a routine procedure, coupled with other fast screening procedures, such as immunoassays. It could also allow the availability of other more expensive and more complex equipment for other purposes, in addition to promoting greater cost-effectiveness of all the equipment available in the laboratory.

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Table 1

Sets' composition and corresponding work range. Working solution concentrations is presented, as well as the IS used for each analyte.

	Work Range	**Substance**	**IS Set** (5000 ng/mL)
Set 1 (10000 ng/mL)	50 - 4000 ng/mL	Tramadol	Tramadol-C_{13}.D_3
		Ketamine	Benzoylecgonine-D_3
		Cocaethylene	
Set 2 (500 ng/mL)	5 - 100 ng/mL	6-MAM	6-MAM-D_3
		Fentanyl	
		PCP	PCP-D_5
		Buprenorphine	Buprenorphine-D_4
Set 3 (5000 ng/mL)	25 - 1000 ng/mL	Pseudoephedrine	EME-D_3
		Ephedrine	
		Norephedrine	
		EME	
		TFMPP	
		d-Propoxyphene	PCP-D_5
		Pethidine	
		N- Desmethyltramadol	Tramadol-C_{13}.D_3
		O- Desmethyltramadol	
		EDDP	EDDP-D_3
		3-MeO-PCP	PCP-D_5
		Methadone	Methadone-D_3
		Cocaine	Cocaine-D_3
		Benzoylecgonine	Benzoylecgonine-D_3
		Codeine	Codeine-D_3
		Morphine	Morphine-D_3

Table 2

Retention times, in minutes, and *m/z* ratios of the three diagnostic ions chosen for each psychotropic drug or metabolite, with the quantification ion highlighted in bolt.

Substance	**Retention Time (min)**	**Diagnostic Ions (*m/z*)**
Pseudoephedrine di-TMS	8.748	**149**, 163, 179
Ephedrine di-TMS	8.805	**149**, 163, 179
Norephedrine di-TMS	9.709	**116**, 149, 280
EME-D_3	10.584	99
EME	10.601	**96**, 82, 83
TFMPP mono-TMS	11.534	**302**, 287, 172
d-Propoxyphene	11.738	**208**, 193, 178
Pethidine	12.089	**247**, 246, 218
Ketamine	13.010	**182**, 209, 152
PCP-D_5	13.165	205
PCP	13.194	**200**, 242, 243
Tramadol-C_{13}.D_3 mono-TMS	13.611	339
Tramadol mono-TMS	13.628	**335**, 245, 320
N-Desmethyltramadol di-TMS	13.829	**189**, 202, 261
O-Desmethyltramadol di-TMS	14.040	**58**, 303, 393
EDDP-D_3	14.143	280
EDDP	14.160	**277**, 276, 262
3-MeO-PCP	14.601	**230**, 272, 273
Methadone-D_3	14.847	297
Methadone	14.859	**294**, 223, 309
Cocaine-D_3	15.271	185
Cocaine	15.282	**182**, 82, 303
Cocaethylene	15.595	**196**, 94, 317
Benzoylecgonine-D_3 mono-TMS	15.631	243
Benzoylecgonine mono-TMS	15.642	**240**, 94, 361
Codeine-D_3 mono-TMS	16.632	237
Codeine mono-TMS	16.638	**234**, 178, 196
Morphine-D_3 di-TMS	16.861	432
Morphine di-TMS	16.873	**429**, 236, 414
6-MAM-D_3 mono-TMS	17.233	402
6-MAM mono-TMS	17.251	**399**, 287, 340
Fentanyl	17.970	**245**, 146, 189
Buprenorphine-D_4 mono-TMS	26.344	454
Buprenorphine mono-TMS	26.420	**450**, 482, 506

Table 3

Obtained data in linearity and variances homocedasticity studies. Variances of the low concentration level (S^2_{lower}) and high concentration level (S^2_{upper}) were calculated for the analytes which coefficient of correlation $r^2 > 0.98$. The value of $F_{calculated}$ was obtained through $S^2_{inferior}$ and $S^2_{superior}$ values.

Set / Work Range	**Analyte**	**r^2**	**S^2_{lower}**	**S^2_{upper}**	**$F_{calculated}$**
Set 1 50 - 4000 ng/mL	Tramadol	0.999	8.24	25528.8	3097.973
	Ketamine	0.990	32.43	63578.4	1960.534
Set 2 5 - 100 ng/mL	Buprenorphine	0.994	0.23	13.19	56.870
	Fentanyl	0.992	4.60	53.06	11.532
	6-MAM	0.999	0.24	4.77	20.038
	Cocaethylene	0.991	0.46	40.20	87.048
	PCP	0.997	0.22	3.98	17.726
Set 3 25 - 1000 ng/mL	Pseudoephedrine	0.832	-	-	-
	Ephedrine	0.878	-	-	-
	Norephedrine	0.853	-	-	-
	EME	0.997	50.16	9294.65	185.311
	TFMPP	0.875	-	-	-
	d-Propoxyphene	0.993	23.17	575.19	24.827
	Pethidine	0.995	36.67	1996.21	54.441
	N- Desmethyltramadol	0.998	10.12	54063.6	5344.046
	O- Desmethyltramadol	0.991	40.49	2230.23	55.076
	EDDP	0.999	45.80	1959.02	42.771
	3-MeO-PCP	0.998	93.50	947.25	10.131
	Methadone	0.996	46.48	38756.4	833.914
	Cocaine	0.997	46.12	1214.42	26.332
	Benzoylecgonine	0.998	41.90	847.48	20.226
	Codeine	0.996	17.99	9487.28	527.217
	Morphine	0.995	10.88	16892.2	1552.65

Table 4

Weight factors (*w*) study results, based on eight calibration curves prepared for each of the 19 quantifiable compounds. The sum of relative errors (Σ%RE) is shown and a classification was assigned to each w, between 1 and 6, in ascending order of Σ%RE. Weight factors with r^2 (mean) lower than 0.99 had no classification.

Weight factors (*w*)	**Tramadol**			**Ketamine**			**Buprenorphine**			**Fentanyl**		
	r^2 (mean)	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***
$1/x^{1/2}$	0.993	835.2%	6	0.994	675.8%	5	0.996	702.8%	4	0.995	664.2%	4
1/x	0.993	483.6%	3	0.992	481.8%	3	0.996	589.3%	3	0.994	562.1%	3
$1/x^2$	0.993	309.6%	2	0.992	302.7%	1	0.992	268.5%	1	0.991	246.5%	1
$1/y^{1/2}$	0.993	817.2%	5	0.995	622.9%	4	0.996	821.4%	6	0.995	765.6%	5
1/y	0.993	492.7%	4	**0.989**	553.8%	-	0.996	774.7%	5	0.995	498.7%	2
$1/y^2$	0.994	294.5%	1	0.991	317.8%	2	0.994	350.9%	2	**0.989**	285.7%	-
Weight factors (*w*)	**Cocaethylene**			**PCP**			**EME**			**d-Propoxyphene**		
	r^2 (mean)	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***	**r^2 (mean)**	**Σ%RE**	***Rank***
$1/x^{1/2}$	0.994	819.9%	4	0.996	874.9%	5	0.995	436.0%	5	0.994	538.4%	5
1/x	0.995	415.1%	2	0.994	666.3%	3	0.994	374.8%	3	0.993	415.9%	3
$1/x^2$	0.994	218.4%	1	0.993	259.1%	1	0.991	246.7%	1	0.993	228.6%	1
$1/y^{1/2}$	0.994	851.7%	5	0.995	1114.8%	6	0.995	501.1%	6	**0.986**	471.4%	-
1/y	0.995	434.1%	3	0.994	750.4%	4	0.994	385.5%	4	0.993	427.7%	4
$1/y^2$	**0.980**	343.5%	-	0.992	284.8%	2	0.992	291.5%	2	0.992	265.6%	2
	Pethidine			**N-DT**			**O-DT**			**EDDP**		

Weight factors (*w*)	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*
$1/x^{1/2}$	0.991	586.5%	4	0.994	527.2%	2	0.996	426.3%	5	0.996	325.3%	5
$1/x$	0.990	446.0%	2	0.991	426.0%	1	0.995	342.8%	4	0.996	299.1%	3
$1/x^2$	**0.988**	277.3%	-	**0.986**	298.1%	-	0.994	249.2%	1	0.994	228.9%	1
$1/y^{1/2}$	0.993	525.7%	3	0.992	545.3%	3	0.995	440.7%	6	0.996	409.8%	6
$1/y$	0.992	422.5%	1	**0.989**	393.3%	-	0.996	320.8%	3	0.995	304.5%	4
$1/y^2$	**0.989**	282.6%	-	**0.984**	318.8%	-	0.995	253.8%	2	0.993	248.3%	2

Weight factors (*w*)	Methadone			3-MeO-PCP			Cocaine			Benzoylecgonine		
	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*
$1/x^{1/2}$	0.997	320.4%	5	0.995	552.1%	6	0.998	336.2%	5	0.996	369.8%	5
$1/x$	0.997	265.7%	4	0.995	311.8%	4	0.997	267.8%	3	0.995	300.9%	2
$1/x^2$	0.995	232.0%	1	0.994	234.2%	1	0.996	218.5%	1	0.994	261.1%	1
$1/y^{1/2}$	0.997	330.5%	6	0.994	551.4%	5	0.998	346.9%	6	0.994	409.7%	6
$1/y$	0.997	251.4%	3	0.995	302.7%	3	0.996	324.5%	4	0.994	350.7%	4
$1/y^2$	0.995	241.3%	2	0.994	252.2%	2	0.996	221.3%	2	0.990	307.6%	3

Weight factors (*w*)	Codeine			Morphine		
	r^2 (mean)	Σ%RE	*Rank*	r^2 (mean)	Σ%RE	*Rank*
$1/x^{1/2}$	0.993	836.0%	3	0.993	815.0%	6
$1/x$	0.991	524.7%	1	0.994	515.8%	3
$1/x^2$	**0.989**	284.8%	-	0.990	332.6%	1
$1/y^{1/2}$	0.993	901.5%	4	0.994	713.3%	5
$1/y$	0.991	697.3%	2	0.994	579.9%	4
$1/y^2$	**0.989**	319.4%	-	0.992	346.6%	2

Table 5

Results of the repeatability limit study, for each of the three quality control levels (QC) using different weight factors. The lowest percentage is classified with the lower rank number, and equal values are classified with the same rank number.

Repeatability limit (%)																		
Weight	**Tramadol**						**Ketamine**						**Buprenorphine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	13.8	2	20.3	2	10.8	2	13.8	2	19.9	2	32.0	2	39.9	2	14.6	4	8.3	2
$1/x$	14.6	3	20.5	4	10.9	3	14.3	3	20.3	4	32.5	3	43.0	3	14.8	5	8.3	2
$1/x^2$	15.1	5	20.7	5	11.0	4	15.2	4	21.0	5	33.5	4	46.1	5	15.4	6	8.3	3
$1/y^{1/2}$	13.7	1	20.2	1	10.8	1	13.8	1	19.9	1	32.0	1	39.5	1	14.5	1	8.3	2
$1/y$	14.6	4	20.5	3	10.9	3	-	-	-	-	-	-	44.5	4	14.6	3	8.3	1
$1/y^2$	15.1	6	20.7	5	11.0	4	15.2	5	21.0	3	33.5	5	46.7	6	14.5	2	8.3	1
Weight	**Fentanyl**						**Cocaethylene**						**PCP**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	35.1	2	19.1	3	11.6	4	20.5	2	10.9	3	17.6	2	24.5	2	13.7	1	14.7	2
$1/x$	36.9	4	19.5	5	11.5	3	23.5	4	11.8	4	17.8	4	25.0	3	13.8	2	14.7	3
$1/x^2$	36.6	3	19.1	2	11.6	5	24.6	5	11.9	5	17.8	5	27.9	5	14.0	5	14.7	5
$1/y^{1/2}$	34.8	1	18.4	1	11.3	1	20.0	1	10.6	2	17.6	1	24.2	1	13.8	3	14.6	1
$1/y$	37.3	5	19.2	4	11.5	2	21.9	3	10.3	1	17.7	3	25.2	4	13.8	4	14.7	5
$1/y^2$	-	-	-	-	-	-	-	-	-	-	-	-	28.3	6	14.2	6	14.7	4
Weight	**EME**						**d-Propoxyphene**						**Pethidine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	19.7	5	28.3	2	22.3	5	27.6	4	18.6	4	22.8	5	30.2	4	29.6	4	31.5	4
$1/x$	19.5	3	28.4	3	22.3	4	25.8	5	18.3	3	22.6	4	27.5	3	29.2	2	31.2	1
$1/x^2$	18.3	1	28.5	4	22.2	1	24.4	2	18.1	1	22.5	1	-	-	-	-	-	-
$1/y^{1/2}$	19.6	4	28.0	1	22.3	3	-	-	-	-	-	-	26.4	2	29.5	3	31.4	3
$1/y$	19.7	2	28.6	5	22.3	6	25.6	3	18.3	2	22.6	3	25.7	1	29.2	1	31.2	2
$1/y^2$	19.1	6	28.6	6	22.2	2	24.4	1	18.1	1	22.5	2	-	-	-	-	-	-

Weight	N-DT						O-DT						EDDP					
factors (*w*)	QC 1	*Rank*	QC 2	*Rank*	QC 3	*Rank*	QC 1	*Rank*	QC 2	*Rank*	QC 3	*Rank*	QC 1	*Rank*	QC 2	*Rank*	QC 3	*Rank*
$1/x^{1/2}$	27.4	1	23.3	1	58.2	3	13.8	2	18.9	2	11.1	3	25.4	2	23.0	3	14.1	3
$1/x$	28.7	3	23.6	3	58.1	2	14.0	3	18.9	3	11.0	2	25.8	4	22.9	2	14.0	2
$1/x^2$	-	-	-	-	-	-	14.4	4	19.1	4	11.0	1	26.4	6	23.2	6	14.1	6
$1/y^{1/2}$	27.5	2	23.4	2	58.0	1	13.7	1	18.9	1	11.1	3	25.1	1	22.4	1	13.8	1
$1/y$	-	-	-	-	-	-	14.8	6	19.3	6	11.0	2	25.8	3	23.0	4	14.0	4
$1/y^2$	-	-	-	-	-	-	14.8	5	19.2	5	11.0	1	26.3	5	23.2	5	14.1	5
Weight	**Methadone**						**3-MeO-PCP**						**Cocaine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	22.0	2	18.1	2	12.3	4	26.5	6	18.4	6	18.7	4	15.6	2	16.6	2	10.1	5
$1/x$	22.0	1	18.1	3	12.3	3	24.7	4	18.2	3	18.6	3	16.9	6	18.5	6	10.0	3
$1/x^2$	22.6	4	18.4	4	12.3	1	24.1	1	18.2	1	18.5	1	16.2	4	16.9	4	10.0	1
$1/y^{1/2}$	22.1	3	18.0	1	12.4	5	25.5	5	18.3	5	18.7	5	15.6	1	16.6	1	10.0	5
$1/y$	23.3	6	18.5	6	12.4	5	24.4	3	18.2	3	18.6	3	15.7	3	16.7	3	10.0	4
$1/y^2$	22.7	5	18.4	5	12.3	2	24.2	2	18.2	2	18.6	2	16.2	5	17.0	5	10.0	2
Weight	**Benzoylecgonine**						**Codeine**						**Morphine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	16.1	3	16.8	4	10.0	4	20.0	3	14.1	3	6.95	3	29.6	4	18.1	5	12.1	5
$1/x$	15.7	2	16.7	3	9.9	2	17.9	1	13.8	1	6.85	1	26.6	3	17.8	3	11.9	3
$1/x^2$	15.5	1	16.6	2	9.9	1	-	-	-	-	-	-	24.6	1	17.5	1	11.8	1
$1/y^{1/2}$	18.3	6	15.7	1	11.5	6	20.7	4	14.2	4	6.97	4	30.4	5	18.1	6	12.1	6
$1/y$	17.2	5	17.6	6	10.0	5	18.8	2	13.9	2	6.89	2	64.9	6	17.8	4	11.9	4
$1/y^2$	16.6	4	17.3	5	9.9	3	-	-	-	-	-	-	25.5	2	17.6	2	11.8	2

Table 6

Results of the expanded uncertainty study, for each of the three quality control levels (QC) using different weight factors. The lowest percentage is classified with the lower rank number, and equal values are classified with the same rank number.

Expanded uncertainty (%)																		
Weight	**Tramadol**						**Ketamine**						**Buprenorphine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	23.52	1	7.84	1	18.05	1	29.08	5	29.08	1	30.21	2	36.46	2	40.37	2	32.89	1
$1/x$	27.75	4	9.26	4	18.99	4	26.82	3	29.89	3	30.44	3	36.40	1	43.02	6	33.16	3
$1/x^2$	27.78	5	9.28	5	19.45	6	24.40	1	32.64	4	32.64	4	38.44	3	40.26	1	53.97	6
$1/y^{1/2}$	24.66	2	8.21	2	18.07	2	27.86	4	29.45	2	30.20	1	41.53	5	41.10	4	32.95	2
$1/y$	27.84	6	9.28	6	19.06	5	-	-	-	-	-	-	41.44	4	42.14	5	33.25	4
$1/y^2$	27.30	3	9.12	3	18.34	3	25.38	2	33.19	5	33.08	5	44.29	6	40.99	3	48.77	5
Weight	**Fentanyl**						**Cocaethylene**						**PCP**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	84.05	2	30.78	2	28.28	3	28.68	2	32.92	1	25.51	2	35.15	2	20.58	2	22.77	1
$1/x$	84.85	3	32.08	3	23.13	2	28.10	1	35.25	3	25.85	3	41.24	4	19.71	1	23.37	3
$1/x^2$	91.05	5	35.68	5	48.00	5	35.12	4	41.51	5	34.23	5	52.26	5	32.23	6	39.70	6
$1/y^{1/2}$	78.39	1	32.75	4	20.68	1	29.29	3	33.37	2	25.50	1	27.80	1	23.30	3	22.98	2
$1/y$	86.22	4	30.52	1	38.12	4	45.75	5	38.95	4	30.26	4	35.61	3	29.85	4	37.52	4
$1/y^2$	-	-	-	-	-	-	-	-	-	-	-	-	51.78	6	31.37	5	38.58	5
Weight	**EME**						**d-Propoxyphene**						**Pethidine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
$1/x^{1/2}$	36.37	4	32.09	4	40.93	6	35.15	1	24.47	2	27.11	2	59.82	1	39.64	3	33.38	4
$1/x$	39.12	5	31.67	2	40.39	4	35.64	2	24.26	1	27.20	3	63.35	3	37.47	1	30.73	1
$1/x^2$	40.74	6	31.39	1	36.86	3	38.54	5	25.96	4	27.33	4	-	-	-	-	-	-
$1/y^{1/2}$	33.81	1	32.01	3	40.49	5	-	-	-	-	-	-	61.94	2	40.66	4	33.37	3

1/y	35.45	3	53.23	5	29.91	2	37.95	4	24.72	3	26.90	1	64.79	4	39.46	2	33.23	2
1/y²	34.37	2	56.56	6	28.23	1	36.91	3	26.05	5	28.96	5	-	-	-	-	-	-
Weight	**N-DT**						**O-DT**						**EDDP**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
1/x^1/2	66.39	3	57.61	2	56.65	2	24.72	2	25.66	3	24.56	5	23.38	4	23.19	3	18.75	1
1/x	65.73	1	56.49	1	56.35	1	28.27	6	25.51	1	24.01	4	27.30	6	21.54	2	24.88	4
1/x²	-	-	-	-	-	-	27.90	5	27.13	4	18.93	2	25.07	5	27.05	5	19.62	3
1/y^1/2	66.23	2	57.63	3	58.64	3	23.76	1	25.60	2	24.58	6	22.17	1	20.73	1	25.02	6
1/y	-	-	-	-	-	-	26.58	3	41.56	6	23.45	1	22.81	3	23.69	4	18.94	2
1/y²	-	-	-	-	-	-	27.51	4	38.96	5	20.94	3	22.16	2	33.61	6	24.89	5
Weight	**Methadone**						**3-MeO-PCP**						**Cocaine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
1/x^1/2	29.12	1	20.88	3	25.23	5	30.58	1	26.54	3	28.77	6	26.09	4	21.31	4	24.94	6
1/x	29.40	3	20.65	1	24.54	4	38.09	3	26.70	6	28.40	3	28.23	6	21.05	1	24.01	3
1/x²	30.12	4	27.05	4	14.39	1	36.89	2	25.50	1	28.51	4	25.22	1	27.20	5	12.55	1
1/y^1/2	29.13	2	20.86	2	25.27	6	39.45	5	26.55	5	28.52	5	25.70	2	21.27	3	24.93	5
1/y	32.19	6	30.29	6	16.73	3	40.05	6	26.54	4	28.34	2	28.20	5	21.17	2	24.01	4
1/y²	30.93	5	28.17	5	15.12	2	39.31	4	25.85	2	27.18	1	25.80	3	28.33	6	13.07	2
Weight	**Benzoylecgonine**						**Codeine**						**Morphine**					
factors (*w*)	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***	**QC 1**	***Rank***	**QC 2**	***Rank***	**QC 3**	***Rank***
1/x^1/2	39.29	2	22.28	3	21.22	6	39.57	4	21.91	3	12.30	3	40.10	1	32.79	2	18.15	2
1/x	45.00	5	21.72	2	20.44	4	36.19	1	20.32	1	10.68	1	41.33	3	34.12	4	18.46	3
1/x²	46.34	6	17.44	1	20.69	5	-	-	-	-	-	-	45.05	5	25.86	1	15.73	1
1/y^1/2	38.88	1	23.35	4	17.80	3	39.54	3	21.87	2	11.74	2	40.12	2	33.86	3	20.37	6
1/y	41.10	3	35.02	6	15.67	2	38.34	2	24.16	4	13.08	4	55.52	6	34.13	5	18.52	4
1/y²	44.53	4	31.13	5	15.12	1	-	-	-	-	-	-	43.88	4	34.49	6	19.05	5

Table 7

Final rank classification for different *w*, based on the partial sums of each evaluated parameter: relative error (%RE), repeatability limit (r) and expanded uncertainty (U(y)). Highlighted in bold are the lowest classifications of the final rank, which correspond to the *w* best fitting the respective DA's work range.

Weight factors (*w*)	**Tramadol**				**Ketamine**				**Buprenorphine**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	6	6	3	15	5	6	8	19	4	8	5	**17**
$1/x$	3	10	12	25	3	10	9	22	3	10	10	23
$1/x^2$	2	14	16	32	1	13	9	23	1	14	10	25
$1/y^{1/2}$	5	3	6	**14**	4	3	7	**14**	6	4	11	21
$1/y$	4	10	17	31	-	-	-	-	5	8	13	26
$1/y^2$	1	15	9	25	2	13	12	27	2	9	14	25
Weight factors (*w*)	**Fentanyl**				**Cocaethylene**				**PCP**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	4	9	7	20	4	7	5	16	5	5	5	**15**
$1/x$	3	12	8	23	2	12	7	21	3	8	8	19
$1/x^2$	1	10	15	26	1	15	14	30	1	15	17	33
$1/y^{1/2}$	5	3	6	**14**	5	4	6	**15**	6	5	6	17
$1/y$	2	11	9	22	3	7	13	23	4	13	11	28
$1/y^2$	-	-	-	-	-	-	-	-	2	16	16	34
Weight factors (*w*)	**EME**				**d-Propoxyphene**				**Pethidine**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	5	12	14	31	5	13	5	23	4	12	8	24

1/x	3	10	11	24	3	12	6	21	2	5	5	**12**
$1/x^2$	1	6	10	**17**	1	4	13	**18**	-	-	-	-
$1/y^{1/2}$	6	8	9	23	-	-	-	-	3	7	9	19
1/y	4	13	10	27	4	8	8	20	1	6	8	15
$1/y^2$	2	14	9	25	2	4	13	19	-	-	-	-

Weight factors (*w*)	**N-DT**				**O-DT**				**EDDP**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	2	5	7	14	5	7	10	22	5	8	8	21
1/x	1	8	3	**12**	4	8	11	23	3	8	12	23
$1/x^2$	-	-	-	-	1	9	11	21	1	18	13	32
$1/y^{1/2}$	3	5	8	16	6	5	9	**20**	6	3	8	**17**
1/y	-	-	-	-	3	14	10	27	4	11	9	24
$1/y^2$	-	-	-	-	2	11	12	25	2	15	13	30

Weight factors (*w*)	**Methadone**				**3-MeO-PCP**				**Cocaine**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	5	8	9	22	6	16	10	32	5	9	14	28
1/x	4	7	8	**19**	4	10	12	26	3	15	10	28
$1/x^2$	1	9	9	**19**	1	3	7	**11**	1	9	7	**17**
$1/y^{1/2}$	6	9	10	25	5	15	15	35	6	7	10	23
1/y	3	17	15	35	3	9	12	24	4	10	11	25
$1/y^2$	2	12	12	26	2	6	7	15	2	12	11	25

Weight factors (*w*)	**Benzoylecgonine**				**Codeine**				**Morphine**			
	%RE	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***	**%RE**	**r**	$U(y)$	***Final Rank***
	Σ *Rank*	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***		**Σ *Rank***	**Σ *Rank***	**Σ *Rank***	
$1/x^{1/2}$	5	11	11	27	3	9	10	22	6	14	5	25
1/x	2	7	11	20	1	3	3	**7**	3	9	10	22
$1/x^2$	1	4	12	**17**	-	-	-	-	1	3	7	**11**

$1/y^{1/2}$	6	13	8	27	4	12	7	23	5	17	11	33
$1/y$	4	16	11	31	2	6	10	18	4	14	15	33
$1/y^2$	3	12	10	25	-	-	-	-	2	6	15	23

Table 8

Selected weight factors for 19 quantifiable analytes, according to the final rank classification.

Set / Work range	Analyte	Weight factor (*w*)
Set 1 50-4000 ng/mL	Tramadol	$1/y^{1/2}$
	Ketamine	$1/y^{1/2}$
Set 2 5-100 ng/mL	Buprenorphine	$1/x^{1/2}$
	Fentanyl	$1/y^{1/2}$
	6-MAM	$1/y^{1/2}$
	Cocaethylene	$1/y^{1/2}$
	PCP	$1/x^{1/2}$
Set 3 25-1000 ng/mL	EME	$1/x^2$
	d-Propoxyphene	$1/x^2$
	Pethidine	$1/x$
	N-Desmetiltramadol	$1/x$
	O-Desmetiltramadol	$1/y^{1/2}$
	EDDP	$1/y^{1/2}$
	Methadone	$1/x^2$
	3-MeO-PCP	$1/x^2$
	Cocaine	$1/x^2$
	Benzoylecgonine	$1/x^2$
	Codeine	$1/x$
	Morphine	$1/x^2$

Table 9

Data from extraction recovery assessment for analytes considered to quantification. Percentages (mean, n=3) obtained at low and high concentration levels are shown. Also, mean extraction recovery values are presented.

Analyte	Low level mean recovery (%)	High level mean recovery (%)	Mean Extraction Recovery (%)
Tramadol	81	85	83
Ketamine	77	86	82
Buprenorphine	44	48	46
Fentanyl	94	96	95
6-MAM	76	78	77
Cocaethylene	86	94	90
PCP	82	88	85
EME	102	92	97
d-Propoxyphene	112	91	101
Pethidine	95	99	97
N-DT	135	179	157
O-DT	93	93	93
EDDP	31	20	25
Methadone	86	86	86
3-MeO-PCP	100	100	100
Cocaine	97	91	94
Benzoylecgonine	78	74	76
Codeine	93	93	93
Morphine	61	63	62

Table 10

Coefficients of variation (CV) and repeatability limits (r) percentages for each of the three QC concentration levels studied for each drug of abuse. Highlighted in bold are the highest r values, chosen as repeatability limits of the method, for the corresponding substances.

Analyte	**CV** (%)	***r*** (%)	**CV** (%)	***r*** (%)	**CV** (%)	***r*** (%)
Set 1 50-4000 ng/mL	**QC 1 (500 ng/mL)**		**QC 2 (1500 ng/mL)**		**QC 3 (3000 ng/mL)**	
Tramadol	4.9	13.7	7.2	**20.2**	3.9	10.8
Ketamine	4.9	13.8	7.1	19.9	11.4	**32.0**
Set 2 5-100 ng/mL	**QC 1 (5 ng/mL)**		**QC 2 (10 ng/mL)**		**QC 3 (70 ng/mL)**	
Buprenorphine	14.3	**39.9**	5.2	14.6	3.0	8.3
Fentanyl	12.4	**34.8**	6.6	18.4	4.1	11.3
6-MAM	7.7	**21.4**	4.8	13.3	4.5	12.5
Cocaethylene	7.2	**20.0**	3.8	10.6	6.3	17.6
PCP	8.8	**24.6**	4.9	13.7	5.2	14.7
Set 3 25-1000 ng/mL	**QC 1 (100 ng/mL)**		**QC 2 (400 ng/mL)**		**QC 3 (700 ng/mL)**	
EME	6.7	18.8	10.2	**28.5**	7.9	22.2
d-Propoxyphene	8.7	**24.4**	6.5	18.1	8.0	22.5
Pethidine	19.2	**53.9**	10.4	29.2	11.1	31.2
N-DT	10.3	28.7	8.4	23.6	20.8	**58.1**
O-DT	4.9	13.7	6.7	**18.9**	3.9	11.1
EDDP	9.0	**25.1**	8.0	22.4	4.9	13.8
Methadone	8.1	**22.6**	6.6	18.4	4.4	12.3
3-MeO-PCP	8.6	**24.1**	6.5	18.2	6.6	18.5
Cocaine	5.8	16.2	6.1	**16.9**	3.6	10.0
Benzoylecgonine	5.5	15.5	5.9	**16.6**	3.5	9.9
Codeine	6.4	**17.9**	4.9	13.8	2.4	6.9
Morphine	8.8	**24.6**	6.3	17.5	4.2	11.8

Table 11

Results obtained in real samples.

Case	Age	Sex	Medico-Legal ethiology	Results (ng/mL)
1	62	M	Accident	ODT (123) ; Tramadol (211)
2	57	M	Overdose	Methadone (904) ; EDDP (446) ; Cocaine (119) EME (535) ; Benzoylecgonine (2868)
3	38	M	Car accident	Cocaine (<25) ; EME (81) Benzoylecgonine (402)
4	62	F	Natural causes	NDT (227) ; ODT (59) ; Tramadol (1998)
5	46	F	Sepsis	ODT (40) ; Tramadol (76)
6	28	M	Motorbike accident	EME (29) ; Benzoylecgonine (534)
7	73	M	Natural causes	Morphine (67) Tramadol (940)
8	60	F	Suicide	NDT (218) ; ODT (138) ; Tramadol (532)
9	60	M	DUID	Morphine (36)
10	21	M	DUID	Morphine (73)
11	U	M	overdose	Codeine (78) ; Morphine (807) ; 6-AM (56) ; Methadone (733) ; NDT (32) ; ODT (80) ; Tramadol (181) ; EME (56) Benzoilecgonine (50)

U- unknown; NDT – N-Desmethyltramadol ; ODT – O-Desmethyltramadol ; EDDP (Methadone metabolite) ; DUID – Traffic control (Driving under the influence of drugs)

Supplementary data 1 – Results obtained in the Specificity/selectivity tests, per compound and per pool.

Ecgonine Methylesther

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **82**	54324	100,0%					23268	100,0%				-	>3	<1
1	*m/z* **83**	38855	71,5%				2	18003	77,4%				67,4/87.4	>3	<1
	m/z **96**	34850	64,2%					16324	70,2%				60.2/80.2	>3	<1
	m/z **82**	23268	100,0%					54324	100,0%				-	>3	<1
2	*m/z* **83**	18003	77,4%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	16324	70,2%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	46760	100,0%					54324	100,0%				-	>3	<1
3	*m/z* **83**	36249	77,5%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	34061	72,8%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	52716	100,0%					54324	100,0%				-	>3	<1
4	*m/z* **83**	34619	65,7%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	31681	60,1%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	27362	100,0%					54324	100,0%				-	>3	<1
5	*m/z* **83**	20602	75,3%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	18768	68,6%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	23358	100,0%					54324	100,0%				-	>3	<1
6	*m/z* **83**	18451	79,0%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	17260	73,9%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	25627	100,0%					54324	100,0%				-	>3	<1
7	*m/z* **83**	19369	75,6%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	18885	73,7%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	5384	100,0%					54324	100,0%				-	>3	<1
8	*m/z* **83**	4000	74,3%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	3669	68,1%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	34376	100,0%					54324	100,0%				-	>3	<1
9	*m/z* **83**	25681	74,7%				1	38855	71,5%				61.5/81.5	>3	<1
	m/z **96**	25040	72,8%					34850	64,2%				54.2/74.2	>3	<1
	m/z **82**	11615	100,0%					34376	100,0%				-	>3	<1
10	*m/z* **83**	8874	76,4%				10	25681	74,7%				64.7/84.7	>3	<1
	m/z **96**	8557	74,0%					25040	72,8%				62.8/82.8	>3	<1

Pseudoephedrine

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **149**	3855	100,0%				3444	100,0%				-	>3	<1
1	*m/z* **163**	817	21,2%			2	592	17,2%				12.2/22.2	>3	<1
	m/z **179**	539	14,0%				376	10,9%				5.9/15.9	>3	<1
	m/z **149**	3444	100,0%				4594	100,0%				-	>3	<1
2	*m/z* **163**	592	17,2%			3	611	13,3%				8.3/18.3	>3	<1
	m/z **179**	376	10,9%				307	6,7%				1.7/11.7	>3	<1
	m/z **149**	4594	100,0%									-	>3	<1
3	*m/z* **163**	611	13,3%			2							>3	<1
	m/z **179**	307	6,7%										>3	<1
	m/z **149**	5095	100,0%				3444	100,0%				-	>3	<1
4	*m/z* **163**	701	13,8%			2	592	17,2%				12.2/22.2	>3	<1
	m/z **179**	463	9,1%				376	10,9%				5.9/15.9	>3	<1
	m/z **149**	3938	100,0%				3855	100,0%				-	>3	<1
5	*m/z* **163**	853	21,7%			1	817	21,2%				16.2/26.2	>3	<1
	m/z **179**	512	13,0%				539	14,0%				9.0/19.0	>3	<1
	m/z **149**	3307	100,0%				3444	100,0%				-	>3	<1
6	*m/z* **163**	428	12,9%			2	592	17,2%				12.2/22.2	>3	<1
	m/z **179**	267	8,1%				376	10,9%				5.9/15.9	>3	<1
	m/z **149**	3922	100,0%				3855	100,0%				-	>3	<1
7	*m/z* **163**	655	17,0%			1	817	21,2%				16.2/26.2	>3	<1
	m/z **179**	389	10,0%				539	14,0%				9.0/19.0	>3	<1
	m/z **149**	5641	100,0%				4594	100,0%				-	>3	<1
8	*m/z* **163**	565	10,0%			3	611	13,3%				8.3/18.3	>3	<1
	m/z **179**	266	4,7%				307	6,7%				1.7/11.7	>3	<1
	m/z **149**	5155	100,0%				3855	100,0%				-	>3	<1
9	*m/z* **163**	1074	20,8%			1	817	21,2%				16.2/26.2	>3	<1
	m/z **179**	613	11,9%				539	14,0%				9.0/19.0	>3	<1
	m/z **149**	2150	100,0%				3444	100,0%				-	>3	<1
10	*m/z* **163**	464	21,6%			2	592	17,2%				12.2/22.2	>3	<1
	m/z **179**	306	14,2%				376	10,9%				5.9/15.9	>3	<1

Ephedrine

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **149**	7600	100,0%				5030	100,0%				-	>3	<1
1	*m/z* **163**	4923	64,8%			6	2844	56,5%				46.5/66.5	>3	<1
	m/z **179**	3327	43,8%				1999	39,7%				31.8/47.7	>3	<1
	m/z **149**	5458	100,0%				5210	100,0%				-	>3	<1
2	*m/z* **163**	2320	42,5%			4	2227	42,7%				34.2/51.3	>3	<1
	m/z **179**	1789	32,8%				1552	29,8%				23.8/35.7	>3	<1
	m/z **149**	3345	100,0%				5458	100,0%				-	>3	<1
3	*m/z* **163**	1322	39,5%			2	2320	42,5%				34.0/51.0	>3	<1
	m/z **179**	996	29,8%				1789	32,8%				26.2/39.3	>3	<1
	m/z **149**	5210	100,0%				5458	100,0%				-	>3	<1
4	*m/z* **163**	2227	42,7%			2	2320	42,5%				34.0/51.0	>3	<1
	m/z **179**	1552	29,8%				1789	32,8%				26.2/39.3	>3	<1
	m/z **149**	5030	100,0%				7600	100,0%				-	>3	<1
5	*m/z* **163**	2844	56,5%			1	4923	64,8%				54.8/74.8	>3	<1
	m/z **179**	1999	39,7%				3327	43,8%				35.0/52.5	>3	<1
	m/z **149**	4038	100,0%				5458	100,0%				-	>3	<1
6	*m/z* **163**	1619	40,1%			2	2320	42,5%				34.0/51.0	>3	<1
	m/z **179**	1195	29,6%				1789	32,8%				26.2/39.3	>3	<1
	m/z **149**	3638	100,0%				3345	100,0%				-	>3	<1
7	*m/z* **163**	942	25,9%			3	1322	39,5%				31.6/47.4	>3	<1
	m/z **179**	714	19,6%				996	29,8%				23.8/35.7	>3	<1
	m/z **149**	5220	100,0%				5458	100,0%				-	>3	<1
8	*m/z* **163**	1992	38,2%			2	2320	42,5%				34.0/51.0	>3	<1
	m/z **179**	1409	27,0%				1789	32,8%				26.2/39.3	>3	<1
	m/z **149**	5086	100,0%				7600	100,0%				-	>3	<1
9	*m/z* **163**	2893	56,9%			1	4923	64,8%				54.8/74.8	>3	<1
	m/z **179**	1987	39,1%				3327	43,8%				35.0/52.5	>3	<1
	m/z **149**	3789	100,0%				7600	100,0%				-	>3	<1
10	*m/z* **163**	2275	60,0%			1	4923	64,8%				54.8/74.8	>3	<1
	m/z **179**	1540	40,6%				3327	43,8%				35.0/52.5	>3	<1

Norephedrine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **116**	469100	100,0%					126286	100,0%				-	>3	<1
1	*m/z* **149**	7850	1,7%				2	1632	1,3%				0.6/1.9	>3	<1
	m/z **280**	10156	2,2%					2598	2,1%				1.0/3.1	>3	<1
	m/z **116**	126286	100,0%					469100	100,0%				-	>3	<1
2	*m/z* **149**	1632	1,3%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	2598	2,1%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	141865	100,0%					469100	100,0%				-	>3	<1
3	*m/z* **149**	3260	2,3%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	3050	2,1%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	297483	100,0%					469100	100,0%				-	>3	<1
4	*m/z* **149**	4556	1,5%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	6503	2,2%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	307015	100,0%					469100	100,0%				-	>3	<1
5	*m/z* **149**	5282	1,7%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	7300	2,4%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	239723	100,0%					469100	100,0%				-	>3	<1
6	*m/z* **149**	3788	1,6%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	5644	2,4%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	132058	100,0%					469100	100,0%				-	>3	<1
7	*m/z* **149**	2618	2,0%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	3085	2,3%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	70615	100,0%					469100	100,0%				-	>3	<1
8	*m/z* **149**	1258	1,8%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	1717	2,4%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	374532	100,0%					469100	100,0%				-	>3	<1
9	*m/z* **149**	4935	1,3%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	8728	2,3%					10156	2,2%				1.1/3.2	>3	<1
	m/z **116**	200829	100,0%					469100	100,0%				-	>3	<1
10	*m/z* **149**	3414	1,7%				1	7850	1,7%				0.8/2.5	>3	<1
	m/z **280**	5188	2,6%					10156	2,2%				1.1/3.2	>3	<1

TFMPP

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **302**	21514	100,0%					7785	100,0%				-	>3	<1
1	*m/z* **287**	6324	29,4%				2	2202	28,3%				22.6/33.9	>3	<1
	m/z **172**	3614	16,8%					1020	13,1%				8.1/18.1	>3	<1
	m/z **302**	7785	100,0%					21514	100,0%				-	>3	<1
2	*m/z* **287**	2202	28,3%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	1020	13,1%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	14018	100,0%					21514	100,0%				-	>3	<1
3	*m/z* **287**	4139	29,5%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	2231	15,9%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	15675	100,0%					21514	100,0%				-	>3	<1
4	*m/z* **287**	4496	28,7%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	2679	17,1%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	16307	100,0%					21514	100,0%				-	>3	<1
5	*m/z* **287**	4818	29,5%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	2427	14,9%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	14449	100,0%					21514	100,0%				-	>3	<1
6	*m/z* **287**	3883	26,9%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	2008	13,9%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	12014	100,0%					21514	100,0%				-	>3	<1
7	*m/z* **287**	3547	29,5%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	1970	16,4%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	8857	100,0%					21514	100,0%				-	>3	<1
8	*m/z* **287**	2288	25,8%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	1254	14,2%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	17314	100,0%					21514	100,0%				-	>3	<1
9	*m/z* **287**	5247	30,3%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	2679	15,5%					3614	16,8%				11.8/21.8	>3	<1
	m/z **302**	8673	100,0%					21514	100,0%				-	>3	<1
10	*m/z* **287**	2631	30,3%				1	6324	29,4%				23.5/35.3	>3	<1
	m/z **172**	1271	14,7%					3614	16,8%				11.8/21.8	>3	<1

Propoxyphene

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **208**	20307	100,0%				8737	100,0%				-	>3	<1
1	*m/z* **193**	13524	66,6%			2	6009	68,8%				58.8/78.8	>3	<1
	m/z **178**	5834	28,7%				2279	26,1%				20.9/31.3	>3	<1
	m/z **208**	8737	100,0%				20307	100,0%				-	>3	<1
2	*m/z* **193**	6009	68,8%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2279	26,1%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	9952	100,0%				20307	100,0%				-	>3	<1
3	*m/z* **193**	6523	65,5%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2582	25,9%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	8932	100,0%				20307	100,0%				-	>3	<1
4	*m/z* **193**	5816	65,1%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2239	25,1%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	8876	100,0%				20307	100,0%				-	>3	<1
5	*m/z* **193**	5606	63,2%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2289	25,8%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	8602	100,0%				20307	100,0%				-	>3	<1
6	*m/z* **193**	6236	72,5%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2625	30,5%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	10051	100,0%				20307	100,0%				-	>3	<1
7	*m/z* **193**	6577	65,4%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2852	28,4%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	3952	100,0%				20307	100,0%				-	>3	<1
8	*m/z* **193**	2504	63,4%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	972	24,6%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	9657	100,0%				20307	100,0%				-	>3	<1
9	*m/z* **193**	6198	64,2%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	2586	26,8%				5834	28,7%				23.0/34.5	>3	<1
	m/z **208**	7694	100,0%				20307	100,0%				-	>3	<1
10	*m/z* **193**	4760	61,9%			1	13524	66,6%				56.6/76.6	>3	<1
	m/z **178**	1890	24,6%				5834	28,7%				23.0/34.5	>3	<1

Pethidine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **247**	39533	100,0%					18886	100,0%				-	>3	<1
1	*m/z* **246**	24570	62,2%				2	12386	65,6%				55.6/75.6	>3	<1
	m/z **218**	34288	86,7%					16249	86,0%				76.0/96.0	>3	<1
	m/z **247**	18886	100,0%					39533	100,0%				-	>3	<1
2	*m/z* **246**	12386	65,6%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	16249	86,0%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	16496	100,0%					39533	100,0%				-	>3	<1
3	*m/z* **246**	10407	63,1%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	14016	85,0%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	25755	100,0%					39533	100,0%				-	>3	<1
4	*m/z* **246**	16690	64,8%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	19779	76,8%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	25333	100,0%					39533	100,0%				-	>3	<1
5	*m/z* **246**	16856	66,5%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	19917	78,6%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	22264	100,0%					39533	100,0%				-	>3	<1
6	*m/z* **246**	14136	63,5%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	18549	83,3%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	23564	100,0%					39533	100,0%				-	>3	<1
7	*m/z* **246**	15560	66,0%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	20595	87,4%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	6704	100,0%					39533	100,0%				-	>3	<1
8	*m/z* **246**	4328	64,6%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	6324	94,3%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	30497	78,6%					39533	100,0%				-	>3	<1
9	*m/z* **246**	19548	50,4%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	28445	93,3%					34288	86,7%				76.7/96.7	>3	<1
	m/z **247**	15831	100,0%					39533	100,0%				-	>3	<1
10	*m/z* **246**	10255	64,8%				1	24570	62,2%				52.2/72.2	>3	<1
	m/z **218**	14609	92,3%					34288	86,7%				76.7/96.7	>3	<1

Ketamine

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **182**	67106	100,0%				66736	100,0%				-	>3	<1
1	*m/z* **209**	51482	76,7%			2	50984	76,4%				66.4/86.4	>3	<1
	m/z **152**	31441	46,9%				30562	45,8%				36.6/55.0	>3	<1
	m/z **182**	66736	100,0%				67106	100,0%				-	>3	<1
2	*m/z* **209**	50984	76,4%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	30562	45,8%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	77523	100,0%				67106	100,0%				-	>3	<1
3	*m/z* **209**	61547	79,4%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	36117	46,6%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	74594	100,0%				67106	100,0%				-	>3	<1
4	*m/z* **209**	51871	69,5%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	34203	45,9%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	71271	100,0%				67106	100,0%				-	>3	<1
5	*m/z* **209**	55576	78,0%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	31730	44,5%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	65806	100,0%				67106	100,0%				-	>3	<1
6	*m/z* **209**	51549	78,3%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	28827	43,8%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	79747	100,0%				67106	100,0%				-	>3	<1
7	*m/z* **209**	62939	78,9%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	34475	43,2%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	21882	100,0%				67106	100,0%				-	>3	<1
8	*m/z* **209**	17892	81,8%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	10006	45,7%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	70520	100,0%				67106	100,0%				-	>3	<1
9	*m/z* **209**	58046	82,3%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	30781	43,6%				31441	46,9%				37.5/56.2	>3	<1
	m/z **182**	45990	100,0%				67106	100,0%				-	>3	<1
10	*m/z* **209**	38335	83,4%			1	51482	76,7%				66.7/86.7	>3	<1
	m/z **152**	21517	46,8%				31441	46,9%				37.5/56.2	>3	<1

PCP

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **200**	7360	100,0%					6184	100,0%				-	>3	<1
1	*m/z* **242**	2073	28,2%				2	1826	29,5%				23.6/35.4	>3	<1
	m/z **243**	1502	20,4%					1565	25,3%				20.2/30.4	>3	<1
	m/z **200**	6184	100,0%					7360	100,0%				-	>3	<1
2	*m/z* **242**	1826	29,5%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	1565	25,3%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	12220	100,0%					7360	100,0%				-	>3	<1
3	*m/z* **242**	3251	26,6%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	2979	24,4%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	7721	100,0%					7360	100,0%				-	>3	<1
4	*m/z* **242**	1999	25,9%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	1442	18,7%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	8824	100,0%					7360	100,0%				-	>3	<1
5	*m/z* **242**	2677	30,3%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	2233	25,3%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	7899	100,0%					7360	100,0%				-	>3	<1
6	*m/z* **242**	1989	25,2%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	1668	21,1%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	10427	100,0%					7360	100,0%				-	>3	<1
7	*m/z* **242**	2367	22,7%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	2544	24,4%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	2582	100,0%					7360	100,0%				-	>3	<1
8	*m/z* **242**	812	31,4%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	570	22,1%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	10054	100,0%					7360	100,0%				-	>3	<1
9	*m/z* **242**	3057	30,4%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	2300	22,9%					1502	20,4%				15.4/25.4	>3	<1
	m/z **200**	5560	100,0%					7360	100,0%				-	>3	<1
10	*m/z* **242**	1819	32,7%				1	2073	28,2%				22.5/33.8	>3	<1
	m/z **243**	1106	19,9%					1502	20,4%				15.4/25.4	>3	<1

TRAMADOL

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **335**	44686	100,0%					47721	100,0%				-	>3	<1
1	*m/z* **245**	44085	98,7%				2	44416	93,1%				83.1/103.1	>3	<1
	m/z **320**	14904	33,4%					15799	33,1%				26.5/39.7	>3	<1
	m/z **335**	47721	100,0%					44686	100,0%				-	>3	<1
2	*m/z* **245**	44416	93,1%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	15799	33,1%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	51040	100,0%					44686	100,0%				-	>3	<1
3	*m/z* **245**	45599	89,3%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	16758	32,8%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	46812	100,0%					44686	100,0%				-	>3	<1
4	*m/z* **245**	45831	97,9%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	15822	33,8%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	58267	100,0%					44686	100,0%				-	>3	<1
5	*m/z* **245**	51679	88,7%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	18556	31,8%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	53326	100,0%					44686	100,0%				-	>3	<1
6	*m/z* **245**	47453	89,0%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	17104	32,1%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	56698	100,0%					44686	100,0%				-	>3	<1
7	*m/z* **245**	50309	88,7%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	18363	32,4%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	17816	100,0%					44686	100,0%				-	>3	<1
8	*m/z* **245**	15836	88,9%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	5874	33,0%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	59433	100,0%					44686	100,0%				-	>3	<1
9	*m/z* **245**	52851	88,9%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	18898	31,8%					14904	33,4%				26.7/40.0	>3	<1
	m/z **335**	39386	100,0%					44686	100,0%				-	>3	<1
10	*m/z* **245**	34965	88,8%				1	44085	98,7%				88.7/108.7	>3	<1
	m/z **320**	12781	32,5%					14904	33,4%				26.7/40.0	>3	<1

N-DT

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **189**	6049	100,0%				2036	100,0%				-	>3	<1
1	*m/z* **202**	2774	45,9%			2	790	38,8%				31.0/46.6	>3	<1
	m/z **261**	1877	31,0%				584	28,7%				22.9/34.4	>3	<1
	m/z **189**	2036	100,0%				6049	100,0%				-	>3	<1
2	*m/z* **202**	790	38,8%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	584	28,7%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	1677	100,0%				6049	100,0%				-	>3	<1
3	*m/z* **202**	862	51,4%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	482	28,7%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	5303	100,0%				6049	100,0%				-	>3	<1
4	*m/z* **202**	1961	37,0%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	1639	30,9%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	4158	100,0%				6049	100,0%				-	>3	<1
5	*m/z* **202**	1961	47,2%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	1368	32,9%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	6973	100,0%				6049	100,0%				-	>3	<1
6	*m/z* **202**	2846	40,8%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	2288	32,8%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	784	100,0%				6049	100,0%				-	>3	<1
7	*m/z* **202**	352	44,9%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	240	30,6%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	1099	100,0%				6049	100,0%				-	>3	<1
8	*m/z* **202**	545	49,6%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	325	29,6%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	2149	100,0%				6049	100,0%				-	>3	<1
9	*m/z* **202**	966	45,0%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	626	29,1%				1877	31,0%				24.8/37.2	>3	<1
	m/z **189**	1888	100,0%				6049	100,0%				-	>3	<1
10	*m/z* **202**	912	48,3%			1	2774	45,9%				36.7/55.0	>3	<1
	m/z **261**	631	33,4%				1877	31,0%				24.8/37.2	>3	<1

O-DT

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **58**	1080238	100,0%					411535	100,0%				-	>3	<1
1	*m/z* **303**	31080	2,9%				2	14477	3,5%				1.8/5.3	>3	<1
	m/z **393**	23043	2,1%					11440	2,8%				1.4/4.2	>3	<1
	m/z **58**	411535	100,0%					1080238	100,0%				-	>3	<1
2	*m/z* **303**	14477	3,5%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	11440	2,8%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	671167	100,0%					1080238	100,0%				-	>3	<1
3	*m/z* **303**	25265	3,8%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	20404	3,0%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	558942	100,0%					1080238	100,0%				-	>3	<1
4	*m/z* **303**	15263	2,7%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	10731	1,9%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	649943	100,0%					1080238	100,0%				-	>3	<1
5	*m/z* **303**	23770	3,7%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	18537	2,9%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	609879	100,0%					1080238	100,0%				-	>3	<1
6	*m/z* **303**	22247	3,6%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	17327	2,8%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	645378	100,0%					1080238	100,0%				-	>3	<1
7	*m/z* **303**	24508	3,8%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	19225	3,0%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	179359	100,0%					1080238	100,0%				-	>3	<1
8	*m/z* **303**	7279	4,1%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	5716	3,2%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	620927	100,0%					1080238	100,0%				-	>3	<1
9	*m/z* **303**	23260	3,7%				1	31080	2,9%				1.4/4.3	>3	<1
	m/z **393**	18978	3,1%					23043	2,1%				1.1/3.2	>3	<1
	m/z **58**	397382	100,0%					411535	100,0%				-	>3	<1
10	*m/z* **303**	16772	4,2%				2	14477	3,5%				1.8/5.3	>3	<1
	m/z **393**	13598	3,4%					11440	2,8%				1.4/4.2	>3	<1

EDDP

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **277**	19660	100,0%					5011	100,0%				-	>3	<1
1	*m/z* **276**	18428	93,7%				2	4793	95,6%				85.6/105.6	>3	<1
	m/z **262**	10160	51,7%					2346	46,8%				37.5/56.2	>3	<1
	m/z **277**	5011	100,0%					19660	100,0%				-	>3	<1
2	*m/z* **276**	4793	95,6%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	2346	46,8%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	50108	100,0%					19660	100,0%				-	>3	<1
3	*m/z* **276**	45299	90,4%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	22308	44,5%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	6572	100,0%					19660	100,0%				-	>3	<1
4	*m/z* **276**	6259	95,2%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	3940	60,0%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	4918	99,0%					19660	100,0%				-	>3	<1
5	*m/z* **276**	4966	100,0%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	2963	59,7%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	4136	100,0%					19660	100,0%				-	>3	<1
6	*m/z* **276**	4020	97,2%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	2440	59,0%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	16325	100,0%					19660	100,0%				-	>3	<1
7	*m/z* **276**	13908	85,2%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	8029	49,2%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	4725	100,0%					19660	100,0%				-	>3	<1
8	*m/z* **276**	4316	91,3%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	2563	54,2%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	17410	100,0%					19660	100,0%				-	>3	<1
9	*m/z* **276**	16047	92,2%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	9784	56,2%					10160	51,7%				41.7/61.7	>3	<1
	m/z **277**	1650	100,0%					19660	100,0%				-	>3	<1
10	*m/z* **276**	1602	97,1%				1	18428	93,7%				83.7/103.7	>3	<1
	m/z **262**	987	59,8%					10160	51,7%				41.7/61.7	>3	<1

3-MeO-PCP

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **230**	165861	100,0%					81307	100,0%				-	>3	<1
1	*m/z* **272**	51433	31,0%				2	25662	31,6%				25.2/37.9	>3	<1
	m/z **273**	49977	30,1%					25339	31,2%				24.9/37.4	>3	<1
	m/z **230**	81307	100,0%					165861	100,0%				-	>3	<1
2	*m/z* **272**	25662	31,6%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	25339	31,2%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	141286	100,0%					165861	100,0%				-	>3	<1
3	*m/z* **272**	43508	30,8%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	42708	30,2%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	96285	100,0%					165861	100,0%				-	>3	<1
4	*m/z* **272**	28747	29,9%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	27899	29,0%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	129557	100,0%					165861	100,0%				-	>3	<1
5	*m/z* **272**	40878	31,6%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	40402	31,2%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	114257	100,0%					165861	100,0%				-	>3	<1
6	*m/z* **272**	35990	31,5%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	35781	31,3%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	136197	100,0%					165861	100,0%				-	>3	<1
7	*m/z* **272**	43446	31,9%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	42668	31,3%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	40878	100,0%					165861	100,0%				-	>3	<1
8	*m/z* **272**	12979	31,8%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	13106	32,1%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	130419	100,0%					165861	100,0%				-	>3	<1
9	*m/z* **272**	40732	31,2%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	40138	30,8%					49977	30,1%				24.1/36.2	>3	<1
	m/z **230**	87293	100,0%					165861	100,0%				-	>3	<1
10	*m/z* **272**	27853	31,9%				1	51433	31,0%				24.8/37.2	>3	<1
	m/z **273**	28112	32,2%					49977	30,1%				24.1/36.2	>3	<1

Methadone

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **294**	17658	100,0%					12289	100,0%				-	>3	<1
1	*m/z* **223**	11210	63,5%				10	7428	60,4%				50.4/70.4	>3	<1
	m/z **309**	1712	9,7%					963	7,8%				2.8/12.8	>3	<1
	m/z **294**	12238	100,0%					21255	100,0%				-	>3	<1
2	*m/z* **223**	4374	35,7%				3	6967	32,8%				26.2/39.3	>3	<1
	m/z **309**	942	7,7%					2182	10,3%				5.3/15.3	>3	<1
	m/z **294**	21255	100,0%					12238	100,0%				-	>3	<1
3	*m/z* **223**	6967	32,8%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	2182	10,3%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	14416	100,0%					12238	100,0%				-	>3	<1
4	*m/z* **223**	4872	33,8%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	1415	9,8%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	17208	100,0%					12238	100,0%				-	>3	<1
5	*m/z* **223**	7038	40,9%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	1741	10,1%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	16027	100,0%					12238	100,0%				-	>3	<1
6	*m/z* **223**	6208	38,7%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	1827	11,4%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	15762	100,0%					12238	100,0%				-	>3	<1
7	*m/z* **223**	4509	28,6%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	1360	8,6%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	7257	100,0%					12238	100,0%				-	>3	<1
8	*m/z* **223**	2100	28,9%				2	4374	35,7%				28.6/42.9	>3	<1
	m/z **309**	760	10,5%					942	7,7%				2.7/12.7	>3	<1
	m/z **294**	12289	100,0%					17658	100,0%				-	>3	<1
9	*m/z* **223**	7428	60,4%				1	11210	63,5%				53.5/73.5	>3	<1
	m/z **309**	963	7,8%					1712	9,7%				4.7/14.7	>3	<1
	m/z **294**	18286	100,0%					21255	100,0%				-	>3	<1
10	*m/z* **223**	4925	26,9%				3	6967	32,8%				26.2/39.3	>3	<1
	m/z **309**	1858	10,2%					2182	10,3%				5.3/15.3	>3	<1

Cocaine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **82**	132950	100,0%					55524	100,0%				-	>3	<1
1	*m/z* **182**	131733	99,1%				2	55538	100,0%				90.0/110.0	>3	<1
	m/z **303**	30739	23,1%					12669	22,8%				17.8/27.8	>3	<1
	m/z **82**	55524	100,0%					132950	100,0%				-	>3	<1
2	*m/z* **182**	55538	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	12669	22,8%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	92572	100,0%					132950	100,0%				-	>3	<1
3	*m/z* **182**	89508	96,7%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	18121	19,6%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	65128	100,0%					132950	100,0%				-	>3	<1
4	*m/z* **182**	62187	95,5%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	14420	22,1%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	66619	91,8%					132950	100,0%				-	>3	<1
5	*m/z* **182**	72566	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	17504	24,1%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	60926	90,8%					132950	100,0%				-	>3	<1
6	*m/z* **182**	67104	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	16221	24,2%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	78563	92,0%					132950	100,0%				-	>3	<1
7	*m/z* **182**	85427	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	21168	24,8%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	18393	98,4%					132950	100,0%				-	>3	<1
8	*m/z* **182**	18686	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	4658	24,9%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	79851	93,9%					132950	100,0%				-	>3	<1
9	*m/z* **182**	85074	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	19489	22,9%					30739	23,1%				18.1/28.1	>3	<1
	m/z **82**	48594	97,2%					132950	100,0%				-	>3	<1
10	*m/z* **182**	49971	100,0%				1	131733	99,1%				89.1/109.1	>3	<1
	m/z **303**	13298	26,6%					30739	23,1%				18.1/28.1	>3	<1

Cocaethylene

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **196**	8834	100,0%				10619	100,0%				-	>3	<1
1	*m/z* **94**	4061	46,0%			3	5743	54,1%				44.1/64.1	>3	<1
	m/z **317**	2078	23,5%				2637	24,8%				19.8/29.8	>3	<1
	m/z **196**	11226	100,0%				9310	100,0%				-	>3	<1
2	*m/z* **94**	7103	63,3%			8	5130	55,1%				45.1/65.1	>3	<1
	m/z **317**	2441	21,7%				2237	24,0%				19.0/29.0	>3	<1
	m/z **196**	10619	100,0%				8834	100,0%				-	>3	<1
3	*m/z* **94**	5743	54,1%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	2637	24,8%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	7643	100,0%				7439	100,0%				-	>3	<1
4	*m/z* **94**	4587	60,0%			10	3951	53,1%				43.1/63.1	>3	<1
	m/z **317**	1890	24,7%				2006	27,0%				21.6/32.4	>3	<1
	m/z **196**	7522	100,0%				8834	100,0%				-	>3	<1
5	*m/z* **94**	3886	51,7%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	1720	22,9%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	7891	100,0%				8834	100,0%				-	>3	<1
6	*m/z* **94**	3807	48,2%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	1826	23,1%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	9310	100,0%				8834	100,0%				-	>3	<1
7	*m/z* **94**	5130	55,1%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	2237	24,0%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	2013	100,0%				8834	100,0%				-	>3	<1
8	*m/z* **94**	1098	54,5%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	518	25,7%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	7439	100,0%				8834	100,0%				-	>3	<1
9	*m/z* **94**	3951	53,1%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	2006	27,0%				2078	23,5%				18.5/28.5	>3	<1
	m/z **196**	7192	100,0%				8834	100,0%				-	>3	<1
10	*m/z* **94**	2862	39,8%			1	4061	46,0%				36.8/55.2	>3	<1
	m/z **317**	1879	26,1%				2078	23,5%				18.5/28.5	>3	<1

Benzoylecgonine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **240**	88279	100,0%					37297	100,0%				-	>3	<1
1	*m/z* **94**	39276	44,5%				2	16604	44,5%				35.6/53.4	>3	<1
	m/z **361**	26392	29,9%					11613	31,1%				24.9/37.4	>3	<1
	m/z **240**	37297	100,0%					88279	100,0%				-	>3	<1
2	*m/z* **94**	16604	44,5%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	11613	31,1%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	62814	100,0%					88279	100,0%				-	>3	<1
3	*m/z* **94**	31619	50,3%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	17150	27,3%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	45373	100,0%					88279	100,0%				-	>3	<1
4	*m/z* **94**	22730	50,1%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	13420	29,6%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	62684	100,0%					88279	100,0%				-	>3	<1
5	*m/z* **94**	28492	45,5%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	19624	31,3%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	56913	100,0%					88279	100,0%				-	>3	<1
6	*m/z* **94**	24547	43,1%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	17989	31,6%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	64802	100,0%					88279	100,0%				-	>3	<1
7	*m/z* **94**	27022	41,7%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	21047	32,5%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	15730	100,0%					88279	100,0%				-	>3	<1
8	*m/z* **94**	6838	43,5%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	5370	34,1%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	69862	100,0%					88279	100,0%				-	>3	<1
9	*m/z* **94**	31333	44,8%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	21593	30,9%					26392	29,9%				23.9/35.9	>3	<1
	m/z **240**	39290	100,0%					88279	100,0%				-	>3	<1
10	*m/z* **94**	16869	42,9%				1	39276	44,5%				35.6/53.4	>3	<1
	m/z **361**	13052	33,2%					26392	29,9%				23.9/35.9	>3	<1

Codeine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **178**	62141	100,0%					27330	100,0%				-	>3	<1
1	*m/z* **196**	49967	80,4%				2	21536	78,8%				68.8/88.8	>3	<1
	m/z **234**	39323	63,3%					16496	60,4%				50.4/70.4	>3	<1
	m/z **178**	27330	100,0%					62141	100,0%				-	>3	<1
2	*m/z* **196**	21536	78,8%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	16496	60,4%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	44539	100,0%					62141	100,0%				-	>3	<1
3	*m/z* **196**	35506	79,7%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	27188	61,0%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	31362	100,0%					62141	100,0%				-	>3	<1
4	*m/z* **196**	24836	79,2%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	18460	58,9%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	38496	100,0%					62141	100,0%				-	>3	<1
5	*m/z* **196**	31117	80,8%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	24723	64,2%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	38756	100,0%					62141	100,0%				-	>3	<1
6	*m/z* **196**	30841	79,6%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	23929	61,7%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	41563	100,0%					62141	100,0%				-	>3	<1
7	*m/z* **196**	34182	82,2%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	26538	63,9%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	12083	100,0%					62141	100,0%				-	>3	<1
8	*m/z* **196**	9709	80,4%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	7400	61,2%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	42189	100,0%					62141	100,0%				-	>3	<1
9	*m/z* **196**	33708	79,9%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	25936	61,5%					39323	63,3%				53.3/73.3	>3	<1
	m/z **178**	28250	100,0%					62141	100,0%				-	>3	<1
10	*m/z* **196**	23186	82,1%				1	49967	80,4%				70.4/90.4	>3	<1
	m/z **234**	18114	64,1%					39323	63,3%				53.3/73.3	>3	<1

Morphine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **429**	23559	100,0%					10588	100,0%				-	>3	<1
1	*m/z* **236**	20072	85,2%				2	8810	83,2%				73.2/93.2	>3	<1
	m/z **414**	11543	49,0%					5258	49,7%				39.7/59.6	>3	<1
	m/z **429**	10588	100,0%					23559	100,0%				-	>3	<1
2	*m/z* **236**	8810	83,2%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	5258	49,7%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	38229	100,0%					23559	100,0%				-	>3	<1
3	*m/z* **236**	34386	89,9%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	19681	51,5%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	18636	100,0%					23559	100,0%				-	>3	<1
4	*m/z* **236**	17123	91,9%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	9771	52,4%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	16517	100,0%					23559	100,0%				-	>3	<1
5	*m/z* **236**	14516	87,9%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	7988	48,4%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	13318	100,0%					23559	100,0%				-	>3	<1
6	*m/z* **236**	11655	87,5%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	6534	49,1%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	51036	100,0%					23559	100,0%				-	>3	<1
7	*m/z* **236**	40560	79,5%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	23781	46,6%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	10555	100,0%					23559	100,0%				-	>3	<1
8	*m/z* **236**	9497	90,0%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	5495	52,1%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	27063	100,0%					23559	100,0%				-	>3	<1
9	*m/z* **236**	23131	85,5%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	12873	47,6%					11543	49,0%				39.2/58.8	>3	<1
	m/z **429**	7802	100,0%					23559	100,0%				-	>3	<1
10	*m/z* **236**	6049	77,5%				1	20072	85,2%				75.2/95.2	>3	<1
	m/z **414**	3470	44,5%					11543	49,0%				39.2/58.8	>3	<1

6-MAM

		POOL					Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT	A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **287**	7194	100,0%				7570	100,0%				-	>3	<1
1	*m/z* **399**	4522	62,9%			3	4184	55,3%				45.3/65.3	>3	<1
	m/z **340**	3431	47,7%				3450	45,6%				36.5/54.7	>3	<1
	m/z **287**	10324	100,0%				7570	100,0%				-	>3	<1
2	*m/z* **399**	4869	47,2%			3	4184	55,3%				45.3/65.3	>3	<1
	m/z **340**	3937	38,1%				3450	45,6%				36.5/54.7	>3	<1
	m/z **287**	7570	100,0%				7194	100,0%				-	>3	<1
3	*m/z* **399**	4184	55,3%			1	4522	62,9%				52.9/72.9	>3	<1
	m/z **340**	3450	45,6%				3431	47,7%				38.2/57.2	>3	<1
	m/z **287**	13678	100,0%				10222	100,0%				-	>3	<1
4	*m/z* **399**	2958	21,6%			6	2407	23,5%				18.5/28.5	>3	<1
	m/z **340**	2622	19,2%				2288	22,4%				17.4/27.4	>3	<1
	m/z **287**	10222	100,0%				13678	100,0%				-	>3	<1
5	*m/z* **399**	2407	23,5%			4	2958	21,6%				16.6/26.6	>3	<1
	m/z **340**	2288	22,4%				2622	19,2%				14.2/24.2	>3	<1
	m/z **287**	7740	100,0%				7194	100,0%				-	>3	<1
6	*m/z* **399**	4442	57,4%			1	4522	62,9%				52.9/72.9	>3	<1
	m/z **340**	3324	42,9%				3431	47,7%				38.2/57.2	>3	<1
	m/z **287**	8554	100,0%				10222	100,0%				-	>3	<1
7	*m/z* **399**	3952	46,2%			6	2407	23,5%				18.5/28.5	>3	<1
	m/z **340**	2447	28,6%				2288	22,4%				17.4/27.4	>3	<1
	m/z **287**	4684	100,0%				10222	100,0%				-	>3	<1
8	*m/z* **399**	1024	21,9%			6	2407	23,5%				18.5/28.5	>3	<1
	m/z **340**	838	17,9%				2288	22,4%				17.4/27.4	>3	<1
	m/z **287**	10893	100,0%				7570	100,0%				-	>3	<1
9	*m/z* **399**	5248	48,2%			3	4184	55,3%				45.3/65.3	>3	<1
	m/z **340**	4025	37,0%				3450	45,6%				36.5/54.7	>3	<1
	m/z **287**	6310	100,0%				13678	100,0%				-	>3	<1
10	*m/z* **399**	1406	22,3%			4	2958	21,6%				16.6/26.6	>3	<1
	m/z **340**	1075	17,0%				2622	19,2%				14.2/24.2	>3	<1

Fentanyl

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **245**	5362	100,0%					5286	100,0%				-	>3	<1
1	*m/z* **146**	2569	47,9%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	3043	56,8%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	5286	100,0%					5362	100,0%				-	>3	<1
2	*m/z* **146**	2513	47,5%				1	2569	47,9%				38.3/57.5	>3	<1
	m/z **189**	2687	50,8%					3043	56,8%				46.8/66.8	>3	<1
	m/z **245**	7089	100,0%					5286	100,0%				-	>3	<1
3	*m/z* **146**	3271	46,1%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	3587	50,6%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	6457	100,0%					5286	100,0%				-	>3	<1
4	*m/z* **146**	3051	47,3%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	2752	42,6%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	6761	100,0%					5362	100,0%				-	>3	<1
5	*m/z* **146**	2727	40,3%				1	2569	47,9%				38.3/57.5	>3	<1
	m/z **189**	3285	48,6%					3043	56,8%				46.8/66.8	>3	<1
	m/z **245**	5816	100,0%					5362	100,0%				-	>3	<1
6	*m/z* **146**	2919	50,2%				1	2569	47,9%				38.3/57.5	>3	<1
	m/z **189**	3187	54,8%					3043	56,8%				46.8/66.8	>3	<1
	m/z **245**	5435	100,0%					5286	100,0%				-	>3	<1
7	*m/z* **146**	2536	46,7%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	2256	41,5%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	7122	100,0%					5286	100,0%				-	>3	<1
8	*m/z* **146**	3961	55,6%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	2947	41,4%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	6976	100,0%					5286	100,0%				-	>3	<1
9	*m/z* **146**	3378	48,4%				2	2513	47,5%				38.0/57.0	>3	<1
	m/z **189**	2871	41,2%					2687	50,8%				40.8/60.8	>3	<1
	m/z **245**	7462	100,0%					5362	100,0%				-	>3	<1
10	*m/z* **146**	3057	41,0%				1	2569	47,9%				38.3/57.5	>3	<1
	m/z **189**	3656	49,0%					3043	56,8%				46.8/66.8	>3	<1

Buprenorphine

		POOL						Control					Criteria		
		Abs area	Rel Area	S/N	Abs RT	Rel RT		A abs.	A rel.	S/N	TRA	TRR	Ionic ratio	S/N	▫Rel RT
	m/z **450**	871	100,0%					485	100,0%				-	>3	<1
1	*m/z* **482**	309	35,5%				2	166	34,2%				27.4/41.1	>3	<1
	m/z **506**	170	19,5%					95	19,6%				14.6/24.6	>3	<1
	m/z **450**	485	100,0%					871	100,0%				-	>3	<1
2	*m/z* **482**	166	34,2%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	95	19,6%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	1773	100,0%					871	100,0%				-	>3	<1
3	*m/z* **482**	504	28,4%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	314	17,7%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	1152	100,0%					871	100,0%				-	>3	<1
4	*m/z* **482**	335	29,1%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	176	15,3%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	1025	100,0%					871	100,0%				-	>3	<1
5	*m/z* **482**	297	29,0%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	194	18,9%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	869	100,0%					871	100,0%				-	>3	<1
6	*m/z* **482**	308	35,4%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	206	23,7%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	2832	100,0%					871	100,0%				-	>3	<1
7	*m/z* **482**	849	30,0%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	511	18,0%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	582	100,0%					871	100,0%				-	>3	<1
8	*m/z* **482**	201	34,5%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	129	22,2%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	1418	100,0%					871	100,0%				-	>3	<1
9	*m/z* **482**	424	29,9%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	255	18,0%					170	19,5%				14.5/24.5	>3	<1
	m/z **450**	723	100,0%					871	100,0%				-	>3	<1
10	*m/z* **482**	212	29,3%				1	309	35,5%				28.4/42.6	>3	<1
	m/z **506**	130	18,0%					170	19,5%				14.5/24.5	>3	<1

Supplementary data S2 – Homocedasticity study results, per compound

Panel /work range	Analite	Level	Inj. 1	Inj. 2	Inj. 3	Inj. 4	Inj. 5	Average	SD	(S^2)	(CV) (%)	$F_{crít}$	F_{calc}
		(ng/mL)											
Set 1 50-4000 ng/mL	**Tramadol**	**50**	97.2	91.2	91.8	92.1	96.6	93.7	2.87	8.24047	3.1	**6.388**	3097.973
		4000	4070	3976	4164	3917	3743	3974	159.8	25528.75	4.0		
	Ketamine	**50**	205	191	197	192	196	196	5.7	32.42913	2.9		1960.534
		4000	4285	4155	4067	4101	3619	4045	252.1	63578.41	6.2		
Set 2 5-100 ng/mL	**Buprenorphine**	**5**	5.39	5.64	4.51	4.66	5.21	5.08	0.482	0.23197	9.5		56.86972
		100	94.5	90.7	96.4	90.3	87.2	91.8	3.63	13.19207	4.0		
	Fentanyl	**5**	8.11	3.07	3.25	3.20	4.73	4.47	2.145	4.601	48.0		11.53239
		100	106	90.4	97.5	97.9	87.1	95.7	7.28	53.06052	7.6		
	6-MAM	**5**	5.0	4.25	3.87	3.94	3.91	4.20	0.492	0.24217	11.7		19.89788
		100	98.9	95.1	96.6	95.3	92.9	95.8	2.20	4.81867	2.3		
	Cocaethylene	**5**	8.4	6.97	6.72	7.04	6.97	7.22	0.680	0.46183	9.4		87.0479
		100	105.5	99.6	102	102	89.0	99.7	6.34	40.20133	6.4		
	PCP	**5**	6.6	5.93	5.55	5.39	5.53	5.79	0.474	0.22442	8.2		17.72645
		100	102	98.1	101	97.0	100	99.6	1.99	3.97817	2.0		
Set 3 25-1000 ng/mL	**EME**	**25**	48.5	43.7	46.3	56.8	37.4	46.5	7.08	50.1569	15.2		185.3114
		1000	1019	961	895	908	760	908	96.4	9294.647	10.6		
	d-Propoxiphene	**25**	-1.04	-1.41	0.37	22.7	-3.23	3.48	10.826	117.2079	311		4.972601
		1000	977	1032	989	994	969	992	24.1	582.8281	2.4		
	Pethidine	25	18.7	-1.90	9.86	29.9	8.84	13.1	11.91	141.9234	911	**6.388**	14.06543
		1000	1024	945	960	990	1053	994	44.7	1996.214	4.5		
	N-Desmehyltramadol	**25**	39.4	41.2	39.5	46.3	38.4	41.0	3.18	10.1166	7.8		5344.046
		1000	982	1160	1083	1042	567	967	232.5	54063.58	24.1		

Painel 3 **(25-1000 ng/mL)**	**O-Desmethyltramadol**	**25**	32.6	26.7	28.0	40.6	24.7	30.5	6.36	40.4935	20.9		55.07628
		1000	1021	1001	1021	977	907	986	47.2	2230.231	4.8		
	EDDP	**25**	37.1	41.1	42.0	54.8	46.7	44.3	6.77	45.80207	15.3		42.77132
		1000	1001	1030	1006	986	913	987	44.3	1959.015	4.5		
	3-Meo-PCP	**25**	21.8	9.2	16.8	34.6	14.1	19.3	9.67	93.50408	50.1		10.13058
		1000	1003	938	969	984	930	965	30.8	947.2508	3.2		
	Methadone	**25**	38.3	31.4	50.4	40.6	41.6	40.5	6.82	46.47527	16.8		833.9143
		1000	999	738	1164	901	1223	1005	196.9	38756.39	19.6		
	Cocaine	**25**	43.1	37.1	40.3	54.4	39.6	42.9	6.79	46.11958	15.8		26.33187
		1000	1037	951	995.2	973	957	983	34.9	1214.415	3.5		
	Benzoylecgonine	**25**	32.6	25.1	26.9	41.0	27.0	30.5	6.47	41.89983	21.2		20.22621
		1000	1004	989	982	950	933	972	29.1	847.4749	3.0		
	Codeine	**25**	1.25	0.27	10.2	4.52	8.66	4.99	4.399	19.35333	88.2		389.3838
		1000	883	833	997	808	987	901	86.8	7535.873	9.6		
	Morphine	**25**	20.0	19.5	27.1	22.4	25.4	22.9	3.30	10.87957	14.4		1552.65
		1000	969	934	1153	863	1144	1013	130.0	16892.17	12.8		

Supplementary data S3 - *Results of the uncertainty study of the proposed method: $u'accuracy$ corresponds to the relative uncertainty associated with precision, Rm is equivalent to the mean recovery, (Rm) indicates the uncertainty associated with fairness, $texp$ represents the $t_{experimental}$ value obtained after the t-student test and $u'(Rm)$ corresponds to the relative uncertainty associated with accuracy.*

Analite/Parameter	$u'_{accuracy}$ (%)	Rm (%)	$u(Rm)$ (%)	t_{exp}	$u'(Rm)$ (%)	$u'_{accuracy}$ (%)	Rm (%)	$u(Rm)$ (%)	t_{exp}	$u'(Rm)$ (%)	$u'_{accuracy}$ (%)	Rm (%)	$u(Rm)$ (%)	t_{exp}	$u'(Rm)$ (%)
Panel 1 50-4000 ng/mL			**CQ 1 (500 ng/mL)**					**CQ 2 (1500 ng/mL)**				**CQ 3 (3000 ng/mL)**			
Tramadol	12.01	93.42	2.80	2.3470	3.00	4.00	91.56	0.92	9.2055	1.00	8.81	90.94	2.00	4.5249	2.20
Ketamine	13.61	86.87	2.96	4.4420	3.40	14.44	80.09	2.89	6.8888	3.61	14.78	84.36	3.12	5.0197	3.69
Panel 2 5-100 ng/mL			**CQ 1 (5 ng/mL)**					**CQ 2 (10 ng/mL)**				**CQ 3 (70 ng/mL)**			
Buprenorphine	17.72	96.35	4.56	0.7996	4.56	19.34	119.43	6.17	3.1467	5.17	15.67	126.84	5.31	5.0515	4.19
Fentanyl	37.03	138.78	13.73	2.8232	9.90	15.84	105.52	4.47	1.3204	4.47	10.10	87.54	2.21	5.6337	2.53
6-MAM	20.62	127.59	6.58	4.1938	5.16	8.68	123.38	2.68	8.7326	2.17	11.04	99.82	2.76	0.0651	2.76
Cocaethilene	14.30	88.13	3.15	3.7691	3.58	16.29	88.66	3.86	2.9386	4.35	12.44	90.28	2.81	3.4610	3.11
PCP	17.03	102.21	4.35	0.5085	4.35	9.99	98.84	2.47	0.4710	2.47	11.15	82.07	2.29	7.8366	2.79
Panel 3 25-1000 ng/mL			**CQ 1 (100 ng/mL)**					**CQ 2 (400 ng/mL)**				**CQ 3 (700 ng/mL)**			
EME	19.79	97.70	4.83	0.4751	4.83	15.25	97.42	3.71	0.6960	3.71	17.91	96.77	4.33	0.7453	4.33
d-Propoxiphene	18.70	99.21	4.96	0.1599	4.96	12.67	89.49	2.83	3.7084	3.17	13.41	78.59	2.82	7.6010	3.58
Pethydine	30.89	90.76	7.49	1.2328	7.49	18.14	103.20	4.68	0.6839	4.68	14.95	94.80	3.79	1.3738	3.79
N-Desmethyltramadol	31.90	99.30	8.46	0.0832	8.46	27.37	101.99	7.46	0.2661	7.46	27.18	109.27	7.94	1.1681	7.94
O-Desmethyltramadol	11.59	90.54	2.62	3.6057	2.90	12.47	92.63	2.89	2.5500	3.12	11.98	91.23	2.73	3.2101	3.00
EDDP	10.81	91.91	2.48	3.2577	2.70	10.07	98.25	2.47	0.7064	2.47	12.13	100.27	3.04	0.0875	3.04
Methadone	14.64	95.87	3.51	1.1761	3.51	13.14	97.54	3.20	0.7686	3.20	6.99	96.39	1.69	2.1413	1.75
3-MeO-PCP	17.84	105.07	4.69	1.0822	4.69	12.35	102.59	3.17	0.8183	3.17	13.87	94.63	3.51	1.5301	3.51
Cocaine	12.29	92.40	2.84	2.6793	3.07	13.19	100.45	3.31	0.1355	3.31	6.10	97.71	1.49	1.5377	1.49
Benzoylecgonine	22.58	91.95	5.19	1.5502	5.19	8.48	95.66	2.03	2.1399	2.12	10.06	95.83	2.41	1.7303	2.41
Codeine	16.46	112.63	4.63	2.7250	4.11	9.80	109.12	2.67	3.4105	2.45	5.20	94.17	1.22	4.7662	1.30
Morphine	21.95	92.36	5.07	1.5073	5.07	12.53	102.24	3.20	0.6994	3.20	7.65	96.36	1.84	1.9775	1.84