Advancing Forensic DUID Screening with Mass Spectrometry

Optimized Evolution of a Toxicology Laboratory from Immunoassay to the SCIEX X500R QTOF System

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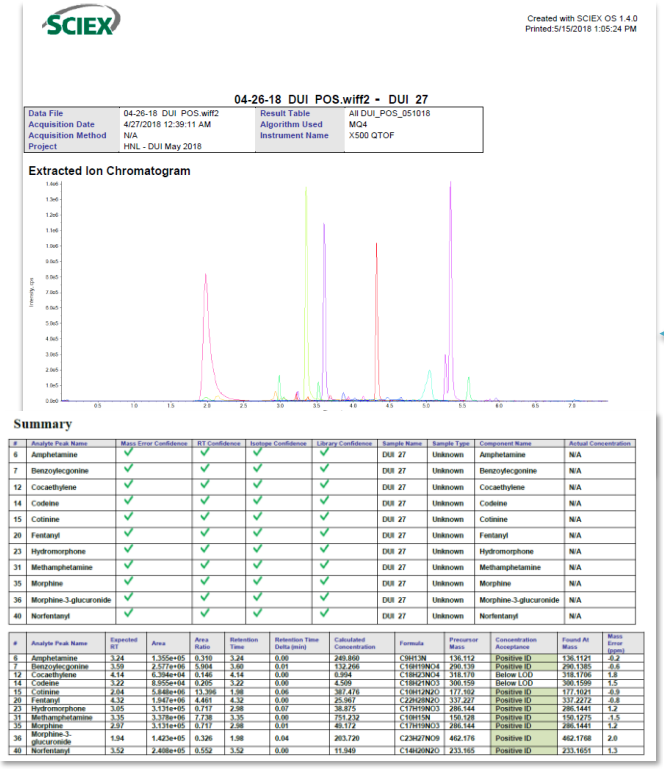
Over the past decade, the National Safety Council's Alcohol, Drugs and Impairment Division (NSC-ADID) started an initiative to standardize forensic toxicology laboratory testing for cases involving driving under the influence of drugs (DUID).

Target forensic compounds of interest were divided into two tiers: Tier I drugs include the most frequently encountered drugs found in DUID casework, and those which could be screened and confirmed with commercially available immunoassay and GC-MS instrumentation. Tier II analytes were those that had limited occurrence or required more advanced instrumentation such as LC-MS/MS, which is typically not readily available in every forensic laboratory.



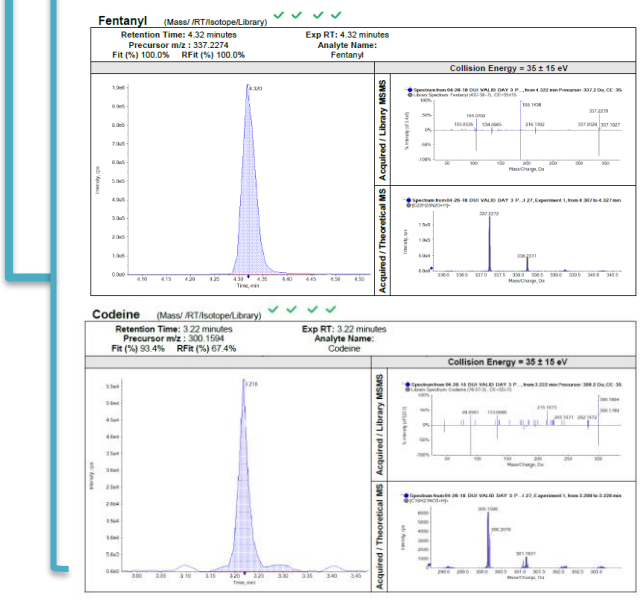


Figure 1. Confidently Identify All Analytes Present Within a Forensic DUID Case Sample. Obtain a simplified sample report showing all positively identified compounds present in a case sample. (Top) Chromatogram and results table showing all target compounds identified in the blood sample based on difference acceptance criteria. (Right) Detailed XIC, TOF MS and MS/MS spectral library identification of fentanyl and codeine present in the screened sample.

More recently, the NSC-ADID made further changes on the list of target analytes for impaired driving and motor vehicle fatality forensic testing, due to recent advances in analytical technology and rapidly growing of novel psychoactive substances (NPS), like synthetic cannabinoids, bath salts and novel opioid analogs.[1]

In this technical note, a comprehensive drug screening workflow for the analysis of forensic DUID blood samples is described. The methodology was developed using a simplified sample preparation approach in combination with the SCIEX X500R QTOF System following the new NSC-ADID recommendations for forensic testing in DUID and motor vehicle fatality cases.

Experimental Details

Sample Preparation: Control whole blood samples were spiked with a stock standard solution mixture containing all the different drugs for initial method development. A detailed list of the forensic compounds targeted, including accurate mass information and limits of detection (LOD) used for this screening are detailed on Supplement A of this technical document. Forensic DUID case samples and controls were extracted for LC-MS screening using the protocol in Figure 2.[2]

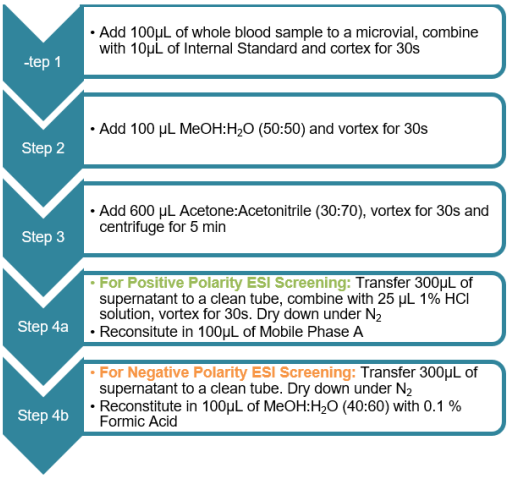


Figure 2. Sample Preparation Protocol.

Liquid Chromatography: HPLC separation was performed at 30 °C on a Phenomenex Kinetex Phenyl-Hexyl column (50 × 2.1 mm, 2.6µm) on the SCIEX ExionLC™ AC system using the following conditions: Mobile Phase A: 10 mM Ammonium Acetate in H_2O:ACN (90:10). Mobile Phase B: 10 mM Ammonium Acetate in ACN:H_2O (90:10) plus 0.1% Formic Acid. LC separation conditions are detailed in Figure 3.

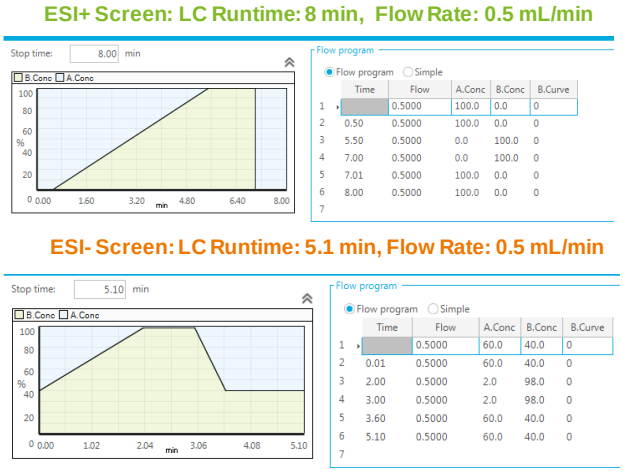


Figure 3. Chromatography Conditions.

Mass Spectrometry and Data Analysis: MS and MS/MS data were collected using the SCIEX X500R QTOF System. For all positive ionizable compounds, an Information Dependent Acquisition (IDA) approach was used. For the negative ionizable target compounds, the MRM^{HR} workflow with the *Apply TOF start/stop* mass feature was used. Both screening strategies included a TOF MS experiment in each cycle. Detailed acquisition parameters are shown in Figure 4.

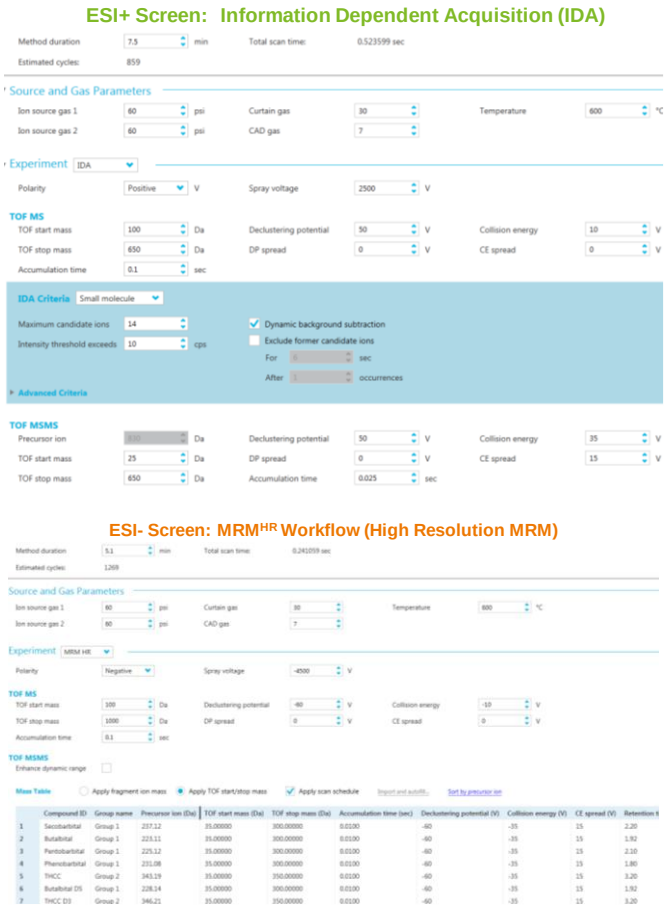
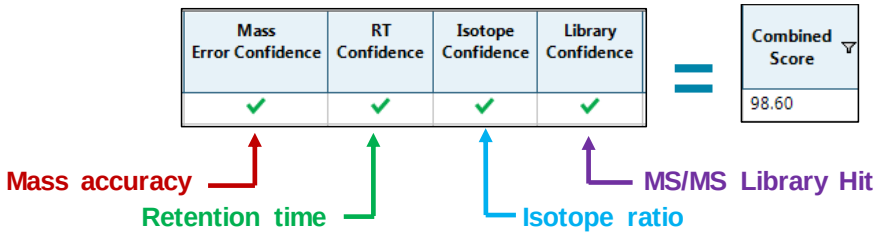


Figure 4. MS Conditions.

Targeted data processing was performed using SCIEX OS Software for positive analyte identification based on previously determined criteria. Four main confidence criteria were used including mass error, retention time, isotope ratio difference, and library score. Subsequently, a combined score was computed based on these four confidence categories with custom weightings.

Table 1. Inter-Day Sverage Combined Scores (n=9) for 60 Compounds Screened in Forensic DUID Samples at the LOD using the SCIEX X500R QTOF System.



6-MAM	*90.0 %*	*Cotinine*	*89.1 %*	*Methadone*	*96.4 %*	*Noroxycodone*	*95.8 %*	*Secobarbital*	*97.1 %*
7-Aminoclonazepam	*90.6 %*	*Diazepam*	*97.6 %*	*Methamphetamine*	*96.7 %*	*O-Desmethyl tramadol*	*97.4 %*	*Butalbital*	*97.2 %*
Alphahydroxyalprazolam	*87.1 %*	*EDDP*	*97.2 %*	*Methylphenidate*	*97.2 %*	*Oxazepam*	*97.2 %*	*Pentobarbital*	*96.9 %*
Alphahydroxymidazolam	*92.2 %*	*Etizolam*	*95.1 %*	*Midazolam*	*96.4 %*	*Oxycodone*	*94.6 %*	*Phenobarbital*	*96.9 %*
Alprazolam	*97.7 %*	*Fentanyl*	*97.2 %*	*Mitragynine*	*95.8 %*	*Oxymorphone*	*90.3 %*	*THC-COOH*	*70.1 %*
Amphetamine	*95.9 %*	*Gabapentin*	*96.8 %*	*Morphine*	*93.6 %*	*Phenazepam*	*94.3 %*		
Benzoylecgonine	*95.2 %*	*Hydrocodone*	*95.5 %*	*Morphine-3-beta-glucuronide*	*93.5 %*	*Phencyclidine*	*98.1 %*		
Beta-Naltrexol	*95.2 %*	*Hydromorphone*	*94.8 %*	*Naltrexone*	*94.0 %*	*Pregabalin*	*84.5 %*		
Buprenorphine	*97.0 %*	*Ketamine*	*97.7 %*	*Norbuprenorphine*	*95.7 %*	*Ritalinic Acid*	*97.8 %*		
Carboxyzolpidem	*97.5 %*	*Lorazepam*	*96.4 %*	*Nordiazepam*	*96.0 %*	*Tapentadol*	*98.4 %*		
Carisoprodol	*97.7 %*	*MDA*	*96.4 %*	*Norfentanyl*	*81.8 %*	*Temazepam*	*97.0 %*		
Cocaethylene	*97.9 %*	*MDMA*	*97.4 %*	*Norhydrocodone*	*97.1 %*	*Tramadol*	*98.4 %*		
Cocaine	*96.0 %*	*Meperidine*	*96.8 %*	*Norketamine*	*96.4 %*	*Zolpidem*	*98.5 %*		
Codeine	*96.8 %*	*Meprobamate*	*97.7 %*	*Normeperidine*	*95.9 %*				

Using a vMethod™ to Develop a Comprehensive Screening Workflow Applied to Forensic DUID Blood Samples

The vMethod™ Application for 664 forensic compounds[3] was initially used to obtain retention times and MS/MS spectra quality to build a data analysis processing method for the 60 target forensic compounds of interest. Two different acquisition strategies were utilized to streamline the screening workflow. For all positive ionizable compounds IDA was chosen as the acquisition mode, as it enabled the acquisition of MS/MS spectra on many precursors, in an intensity dependent manner. Subsequently, resulting MS/MS spectra is the used to match to potential analytes using MS/MS library spectral matching.

For the 5 target compounds (barbiturates and THC-COOH) that favor negative electrospray ionization, MRM^{HR} workflow was used as targeted acquisition strategy. MRM^{HR} workflow was performed using full scan MS/MS acquisition; by

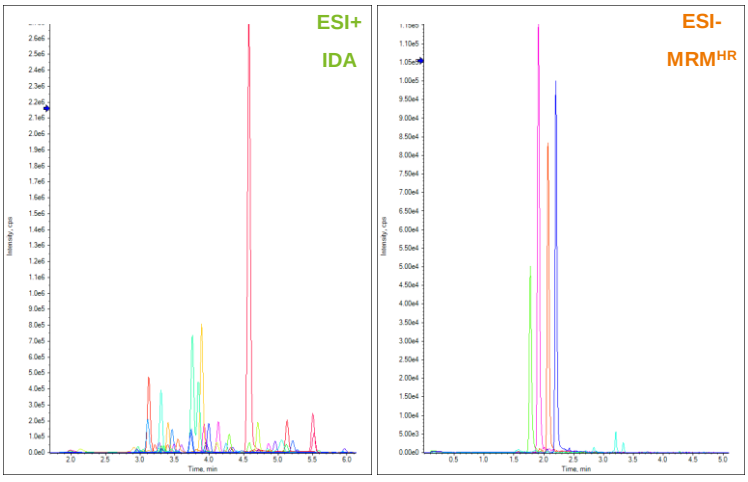


Figure 5. Obtaining Fast and Confident Identification of Forensic Compounds of Interest in Biological Matrices. (Left) Extracted Ion Chromatogram shows a rapid LC separation (6 min) and identification of 55 forensic compounds of interest spiked in whole blood at LOD concentrations using IDA-MS/MS.(Right) Extracted Ion Chromatogram shows the rapid identification of barbiturates and THC-COOH spiked in whole blood at LOD concentrations using MRM^{HR} workflow.

defining the m/z range desired using the *Apply TOF start/stop mass feature*. This mode was beneficial as it enhanced compound identification at the LOD when performing MS/MS spectral library matching.

Figure 5 displays XIC chromatograms showing the detection of all target compounds analyzed with both positive and negative electrospray ionization modes in control blood samples spiked at the LODs, based on the latest NSC-ADID recommendations.[1]

Throughout the method development process, it was important to obtain high combined scores for all compounds based on the four main confidence criteria defined in the processing method. Additional qualification criteria were implemented by setting an analyte concentration threshold based on the LODs to minimize false positives and/or false negative hits. Figure 6 shows the successful detection of 6-MAM and Fentanyl at their corresponding LODs, with mass errors less than 2ppm and MS/MS scores over 90%.

Table 1 shows the average (n=9) combined scores obtained for all 55 target compounds, in control blood samples spiked at the LOD analyzed over the course of 3 days. Inter-day reproducibility resulted in %RSDs ranging between 1-10% for the target analytes.

It was found that THC-COOH had sufficient S/N ratios (> 200) and mass error less than 1 ppm at the LOD (10 ng/mL) for positive identification. However, low-abundance MS/MS spectra were obtained at that concentration level, subsequently resulting in an average combined score of 70%. Further optimization on the sample extraction protocol is recommended to enhance THC-COOH sensitivity and MS/MS fragmentation.

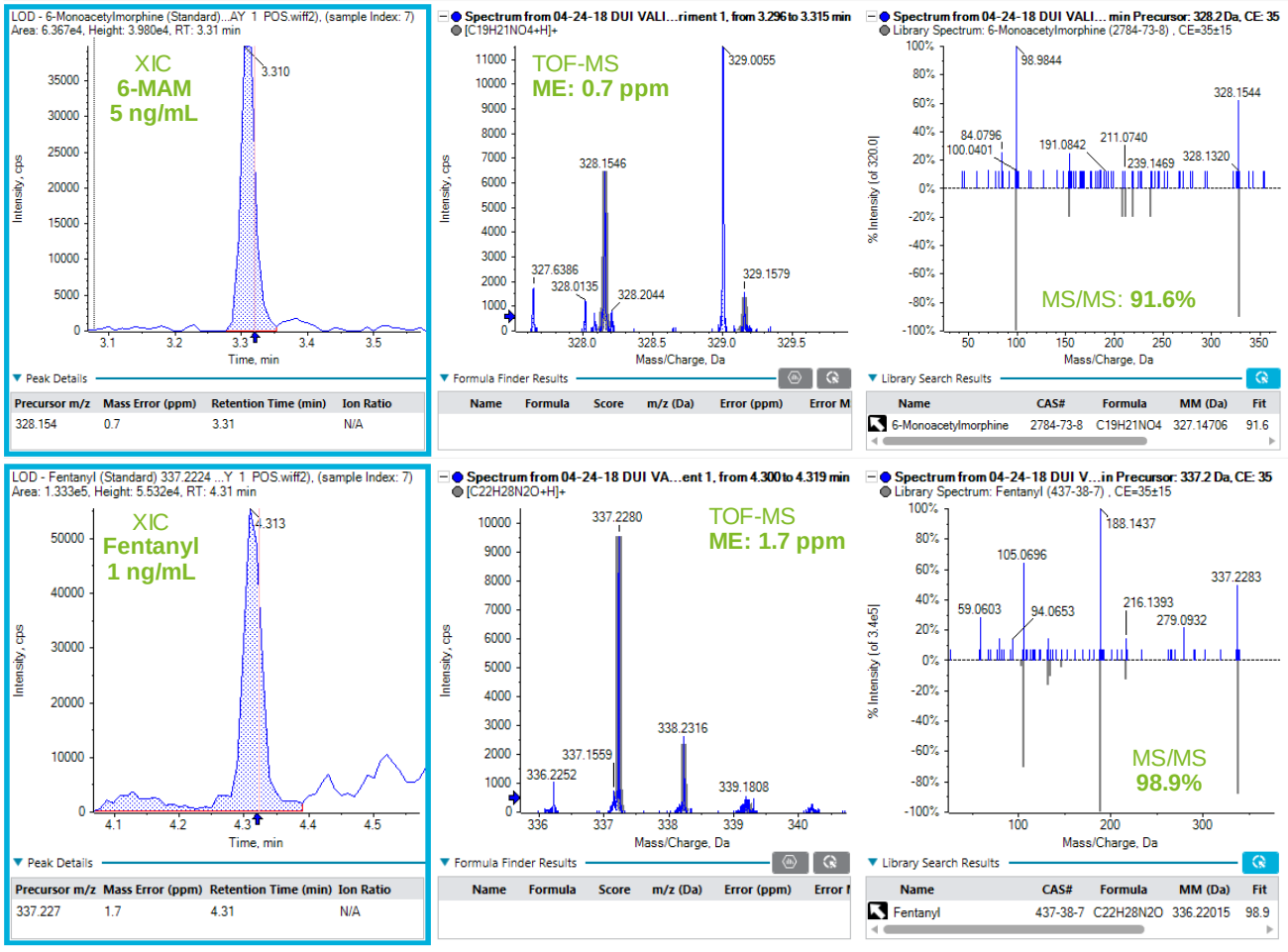


Figure 6. Successful Application of the SCIEX X500R QTOF System for Enhanced Compound Identification at Trace Concentration Levels. XICs, TOF MS and MS/MS spectra obtained showing confident and detailed identification of 6-MAM (Top) and fentanyl (bottom) spiked in whole blood at low ng/mL levels.

Forensic DUID Case Sample #4

Component...	Actual Concentr...	Expected RT	Area	Area R...	Retent... Time	Retenti... Time D...	U...	Calculated Concentrat...	Adduct / C...	Formula	Precursor Mass	Co... Ac...	Mass Error...	RT Confi...	Isotope Confi...	Library Confi...	Found At Mass	Mass Error (...	Library Hit	Library Score
Cocaethylene	N/A	4.14	5.586e4	0.110	4.14	0.00	☑	0.747	[M+H]+	C18H23N...	318.170		✓	✓	✓	✓	318.1704	1.4	Cocaethylene	97.7
Cocaine	N/A	3.93	3.241e4	0.064	3.94	0.01	☑	0.430	[M+H]+	C17H21N...	304.154		✓	✓	▲	✓	304.1544	0.1	Cocaine	86.7
Codeine	N/A	3.22	1.753e4	0.035	3.30	0.08	☑	0.759	[M+H]+	C18H21N...	300.159		✓	✓	▲	✓	300.1603	3.0	Codeine	80.6
Cotinine	N/A	2.04	8.459e6	16.675	1.96	0.08	☑	482.317	[M+H]+	C10H12N...	177.102	!	✓	✓	✓	✓	177.1021	-0.9	Cotinine	100.0
Diazepam D5	1.00	5.51	5.073e5	N/A	5.51	0.00		N/A	[M+H]+	C16H8[2H...	290.110		✓	✓	✓	✓	290.1106	0.9	Diazepam D5	96.8
Fentanyl	N/A	4.32	1.824e5	0.360	4.33	0.01	☑	2.093	[M+H]+	C22H28N...	337.227	!	✓	✓	✓	✓	337.2276	0.3	Fentanyl	98.3
Norfentanyl	N/A	3.52	3.102e4	0.061	3.52	0.00	☑	1.324	[M+H]+	C14H20N...	233.165	!	✓	✓	▲	▲	233.1651	1.0	Norfentanyl	53.9

Component...	Actual Concentr...	Expected RT	Area	Area R...	Retent... Time	Retenti... Time D...	U...	Calculated Concentrat...	Adduct / C...	Formula	Precursor Mass	Co... Ac...	Mass Error...	RT Confi...	Isotope Confi...	Library Confi...	Found At Mass	Mass Error (...	Library Hit	Library Score
THC-COOH	N/A	3.19	3.637e4	0.372	3.16	0.03	☑	92.518	[M-H]-	C21H28O4	343.191	!	✓	✓	✓	✓	343.1918	0.8	THC-COOH Negative	97.0

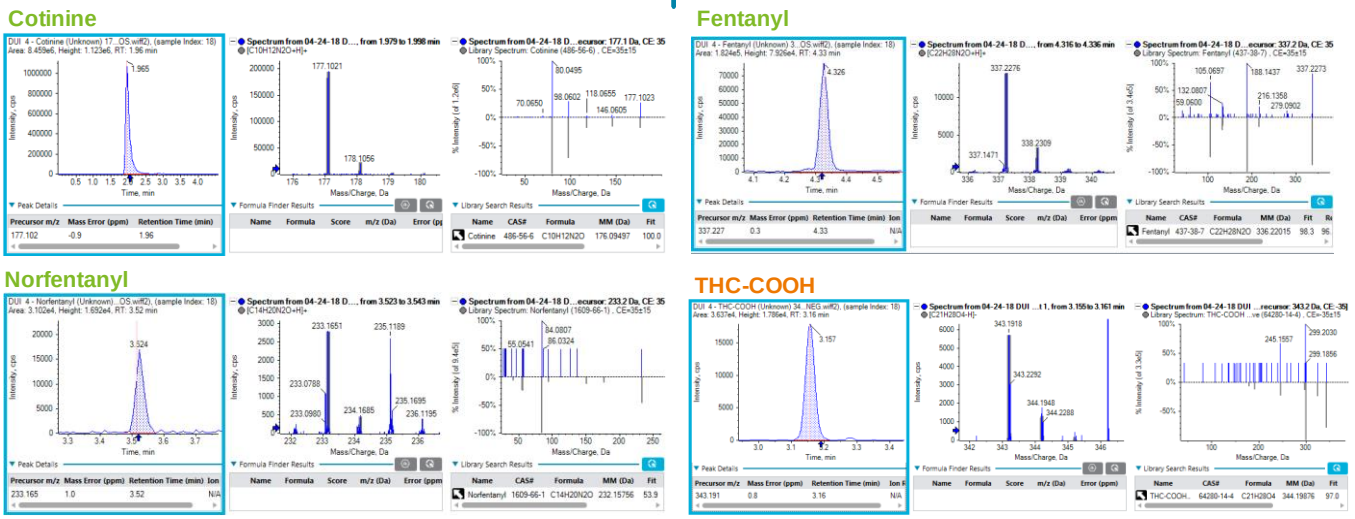


Figure 7. Minimize False Positives/Negatives by Streamlining Accurate Mass Data Processing of all Compounds of Interest Present in a Forensic DUID Case Sample using SCIEX OS Software. Using multiple acceptance criteria enabled the accurate identification of target analytes present in a forensic blood sample. (Top) Sample list of all compounds passing the acceptance criteria (green traffic lights) and concentration thresholds (cells highlighted in red) set within the processing method. (Bottom) XICs of all compounds identified in the sample, showcasing TOF MS and MS/MS spectral library identification details.

Enhanced Forensic Compound Identification using the SCIEX X500R QTOF System

One of the principal goals of developing this comprehensive analysis workflow was to successfully migrate the current immunoassay approach to the SCIEX X500R QTOF System. The current immunoassay sample preparation and analysis workflow utilizes 1mL of forensic blood sample and 2mL of acetonitrile for extraction, whereas with the QTOF MS strategy the laboratory was able to reduce the sample size to 100 µL while still meeting the NSC-ADID recommended cutoffs.

The ability of meeting these cutoffs with minimal sample is ideal, as often forensic case samples are limited in volume. Additionally, it eliminates the laboratory's need for using multiple reagent kits (9 kits currently utilized) as the QTOF MS approach provides the enhanced selectivity and sensitivity to streamline the detection of Tier I and Tier II compounds.

As part of the implementation plan, 30 forensic DUID case samples were screened with both immunoassay and QTOF MS for results comparison.

Table 2 shows all compounds detected in the 30 forensic DUID samples examined with both immunoassay analyzer and the SCIEX X500R QTOF system. Compounds highlighted in green were specifically detected using QTOF MS but missed or classified as a single compound class (e.g., *OPI* for Opiates and metabolites) by the immunoassay approach.

Figures 1 and 7 show the detailed analysis of two different DUID samples in the study. In reference to the sample displayed on Figure 7, the immunoassay analyzer detected THC-COOH exclusively.

Table 2. List of Compounds Identified in Forensic DUID Samples using Immunoassay Analyzer and the SCIEX X500R QTOF System.

ImmunoAssay Results		Mass Spectrometry Results								
DUI 1	COKE	Benzoylecgonine	Cocaethylene	Cocaine	Cotinine	Nordiazepam				
DUI 2	THC	Cotinine	THC-COOH							
DUI 3	NEG	NEG								
DUI 4	THC	Cotinine	Fentanyl	Norfentanyl	THC-COOH					
DUI 5	THC COKE	Benzoylecgonine	Cocaine	Cotinine	THC-COOH					
DUI 6	THC	Cotinine	THC-COOH							
DUI 7	AMPH	Amphetamine	Cotinine	Methamphetamine						
DUI 8	NEG	Cotinine	Lorazepam							
DUI 9	PCP THC	Cotinine	PCP	THC-COOH						
DUI 10	AMPH	Amphetamine	Cotinine	Ritalinic Acid	Methamphetamine					
DUI 11	THC BENZO	Cotinine	Diazepam	THC-COOH	Nordiazepam					
DUI 12	THC	Fentanyl	Norfentanyl	THC-COOH						
DUI 13	THC	Cotinine	THC-COOH							
DUI 14	THC	Cotinine	THC-COOH							
DUI 15	THC	Cotinine	THC-COOH							
DUI 16	THC	Cotinine	THC-COOH							
DUI 17	THC	Cotinine	THC-COOH							
DUI 18	THC	Cotinine	THC-COOH							
DUI 19	THC	Cotinine	THC-COOH							
DUI 20	THC	Cotinine	THC-COOH							
DUI 21	THC	Cotinine	THC-COOH							
DUI 22	THC	Cotinine	THC-COOH							
DUI 23	THC	Cotinine	THC-COOH							
DUI 24	COKE OPI	Benzoylecgonine	Buprenorphine	Cocaine	Codeine	Cotinine	Hydromorphone	Morphine	Metamphetamine	Morphine-3-Glucuronide
DUI 25	COKE	Benzoylecgonine	Cocaethylene	Cocaine	Cotinine					
DUI 26	OPI	Codeine	Cotinine	Fentanyl	Morphine	Morphine-3-Glucuronide	Hydromorphone			
DUI 27	AMPH COKE OPI	Amphetamine	Benzoylecognine	Cotinine	Fentanyl	Hydromorphone	Metamphetamine	Morphine	Morphine-3-Glucuronide	Norfentanyl
DUI 28	OPI	Benzoylecgonine	Codeine	Cotinine	Fentanyl	Hydromorphone	Morphine	Morphine-3-Glucuronide		
DUI 29	AMPH	Amphetamine	Cotinine	Fentanyl	Norfentanyl	Metamphetamine				
DUI 30	THC	Cotinine	THC-COOH							

*Compounds highlighted in **GREEN** are not screened for using the immunoassay analyzer operating in the laboratory but were detected in the MS assay.*

However, when analyzed with the SCIEX X500R QTOF System, the same compound was identified but also three compounds of interest, which were not tested by immunoassay were detected:

- Cotinine (~ 482.32 ng/mL) Combined Score 100%
- Fentanyl (~2.1 ng/mL) Combined Score 98.3%
- Norfentanyl (~1.32 ng/mL) Combined Score 53.9%
- THC-COOH (~92.52 ng/mL) Combined Score: 97%

It is important to highlight that norfentanyl was considered a positive hit although obtaining a combined score of 53.9%. Analyte review based on the acceptance criteria like retention time, mass error on the TOF MS scan, concentration threshold (> 1 ng/mL) as well as parent drug metabolism pathway knowledge, were supporting evidence of compound presence in the forensic DUID sample.

Conclusions

A comprehensive drug screening workflow for the analysis of forensic DUID blood samples has been successfully developed using the SCIEX X500R QTOF System based on the new NSC-ADID recommendations.

- The vMethod™ Application for forensic compound screening was successfully used to obtain retention times and MS/MS spectra necessary to build a targeted analysis workflow for the 60 forensic compounds of interest in DUID case samples.
- Average combined scores based on multiple acceptance criteria (Ret. Time, Mass error, Isotope ratio, MS/MS library hit and concentration) ranged between 70-98% for all target analytes, resulting in successful compound identification.
- The developed QTOF MS screening approach enabled the identification of multiple number of the targeted compounds present in authentic forensic DUID case samples in comparison to immunoassay based screening.
- The adaptation of QTOF MS technology enabled the use of microliter volumes of forensic blood samples, while meeting NSC-ADID cutoff recommendations. Thus, eliminating the use of multiple immunoassay reagent kits used for screening.

References

1. Logan B. et al., Recommendations for Toxicological Investigation of Drug-Impaired Driving and Motor Vehicle Fatalities-2017 Update. J Anal Toxicol 2018, 42 (2), 63-68. https://doi.org/10.1093/jat/bkx082
2. Desharnais B. et al., Protein precipitation of whole blood for quantification of 58 different analytes by LC-MS/MS: method development challenges, https://goo.gl/2Ma9RU
3. vMethod™ Application - Single-Injection Screening of 664 Forensic Toxicology Compounds on a SCIEX X500R QTOF System.

Supplement A. List of Target Forensic DUID Compounds.

Component Name	Retention Time	Formula	Precursor (Q1) Mass (Da)	Adduct & Charge	LOD (ng/mL)
6-Monoacetylmorphine	3.32	$C_{19}H_{21}NO_4$	328.1543	[M+H]+	5
7-Aminoclonazepam	3.97	$C_{15}H_{12}ClN_3O$	286.0742	[M+H]+	10
Alpha-hydroxyalprazolam	4.71	$C_{17}H_{13}ClN_4O$	325.0851	[M+H]+	10
Alpha-hydroxymidazolam	4.36	$C_{18}H_{13}ClFN_3O$	342.0804	[M+H]+	10
Alprazolam	4.95	$C_{17}H_{13}ClN_4$	309.0902	[M+H]+	10
Amphetamine	3.24	$C_9H_{13}N$	136.1121	[M+H]+	20
Benzoylecgonine	3.59	$C_{16}H_{19}NO_4$	290.1387	[M+H]+	5
6-Beta-Naltrexol	3.28	$C_{20}H_{25}NO_4$	344.1856	[M+H]+	10
Buprenorphine	4.39	$C_{29}H_{41}NO_4$	468.3108	[M+H]+	1
Zolpidem Phenyl-4-carboxylic acid	3.5	$C_{19}H_{19}N3O3$	338.1499	[M+H]+	5
Carisoprodol	4.86	$C_{12}H_{24}N2O_4$	261.1809	[M+H]+	50
Cocaethylene	4.14	$C_{18}H_{23}NO_4$	318.1700	[M+H]+	5
Cocaine	3.93	$C_{17}H_{21}NO_4$	304.1543	[M+H]+	5
Codeine	3.22	$C_{18}H_{21}NO_3$	300.1594	[M+H]+	5
Cotinine	2.04	$C_{10}H_{12}N_2O$	177.1022	[M+H]+	5
Delorazepam	5.2	$C_{15}H_{10}Cl_2N_2O$	305.0243	[M+H]+	10
Diazepam	5.53	$C_{16}H_{13}ClN_2O$	285.0789	[M+H]+	10
EDDP	4.59	$C_{20}H_{23}N$	278.1903	[M+H]+	50
Etizolam	5.12	$C_{17}H_{15}ClN_4S$	343.0779	[M+H]+	10
Fentanyl	4.32	$C_{22}H_{28}N_2O$	337.2274	[M+H]+	1
Gabapentin	3.12	$C_9H_{17}NO_2$	172.1332	[M+H]+	250
Hydrocodone	3.41	$C_{18}H_{21}NO_3$	300.1594	[M+H]+	5
Hydromorphone	3.05	$C_{17}H_{19}NO_3$	286.1438	[M+H]+	5
Ketamine	3.55	$C_{13}H_{16}ClNO$	238.0993	[M+H]+	5
Lorazepam	4.9	$C_{15}H_{10}Cl_2N_2O_2$	321.0192	[M+H]+	10
MDA	3.3	$C_{10}H_{13}NO_2$	180.1019	[M+H]+	20
MDMA	3.4	$C_{11}H_{15}NO_2$	194.1176	[M+H]+	20
Meperidine	3.89	$C_{15}H_{21}NO_2$	248.1645	[M+H]+	25
Meprobamate	4.11	$C_9H_{18}N_2O_4$	219.1339	[M+H]+	500
Methadone	4.71	$C_{21}H_{27}NO$	310.2165	[M+H]+	5
Methamphetamine	3.35	$C_{10}H_{15}N$	150.1277	[M+H]+	20

Component Name	Retention Time	Formula	Precursor (Q1) Mass (Da)	Adduct & Charge	LOD (ng/mL)
Methylphenidate	3.77	$C_{14}H_{19}NO_2$	234.1489	[M+H]+	25
Midazolam	4.3	$C_{18}H_{13}ClFN_3$	326.0855	[M+H]+	10
Mitragynine	4.59	$C_{23}H_{30}N_2O_4$	399.2278	[M+H]+	2.5
Morphine	2.97	$C_{17}H_{19}NO_3$	286.1438	[M+H]+	10
Morphine-3-glucuronide	1.94	$C_{23}H_{27}NO_9$	462.1759	[M+H]+	49.4
Naltrexone	3.32	$C_{20}H_{23}NO_4$	342.1700	[M+H]+	10
Norbuprenorphine	3.95	$C_{25}H_{35}NO_4$	414.2639	[M+H]+	2.5
Nordiazepam	5.12	$C_{15}H_{11}ClN_2O$	271.0633	[M+H]+	10
Norfentanyl	3.52	$C_{14}H_{20}N_2O$	233.1648	[M+H]+	1
Norhydrocodone	3.34	$C_{17}H_{19}NO_3$	286.1438	[M+H]+	25
Norketamine	3.46	$C_{12}H_{14}ClNO$	224.0837	[M+H]+	5
Normeperidine	3.85	$C_{14}H_{19}NO_2$	234.1489	[M+H]+	25
Noroxycodone	3.28	$C_{17}H_{19}NO_4$	302.1387	[M+H]+	10
O-Desmethyl-cis-tramadol	3.31	$C_{15}H_{23}NO_2$	250.1802	[M+H]+	25
Oxazepam	4.84	$C_{15}H_{11}ClN_2O_2$	287.0582	[M+H]+	10
Oxycodone	3.34	$C_{18}H_{21}NO_4$	316.1543	[M+H]+	5
Oxymorphone	3	$C_{17}H_{19}NO_4$	302.1387	[M+H]+	5
Phenazepam	5.28	$C_{15}H_{10}N_2OBrCl$	348.9738	[M+H]+	10
Phencyclidine	4.25	$C_{17}H_{25}N$	244.2060	[M+H]+	5
Pregabalin	3.11	$C_8H_{17}NO_2$	160.1332	[M+H]+	250
Ritalinic acid	3.46	$C_{13}H_{17}NO_2$	220.1332	[M+H]+	25
Tapentadol	3.74	$C_{14}H_{23}NO$	222.1852	[M+H]+	5
Temazepam	5.21	$C_{16}H_{13}ClN_2O_2$	301.0738	[M+H]+	10
Tramadol	3.74	$C_{16}H25NO_2$	264.1958	[M+H]+	5
Zolpidem	4	$C_{19}H_{21}N_3O$	308.1757	[M+H]+	5
Secobarbital	2.19	$C_{12}H_{18}N_2O_3$	237.1245	[M-H]-	250
Butalbital	1.9	$C_{11}H_{16}N_2O_3$	223.1088	[M-H]-	250
Pentobarbital	2.05	$C_{11}H_{18}N_2O_3$	225.1245	[M-H]-	250
Phenobarbital	1.76	$C_{12}H_{12}N_2O_3$	231.0775	[M-H]-	250
THC-COOH	3.19	$C_{21}H_{28}O_4$	343.1915	[M-H]-	10

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