Drug Screen Suite: Streamlined LC-HRMS Toxicological Screening for Routine and Post-Mortem Casework

Birgit Schneider[1], Juergen Kempf[2], Laura M. Huppertz[2], Carsten Baessmann[1], Eva Niehaus[1], Sam Putnam[3]
1: Bruker Daltonics GmbH & Co. KG, Bremen, Germany 2: Institute of Forensic Medicine, Medical Center – University of Freiburg, Freiburg, Germany 3: Bruker Scientific LLC, Billerica, MA, USA

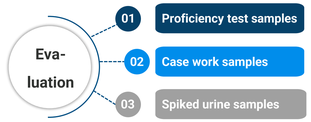
Introduction

In high-throughput forensic labs, robust, user-friendly automated solutions are essential, as screening evaluation often creates bottlenecks. LC-HRMS remains a powerful screening technique, enabling reliable identification via retention time, exact mass, and HRMS/MS spectra. With the rapid emergence of new psychoactive substances (NPS), workflows must also be adaptable. The Drug Screen Suite meets these needs by offering an efficient, fully integrated approach to toxicological screening: from sample to report.

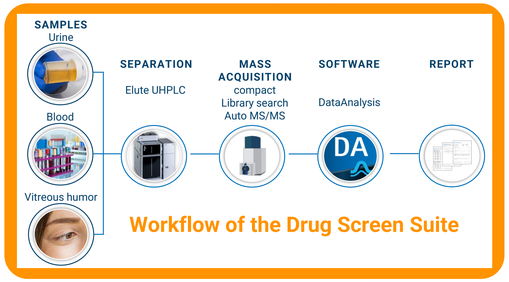
Methods

LC-System: Bruker Elute⁺ UHPLC
Eluent A: H_2O, 0.2% buffer mix, 1% eluent B
Eluent B: Methanol, 0.2% buffer mix
Gradient: 20 min gradient elution
Column: Intensity Solo 1.8 C18-2 100 x 2.1 mm

MS-System: Bruker OTOF
Ion source: VIP HESI source, positive mode
Scan mode: AutoMS/MS @ 12 Hz
Scan range: *m/z* 30 -1,000



Different sample types were used to evaluate the screening approach. Preparation included liquid-liquid extraction (serum, blood), cold ACN precipitation (urine, serum), and solid-phase extraction (vitreous humor) following the respective protocols.



Results

Several 2024 Society of Toxicological and Forensic Chemistry (GTFCh) proficiency tests were analyzed, including urine screening (UF), abstinence monitoring (SFD), general unknown analysis (QSA), and serum tests for benzodiazepines (BZF), neuroleptics (TDMA), and narcotics (BTMF).

01 Proficiency test samples

Urine screening

UF 1/24

Substance	Conc. [µg/L]	
Methamphetamine	1,350	✓
Nordazepam	500	✓
Benzoylecgonine	400	✓
Dihydrocodeine	450	✓
Doxylamine	800	✓
Norbuprenorphine	250	X
Oxycodone	250	✓

UF 2/24

Substance	Conc. [µg/L]	
MDMA	450	✓
Nordazepam	500	✓
THC-COOH	150	✓
EDDP	350	✓
Norbuprenorphine	200	X
GHB	30,000	◆
O-Desmethyltramadol	400	✓

UF 3/24

Substance	Conc. [µg/L]	
Amphetamine	1,100	✓
Nitrazepam	600	✓
Benzoylecgonine	250	✓
Dihydrocodeine	750	✓
Nortriptyline	800	✓
LSD	6	✓
Tramadol	700	✓

Abstinence monitoring

SFD 1/24

Substance	Conc. [µg/L]	
MDMA	200	✓
Nordazepam	95	✓
THC-COOH	40	✓
Codeine	200	✓
Norfentanyl	25	✓
Ethylglucuronide	175	⌘
Norbuprenorphine	15	X

SFD 2/24

Substance	Conc. [µg/L]	
Amphetamine	500	✓
Benzoylecgonine	150	✓
Dihydrocodeine	300	✓
Nortilidine	125	✓
Oxycodone	75	✓
EDDP	200	✓
O-Desmethyltramadol	250	✓

SFD 3/24

Substance	Conc. [µg/L]	
Methamphetamine	350	✓
THC-COOH	85	✓
Benzoylecgonine	350	✓
Ethylglucuronide	300	⌘
Norbuprenorphine	75	X
Norfentanyl	125	✓
7-Aminoflunitrazepam	100	✓

General unknown analysis

QSA 1/24

Substance	Conc. [µg/L]	
Fentanyl	40	✓
Norfentanyl	25	✓
Methadon	250	✓
EDDP	200	✓

QSA 2/24

Substance	Conc.	
GHB	550 mg/L	◆
Ethanol	1.5 g/L	●

⌦ no false positives

QSA3/24

Substance	Conc. [µg/L]	
Ketamine	7,500	✓
Norketamine	1,500	✓
MDMA	500	✓
MDA	50	✓
2C-B	200	✓

Neutoleptics

TDMA 1/24

Substance	Conc. [µg/L]	
Clozapine	180	✓
Desmethylclozapine	170	✓
Olanzapine	50	✓
Norolanzapine	30	✓
Quetiapine	60	✓
Norquetiapine	60	✓
Amisulpride	125	✓
Thioridazine	95	✓
Chlorprothixene	95	✓

For serum samples, precipitation with ice-cold acetonitrile and alkaline liquid-liquid extraction using chlorobutane were applied for sample preparation. The results demonstrate that the Drug Screen Suite is also suitable for serum, enabling the detection of a broad range of medications and drugs. Limitations arise from simplified sample preparation, especially for chlorobutane-incompatible compounds (e.g., THC-COOH, detectable only with ACN).

Benzodiazepines

BZF 1/24

Substance	Conc. [µg/L]	
Clobazam	295	✓
Norclobazam	12,000	◆
Flurazepam	45	✓
Disalkylflurazepam	65	✓
Triazolam	27	✓
α-OH-Triazolam	22	✓
Chlordiazepoxide	1,150	✓
Demoxepam	925	✓
3-OH-Bromazepam	95	✓
7-Aminoclonazepam	28	✓
7-Aminonitrazepam	120	✓
α-OH-Alprazolam	32	✓
Estazolam	260	✓
Medazepam	235	✓
Prazepam	470	✓

BTMF 3/24 A

Substance	Conc. [µg/L]	
THC	6	✓
11-OH-THC	2.5	⌘
THC-COOH	120	✓
Cocaine	30	✓
Benzoylecgonine	185	✓
Ecgoninemethylester	20	✓
Cocaethylene	17	✓
Morphine	40	✓
6-Monoacetylmorphine	17	✓
Codeine	85	✓
Dihydrocodeine	200	✓
Amphetamine	80	✓
MDMA	55	✓
MDA	25	✓
MDEA	65	✓
Methamphetamine	125	✓

BTMF 3/24 B

Substance	Conc. [µg/L]	
THC	10	✓
11-OH-THC	5	⌘
THC-COOH	75	✓
Cocaine	50	✓
Benzoylecgonine	250	✓
Ecgoninemethylester	37.5	✓
Cocaethylene	37.5	✓
Morphine	50	✓
6-Monoacetylmorphine	25	✓
Codeine	75	✓
Dihydrocodeine	100	✓
Amphetamine	75	✓
MDMA	75	✓
MDA	50	✓
MDEA	75	✓
Methamphetamine	75	✓

02 Case work samples

To evaluate performance under high matrix conditions, several post-mortem extracts were reanalyzed. The tables below present representative findings from a driver involved in a fatal traffic accident. Routine screening was conducted using immunoassays and the Toxtyper®, followed by targeted quantitation of relevant compounds by LC-MS/MS.

Femoral blood

Substance	Routine Analysis	Drug Screen Suite
Amlodipine	60 µg/L	✓
Fentanyl	< 1.0 µg/L	✓
Ketamin	220 µg/L	✓
Metoprolol	230 µg/L	✓
Midazolam	16 µg/L	✓
Paroxetine	200 µg/L	✓
Ramipril	1,1 µg/L	✓
Ephedrine	350 µg/L	✓
Norephedrine	21 µg/L	✓
Tilidine	110 µg/L	✓
Nortilidine	160 µg/L	✓
Naloxone	detected	✓
4-Acetylaminoantipyrine	detected	✓
4-Formylaminoantipyrene	detected	✓
4-Methylaminoantipyrine	detected	✓
Aminoantipyrine	detected	✓
Ethyl glucuronide	detected	⌘
Ethyl sulfate	detected	⌘
Ondansetrone	detected	✓
Torasemide	detected	✓

Vitreous humor

Substance	Drug Screen Suite
4-Acetylaminoantipyrine	✓
4-Formylaminoantipyrene	✓
4-Methylaminoantipyrine	✓
Aminoantipyrine	✓
Amlodipine	✓
Clopidogrel	✓
Ephedrine	✓
Ketamine	✓
Metoprolol	✓
Midazolam	✓
Naloxone	✓
Nortilidine	✓
Ondansetrone	✓
Paroxetine	✓
Tilidine	✓

Urine

Substance	Drug Screen Suite
4-Acetylaminoantipyrine	✓
4-Formylaminoantipyrene	✓
4-Methylaminoantipyrine	✓
Aminoantipyrine	✓
Amlodipine	✓
Clopidogrel	✓
Metoprolol	✓
Naloxone glucuronide	✓
Nortilidine	✓
Paroxetine	✓
Ramipril	✓
Tilidine	✓
Torasemide	✓

All substances detected during toxicological analysis in femoral blood, vitreous humor, and urine were successfully identified using the Drug Screen Suite except for EtG and EtS that are analyzed in negative mode.

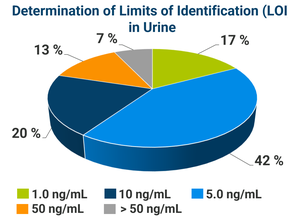
03 Spiked urine samples

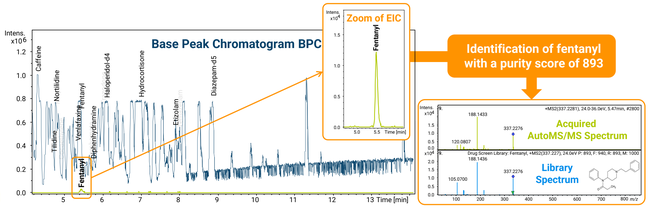
To determine limits of identification (LOI), 100 µL of blank urine was spiked with 120 substances most commonly detected in routine cases at concentrations of 50, 10, 5.0, and 1.0 ng/mL.

Approximately 80% of the substances could be identified at concentrations of 10 ng/mL or lower.

Although some substances could still be detected at lower concentrations (e.g. fentanyl), review of the raw data also showed that, especially at low concentrations, low *m/z* interference signals may prevent successful library matching.

One possible workaround strategy here could be the substance-specific use of fit or purity value as identification criterium.





Conclusions

- **Ready-to-use solution** for **rapid compound detection and identification** in clinical research and forensic toxicology
- **High sensitivity enables detection of a broad range of substances**, including proficiency test samples
- **High-resolution MS minimizes false positives** even in complex matrices, with the method set to ±5 mDa tolerance
- **Open library** supports continuous and timely method updates
- **Automated data processing and reporting** reduce turnaround time and enable routine HRMS use
- Additional capabilities:
  - Identification of unknowns via accurate mass, isotope pattern, and MS/MS
  - Full quantitation and semi-quantitative analysis

Drug Screen Suite

© 2026 Bruker

◆: Compound is not included in library; ●: not suitable for ESI; ⌘: ESI negative mode; X: not detected

For Research Use Only. Not for use in diagnostic procedures.