



# Screening Method for Acidic, Neutral and Basic Drug Analytes in Oral Fluid by LC-MS/MS Using CLEAN SCREEN® XCEL I

## UCT Part Numbers

### CSXCE106

Clean Screen® XCEL I  
130mg / 6mL SPE Cartridge

### SPPHO6001-5

Select pH Buffer  
100 mM Phosphate pH 6.0

### SLDA50ID21-5UM

Selectra® DA LC column  
50 x 2.1 mm, 5 µm

### SLDAGDC21-5UM

Selectra® DA guard column  
10 x 2.1 mm, 5µm

### SLGRDHLDR

Guard Column Holder



## Summary:

When compared to urine and hair drug tests, oral fluid is best at detecting recent drug use. Drugs take time to metabolize and pass through the system in a urine test, and the same drugs are incorporated as hair grows and it takes time for the drug to be present in the hair above the scalp. But an oral fluid test will often detect drugs in a donor's system immediately after use. This makes oral fluid testing ideal for a broad range of situations ranging from pre-employment, to reasonable suspicion, to post-accident testing where the employer is interested in assessing what's in the donor's system at the time of the drug test collection.

Oral fluid levels largely correlate with the amount of drug in the blood (dependent on the saliva/plasma ratio for each drug). Higher drug and drug metabolite levels are found in urine because they are concentrated by the kidneys during the excretion process. The SAMHSA cut-off levels for oral fluid are very much lower than those for urine and hence more sensitive screening and confirmatory assays are required for oral fluid analysis often times with the incorporation of a concentration step to enhance sensitivity.

The below Clean Screen® XCEL I method can be utilized for both universal screening and confirmatory purposes when extracting various drugs from oral fluid prior to analysis by LC-MS/MS. By evaporating to completion, final extracts are purified and highly concentrated to achieve required levels of detection/quantitation.



CLINICAL



FORENSICS

## Sample Pretreatment:

### NEAT ORAL FLUID:

- Add 100 - 500  $\mu\text{L}$  of neat oral fluid sample to a clean tube.
- Add internal standard(s) and let sit for 10 minutes at room temperature.
- Add 800  $\mu\text{L}$  of 100 mM phosphate buffer (pH= 6.0).
- Mix/vortex for 10 seconds. Sample pH should be  $6.0 \pm 0.5$ .
- Adjust pH accordingly with 100 mM monobasic or dibasic sodium phosphate.

### ORAL FLUID COLLECTION DEVICE:

To 1mL of oral fluid specimen, (diluted in Quantisal™ Buffer), add appropriate internal standards. Mix/vortex for 30 seconds.

## SPE Procedure:

### 1. Sample Extraction

- a) Apply the sample directly to the SPE cartridge (if required, use a low vacuum to draw the sample through at  $\leq 3$  mL/min).

### 2. Wash cartridge

- a) 1  $\times$  3 mL D.I. H<sub>2</sub>O.
- b) 1  $\times$  3 mL 1% HCl Solution.
- c) Dry cartridges for  $\sim 10$  minutes under a high vacuum.

Note: A Hexane wash may be added if not looking for parent THC.

### 3. Elution

- a) Elute with 1  $\times$  3 mL MEOH containing 2% Ammonium Hydroxide (MEOH: NH<sub>4</sub>OH, 98:2 v/v).
- b) Evaporate the sample to dryness under a gentle stream of nitrogen. Take care not to overheat or over evaporate. Certain compounds are heat labile, such as the amphetamines and phencyclidine. A 1% HCl in MEOH solution may be used to prevent volatilization by the formation of the hydrochloric salt of the drugs. Add 1 drop of the solution prior to evaporating than continue to dryness.
- c) Reconstitute in 100  $\mu\text{L}$  of Mobile Phase and vortex for 1 minute.
- d) Transfer sample to an autosampler vial containing a low volume insert.



## LC-MS/MS Parameters:

| Instrumentation     |   |
|---------------------|---|
| HPLC system         | Agilent 1200 Binary Pump SL                               |
| MS system           | API 4000 QTRAP (MS/MS)                                    |
| HPLC column         | UCT Selectra® DA, 50 × 2.1 mm, 5 µm (p/n: SLDA50ID21-5UM) |
| Guard column        | UCT Selectra® DA, 10 × 2.1 mm, 5 µm (p/n: SLDAGDC21-5UM)  |
| Guard column holder | p/n: SLGRDHLDR  |
| Column temperature  | 40°C  |
| Flow rate           | 300 µL/min  |
| Injection volume    | 10 µL   |

| Mobile Phase Gradient |   |  |
|-----------------------|---|--|
| Time (min)            | % Mobile Phase A<br>(0.1% Formic Acid in Water) | % Mobile Phase B<br>(0.1% Formic Acid in MEOH) |
| 0.0                   | 90  | 10   |
| 0.5                   | 90  | 10   |
| 4.0                   | 60  | 40   |
| 7.5                   | 15  | 85   |
| 8.5                   | 10  | 90   |
| 8.51                  | 90  | 10   |
| 10.0                  | STOP  |  |

## Results:

| ANALYTE                       | Relative Retention Time (min) | Q1    | Q3    |
|-------------------------------|-------------------------------|-------|-------|
| Ecgoninemethylester           | 0.5                           | 200.1 | 182.1 |
| Phenylpropanolamine           | 0.9                           | 152.2 | 134.2 |
| Morphine                      | 1.4                           | 286   | 152   |
| Oxymorphone                   | 1.5                           | 302   | 227   |
| Pregabalin                    | 1.5                           | 160.2 | 97    |
| Pseudoephedrine               | 1.9                           | 166.1 | 148.1 |
| Hydromorphone                 | 1.9                           | 286   | 185   |
| Ephedrine                     | 1.9                           | 166.2 | 148.3 |
| Amphetamine                   | 2                             | 136.1 | 91.1  |
| Paracetamol                   | 2                             | 152   | 110   |
| Gabapentin                    | 2.2                           | 172.1 | 67.1  |
| 3,4-Methylenedioxyamphetamine | 2.5                           | 180.1 | 105   |
| Atropine                      | 2.5                           | 290.2 | 124.1 |
| Buspirone                     | 2.5                           | 386.2 | 122.1 |
| Clonidine                     | 2.5                           | 230   | 213   |
| Metamphetamine                | 2.5                           | 150.1 | 91.1  |
| Nicotine                      | 2.5                           | 163.1 | 132.1 |
| Phenylephrine                 | 2.5                           | 168.1 | 91.1  |
| Theobromine                   | 2.5                           | 181.1 | 138   |
| Theophylline                  | 2.5                           | 181.1 | 124   |
| Mephedrone                    | 2.5                           | 178.2 | 160.1 |
| Phentermine                   | 2.5                           | 150.2 | 91.2  |
| 6-O-Monoacetylmorphine        | 2.6                           | 328.1 | 165.1 |
| Naloxone                      | 2.8                           | 328.2 | 310.2 |
| Methylone                     | 2.8                           | 208   | 160.1 |



| ANALYTE                       | Relative Retention Time (min) | Q1    | Q3    |
|-------------------------------|-------------------------------|-------|-------|
| Phenmetrazine                 | 2.8                           | 178.2 | 115.1 |
| Phendimetrazine               | 2.8                           | 192.2 | 147.1 |
| Caffeine                      | 3.0                           | 195.1 | 122.9 |
| Dihydrocodeine                | 3                             | 302.2 | 199.1 |
| Codeine                       | 3                             | 300   | 152   |
| Desmethyltramadol             | 3                             | 250.2 | 58.2  |
| MDMA                          | 3.1                           | 194.1 | 105.1 |
| 7-Aminonitrazepam             | 3.1                           | 252.1 | 121.1 |
| Oxycodone D6                  | 3.1                           | 322.3 | 304.1 |
| Oxycodone                     | 3.2                           | 316.1 | 298.1 |
| Hydrocodone                   | 3.4                           | 300   | 199   |
| Diethylpropion                | 3.4                           | 206.2 | 100.2 |
| MDEA                          | 3.6                           | 208.1 | 77.1  |
| Naltrexol                     | 3.6                           | 344.3 | 308.4 |
| Pheniramine                   | 3.8                           | 241.2 | 167.2 |
| Olanzapine                    | 4                             | 313.1 | 256.1 |
| Norketamine                   | 4                             | 224.1 | 207.1 |
| Methylphenidate               | 4.1                           | 234.1 | 84.1  |
| Norfentanyl                   | 4.1                           | 233.2 | 84.1  |
| Doxylamine                    | 4.1                           | 271.3 | 167.2 |
| Nalbuphine                    | 4.1                           | 358.4 | 185.2 |
| Tramadol                      | 4.3                           | 264.2 | 58    |
| Tapentadol                    | 4.3                           | 222.3 | 107.2 |
| Benzoyllecgonine              | 4.4                           | 290.1 | 168.1 |
| 7-Aminoclonazepam             | 4.5                           | 286.1 | 121.1 |
| Ketamine                      | 4.5                           | 238.1 | 125   |
| Meperidine                    | 4.5                           | 248.2 | 220   |
| Meprobamate                   | 4.6                           | 219.1 | 158.2 |
| Normeperidine                 | 4.7                           | 234.1 | 91.2  |
| Cocaine                       | 4.9                           | 304.1 | 182.1 |
| MDPV                          | 5                             | 276.2 | 126.2 |
| Midazolam                     | 5                             | 326.1 | 291.3 |
| Bupropion                     | 5                             | 240.2 | 184   |
| alpha-pyrrolidinopentophenone | 5                             | 272.3 | 110.1 |
| 5-methoxy DALT                | 5                             | 272.3 | 110   |
| 7-Aminoflunitrazepam          | 5.2                           | 284.1 | 135.1 |
| Chlorpheniramine              | 5.2                           | 275.1 | 230.1 |
| Venlafaxine                   | 5.2                           | 278.2 | 260.2 |
| Mirtazapine                   | 5.3                           | 266.2 | 195.1 |
| Pentazocine                   | 5.3                           | 286.3 | 175.1 |
| Norbuprenorphine              | 5.4                           | 414.2 | 187.1 |
| Butorphanol                   | 5.4                           | 328.4 | 131.2 |
| Brompheniramine               | 5.5                           | 319.1 | 274.1 |
| Clozapine                     | 5.5                           | 327.1 | 270.1 |
| Zolpidem                      | 5.6                           | 308.2 | 235.2 |
| Diphenhydramine               | 5.8                           | 256.2 | 165.1 |
| Buprenorphine                 | 5.8                           | 468.2 | 396.2 |
| Citalopram                    | 5.9                           | 325.2 | 109   |
| D3-Doxepin                    | 5.9                           | 283   | 107.1 |
| Trazodone                     | 5.9                           | 372.2 | 176.1 |



| ANALYTE                  | Relative Retention Time (min) | Q1    | Q3    |
|--------------------------|-------------------------------|-------|-------|
| Doxepin                  | 6                             | 280.2 | 107.1 |
| Fentanyl                 | 6                             | 337.2 | 188.2 |
| Fluoxetine               | 6                             | 310.1 | 117.1 |
| Haloperidol              | 6                             | 376.1 | 123   |
| Clomipramine             | 6                             | 315.2 | 86.1  |
| Phencyclidine-D5         | 6                             | 249.2 | 164.2 |
| Dextromethorphan         | 6.1                           | 272.2 | 171.2 |
| Mianserin                | 6.1                           | 265.2 | 208.2 |
| Phencyclidine            | 6.1                           | 244.2 | 86.1  |
| Carisoprodol             | 6.1                           | 261.2 | 176.1 |
| Quetiapine               | 6.2                           | 384.2 | 253.1 |
| Zopiclone                | 6.2                           | 389.1 | 245   |
| Dextropropoxyphene       | 6.3                           | 340.2 | 266.2 |
| Propoxyphene             | 6.3                           | 340   | 58    |
| alpha-hydroxymidazolam   | 6.3                           | 342.1 | 168.1 |
| Desipramine              | 6.4                           | 267.2 | 72.1  |
| Imipramine               | 6.4                           | 281.2 | 86.1  |
| EDDP                     | 6.4                           | 278.2 | 234.1 |
| Cyclobenzaprine          | 6.4                           | 276.2 | 215   |
| Bromazepam               | 6.5                           | 316   | 182.1 |
| Nortriptyline            | 6.5                           | 264.2 | 233.1 |
| Paroxetine               | 6.5                           | 330.1 | 192.1 |
| Carbamazepine            | 6.5                           | 237.1 | 194.2 |
| Amitriptyline            | 6.6                           | 278.2 | 233.2 |
| Lorazepam                | 6.8                           | 321   | 229.1 |
| Methadone                | 6.8                           | 310.2 | 265.2 |
| Clonazepam               | 6.9                           | 316.1 | 270.1 |
| Oxazepam                 | 6.9                           | 287.1 | 241.1 |
| alpha-Hydroxytriazolam   | 6.9                           | 359   | 331.1 |
| 2-Hydroxyethylflurazepam | 7                             | 333.1 | 211.2 |
| Triazolam                | 7                             | 343   | 239   |
| alpha-Hydroxyalprazolam  | 7                             | 325.1 | 297.2 |
| Norfluoxetine            | 7                             | 296.2 | 134.2 |
| Nordiazepam              | 7.2                           | 271.1 | 140.1 |
| Sertraline               | 7.2                           | 306.1 | 159   |
| Estazolam                | 7.3                           | 295.1 | 205.2 |
| Flunitrazepam            | 7.3                           | 314.1 | 268.1 |
| Alprazolam-D5            | 7.3                           | 314.2 | 286.3 |
| Alprazolam               | 7.4                           | 309.1 | 281.1 |
| Temazepam                | 7.4                           | 301.1 | 255.1 |
| D5-Diazepam              | 7.5                           | 290   | 198.2 |
| Diazepam                 | 7.7                           | 285.1 | 193.2 |
| Methaqualone-d7          | 8                             | 259.2 | 98.2  |
| Flurazepam               | 8.3                           | 388.1 | 315.1 |
| THC-COOH                 | 8.4                           | 345.1 | 299.1 |
| THC                      | 8.5                           | 315.2 | 193.2 |



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