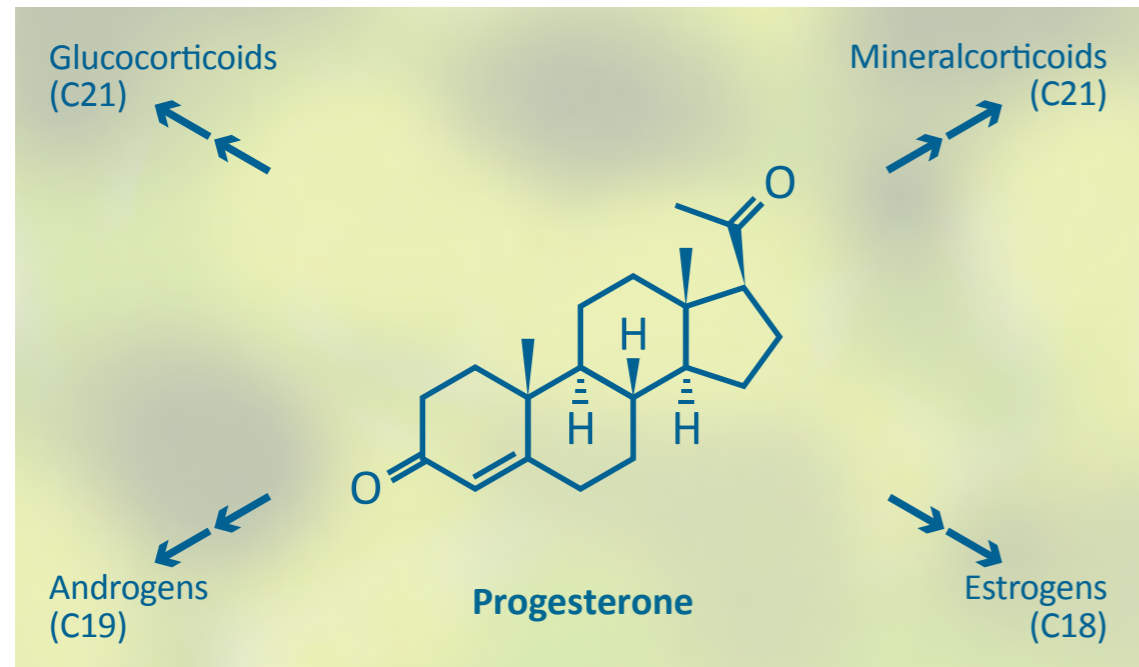




## Smart Steroid Profiling



Detection of metabolic disorders

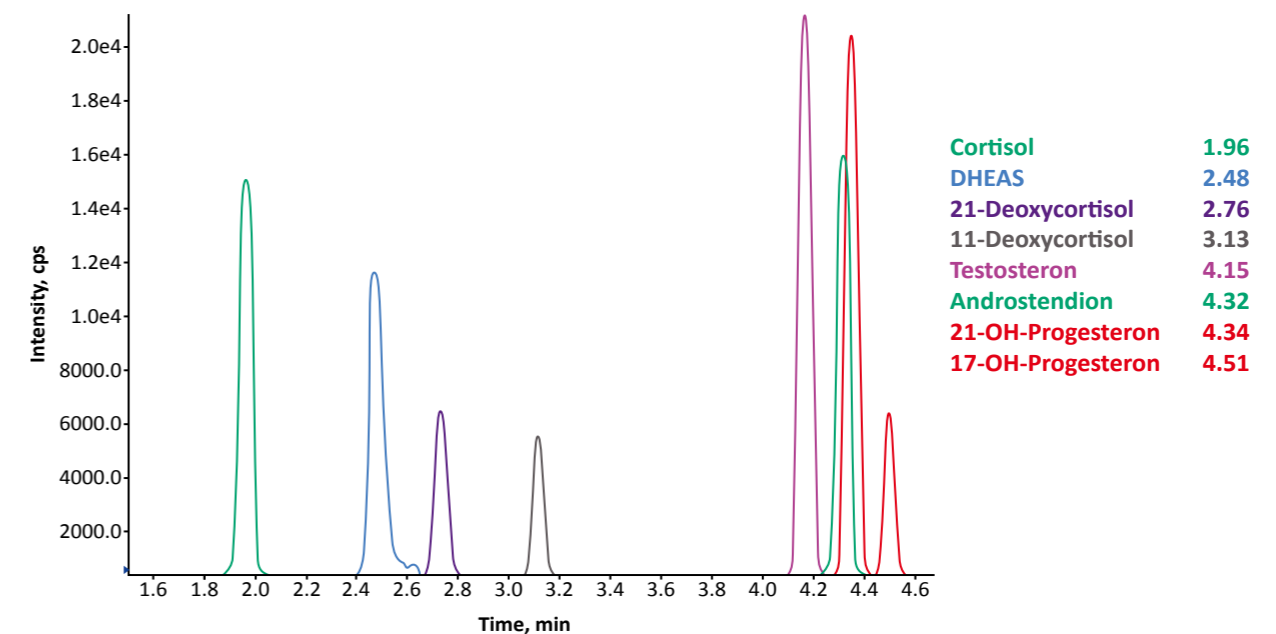


## Smart Metabolic Profiling of Steroid Hormones

Steroid hormones are synthesised from cholesterol. The majority of these powerful molecules are produced by the adrenal glands, testes or ovaries. They fulfill a wide range of physiological functions after binding to specific cell receptors of various target organs. Mainly, they are involved in the carbohydrate, lipid and protein metabolism, stress response, regulation of the water and mineral balance, reproductive processes and development of secondary sex characteristics. Consequently, steroid hormones are also involved in a variety of diseases, like adrenal tumors, the Adrenogenital

Syndrome (CAH), the Cushing's Syndrome or the Polycystic Ovarian Syndrome. Synthetic steroids are used in medical treatment of acute and chronic diseases, e.g. gonadal dysfunction, allergies and suppression of immune responses. Quantitative profiling of steroids is essential in diagnosis and evaluation of pathologic conditions and therapeutic responses. RECIPE developed a fast and simple quantitative Steroid Profiling LC-MS/MS method that covers the most relevant steroid hormones. Thus, enables the recognition of significant changes of individual steroid profiles.

Chromatogram of the ClinChek® Serum Control Level II (order no. MS12081)



### The Analytes and labelled Internal Standards (IS)

- + Cortisol / Cortisol-d4
- + Testosterone / Testosterone-d3
- + Androstenedione / Androstenedione-d7
- + 11-Deoxycortisol / 11-Deoxycortisol-d5
- + 21-Deoxycortisol / 11-Deoxycortisol-d5
- + 17-OH-Progesterone / 17-OH-Progesterone-d8
- + 21-OH-Progesterone / 17-OH-Progesterone-d8
- + DHEAS / DHEAS-d5

### Smart Profiling

- + Covers the most recognised steroid metabolites for diagnostic purposes in one kit
- + Suitable for CAH, PCOS and Hypercorticism (Cushing Syndrome) testing
- + All steroid metabolites in a 6 min run
- + Sample preparation in a few minutes

## Your choice in HPLC & LC-MS/MS diagnostics

- + Certified and quality approved CE-IVD solutions
- + Unique metabolic profiling of steroid hormones
- + Preferred partner in more than 80 countries



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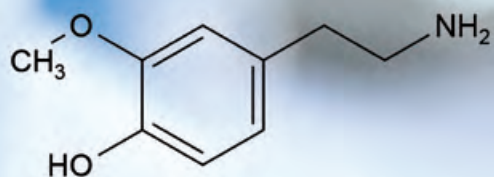
PROTON IMPEX 2000 SRL

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[www.shimadzumedical.ro](http://www.shimadzumedical.ro)

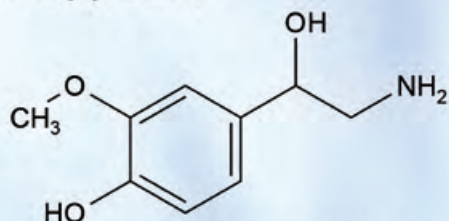


# RECIPE®

 **SHIMADZU**  
Excellence in Science



3-Methoxytyramine



Normetanephrine



ClinMass® LC-MS/MS Complete Kits for

## Free Metanephrines in Plasma

SPE-column extraction or  
ONE-STEP sample preparation

### Benefits:

- Highly sensitive and selective CE-IVD LC-MS/MS methods
- Fast and easy sample preparation
- Isotope labelled internal standards for all analytes

Two  
methods  
available

# ClinMass® LC-MS/MS Complete Kits for Free Metanephrines in Plasma

## Clinical Background

Pheochromocytomas and paragangliomas (PPGL) are rare tumors that arise from adrenal and extraadrenal chromaffin tissue. PPGL produce excessive amounts of catecholamines (epinephrine, norepinephrine, dopamine) and their metabolites, the metanephrines (metanephrine, normetanephrine and 3-methoxytyramine). Measurement of metanephrines provides a particularly sensitive test for the diagnosis of pheochromocytoma [1]. Compared to tests using catecholamines or other metabolites it offers the best diagnostic performance [2].

## Higher accuracy of plasma over urinary metanephrines

Plasma free metanephrines (PFM) are well-established parameters with adequate reference values [3, 4] and have a higher diagnostic accuracy than metanephrines in urine, which has been confirmed by several independent studies (Table 1) [5, 6]. These results suggest higher sensitivity and specificity of the plasma than the urine test [2].

**Table 1:** Comparison of diagnostic performance of plasma free vs. urinary fractionated metanephrines [6]

|        | Sensitivity | Specificity |
|--------|-------------|-------------|
| Plasma | 99 %        | 89 %        |
| Urine  | 97 %        | 69 %        |

## LC-MS/MS is the method of choice

To establish a biochemical diagnosis of PPGL, the use of liquid chromatography with tandem mass spectrometric detection (LC-MS/MS) is suggested rather than other laboratory methods [6]. LC-MS/MS represents the method of choice for high-throughput, low-cost, precise and accurate measurements of the catecholamine metabolites [7].



The ClinMass® LC-MS/MS Complete Kits represent highly sensitive and selective CE-IVD methods for the determination of plasma free metanephrines (PFM). **There are two methods available:**

### PFM analysis with SPE-column extraction using standard LC systems (MS11100)

- No dilution or evaporation steps required
- measurement of highly concentrated samples guaranteed
- injection interval of 4 min

### PFM analysis with one-step sample preparation using two-dimensional LC-systems (on-line, MS1000)

- LC-MS/MS Complete Kit with simple and short one-step sample pretreatment (protein precipitation)
- designed for high sample throughput via on-line SPE
- injection interval of 6 min

Our calibrators are intended for calibration of the LC-MS/MS system. For this, we offer matrix based ClinCal® Multilevel Calibrator Sets (5 levels). For internal quality assurance, matrix based ClinChek® Controls are available in 3 levels. The accuracy is being checked by regular successful participation at RCPA Quality Assurance Programs (RCPAQAP). Matrix effects are compensated using isotope labelled internal standards.

## References:

- [1] Lenders JWM, Willemsen JJ, Eisenhofer G, Ross HA, Pacak K, Timmers HJ, Sweep CG. Is supine rest necessary before blood sampling for plasma metanephrines? *Clin Chem*. 2007; 53:352–354.
- [2] van Berkel A, Lenders JWM, Timmers HJLM. Diagnosis of endocrine disease: biochemical diagnosis of pheochromocytoma and paraganglioma. *European Journal of Endocrinology*. 2014; 170 R109–R119.
- [3] Eisenhofer G, Lenders JWM, Siegert G, Bornstein SR, Friberg P, Milosevic D, Mannelli M, Marston Linehan W, Adams K, Timmers HJ, Pacak K. Plasma methoxytyramine: A novel biomarker of metastatic pheochromocytoma and paraganglioma in relation to established risk factors of tumor size, location and SDHB mutation status. *Eur J Cancer*. 2012; 48(11), 1739–1749.
- [4] Eisenhofer G, Lattke P, Herberg M, Siegert G, Qin N, Därr R, Hoyer J, Willringer A, Prejbisz A, Januszewicz A, Remaley A, Martucci V, Pacak K, Alec Ross H, Sweep FCGJ, Lenders JWM. Reference intervals for plasma free metanephrines with an age adjustment for normetanephrine for optimized laboratory testing of pheochromocytoma. *Ann Clin Biochem*. 2013; 50:62–69.
- [5] Lenders JWM, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, Keiser HR, Goldstein DS, Eisenhofer G. Biochemical diagnosis of pheochromocytoma: which test is best? *Jama*. 2002; 287(11): 1427–34.
- [6] Lenders JWM, Duh Q-Y, Eisenhofer G, Gimenez-Roqueplo A-P, Grebe SKG, Murad MH, Naruse M, Pacak K, Young WF. Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2014; 99(6), 1915–1942.
- [7] Eisenhofer G, Peitzsch M, McWhinney BC. Impact of LC-MS/MS on the laboratory diagnosis of catecholamine-producing tumors. *Trends in Analytical Chemistry*. 2016; 84, 106–116

## LC-MS/MS Parameters

### LC-Parameters

Binary HPLC pump: Mobile Phases A / B (0.6 ml/min)  
 Injection volume: 20 - 50 µl  
 Injection interval: 4.0 min  
 Column heater: 25 °C

### MS-Parameters

Ion-Source: ESI positive  
 MS/MS-Mode: MRM

### Test Data

Linearity (up to): 20970 ng/l (M), 19860 ng/l (NM), 5094 ng/l (MT)  
 Recovery: 95 - 98 %  
 LOD: 0.97 ng/l (M), 0.92 ng/l (NM), 0.94 ng/l (MT)  
 LLOQ: 2.91 ng/l (M), 2.76 ng/l (NM), 2.83 ng/l (MT)  
 Intraassay precision: 2.0 % (M), 4.4 % (NM), 3.7 % (MT)  
 Interassay precision: 3.1 % (M), 3.2 % (NM), 3.4 % (MT)

M: Metanephrine  
 NM: Normetanephrine  
 MT: 3-Methoxytyramine

## Sample Preparation

### Extraction:

|   |                             |
|---|-----------------------------|
| Apply (conditioned* sample preparation column): |                             |
| 500 µl Sample (calibrator, control, patient)    | 500 µl Internal Standard IS |

↓ wash with Washing Solution W2, W1 and W3

### Elution:

|   |
|---|
| Elute with 2 x 100 µl Eluting Reagent E |
|---|

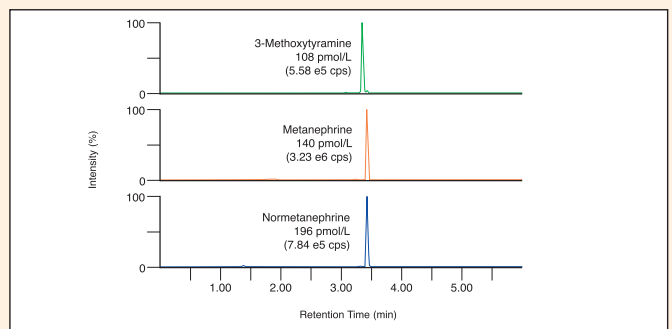
↓ collect the eluate

### LC-MS/MS Analysis:

|                   |
|-------------------|
| Inject 20 - 50 µl |
|-------------------|

\* Conditioning with Washing Solution W1 and W2

### Chromatogram of the ClinCal® Calibrator, Level 1 (order no. MS11013)



## LC-MS/MS Parameters

### LC-Parameters

Pump 1: SPE-buffer (0.1 - 1.0 ml/min)  
 Pump 2: Mobile phase A / B (0.6 ml/min)  
 Injection volume: 50 µl  
 Injection interval: 6.0 min  
 Switching valve: automatic switching valve, 6-port/3-channel  
 Column heater: 25 °C

### MS-Parameters

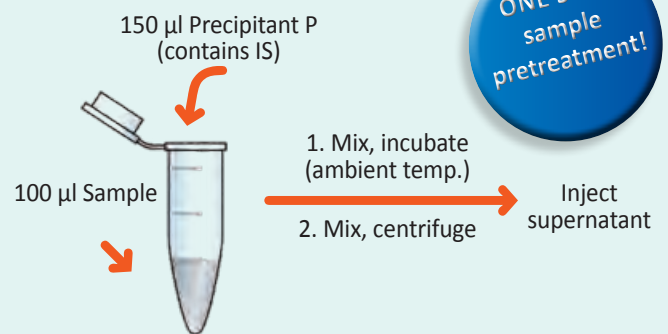
Ion-Source: ESI positive  
 MS/MS-Mode: MRM

### Test Data

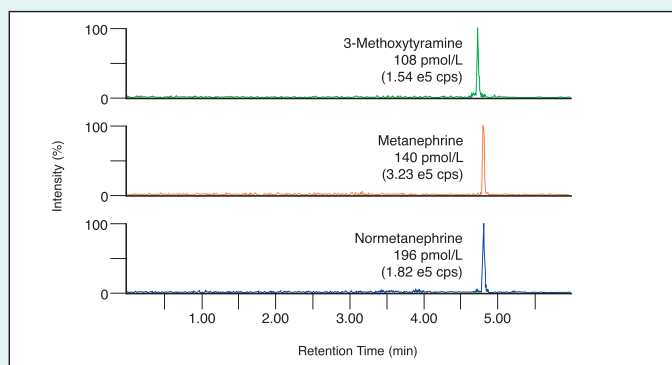
Linearity (up to): 5200 ng/l (M), 10000 ng/l (NM, MT)  
 Recovery: 83 - 116 %  
 LOD: 1.94 ng/l (M), 3.67 ng/l (NM), 0.94 ng/l (MT)  
 LLOQ: 5.82 ng/l (M), 11.0 ng/l (NM), 2.83 ng/l (MT)  
 Intraassay precision: 3.1 % (M), 4.5 % (NM), 3.4 % (MT)  
 Interassay precision: 3.2 % (M), 4.7 % (NM), 4.1 % (MT)

M: Metanephrine  
 NM: Normetanephrine  
 MT: 3-Methoxytyramine

## Sample Preparation



### Chromatogram of the ClinCal® Calibrator, Level 1 (order no. MS11013)



## Analysis with SPE-column extraction

| Order No.                           | Description  | Quantity                  |
|-------------------------------------|--|---------------------------|
| <b>MS11100</b>                      | <b>ClinMass® Complete Kit for Free Metanephrines in Plasma, for 200 assays</b> | <b>1 pce.</b>             |
| <b>Contents (order no. MS11100)</b> |  |                           |
| MS11005                             | Autosampler Washing Solution   | 1000 ml                   |
| MS11007                             | Mobile Phase A   | 250 ml                    |
| MS11008                             | Mobile Phase B   | 2 x MS11008 (2 x 1000 ml) |
| MS11112                             | Internal Standard IS   | 2 x MS11112 (2 x 50 ml)   |
| MS11013                             | Serum Calibrator Set, lyophil. (Level 0 - 4)                                   | 5 x 1 x 3 ml              |
| MS11120                             | Sample Preparation Columns   | 4 x MS11120 (4 x 50 pcs.) |
| MS11121                             | Washing Solution W1  | 400 ml                    |
| MS11122                             | Washing Solution W2  | 400 ml                    |
| MS11123                             | Washing Solution W3  | 200 ml                    |
| MS11124                             | Eluting Reagent E  | 40 ml                     |
|                                     | Manual   |                           |
| <b>Additional Components</b>        |  |                           |
| MS11014                             | Optimisation Mix   | 2 ml                      |
| <b>Start Accessories</b>            |  |                           |
| MS11030                             | Analytical Column with test chromatogram                                       | 1 pce.                    |
| <b>Accessories</b>                  |  |                           |
| MS11161                             | Elution Vials  | 100 pcs.                  |
| <b>ClinChek® Controls</b>           |  |                           |
| MS11080                             | Serum Control, lyophil., Level I   | 10 x 3 ml                 |
| MS11081                             | Serum Control, lyophil., Level II  | 10 x 3 ml                 |
| MS11082                             | Serum Control, lyophil., Level III   | 10 x 3 ml                 |
| MS11083                             | Serum Control, lyophil., Level I, II, III                                      | 3 x 3 x 3 ml              |

## Analysis with one-step sample preparation (on-line)

| Order No.                           | Description   | Quantity                   |
|-------------------------------------|---|----------------------------|
| <b>MS11000</b>                      | <b>ClinMass® Complete Kit for Free Metanephrines in Plasma – on-line Analysis, for 200 assays</b> | <b>1 pce.</b>              |
| <b>Contents (order no. MS11000)</b> |   |                            |
| MS11005                             | Autosampler Washing Solution  | 1000 ml                    |
| MS11007                             | Mobile Phase A  | 250 ml                     |
| MS11008                             | Mobile Phase B  | 2 x MS11008 (2 x 1000 ml)  |
| MS11009                             | SPE-Buffer Load L   | 2 x MS11009 (2 x 1000 ml)  |
| MS11010                             | SPE-Buffer Wash W   | 1000 ml                    |
| MS11012                             | Precipitant P with Internal Standard  | 30 ml                      |
| MS11013                             | Serum Calibrator Set, lyophil. (Level 0 - 4)  | 5 x 1 x 3 ml               |
| MS11020                             | Sample Pretreatment Vials   | 2 x MS11020 (2 x 100 pcs.) |
|                                     | Manual  |                            |
| <b>Additional Components</b>        |   |                            |
| MS11014                             | Optimisation Mix  | 2 ml                       |
| <b>Start Accessories</b>            |   |                            |
| MS11030                             | Analytical Column with test chromatogram  | 1 pce.                     |
| MS11031                             | SPE-Column  | 1 pce.                     |
| <b>ClinChek® Controls</b>           |   |                            |
| MS11080                             | Serum Control, lyophil., Level I  | 10 x 3 ml                  |
| MS11081                             | Serum Control, lyophil., Level II   | 10 x 3 ml                  |
| MS11082                             | Serum Control, lyophil., Level III  | 10 x 3 ml                  |
| MS11083                             | Serum Control, lyophil., Level I, II, III   | 3 x 3 x 3 ml               |



# RECIPE®

**SHIMADZU**  
Excellence in Science



Screening / Detection of

## Inborn Errors of Metabolism

CE-IVD certified products for HPLC & LC-MS/MS

### Complete Kits for HPLC and LC-MS/MS Analysis

- Amino Acids and Acylcarnitines in Dried Blood Spots, derivatised and non-derivatised
- Aromatic Amino Acids in Plasma
- Homocysteine in Dried Blood Spots
- Homocysteine in Plasma / Serum
- Methylmalonic Acid in Serum / Plasma / Urine



Reference Material for Amino Acid Analyser



Complete Kits for HPLC and LC-MS/MS Analysis

# Neonatal Screening



## ClinSpot® LC-MS/MS Complete Kit

**Amino Acids and Acylcarnitines in Dried Blood Spots (DBS), *derivatised*** Order nos. MS10000, MS10100 (with filter plates)

- Method according to CLSI NBS-04A
- Reliable screening in 1.6 min only
- Dried blood spots controls included

The RECIPE ClinSpot® Complete Kit provides reliable screening by determination of the amino acids and acylcarnitines profile. The entire sample preparation is performed with 96-well plates (MS10000), alternatively also in combination with filter plates (MS10100) in order to ensure a high sample throughput.

### Analytes:

| Amino acids   | Acylcarnitines | Additional acylcarnitines |                  |
|---------------|----------------|---------------------------|------------------|
| Alanine       | Carnitin       | C3DC-Carnitin             | C16:1-Carnitin   |
| Arginine      | C2-Carnitin    | C4OH-Carnitin             | C16:1OH-Carnitin |
| Aspartic acid | C3-Carnitin    | C4DC-Carnitin             | C16OH-Carnitin   |
| Citrulline    | C4-Carnitin    | C5:1-Carnitin             | C18:2-Carnitin   |
| Glutamic acid | C5-Carnitin    | C5OH-Carnitin             | C18:1-Carnitin   |
| Glycine       | C5DC-Carnitin  | C6DC-Carnitin             | C18:2OH-Carnitin |
| Leucine       | C6-Carnitin    | C8:1-Carnitin             | C18:1OH-Carnitin |
| Methionine    | C8-Carnitin    | C10:2-Carnitin            | C18OH-Carnitin   |
| Ornithine     | C10-Carnitin   | C10:1-Carnitin            |                  |
| Phenylalanine | C12-Carnitin   | C12:1-Carnitin            |                  |
| Proline       | C14-Carnitin   | C14:2-Carnitin            |                  |
| Tyrosine      | C16-Carnitin   | C14:1-Carnitin            |                  |
| Valine        | C18-Carnitin   | C14OH-Carnitin            |                  |

## ClinSpot® LC-MS/MS Complete Kit

**Amino Acids and Acylcarnitines in Dried Blood Spots (DBS), *non-derivatised*** Order nos. MS10200, MS10300 (with filter plates)

This ClinSpot® Complete Kit, non-derivatised, stands out for its fast and easy sample preparation. Samples can be injected directly after an extraction step. The entire sample preparation is performed with 96-well plates (MS10200), alternatively also in combination with filter plates (MS10300) in order to ensure a high sample throughput.

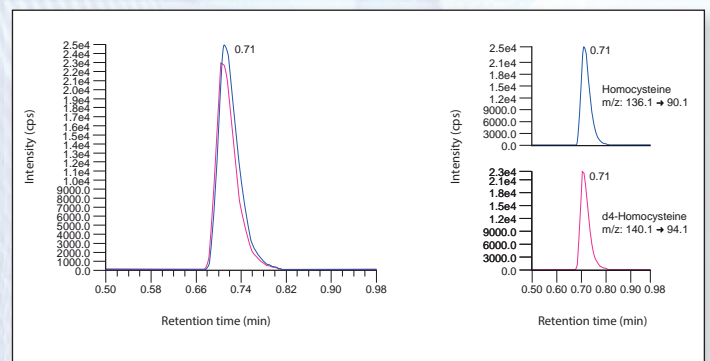


## ClinSpot® LC-MS/MS Complete Kit

**Homocysteine in Dried Blood Spots (DBS)** Order no. MS2100

- Reliable determination of total homocysteine
- Simple and quick two-step sample preparation
- Injection interval: 1.0 min

The determination of homocysteine in dried blood spots (DBS) is used for the newborn screening for inherited defects of the methionine metabolism (homocystinuria). The RECIPE ClinMass® Complete Kit allows a reliable determination of total homocysteine from filter spot specimen with a simple and quick sample preparation and an injection interval of 1 min only.



# Detection of Metabolic Diseases

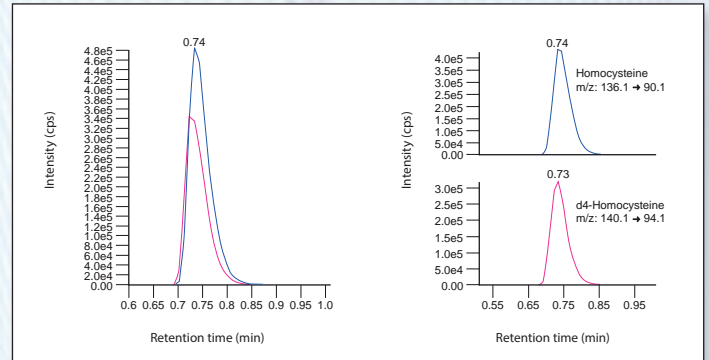


## ClinMass® LC-MS/MS Complete Kit

### Homocysteine in Plasma / Serum Order no. MS2000

- Reliable monitoring of total homocysteine
- Simple and quick two-step sample preparation
- Injection interval: 1.0 min only

The ClinMass® Complete Kit allows a reliable determination of total homocysteine for the detection of hyperhomocysteinemia. After an easy sample preparation the samples are analysed with an injection interval of 1.0 min only.

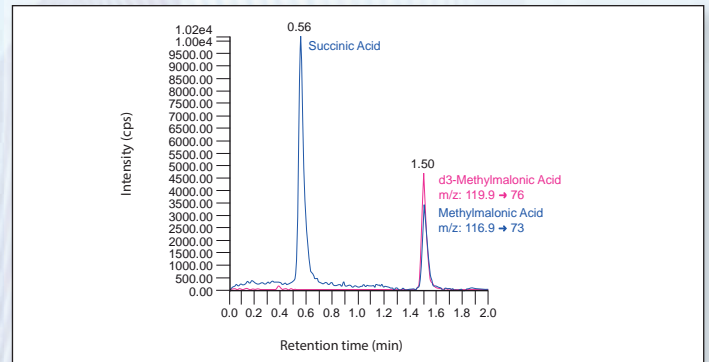


## ClinMass® LC-MS/MS Complete Kit

### Methylmalonic Acid in Serum / Plasma / Urine, *advanced* Order no. MS5100

- Easy one-step sample preparation (serum / plasma)
- Reliable separation of succinic acid
- Injection interval: 2.0 min

This ClinMass® Complete Kit provides a fast and time saving analysis of methylmalonic acid (MMA) for the detection of methylmalonic acidemia. Sample preparation is performed with only one pipetting step (serum, plasma) or direct injection of samples after dilution and addition of internal standard (urine). With subsequent LC-MS/MS analysis within a 2 min injection interval only, the isobar component succinic acid, which may interfere with MMA, is separated reliably.



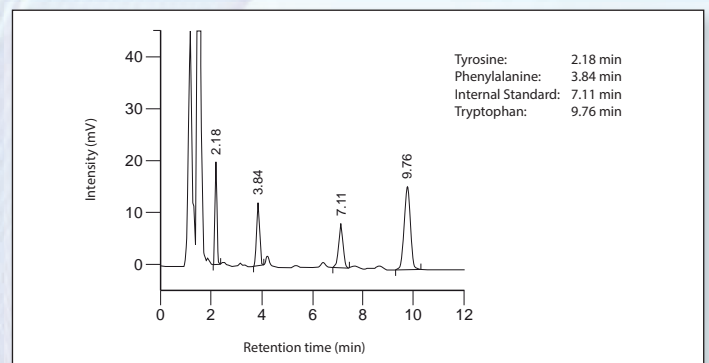
## ClinRep® HPLC Complete Kit

### Aromatic Amino Acids in Plasma Order no. 10000

- Easy sample preparation
- High analytical sensitivity
- Reliable monitoring

Several metabolic disorders result from an impaired amino acid metabolism. The ClinRep® Complete Kit serves for the analysis of the amino acids phenylalanine, tyrosine and tryptophan and may be used for the monitoring of the blood plasma level within a dietary therapy.

**Important notice:** This kit is not intended for use in neonatal screening programmes and especially not for PKU diagnosis. For this diagnostic purpose two legally approved ClinMass® LC-MS/MS Complete Kits (MS10000, MS10100) are provided.



# Reference Material for Amino Acid Analyser



## ClinCal® Plasma Calibrator for Amino Acids

### Intended use:

ClinCal® Plasma Calibrators are used for calibration of your analysis system. This lyophilised calibrator is based on human plasma and is intended for a singlepoint calibration.

### Analytes:

|                     |                  |                   |            |
|---------------------|------------------|-------------------|------------|
| Alanine             | Glutamine        | Lysine            | Serine     |
| α-Aminobutyric Acid | Glycine          | Methionine        | Taurine    |
| Arginine            | Histidin         | 1-Methyl-Histidin | Threonine  |
| Asparagine          | 4-Hydroxyproline | 3-Methyl-Histidin | Tryptophan |
| Aspartic Aci        | allo-Isoleucine  | Ornithine         | Tyrosine   |
| Citrulline          | Isoleucine       | Phenylalanine     | Urea       |
| Glutamic Acid       | Leucine          | Proline           | Valine     |

| Order No. | Description  | Quantity |
|-----------|--|----------|
| 10213     | Plasma Calibrator, lyophilised, for Amino Acids (by Amino Acid Analyser) | 5 x 3 ml |

## ClinChek® Plasma Control for Amino Acids

### Intended use:

ClinChek® Plasma Controls are used for internal quality assurance in clinical-chemical laboratories. These lyophilised controls are based on human plasma and are available with mean values in the normal as well as in the pathological range.

### Analytes:

|                     |                  |                   |            |
|---------------------|------------------|-------------------|------------|
| Alanine             | Glutamine        | Lysine            | Serine     |
| α-Aminobutyric Acid | Glycine          | Methionine        | Taurine    |
| Arginine            | Histidin         | 1-Methyl-Histidin | Threonine  |
| Asparagine          | 4-Hydroxyproline | 3-Methyl-Histidin | Tryptophan |
| Aspartic Aci        | allo-Isoleucine  | Ornithine         | Tyrosine   |
| Citrulline          | Isoleucine       | Phenylalanine     | Urea       |
| Glutamic Acid       | Leucine          | Proline           | Valine     |

| Order No. | Description  | Quantity     |
|-----------|--|--------------|
| 10280     | Plasma Control, lyophilised, for Amino Acids (by Amino Acid Analyser), Level I     | 10 x 3 ml    |
| 10281     | Plasma Control, lyophilised, for Amino Acids (by Amino Acid Analyser), Level II    | 10 x 3 ml    |
| 10282     | Plasma Control, lyophilised, for Amino Acids (by Amino Acid Analyser), Level I, II | 2 x 5 x 3 ml |



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[www.proton.com.ro](http://www.proton.com.ro) | [www.imagisticamedicala.ro](http://www.imagisticamedicala.ro) |  
[www.shimadzumedical.ro](http://www.shimadzumedical.ro)

# ClinMass<sup>®</sup> TDM 200 Kit System

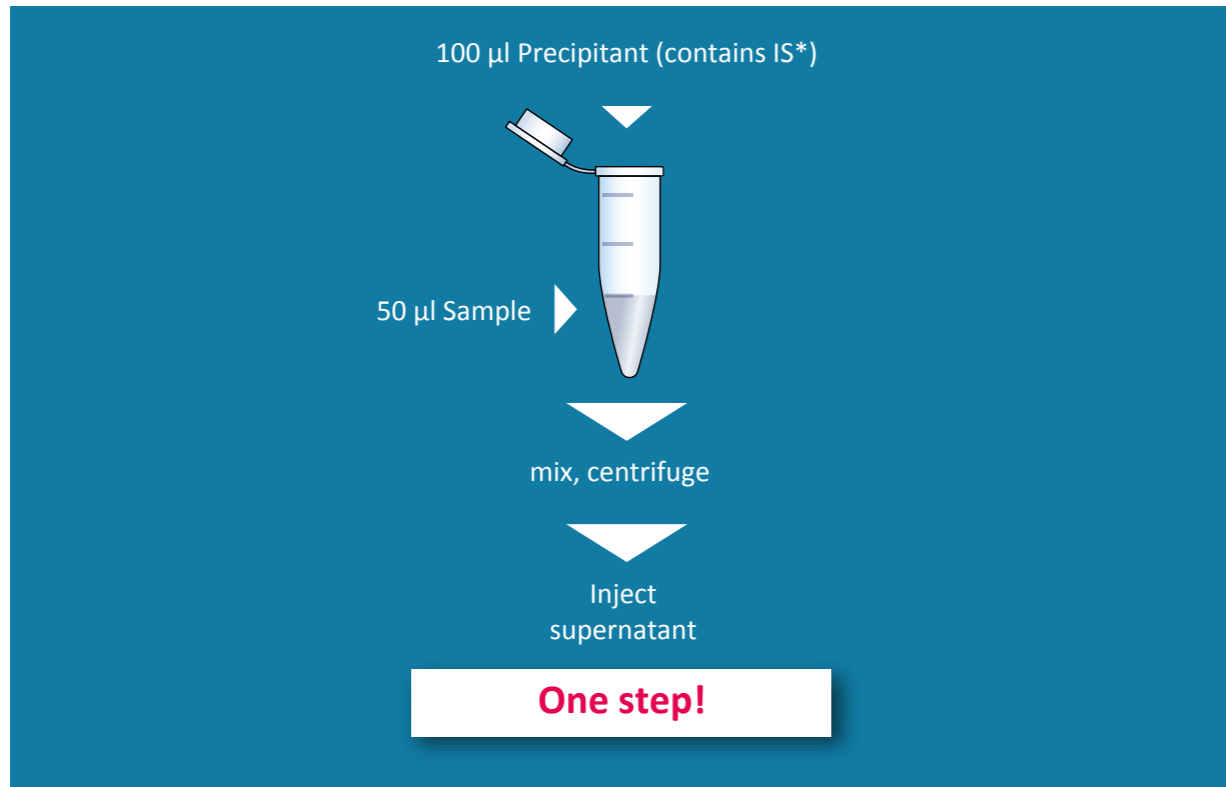


*also available:*  
**TDM<sup>i</sup>**



**Therapeutic Drug Monitoring (TDM)  
by LC-MS/MS**

# The RECIPE TDM 200 Kit System



The **ClinMass® TDM Kit System** offers you the possibility to determine more than 155 different analytical parameters with **one** Kit System (sample preparation, mobile phases and analytical column).

**155 analytical parameters  
in 7 Add-on Sets**



\* Internal Standards available for most analytes.

# The RECIPE TDM<sup>i</sup> Kit Solution



The **TDM 200 Kit System** is also available as **TDM<sup>i</sup> Kit Solution** with direct injection of matrix.

## Direct Injection Technology

Internal Standard is added to native serum or plasma sample, calibrator or control automatically by just one simple pipetting step of the autosampler followed by direct injection of the individual samples into the chromatographic system. Subsequently, the analytes are separated and determined by on-line analysis.

## Simplify your lab-routine

- + By direct injection of matrix
- + Retention times < 7 min.
- + Small sample volume needed < 20 µl

| ADP                       | 37 Antidepressants     | Order no. MS9400        |
|---------------------------|------------------------|-------------------------|
| Agomelatine               | Fluoxetine             | Paroxetine              |
| Atomoxetine               | Fluvoxamine            | Reboxetine              |
| Bupropion                 | Guanfacine             | Ritalinic Acid          |
| Citalopram                | Hydroxybupropion       | Sertraline              |
| Clomethiazole             | Methylphenidate        | threo-Dihydro-Bupropion |
| Desmethylcitalopram       | Mianserine             | Tianeptine              |
| Desmethylfluoxetine       | Milnacipran            | Tramadol                |
| Desmethylmianserine       | Mirtazapine            | Tranlycypromine         |
| Desmethylmirtazapine      | Moclobemide            | Trazodone               |
| Desmethylsertraline       | Nefazodone             | Venlafaxine             |
| Dosulepin                 | O-Desmethyltramadol    | Vortioxetine            |
| Duloxetine                | O-Desmethylvenlafaxine |                         |
| erythro-Dihydro-Bupropion | Opipramol              |                         |

| 36 Benzodiazepines   |                        | Order no. MS9500 | BZP |
|----------------------|------------------------|------------------|-----|
| 3-Hydroxybromazepam  | Demoxepam              | Nordiazepam      |     |
| 7-Aminoclonazepam    | Desalkylflurazepam     | Oxazepam         |     |
| 7-Aminoflunitrazepam | Desmethylflunitrazepam | Prazepam         |     |
| 7-Aminonitrazepam    | Diazepam               | Temazepam        |     |
| α-Hydroxyalprazolam  | Estazolam              | Tetrazepam       |     |
| α-Hydroxymidazolam   | Flunitrazepam          | Trazodone        |     |
| Alprazolam           | Flurazepam             | Triazolam        |     |
| Bromazepam           | Lorazepam              | Zaleplon         |     |
| Brotizolam           | Lormetazepam           | Zolpidem         |     |
| Chlordiazepoxide     | Medazepam              | Zopiclone        |     |
| Clobazam             | Midazolam              |                  |     |
| Clonazepam           | Nitrazepam             |                  |     |
|                      | Norclonazepam          |                  |     |

| AED                   | 26 Antiepileptic Drugs  | Order no. MS9200 |
|-----------------------|-------------------------|------------------|
| 10-OH-Carbamazepine   | Levetiracetam           | Retigabine       |
| Carbamazepine         | N-Desmethylnethsuximide | Rufinamide       |
| Carbamazepine-diol    | Oxcarbazepine           | Stiripentol      |
| Carbamazepine-epoxide | PEMA                    | Sulthiame        |
| Ethosuximide          | Perampanel              | Tiagabine        |
| Felbamate             | Phenobarbital           | Topiramate       |
| Gabapentine           | Phenytoin               | Valproic Acid    |
| Lacosamide            | Pregabalin              | Zonisamide       |
| Lamotrigine           | Primidone               |                  |

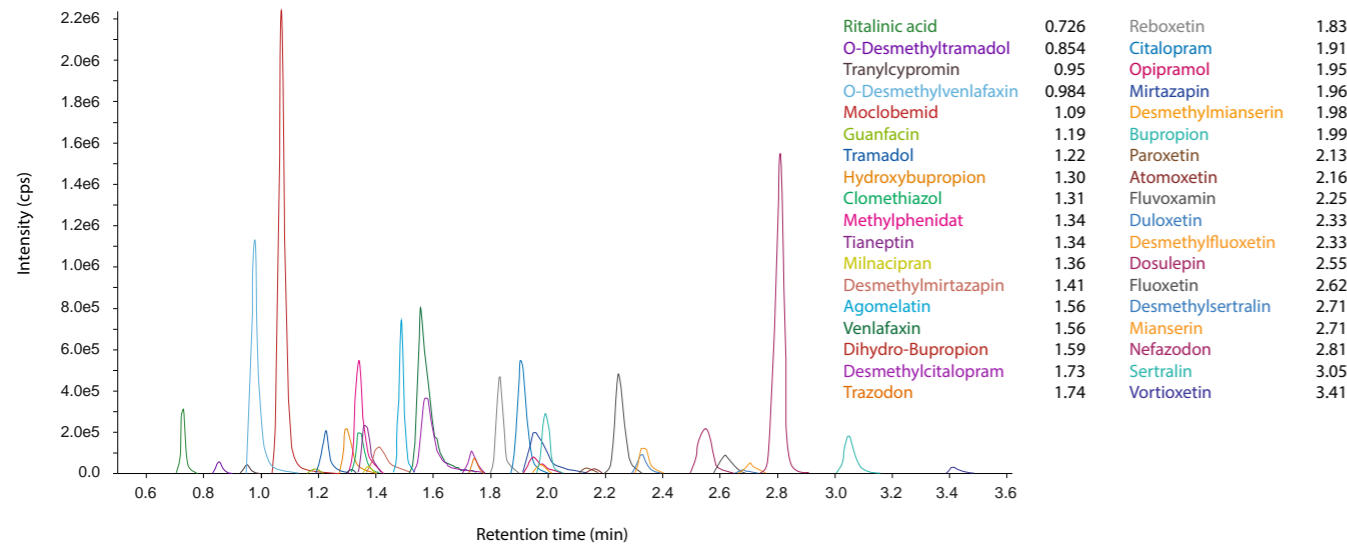
| 2 Mycophenolic Acid | Order no. MS99100             | MPA |
|---------------------|-------------------------------|-----|
| Mycophenolic acid   | Mycophenolic acid glucuronide |     |

| 28 Neuroleptics      | Order no. MS9300                | NLP            |
|----------------------|---------------------------------|----------------|
| Amisulpride          | Melperone                       | Sertindole     |
| Aripiprazole         | Norclozapine                    | Sulpiride      |
| Chlorpromazine       | Norquetiapine                   | Thioridazine   |
| Chlorprothixene      | Olanzapine                      | Ziprasidone    |
| Clozapine            | Paliperidone (9-OH-Risperidone) | Zotepine       |
| Dehydro-Aripiprazole | Perazine                        | Zuclopenthixol |
| Desmethylolanzapine  | Pipamperone                     |                |
| Flupentixol          | Promethazine                    |                |
| Fluphenazine         | Prothipendyl                    |                |
| Haloperidol          | Quetiapine                      |                |
| Levomepromazine      | Risperidone                     |                |

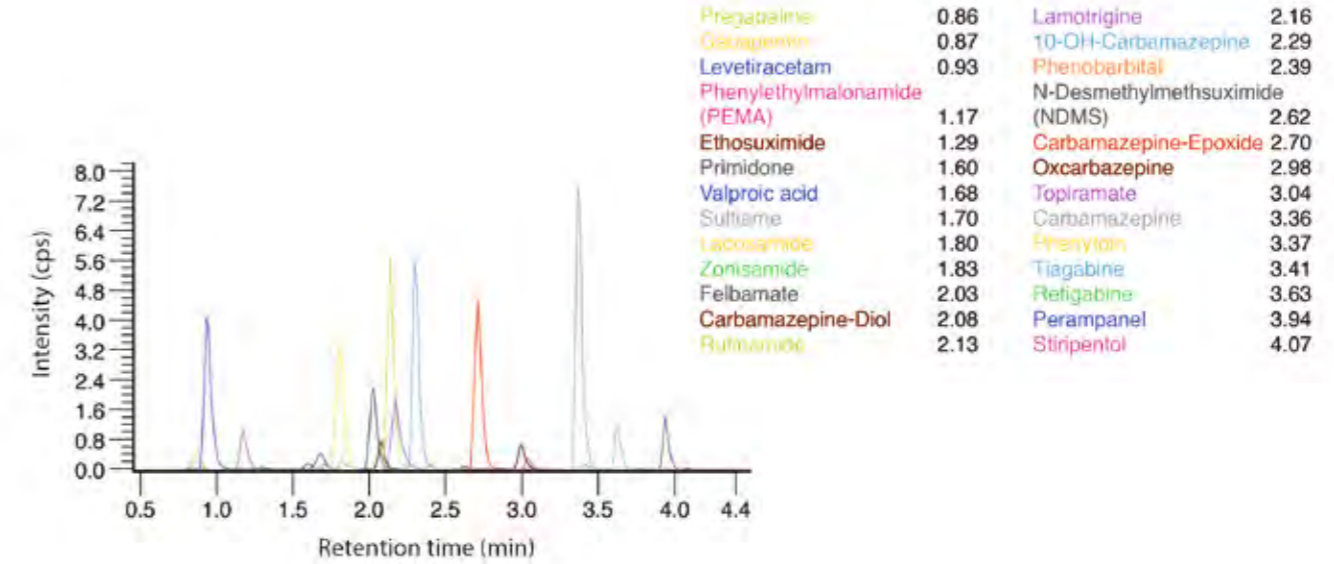
| AMC              | 11 Antimycotics | Order no. MS9600 |
|------------------|-----------------|------------------|
| 5-Fluorocytosine | Isavuconazole   | OH-Itraconazole  |
| Amphotericin B   | Itraconazole    | Posaconazole     |
| Anidulafungin    | Ketoconazole    | Voriconazole     |
| Fluconazole      | Micafungin      |                  |

| 15 Tricyclic Antidepressants | Order no. MS9100 | TCA             |
|------------------------------|------------------|-----------------|
| Amitriptyline                | Imipramine       | Normaprotiline  |
| Clomipramine                 | Maprotiline      | Nortrimipramine |
| Clozapine                    | Norclomipramine  | Nortriptyline   |
| Desipramine                  | Norclozapine     | Protriptyline   |
| Doxepin                      | Nordoxepin       | Trimipramine    |

ADP TDM Antidepressants

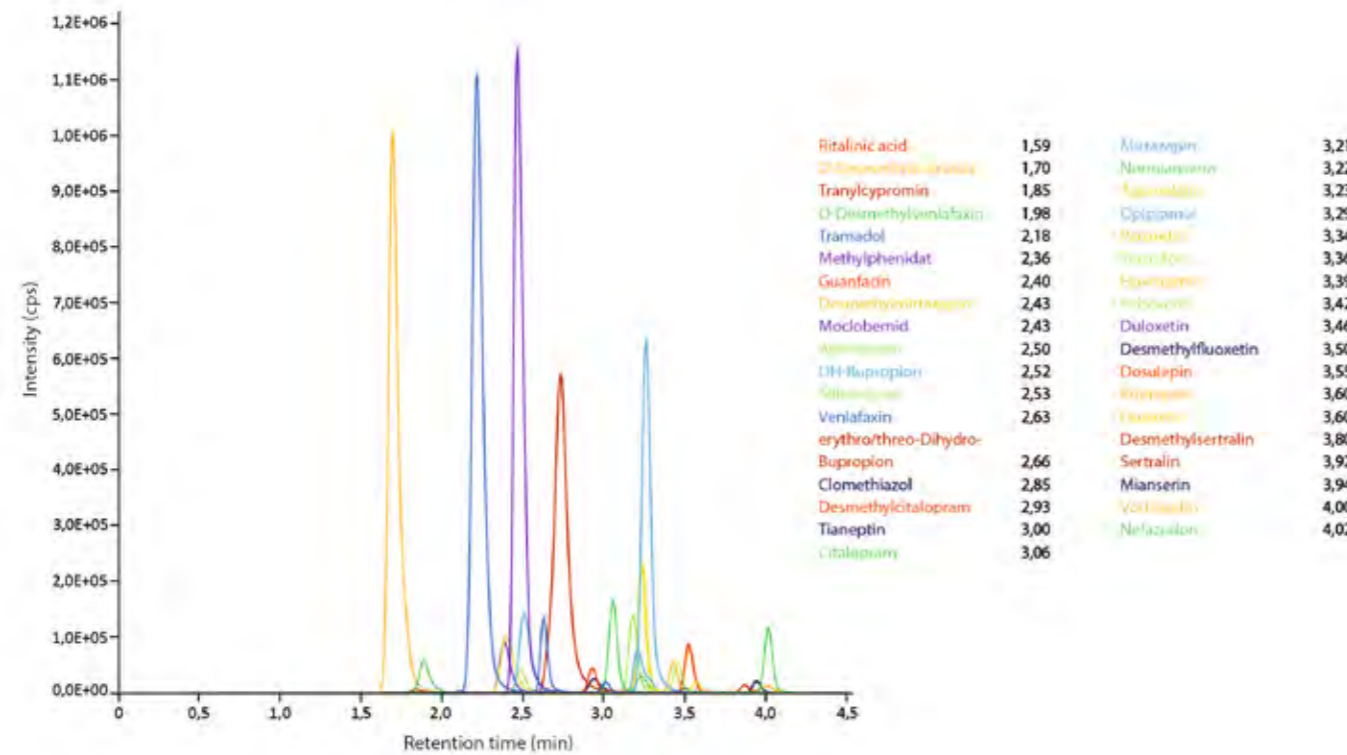


TDM Antiepileptic Drugs AED



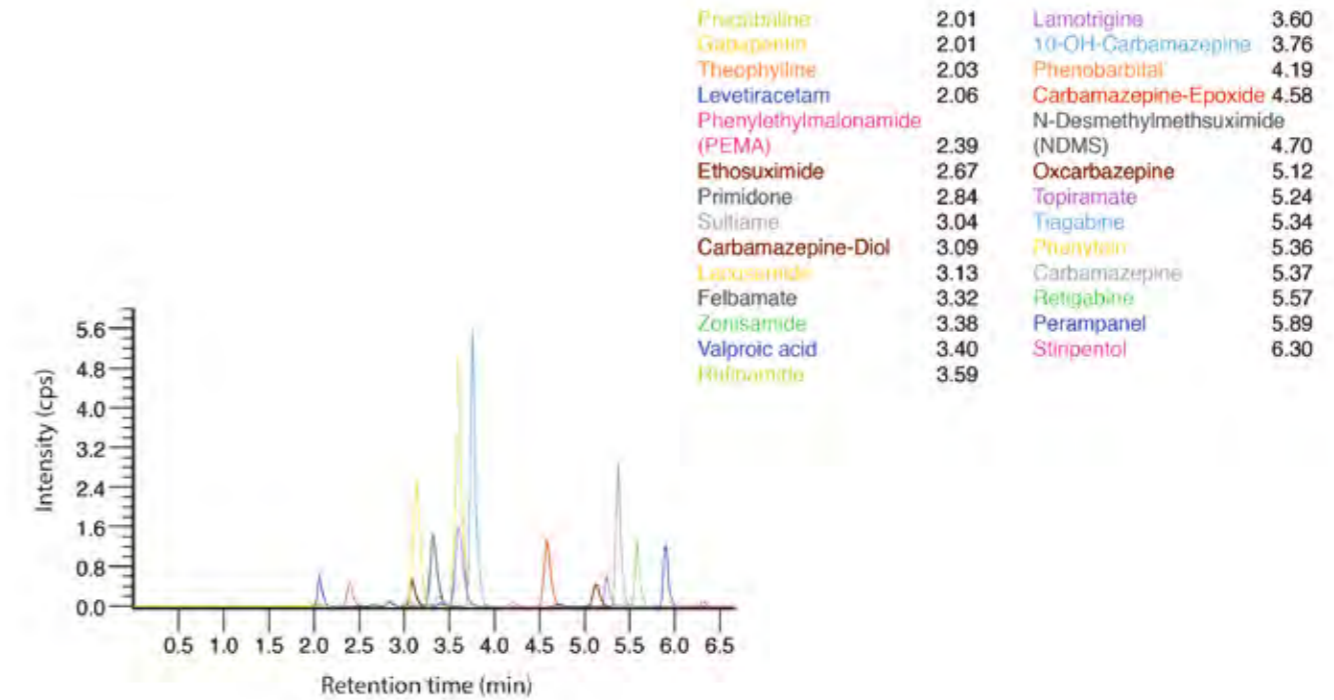
ADP TDM Antidepressants

Direct Injection

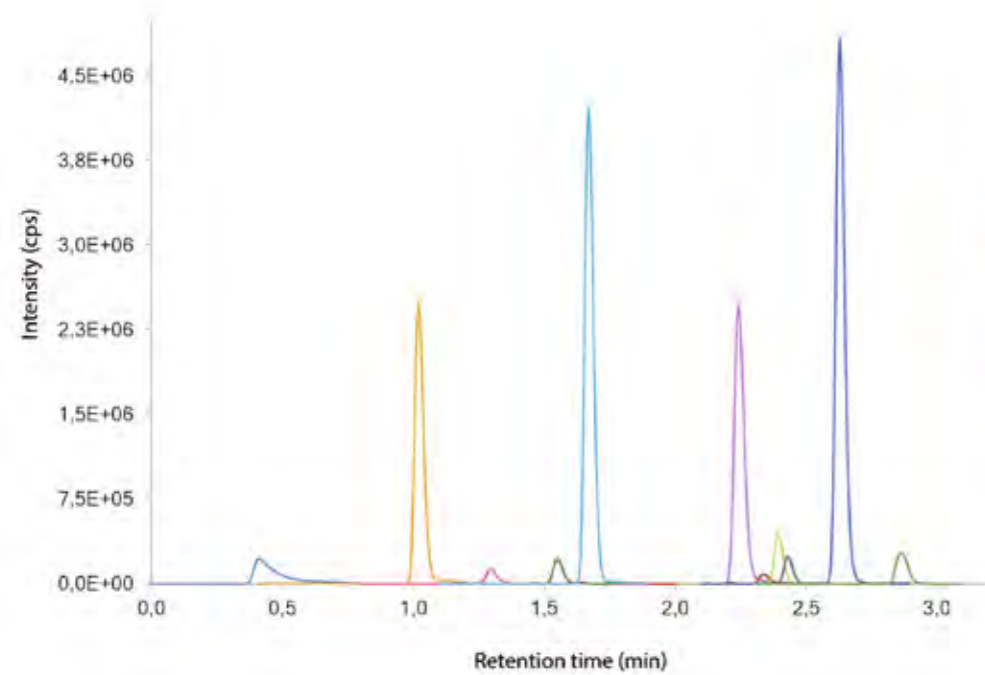


TDM Antiepileptic Drugs AED

Direct Injection

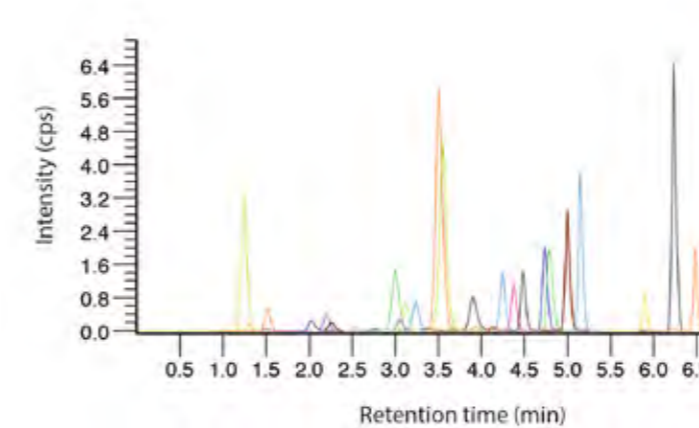


**AMC** **TDM** **Antimycotics**



|                      |      |
|----------------------|------|
| 5-Fluorocytosine     | 0.41 |
| Fluconazole          | 1.02 |
| Amphotericin B       | 1.30 |
| Micafungin           | 1.55 |
| Voriconazole         | 1.67 |
| Ketoconazole         | 2.24 |
| Anidulafungin        | 2.34 |
| Posaconazole         | 2.39 |
| Hydroxy-Itraconazole | 2.43 |
| Isavuconazole        | 2.63 |
| Itraconazole         | 2.86 |

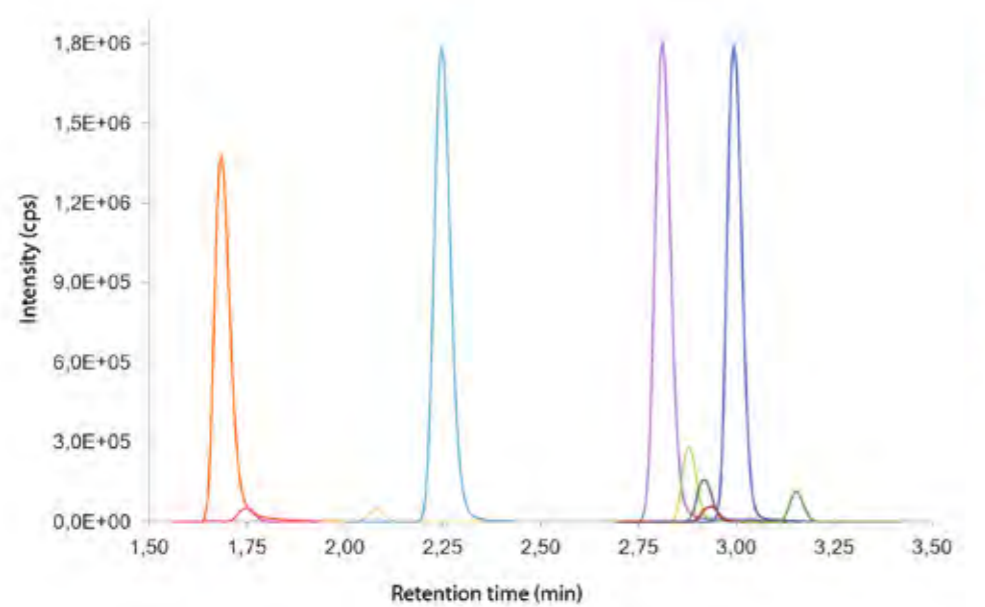
**TDM** **Benzodiazepines** **BZP**



|                        |      |                    |      |
|------------------------|------|--------------------|------|
| 7-Aminonitrazepam      | 1.24 | Chloriazepoxide    | 3.55 |
| 7-Aminoclonazepam      | 1.30 | Alprazolam         | 3.67 |
| 3-Hydroxybromazepam    | 1.50 | α-OH-Midazolam     | 3.90 |
| 7-Aminoflunitrazepam   | 1.51 | Triazolam          | 3.93 |
| Bromazepam             | 2.02 | Desalkylflurazepam | 4.12 |
| Demoxepam              | 2.19 | Flunitrazepam      | 4.13 |
| Zopiclon               | 2.26 | Temazepam          | 4.24 |
| Zolopion               | 2.52 | Brotizolam         | 4.35 |
| α-OH-Triazolam         | 2.74 | Nordiazepam        | 4.37 |
| α-OH-Alprazolam        | 2.75 | Clobazam           | 4.48 |
| Desmethylflunitrazepam | 2.89 | Lometazepam        | 4.61 |
| Oxazepam               | 3.00 | Trazodone          | 4.73 |
| Nitrazepam             | 3.06 | Flurazepam         | 4.79 |
| Estazolam              | 3.11 | Midazolam          | 4.99 |
| Norclonazepam          | 3.23 | Diazepam           | 5.14 |
| Lorazepam              | 3.37 | Tetraepam          | 5.90 |
| Clonazepam             | 3.44 | Prazepam           | 6.23 |
| Zolpidem               | 3.50 | Medazepam          | 6.48 |

**AMC** **TDM<sup>i</sup>** **Antimycotics**

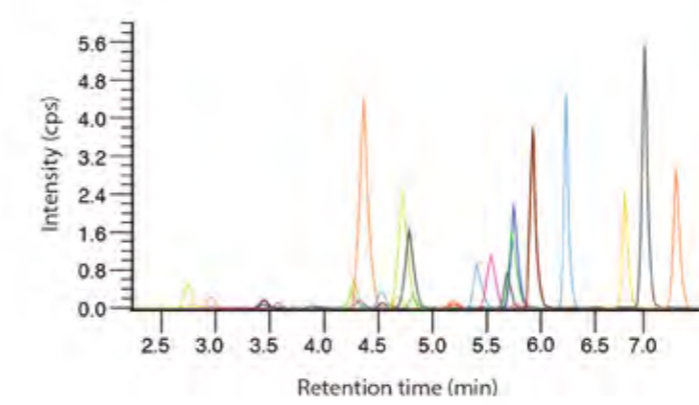
Direct Injection



|                      |      |
|----------------------|------|
| Fluconazole          | 1.69 |
| Amphotericin B       | 1.74 |
| Micafungin           | 2.09 |
| Voriconazole         | 2.25 |
| Ketoconazole         | 2.81 |
| Posaconazole         | 2.88 |
| Hydroxy-Itraconazole | 2.92 |
| Anidulafungin        | 2.94 |
| Isavuconazole        | 2.99 |
| Itraconazole         | 3.15 |

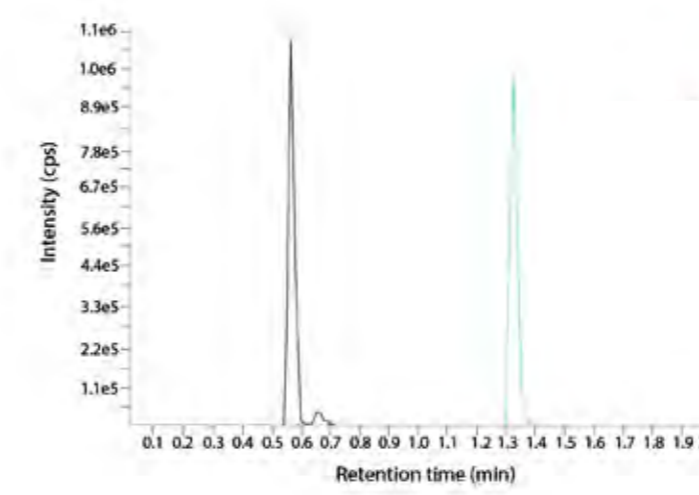
**TDM<sup>i</sup>** **Benzodiazepines** **BZP**

Direct Injection



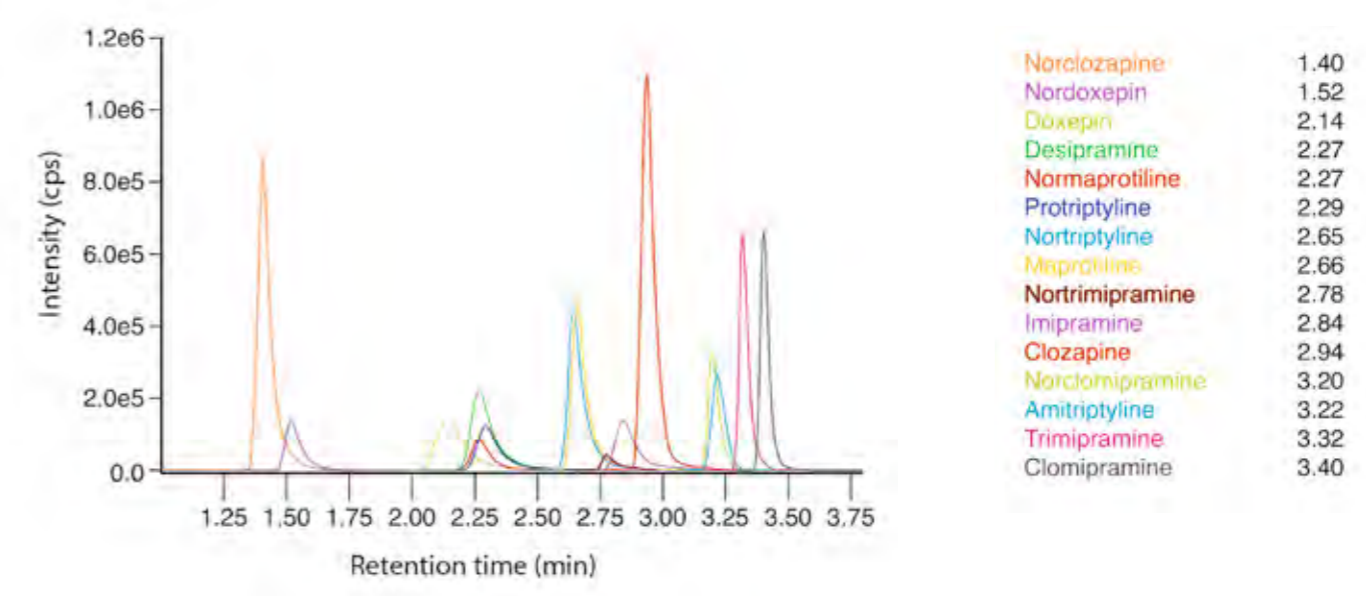
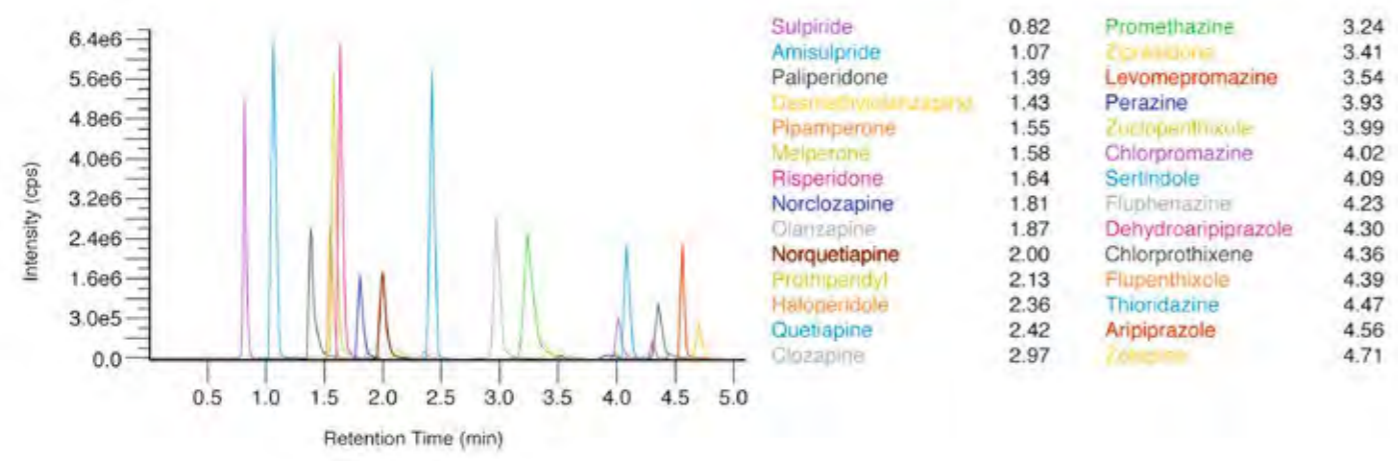
|                        |      |                    |      |
|------------------------|------|--------------------|------|
| 7-Aminonitrazepam      | 2.74 | Alprazolam         | 4.67 |
| 7-Aminoclonazepam      | 2.80 | Chloriazepoxide    | 4.72 |
| 3-Hydroxybromazepam    | 2.96 | α-OH-Midazolam     | 4.78 |
| 7-Aminoflunitrazepam   | 2.96 | Triazolam          | 4.81 |
| Bromazepam             | 3.43 | Desalkylflurazepam | 5.19 |
| Zopiclon               | 3.45 | Flunitrazepam      | 5.19 |
| Demoxepam              | 3.57 | Brotizolam         | 5.21 |
| Zolopion               | 3.71 | Temazepam          | 5.40 |
| α-OH-Triazolam         | 3.86 | Nordiazepam        | 5.54 |
| α-OH-Alprazolam        | 3.88 | Clobazam           | 5.68 |
| Desmethylflunitrazepam | 4.15 | Flurazepam         | 5.73 |
| Oxazepam               | 4.26 | Trazodone          | 5.74 |
| Estazolam              | 4.27 | Lometazepam        | 5.77 |
| Nitrazepam             | 4.33 | Midazolam          | 5.92 |
| Zolpidem               | 4.36 | Diazepam           | 6.23 |
| Norclonazepam          | 4.53 | Tetraepam          | 6.77 |
| Lorazepam              | 4.53 | Prazepam           | 6.95 |
| Clonazepam             | 4.60 | Medazepam          | 7.25 |

**TDM** **Mycophenolic Acid** **MPA**

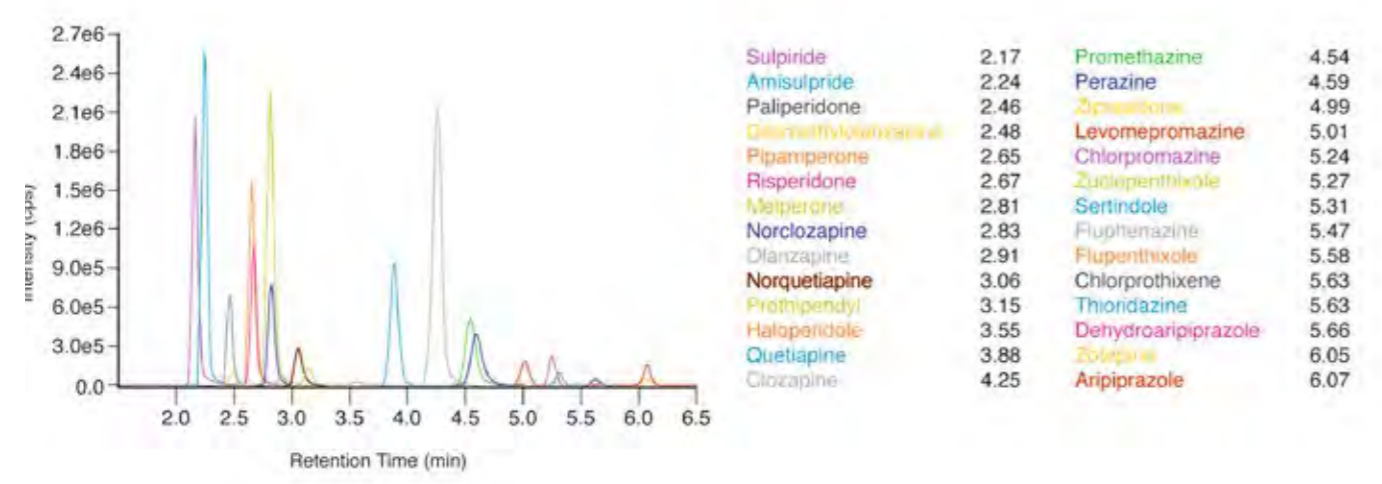


|                                      |      |
|--------------------------------------|------|
| Mycophenolic acid glucuronide (MPAG) | 0.56 |
| Mycophenolic acid                    | 1.32 |

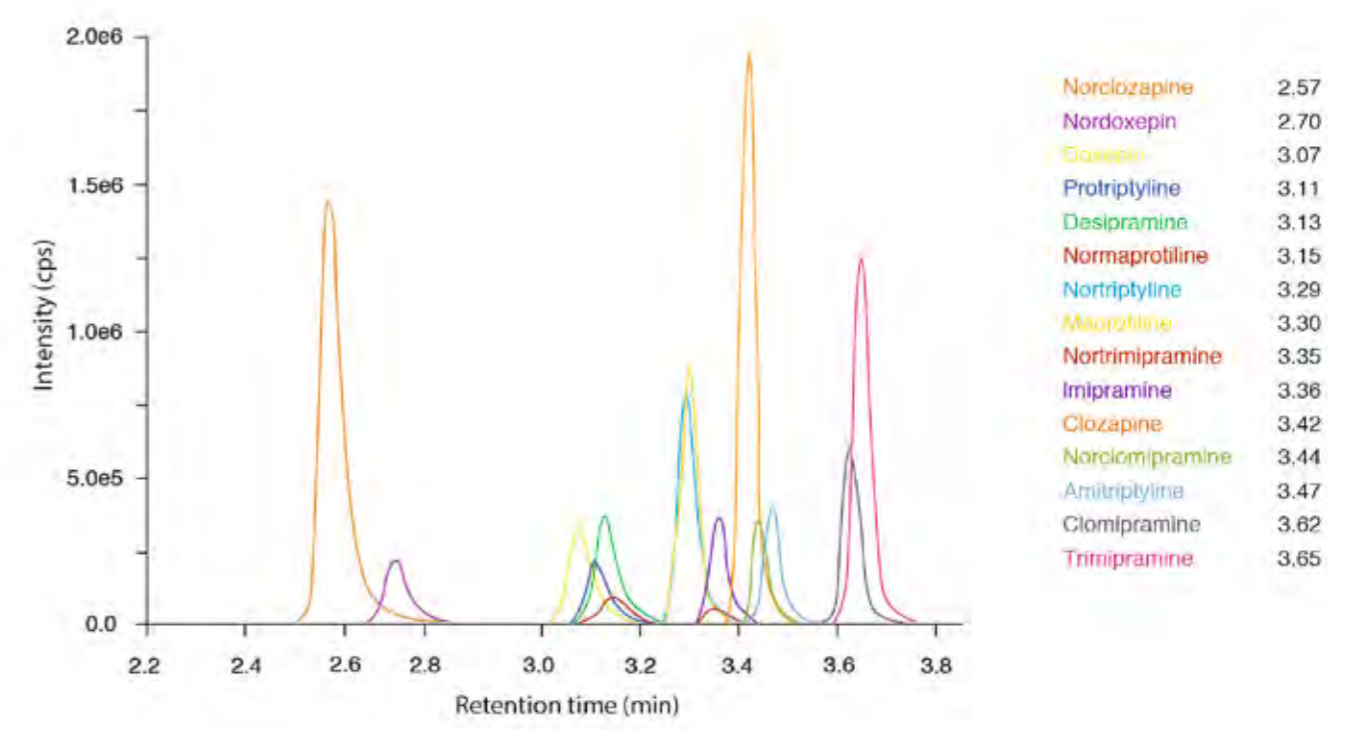




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