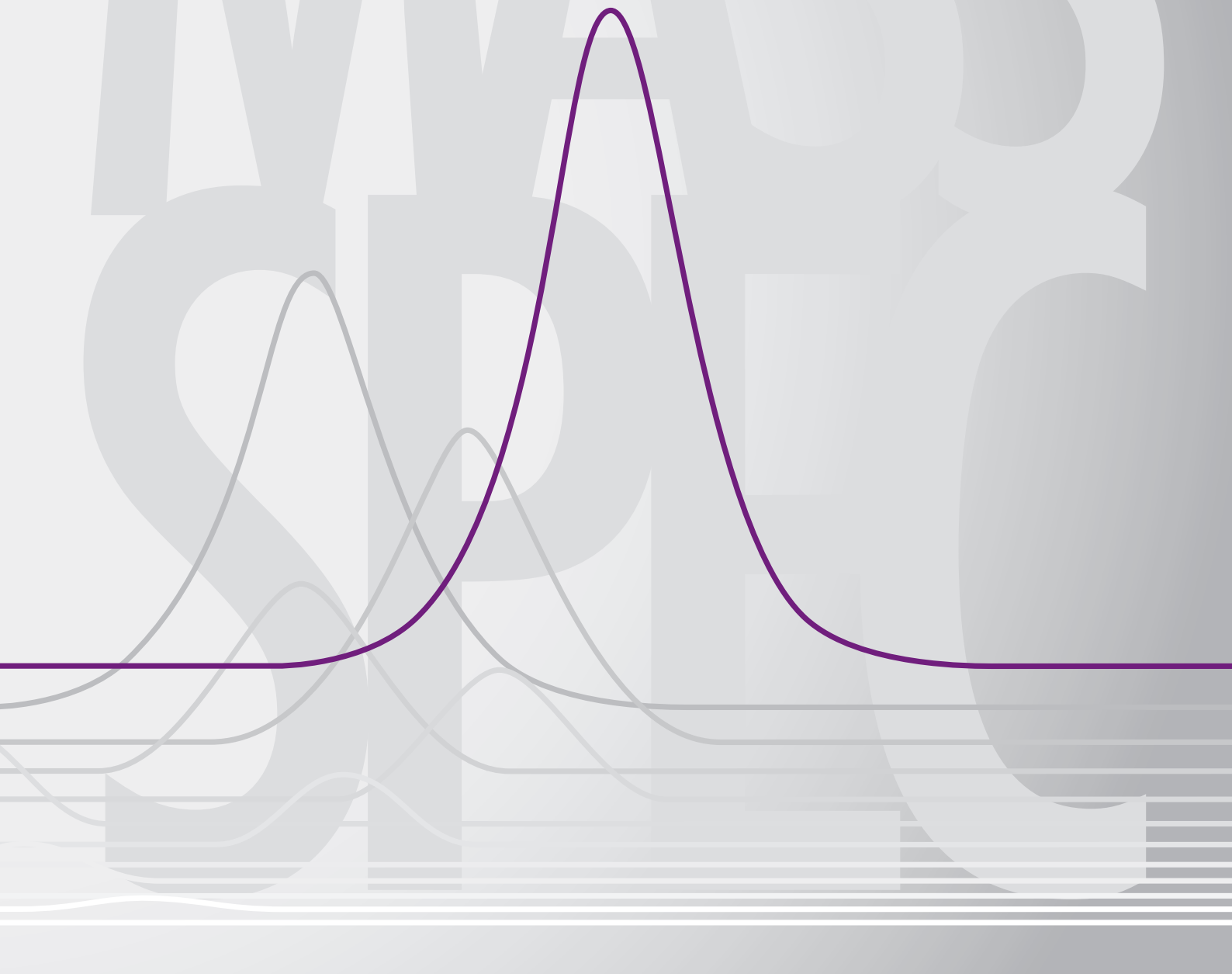
CHROMSYSTEMS

DIAGNOSTICS BY HPLC & LC-MS/MS

LC-MS/MS

Clinical LC-MS/MS Product Catalogue

Assays, Calibrators & Controls



CHROMSYSTEMS®

DIAGNOSTICS BY HPLC & LC-MS/MS

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CHROMSYSTEMS

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More automated solutions under development. Please refer to our website.

About Chromsystems

Chromsystems is a leading global company providing ready-to-use solutions for routine clinical diagnostics by high performance liquid chromatography (HPLC) and tandem mass spectrometry (LC-MS/MS). Our product portfolio includes complete assays as well as quality controls and calibrators, all ensuring highly accurate as well as cost-effective methods for the laboratory. We continuously optimise our assays and expand our broad range of products with new tests, automated solutions or with other techniques such as UHPLC.

All products are CE-IVD compliant, satisfying most stringent requirements for your laboratory. Quality controls and calibrators are uniquely based on human matrices such as serum, plasma and urine, ensuring you achieve maximum result accuracy and regulatory fulfillment. Benefit from our know-how in clinical diagnostics with in-depth HPLC/UHPLC and LC-MS/MS workshops. They provide you with essential and helpful theory as well as practical courses, aimed at enabling you to achieve quick and reliable results in the laboratory. Moreover you are in the best hands with our excellent support: our competent and dedicated team will enable any laboratory to implement HPLC and LC-MS/MS methods without specific prior knowledge in the diagnostic routine.

Über Chromsystems

Chromsystems ist weltweit einer der führenden Hersteller von Lösungen für die klinische Routinediagnostik mittels Hochleistungs-Flüssigkeitschromatographie (HPLC) und Tandem-Massenspektrometrie (LC-MS/MS). Unser Produktportfolio, das sowohl komplette Kits als auch Qualitätskontrollen und Kalibratoren umfasst, garantiert Ihnen präzise und ökonomische Methoden im Routinelabor. Wir optimieren unsere Kits und erweitern unser Produktportfolio mit neuen Tests, Automationslösungen sowie weiteren Technologien wie der UHPLC.

Alle Produkte sind CE-IVD konform, was es Ihrem Labor wesentlich erleichtert selbst strengsten Anforderungen gerecht zu werden. Ergänzend basieren die Qualitätskontrollen und Kalibratoren auf Humanmatrizes wie Serum, Plasma und Urin, wodurch Sie eine maximale Genauigkeit der Ergebnisse erreichen und regulatorische Ansprüche erfüllen. Profitieren Sie von unserem Know-how in der klinischen Diagnostik durch unsere praxisbezogenen Workshops: Erweitern Sie Ihr theoretisches Wissen und vertiefen Sie das Erlernte im praktischen Teil, sodass Sie schnell zuverlässige Ergebnisse erhalten. Darüber hinaus sind Sie bei unserem ausgezeichneten Support in den besten Händen: Kompetente und spezialisierte Mitarbeiter ermöglichen es jedem Labor, HPLC- und LC-MS/MS-Methoden ohne spezifische Vorkenntnisse in die diagnostische Routine zu implementieren.

Drugs of Abuse Testing

Drug abuse is one of the most pressing public health issues worldwide, including the use of both illegal drugs and prescription medicines. Cannabis is by far the most commonly consumed illegal drug in Europe. Distant runners-up are the stimulants cocaine, MDMA and amphetamines. Within the class of opioids, heroin continues to be the most widely abused drug.

Drug of abuse testing in forensic medicine can establish both illicit drug use and whether crimes were committed under the influence of drugs. During the treatment of drug addicts, it is also performed to verify the abstinence of illicit drugs during replacement and maintenance therapy. In occupational medicine, drug screening is used to check for abstinence and to determine if a patient is fit to drive. Accurate testing can also help to save lives when someone is intoxicated.

2

Drogenanalytik

Der Drogenmissbrauch ist weltweit ein großes Problem im Gesundheitswesen. Dies gilt sowohl für den Missbrauch illegaler Drogen als auch für verschreibungspflichtige Medikamente. Unter den illegalen Drogen wird Cannabis in Europa am weitaus häufigsten konsumiert. Mit einigem Abstand folgen die stimulierenden Substanzen Kokain, MDMA und Amphetamine. Aus der Gruppe der Opioide hat nach wie vor der Heroinkonsum die größte Bedeutung.

In der Forensik kann mit der Drogenanalytik der Konsum illegaler Drogen festgestellt oder die Begehung von Straftaten unter Drogeneinfluss getestet werden. Bei der Therapie Suchtkranker dient es dem Nachweis der Abstinenz oder dem Ausschluss eines Beikonsums bei der Substitutionstherapie. Auch in der Arbeitsmedizin werden Drogenscreenings zur Abstinenzkontrolle durchgeführt, insbesondere wenn es um sicherheitsrelevante Tätigkeiten oder die Fahreignung geht. Bei Intoxikationen kann eine korrekte Analytik lebensrettend sein.

2.1 *MassTox*® Drugs of Abuse Testing in Urine

The LC-MS/MS-based assay ***MassTox***® Drugs of Abuse Testing offers the target screening of more than 100 drugs and metabolites with an analysis time of approximately 12 minutes. A quantitative confirmation can also be performed within the same run.

The assay includes everything required, thereby eliminating the need for developing and maintaining in-house methods or specific QC materials. It also provides a significantly higher selectivity and sensitivity than current immunoassays and is designed to work below cut-offs applied in forensic labs. Semiquantitative statements are also possible.

Nearly all analytes are safeguarded by isotopically labelled internal standards. The high stability of the 6PLUS1® Multilevel Urine Calibrator Set and three ***MassCheck***® urine controls ensure reliable results with highest precision. A specific urine control with a carefully selected set of glucuronide metabolites allows to control the proper functioning of the hydrolysis process. This Hydrolysis Control can also be used in laboratories working with their own developed methods and enzymes.

> Target screening of 108 drugs and metabolites in a single run
> Quantitative confirmation within the same run possible
> Simple sample prep combined with great selectivity and sensitivity
> Internal standards for nearly all analytes

Der LC-MS/MS-basierte Assay ***MassTox***® Drugs of Abuse Testing ermöglicht das Target Screening von mehr als 100 Drogen und Metaboliten mit einer Laufzeit von etwa 12 Minuten. Die quantitative Bestätigungsanalyse kann auch im selben Lauf durchgeführt werden.

Der Assay umfasst alle benötigten Materialien, wodurch der Aufwand für die Eigenentwicklung und der Betrieb von Inhouse-Methoden und QC-Materialien eingespart werden kann. Die Methode verfügt über eine deutlich höhere Empfindlichkeit und Selektivität als Immunoassays und wurde so entwickelt, dass die in der Forensik wichtigen Cut-Off-Werte abgedeckt sind. Semiquantitative Aussagen sind ebenfalls möglich.

Nahezu alle Analyten sind durch einen isotopenmarkierten internen Standard abgesichert. Die hohe Stabilität des 6PLUS1® Multilevel Urine Calibrator Sets und die drei ***MassCheck***® Urinkontrollen sorgen für präzise und zuverlässige Ergebnisse. Eine spezielle Urinkontrolle mit einer Auswahl an Glucuronid-Metaboliten ermöglicht die Überprüfung des Hydrolyse-Prozesses im Routinebetrieb. Diese Hydrolysekontrolle kann speziell in Laboratorien eingesetzt werden, die ihre eigenen Methoden und Enzyme einsetzen.

> Target Screening von 108 Drogen/Metaboliten in einem Lauf
> Quantitative Bestätigung im gleichen Lauf möglich
> Einfache Probenvorbereitung
> Interne Standards für nahezu alle Analyten

Parameters

Amphetamines

Amphetamine
BDB
Butylone
2C-B
2C-I
Cathinone
MBDB
MDA
MDEA
MDMA
MDPV
Mephedrone
Methamphetamine
Methaqualone
Methylone
Methylphenidate
PMA
Ritalinic acid

Barbiturates

Allobarbital
Amobarbital
Barbital
Butalbital
Hexobarbital
Pentobarbital
Phenobarbital
Secbutabarbital
Secobarbital
Thiopental

Benzodiazepines

Alprazolam
7-Aminoclonazepam
7-Aminoflunitrazepam
7-Aminonitrazepam
Bromazepam
Brotizolam
Chlordiazepoxide
Clobazam
Clonazepam
Demoxepam
Desalkylflurazepam
Desmethylflunitrazepam
Diazepam
Estazolam
Flunitrazepam
Flurazepam
Lorazepam
Lormetazepam
Medazepam
Midazolam
Nitrazepam
Norclobazam
Nordiazepam
a-OH-Alprazolam
3-OH-Bromazepam
a-OH-Midazolam
a-OH-Triazolam
Oxazepam
Prazepam
Temazepam
Triazolam

Booster

Gabapentin
Pregabalin
Promethazine
Quetiapine

Cannabinoides

THC-COOH

Cocaine

Benzoylecgonine
Cocaethylene
Cocaine
Norcocaine

Opiates/Opioids

Acetylcodeine
Buprenorphine
Codeine
Dihydrocodeine
EDDP
Fentanyl
Hydrocodone
Hydromorphone
Meconin
Meperidine
Methadone
6-Monoacetylmorphine
Morphine
Naloxone
Naltrexone
Norbuprenorphine
Norcodeine
Norfentanyl
Normeperidine
Nortapentadol
Nortilidine
O-Desmethyltramadol
Oxycodone
Oxymorphone
Papaverine
Propoxyphene
Sufentanil
Tapentadol
Thebaine
Tilidine
Tramadol

Others

Ketamine
LSD
Mescaline
Norketamine
2-Oxo-3-hydroxy-LSD
PCP

Z-Drugs

Zaleplon
Zolpidem
Zopiclone

2.1.1 *MassTox®* Drugs of Abuse Testing in Urine

Order no.	Product
96000	***MassTox®*** Drugs of Abuse Testing in Urine with Reaction Vials For 400 tests
	Components available separately
96001	Mobile Phase A, 700 ml
96002	Mobile Phase B, 700 ml
96005	Precipitation Reagent, 40 ml
96009	Rinsing Solution, 500 ml
96010	Dilution Buffer, 30 ml
96046	Internal Standard Set, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
96078	Enzyme Solution Set, consisting of: Enzyme Reagent (lyoph.) 2 x 8 ml Hydrolysis Buffer, 20 ml
33006	Reaction Vials, 100 pcs.
	Startup Accessories
96100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
96012	System Check Solution, 1 ml
96015	Tuning Mix 1, Analytes and Internal Standards, 1 ml
96016	Tuning Mix 2, Analytes and Internal Standards, 1 ml
96017	Tuning Mix 3, Analytes and Internal Standards, 1 ml
0470	***MassCheck®*** Drugs of Abuse Testing Urine Hydrolysis Control Set (lyoph.), 4 x 1 ml
96033	Urine Screening Standard Set (lyoph.), 4 x 1 ml
15090	UHPLC Stainless Steel Prefilter Housing, 1 pc.
15091	Stainless Steel Prefilter, 0.2 µm, 3 pcs.
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0410	PP Screw-on Caps, pierceable silicone/PTFE septa, 1.0 mm, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
J0505	Micro-inserts for autosampler vials, clear glass, flat bottom, 100 pcs.

	Multilevel Calibrator and Controls
96040	6PLUS1® Multilevel Urine Calibrator Set (lyoph.), 7 x 1 ml
0410	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level I (lyoph.), 4 x 1 ml
0420	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level II (lyoph.), 4 x 1 ml
0430	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level III (lyoph.), 4 x 1 ml

Specifications

Linearity for all analytes:	from 0.25 to 30 x of cut-off value
Limit of quantification:	down to 13 ng/l
Intraassay:	CV = 1–9 %
Interassay:	CV = 1–11 %
Recovery:	85–15 %
Analysis time:	12.5 min

Pre-analytic Treatment

Specimen: urine.
Stability: according to the Swiss Guidelines Committee for Drugs of Abuse Testing (SCDAT), samples are stable for seven days at +2 to +8 °C and for six months at -18 °C.

Sample Preparation

→ Pipette 50 µl sample/calibrator/***MassCheck®*** control into a reaction vial.
→ Add 10 µl Internal Standard.
→ Add 40 µl Enzyme Buffer Mix and vortex.
→ Incubate for 120 minutes at 45 °C.
→ Add 100 µl Precipitation Reagent, mix briefly.
→ Centrifuge for 5 min at 15 000 x g.
→ Dilute 100 µl supernatant with 150 µl Dilution Buffer.
→ Close autosampler vial and vortex.
→ Inject ≤ 20 µl into the LC-MS/MS system.

LC-MS/MS Parameters

Injection volume:	2–20 µl
Flow rate:	0.4 ml/min
Column temperature:	30 °C
Ionisation:	ESI positive and negative
MS/MS Mode:	MRM
Gradient:	binary

2.1.2 *MassTox®* Drugs of Abuse Testing in Urine with 96 Well Plates

Order no.	Product
96000/WP	***MassTox®*** Drugs of Abuse Testing in Urine with 96 Well Plates For 400 tests
	Components available separately
96001	Mobile Phase A, 700 ml
96002	Mobile Phase B, 700 ml
96005	Precipitation Reagent, 40 ml
96009	Rinsing Solution, 500 ml
96010	Dilution Buffer, 30 ml
96046	Internal Standard Set, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
96078	Enzyme Solution Set, consisting of: Enzyme Reagent (lyoph.) 2 x 8 ml Hydrolysis Buffer, 20 ml
96057	96 Well Plates, 5 pcs.
96058	Collection Plates, 5 pcs.
96059	Pierceable Adhesive Seals for 96 Well Plates, 5 pcs.
	Startup Accessories
96100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
96012	System Check Solution, 1 ml
96015	Tuning Mix 1, Analytes and Internal Standards, 1 ml
96016	Tuning Mix 2, Analytes and Internal Standards, 1 ml
96017	Tuning Mix 3, Analytes and Internal Standards, 1 ml
0470	***MassCheck®*** Drugs of Abuse Testing Urine Hydrolysis Control Set (lyoph.), 4 x 1 ml
96033	Urine Screening Standard Set (lyoph.), 4 x 1 ml
15090	UHPLC Stainless Steel Prefilter Housing, 1 pc.
15091	Stainless Steel Prefilter, 0.2 µm, 3 pcs.
	Multilevel Calibrator and Controls
96040	6PLUS1® Multilevel Urine Calibrator Set (lyoph.), 7 x 1 ml
0410	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level I (lyoph.), 4 x 1 ml
0420	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level II (lyoph.), 4 x 1 ml
0430	***MassCheck®*** Drugs of Abuse Testing Urine Control Set, Level III (lyoph.), 4 x 1 ml

Specifications

Linearity for all analytes:	from 0.25 to 30 x of cut-off value
Limit of quantification:	down to 13 ng/l
Intraassay:	CV = 1–9 %
Interassay:	CV = 1–11 %
Recovery:	85–15 %
Analysis time:	12.5 min

Pre-analytic Treatment

Specimen: urine.
Stability: according to the Swiss Guidelines Committee for Drugs of Abuse Testing (SCDAT), samples are stable for seven days at +2 to +8 °C and for six months at -18 °C.

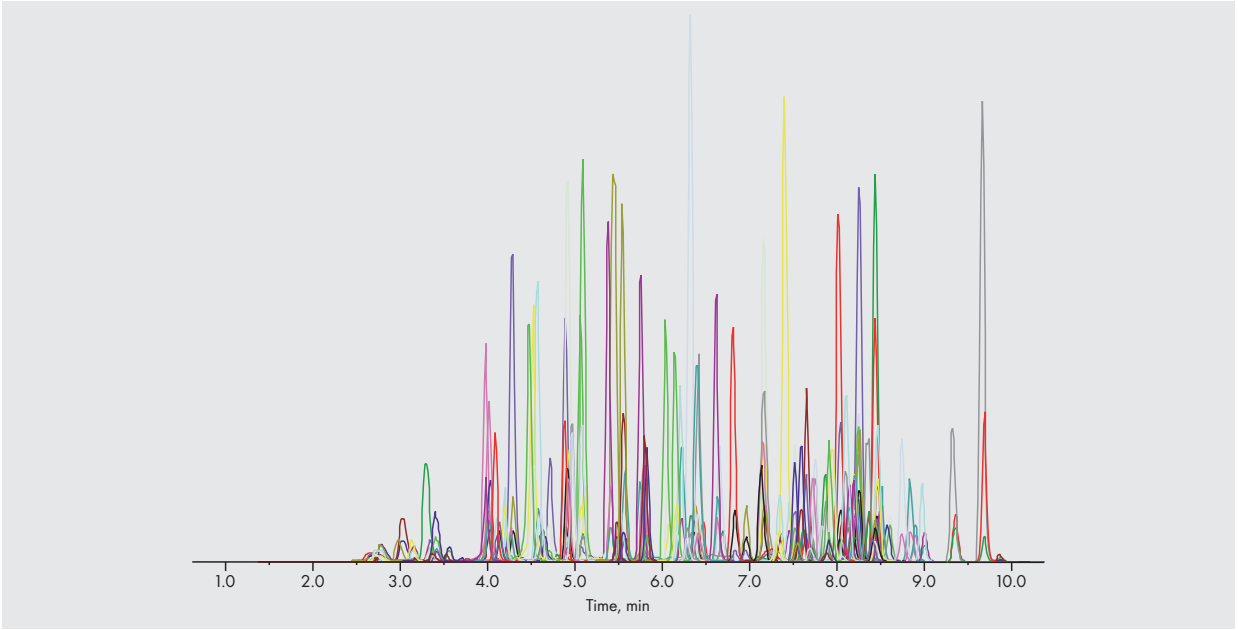
Sample Preparation

→ Pipette 50 µl sample/calibrator/***MassCheck®*** control into a well plate.
→ Add 10 µl Internal Standard.
→ Add 40 µl Enzyme Buffer Mix and shake 10 s at 500 rpm.
→ Incubate for 120 minutes at 45 °C.
→ Add 100 µl Precipitation Reagent and shake for 10 s at 500 rpm.
→ Centrifuge for 5 min at 2000 x g.
→ Transfer 100 µl supernatant into another well plate, add 150 µl Dilution Buffer.
→ Seal the well plate with a pierceable adhesive seal and shake for 10 s at 500 rpm.
→ Inject ≤ 20 µl into the LC-MS/MS system.

LC-MS/MS Parameters

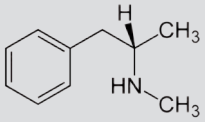
Injection volume:	2–20 µl
Flow rate:	0.4 ml/min
Column temperature:	30 °C
Ionisation:	ESI positive and negative
MS/MS Mode:	MRM
Gradient:	binary

MassTox® Drugs of Abuse Testing



Amphetamines

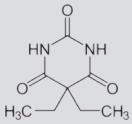
e.g. Methamphetamine



Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Amphetamine	50	200	MDMA	–	200
BDB	–	200	MDPV	50	200
Butylone	–	200	Mephedrone	50	200
2C-B	–	200	Methamphetamine	50	200
2C-I	–	200	Methaqualone	–	200
Cathinone	–	200	Methylone	–	200
MBDB	50	200	Methylphenidate	–	200
MDA	–	200	PMA	50	200
MDEA	–	200	Ritalinic acid	–	200

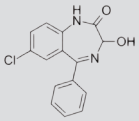
Barbiturates

e.g. Barbital



Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Allobarbital	–	150	Pentobarbital	–	150
Amobarbital	–	150	Phenobarbital	–	150
Barbital	–	150	Secbutabarbital	–	150
Butalbital	–	150	Secobarbital	–	150
Hexobarbital	–	150	Thiopental	–	150

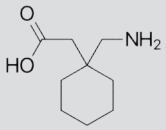
Benzodiazepines



e.g. Oxazepam

Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Alprazolam	50	100	a-Hydroxyalprazolam	50	100
7-Aminoclonazepam	50	100	a-Hydroxymidazolam	50	100
7-Aminoflunitrazepam	50	100	a-Hydroxytriazolam	50	100
7-Aminonitrazepam	50	100	3-Hydroxybromazepam	50	100
Bromazepam	50	100	Lorazepam	50	100
Brotizolam	–	–	Lormetazepam	50	100
Chlordiazepoxide	50	100	Medazepam	50	100
Clobazam	50	100	Midazolam	50	100
Clonazepam	50	100	Nitrazepam	50	100
Demoxepam	50	100	Norclobazam	50	100
Desalkylflurazepam	50	100	Nordiazepam	50	100
Desmethylflunitrazepam	50	100	Oxazepam	50	100
Diazepam	50	100	Prazepam	50	100
Estazolam	–	–	Temazepam	50	100
Flunitrazepam	50	100	Triazolam	50	100
Flurazepam	50	100			

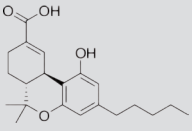
Booster



e.g. Gabapentin

Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Gabapentin	–	–	Promethazine	–	–
Pregabalin	–	–	Quetiapine	–	–

Cannabinoides

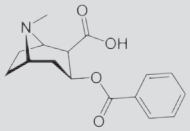


e.g. 11-nor-9-Carboxy-Δ9-THC

Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
11-nor-9-Carboxy-Δ9-THC	10	15

Cocaine

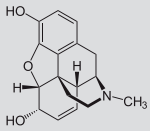
e.g. Benzoylecgonine



Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Benzoylecgonine	30	100	Cocaine	–	–
Cocaethylene	–	–	Norcocaine	–	–

Opiates/Opioides

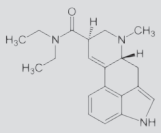
e.g. Morphine



Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Acetylcodeine	25	–	Norcodeine	–	–
Buprenorphine	1	2	Norfentanyl	10	–
Codeine	25	300	Normeperidine	–	–
Dihydrocodeine	25	300	Nortapentadol	–	–
EDDP	50	75	Nortilidine	50	–
Fentanyl	10	–	O-Desmethyltramadol	50	–
Hydrocodone	–	–	Oxycodone	50	–
Hydromorphone	–	–	Oxymorphone	–	–
Meconin	–	–	Papaverine	–	–
Meperidine	–	–	Propoxyphene	–	300
Methadone	50	250	Sufentanil	–	–
6-Monoacetylmorphine	–	10	Tapentadol	–	–
Morphine	25	300	Thebaine	–	–
Naloxone	–	–	Tilidine	50	–
Naltrexone	–	–	Tramadol	50	–
Norbuprenorphine	1	2			

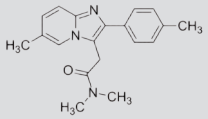
Others

e.g. LSD



Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Ketamine	–	–	Norketamine	–	–
LSD	–	1	2-Oxo-3-hydroxy-LSD	–	–
Mescaline	–	–	PCP	–	25

Z-drugs



e.g. Zalpidem

Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)	Analyte	Cut-off-values GTFCh [1] (µg/l)	Cut-off-values EWDTS [2] (µg/l)
Zaleplon	–	–	Zopiclone	–	–
Zolpidem	–	–			

6PLUS1® Multilevel Urine Calibrator Set Drugs of Abuse Testing

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Amphetamines							
Amphetamine	30.2	49.4	119	234	395	781	< LOQ
BDB	26.9	44.4	109	222	380	774	< LOQ
Butylone	24.3	40.3	99.3	199	353	756	< LOQ
2C-B	27.6	45.7	107	197	348	701	< LOQ
2C-I	24.1	39.2	94	187	321	688	< LOQ
Cathinone	27.6	44.6	108	214	371	745	< LOQ
MBDB	24.7	40.8	101	212	354	734	< LOQ
MDA	25.9	42.9	103	212	375	853	< LOQ
MDEA	24.4	40.2	99.8	203	364	788	< LOQ
MDMA	22	36.4	90	184	327	708	< LOQ
MDPV	23.9	41	103	222	378	813	< LOQ
Mephedrone	24.9	40.8	99.4	208	365	793	< LOQ
Methamphetamine	22.3	35.8	88.2	176	298	595	< LOQ
Methaqualone	27.2	44.6	106	210	364	796	< LOQ
Methylone	22.3	36.7	89.6	179	327	710	< LOQ
Methylphenidate	28.4	46.6	114	236	403	819	< LOQ
PMA	22.9	38.2	110	200	352	705	< LOQ
Ritalinic acid	23	37.7	90.8	178	300	609	< LOQ
Barbiturates							
Allobarbital	67.3	119	283	572	1011	2332	< LOQ
Amobarbital	86.9	142	338	752	1135	2313	< LOQ
Barbital	77.9	127	331	711	1193	2479	< LOQ
Butalbital	65.5	107	265	549	1008	2342	< LOQ
Hexobarbital	72.3	117	337	845	1197	2496	< LOQ
Pentobarbital	74.1	117	274	542	971	2105	< LOQ
Phenobarbital	63.1	106	258	543	983	2293	< LOQ
Secbutabarbital	65	105	260	558	1002	2303	< LOQ
Secobarbital	68.4	112	273	554	989	2174	< LOQ
Thiopental	76	134	336	679	1175	2424	< LOQ
Benzodiazepines							
Alprazolam	26.5	42.4	102	209	370	799	< LOQ
7-Aminoclonazepam	21.7	34.3	94.5	204	352	747	< LOQ
7-Aminoflunitrazepam	18.2	31.3	88	187	334	732	< LOQ
7-Aminonitrazepam	24.3	39.8	101	208	345	690	< LOQ
Bromazepam	26.8	43.6	106	205	359	763	< LOQ
Brotizolam	25.6	42.8	103	211	371	785	< LOQ
Chlordiazepoxide	25.9	43.5	107	216	372	820	< LOQ
Clobazam	26.4	41.1	107	213	369	731	< LOQ
Clonazepam	25.5	43.2	102	200	355	765	< LOQ
Demoxepam	26.4	45.5	105	208	379	815	< LOQ
Desalkylflurazepam	26.6	42.5	103	211	365	743	< LOQ
Desmethylflunitrazepam	25.9	41.7	97.2	197	354	752	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

6PLUS1® Multilevel Urine Calibrator Set Drugs of Abuse Testing

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Benzodiazepines							
Diazepam	25.3	42.5	103	211	371	793	< LOQ
Estazolam	25.3	41.5	102	213	366	773	< LOQ
Flunitrazepam	25	39.3	100	207	373	781	< LOQ
Flurazepam	23.6	37.9	92.8	197	332	741	< LOQ
a-Hydroxyalprazolam	21.3	36.2	91.3	194	357	779	< LOQ
a-Hydroxymidazolam	21.3	33.5	85.2	171	294	591	< LOQ
a-Hydroxytriazolam	24.3	40.9	99.2	204	351	744	< LOQ
3-Hydroxybromazepam	58.8	91	220	417	733	1453	< LOQ
Lorazepam	23.8	38	97	195	346	736	< LOQ
Lormetazepam	25.7	40.7	100	206	372	788	< LOQ
Medazepam	25.1	41.3	101	207	359	762	< LOQ
Midazolam	23.1	36.1	95.9	198	348	776	< LOQ
Nitrazepam	25.5	41.8	99.6	202	352	788	< LOQ
Norclobazam	19.5	33.4	81.9	165	305	651	< LOQ
Nordiazepam	25.5	42.2	106	206	360	776	< LOQ
Oxazepam	24.4	39.2	94.9	198	346	758	< LOQ
Prazepam	25.1	41.6	99.9	205	354	756	< LOQ
Temazepam	24.7	39	96.1	196	352	761	< LOQ
Triazolam	25.6	41.9	105	216	373	783	< LOQ
Booster							
Gabapentin	23.6	39	97	202	346	753	< LOQ
Pregabalin	21.2	35.8	91.7	191	337	719	< LOQ
Promethazine	20.8	32.9	96.3	202	362	800	< LOQ
Quetiapine	26.9	45.1	109	231	408	880	< LOQ
Cannabinoides							
11-nor-9-Carboxy-Δ9-THC	3.96	7.46	18.6	38.3	65.6	144	< LOQ
Cocaine							
Benzoylecgonine	14.7	23.9	59.1	121	212	463	< LOQ
Cocaethylene	15.2	25.4	62.5	129	227	489	< LOQ
Cocaine	13.8	22.6	55.9	112	202	444	< LOQ
Norcocaine	12.7	21.2	53.2	110	197	433	< LOQ
Opiates/Opioides							
Acetylcodeine	2.43	3.98	9.93	20.6	36.3	81.4	< LOQ
Buprenorphine	0.453	0.717	1.78	3.52	6.46	14.3	< LOQ
Codeine	13.2	21.9	56.6	123	228	519	< LOQ
Dihydrocodeine	14.6	23.2	59	113	190	368	< LOQ
EDDP	24.6	40.5	99.6	204	360	789	< LOQ
Fentanyl	4.53	7.59	18.9	37.4	66.8	139	< LOQ
Hydrocodone	13	21.9	54.1	111	197	435	< LOQ
Hydromorphone	3.83	6.46	16.6	35.8	62.2	136	< LOQ
Meconin	25	40.2	96.8	199	357	782	< LOQ
Meperidine	12.4	20.4	51.2	103	184	393	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

6PLUS1® Multilevel Urine Calibrator Set Drugs of Abuse Testing

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Opiates/Opioides							
Methadone	25.2	41.8	102	205	356	766	< LOQ
6-Monoacetylmorphine	2.24	3.73	9.55	20.3	37.8	80.8	< LOQ
Morphine	15.9	26.5	64.6	132	226	489	< LOQ
Naloxone	31.4	51.9	127	248	418	795	< LOQ
Naltrexone	24.5	40.7	102	207	361	777	< LOQ
Norbuprenorphine	0.459	0.843	1.89	3.94	7.02	14.9	< LOQ
Norcodeine	15.1	24.7	60.4	122	210	435	< LOQ
Norfentanyl	4.32	7.25	17.9	35.7	63	134	< LOQ
Normeperidine	12.3	20.7	49	97	170	353	< LOQ
Nortapentadol	14.3	23.3	56.7	118	206	446	< LOQ
Nortilidine	24.3	39.8	101	208	373	820	< LOQ
O-Desmethyltramadol	25	42.3	105	218	381	801	< LOQ
Oxycodone	30	49.7	124	247	395	720	< LOQ
Oxymorphone	20.7	34.8	85.7	180	312	650	< LOQ
Papaverine	23.1	38.8	98.3	206	363	839	< LOQ
Propoxyphene	24.1	38.8	97.9	198	346	740	< LOQ
Sufentanil	23.6	39.1	99.9	213	373	834	< LOQ
Tapentadol	13.3	21.9	53.5	110	192	421	< LOQ
Thebaine	22	32.4	94.3	213	366	824	< LOQ
Tilidine	24.2	41.2	100	206	362	805	< LOQ
Tramadol	25.5	41.9	103	220	375	821	< LOQ
Others							
Ketamine	26.9	44.2	111	236	403	896	< LOQ
LSD	0.338	0.444	1.46	3.3	6.02	12.8	< LOQ
Mescaline	5.07	8.51	20.5	42.1	71.8	152	< LOQ
Norketamine	21.5	35.8	85.9	171	298	612	< LOQ
2-Oxo-3-hydroxy-LSD	0.368	0.601	1.56	3.37	6.07	14.1	< LOQ
PCP	4.16	6.75	18.8	38.5	69.4	151	< LOQ
Z-Drugs							
Zaleplon	23.8	39.8	100	201	356	763	< LOQ
Zolpidem	25.3	42.1	105	190	360	783	< LOQ
Zopiclone	23.7	40.7	96.4	193	356	733	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Drugs of Abuse Testing Urine Controls

Substance	Target Value Level I * (µg/l)	Target Value Level II * (µg/l)	Target Value Level III * (µg/l)
Amphetamines			
Amphetamine	59	175	597
BDB	54.2	164	562
Butylone	48.9	149	554
2C-B	55.9	159	526
2C-I	51.1	145	517
Cathinone	55.4	163	569
MBDB	46.8	143	520
MDA	52.1	152	585
MDEA	50	154	582
MDMA	43.4	134	506
MDPV	48.4	155	582
Mephedrone	49.9	152	571
Methamphetamine	45.1	131	442
Methaqualone	52.8	166	588
Methylone	45.2	134	516
Methylphenidate	59.2	176	610
PMA	48.8	157	537
Ritalinic acid	46.2	133	449
Barbiturates			
Allobarbital	126	436	1749
Amobarbital	163	482	1567
Barbital	156	479	1713
Butalbital	129	402	1657
Hexobarbital	151	508	1710
Pentobarbital	141	403	1512
Phenobarbital	126	393	1588
Secbutabarbital	123	383	1526
Secobarbital	134	409	1541
Thiopental	139	502	1713
Benzodiazepines			
Alprazolam	51.3	157	579
7-Aminoclonazepam	43.4	146	507
7-Aminoflunitrazepam	36.7	127	497
7-Aminonitrazepam	55	169	582
Bromazepam	52.6	161	568
Brotizolam	53.1	159	578
Chlordiazepoxide	51.4	161	590
Clobazam	53.9	157	551
Clonazepam	51.5	154	567
Demoxepam	55.3	170	606
Desalkylflurazepam	52.2	151	535
Desmethylflunitrazepam	51.6	156	550
Diazepam	52.2	158	577

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Drugs of Abuse Testing Urine Controls

Substance	Target Value Level I * (µg/l)	Target Value Level II * (µg/l)	Target Value Level III * (µg/l)
Benzodiazepines			
Estazolam	52.9	161	562
Flunitrazepam	49.6	154	564
Flurazepam	46.9	142	511
a-Hydroxyalprazolam	46.4	142	538
a-Hydroxymidazolam	42.9	131	457
a-Hydroxytriazolam	49.7	149	551
3-Hydroxybromazepam	114	328	1135
Lorazepam	50.4	146	548
Lormetazepam	51.4	156	576
Medazepam	50.2	152	556
Midazolam	47.2	147	537
Nitrazepam	49.9	150	588
Norclobazam	39.1	125	470
Nordiazepam	52.5	156	533
Oxazepam	50.3	150	551
Prazepam	50.9	152	562
Temazepam	49.5	147	560
Triazolam	51.5	161	577
Booster			
Gabapentin	47.8	145	540
Pregabalin	45.2	140	528
Promethazine	36.5	150	580
Quetiapine	54.8	169	631
Cannabinoides			
11-nor-9-Carboxy-Δ9-THC	9.21	26.3	105
Cocaine			
Benzoylecgonine	29.2	88.9	333
Cocaethylene	29.9	95.2	361
Cocaine	27.2	84.1	320
Norcocaine	26.3	81.2	312
Opiates/Opioids			
Acetylcodeine	4.92	15	58.1
Buprenorphine	0.948	2.76	10.3
Codeine	27.6	86	346
Dihydrocodeine	28	86.6	284
EDDP	49.8	151	569
Fentanyl	9.13	28	105
Hydrocodone	26.4	81	314
Hydromorphone	7.58	24.4	96.4
Meconin	48.8	148	563
Meperidine	25.6	79.4	294
Methadone	50.1	152	556
6-Monoacetylmorphine	4.69	14.4	54.9

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Drugs of Abuse Testing Urine Controls

Substance	Target Value Level I * (µg/l)	Target Value Level II * (µg/l)	Target Value Level III * (µg/l)
Opiates/Opioids			
Morphine	32.5	97.7	356
Naloxone	62.7	195	614
Naltrexone	48.6	151	554
Norbuprenorphine	0.963	2.87	10.4
Norcodeine	29.9	90.9	321
Norfentanyl	9.36	28.2	102
Normeperidine	23.8	71.6	257
Nortapentadol	29	86.9	319
Nortilidine	49.4	152	590
O-Desmethyltramadol	53	155	572
Oxycodone	63.1	187	574
Oxymorphone	40.5	122	461
Papaverine	49.2	148	533
Propoxyphene	50.7	143	544
Sufentanil	49.8	156	603
Tapentadol	26.9	81.3	306
Thebaine	34.8	156	585
Tilidine	51.6	156	593
Tramadol	53.3	163	605
Others			
Ketamine	58.4	177	661
LSD	0.469	2.43	9.22
Mescaline	10.2	31.3	114
Norketamine	40.5	121	430
2-Oxo-3-hydroxy-LSD	0.776	2.46	10.2
PCP	9.14	28.5	109
Z-Drugs			
Zaleplon	48.8	148	532
Zolpidem	46.7	158	561
Zopiclone	46.2	142	512

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
96040	6PLUS1® Multilevel Urine Calibrator Set (lyoph.), 7 x 1 ml
0410	***MassCheck***® Drugs of Abuse Testing Urine Control Set, Level I (lyoph.), 4 x 1 ml
0420	***MassCheck***® Drugs of Abuse Testing Urine Control Set, Level II (lyoph.), 4 x 1 ml
0430	***MassCheck***® Drugs of Abuse Testing Urine Control Set, Level III (lyoph.), 4 x 1 ml

Stability of Urine Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to one week at +2 °C to +8 °C

3

Metabolic Diseases and Newborn Screening

Metabolic disorders are caused by the failure of specific metabolic pathways in the human body. They are often based on hereditary enzyme defects, which leads to a decrease or suppression of enzyme activity. Subsequently, this can result in the accumulation of potentially toxic metabolites, which can cause organ defects and multi-systemic diseases.

The identification of metabolic diseases is routinely performed by newborn screening. Once identified, a life-long, specific, low-protein diet can prevent symptoms from occurring. Continuous monitoring of the plasma concentrations of the metabolic products is required to monitor and adjust the patient's dietary prescription. Furthermore, an amino acid analysis can also be performed for patients with unclear clinical signs.

Stoffwechselerkrankungen und Neugeborenen-Screening

Stoffwechselerkrankungen werden durch das Versagen bestimmter Stoffwechselwege im menschlichen Körper verursacht. Diese Krankheiten sind häufig angeborene Enzymdefekte, die zu einer erniedrigten oder unterdrückten Enzymaktivität führen. Als Folge kommt es zur Anreicherung potentiell toxischer Metaboliten, was zu Organschädigungen und Multisystemerkrankungen führen kann.

Die Identifizierung von Stoffwechselerkrankungen erfolgt daher routinemäßig über das Neugeborenen-Screening. Nach Erkennung der Krankheit kann eine lebenslange und häufig proteinarme Ernährung die Entstehung von Symptomen verhindern. Durch regelmäßiges Monitoring der Metabolitkonzentrationen im Plasma kann die Ernährungsumstellung des Patienten überprüft und gegebenenfalls angepasst werden. Außerdem wird die Aminosäure-Analytik auch eingesetzt, um eine unklare Symptomatik von Patienten zu klären.

Overview Amino Acid Analysis (AAA)

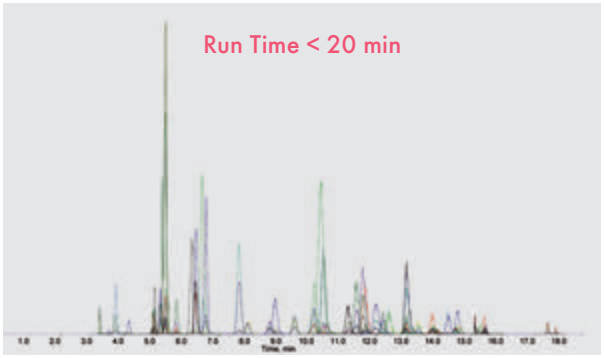
Chromsystems offers a flexible assay for the diagnosis of metabolic diseases that allows the quantification of a full range of 48 amino acids in plasma/serum within 20 min. It is aimed at identifying and testing of a large range of diseases, including rare diseases such as saccharopinuria. Alternatively, the same assay offers the flexibility to be used for PKU and MSUD testing only – with an even faster run time of less than 8 minutes.

Chromsystems bietet einen flexiblen Assay zur Diagnostik von Stoffwechselstörungen und ermöglicht die Bestimmung von 48 Aminosäuren im Plasma/Serum in unter 20 Minuten. Es dient der Testung auf eine Vielzahl an Stoffwechselstörungen, die auch seltenere Krankheiten wie die Saccharopinurie umfasst. Alternativ kann der gleiche Assay ausschließlich für die PKU und MSUD-Testung eingesetzt werden – mit einer noch schnelleren Laufzeit von unter 8 Minuten.

One Assay – 2 Test Modes

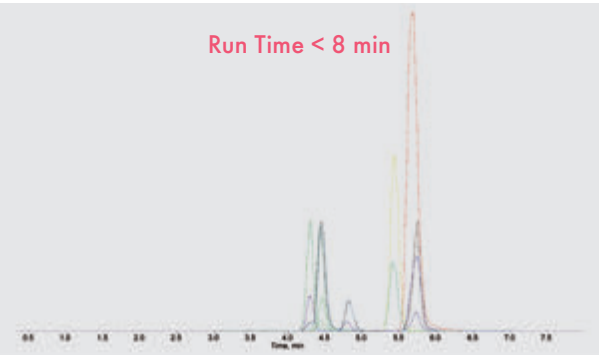
MassChrom® Amino Acid Analysis in Plasma/Serum
75111 – with reaction vials
75111/DWP – with 96 deep well plates

Complete range of diseases



Full Panel	
Acetyltyrosine	1-Methylhistidine
Adenosylhomocysteine	3-Methylhistidine
Alanine	Homocitrulline
β-Alanine	Leucine
α-Aminoadipic acid	Allo-Isoleucine
α-Aminobutyric acid	Isoleucine
β-Aminobutyric acid	Lysine
γ-Aminobutyric acid	Hydroxylysine
Anserine	Methionine
Arginine	Ornithine
Argininosuccinic acid	Phenylalanine
Asparagine	Phosphorylethanolamine
Aspartic acid	Phosphoserine
Carnosin	Pipecolinic acid
Citrulline	Proline
Cystathionine	4-Hydroxyproline
Cystine	Saccharopine
Cysteine S-sulfate	Sarcosine
Homocystine	Serine
Ethanolamine	Taurine
Glutamic Acid	Threonine
Glutamine	Tryptophan
Glycine	Tyrosine
Histidine	Valine

Specific disease testing of PKU and MSUD



PKU/MSUD Panel
Leucine
Allo-Isoleucine
Isoleucine
Methionine
Phenylalanine
Tyrosine
Valine

3.1 *MassChrom®* Amino Acid Analysis in Plasma/Serum

This assay is designed for the quantitative determination of amino acids in plasma/serum. It can be used for a range of applications including follow-up testing in newborn screening, therapy monitoring as well as for other amino acid testing purposes, such as aminoacidopathy diagnosis or nutritional research. The kit covers the 48 most important amino acids that are analysed within 20 min. Alternatively, the same assay allows the determination of 7 parameters for the common metabolic diseases PKU and MSUD in less than 8 min. The method runs on the same chromatographic setup and includes a shorter gradient. The sample prep consists of a very fast and simple protein precipitation, eliminating the need of time consuming and error-prone derivatisation steps. The use of stable isotope-labelled, co-eluting internal standards, and the multilevel calibrators ensures reproducible and dependable quantification of the analytes. The assay is available in 2 versions either with reaction vials or with 96 deep well plates.

> Quantitative Amino Acid Analysis (AAA) of 48 amino acids
> Chromatographic separation of isobaric compounds
> Each analyte safeguarded by its own internal standard
> Full test menu in 20 min or PKU/MSUD panel in less than 8 min
> Available with reaction vials or 96 deep well plates

Dieser Assay ermöglicht die quantitative Bestimmung von Aminosäuren in Plasma/Serum und kann vielfältig eingesetzt werden. Dazu gehören unter anderem die Bestätigungsanalytik, die Therapieüberwachung sowie diverse andere Anwendungen wie die Diagnostik der Aminoazidopathie oder der Ernährungsforschung. Der Kit umfasst 48 wichtige Aminosäuren, die innerhalb von 20 Minuten bestimmt werden können. Alternativ ist die Bestimmung von 7 Aminosäuren für die häufigen Erkrankungen wie die PKU und Ahornsirupkrankheit mit dem selben Assay möglich, wobei hier lediglich 8 Minuten benötigt werden. Das chromatographischen Setup ist identisch, jedoch mit einem kürzeren Gradienten. Die Probenvorbereitung besteht aus einer sehr schnellen und einfachen Proteinfällung, eine in der Regel fehleranfällige und zeitaufwendige Derivatisierung ist nicht erforderlich. Die Verwendung von stabilen isotopenmarkierten und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyten. Der Assay ist verfügbar mit Reaktionsgefäßen sowie mit 96-Deep-Well-Platten.

> Quantitative Aminosäure-Analytik (AAA) von 48 Aminosäuren
> Chromatographische Trennung isobarer Verbindungen
> Jeder Analyt mit eigenem internen Standard
> Komplettes Menü in weniger als 20 min oder PKU/MSUD-Panel in weniger als 8 min
> Verfügbar mit Reaktionsgefäßen oder 96-Deep-Well-Platten

3.1.1 *MassChrom*® Amino Acid Analysis with Reaction Vials

Parameters Full Panel:
acetyltyrosine, adenosylhomocysteine, alanine, β-alanine, a-aminoadipic acid, a-aminobutyric acid, β-aminobutyric acid, γ-aminobutyric acid, anserine, arginine, argininosuccinic acid, asparagine, aspartic acid, carnosin, citrulline, homocitrulline, cystathionine, cysteine-S-sulfate, cystine, homocystine, ethanolamine, phosphoethanolamine, glutamic acid, glutamine, glycine, histidine, 1-methylhistidine, 3-methylhistidine, **leucine**, **isoleucine**, **allo-isoleucine**, lysine, hydroxylysine, **methionine**, ornithine, **phenylalanine**, pipecolinic acid, proline, 4-hydroxyproline, saccharopine, sarcosine, serine, phosphoserine, taurine, threonine, tryptophan, **tyrosine**, **valine**.

Parameters PKU/MSUD:
leucine, isoleucine, allo-isoleucine, methionine, phenylalanine, tyrosine, valine.

Order no.	Product
75111	***MassChrom***® Amino Acid Analysis in Plasma/ Serum with Reaction Vials For 3 x 96 tests

Components available separately

75001	Mobile Phase A, 950 ml
75002	Mobile Phase B, 950 ml
75009	Rinsing Solution, 500 ml
75146	Internal Standard Set Amino Acid Analysis, consisting of: Internal Standard Mix (lyoph.), 3 x 5 ml Reconstitution Buffer, 3 x 5.5 ml
75105	Precipitation Reagent, 40 ml
33006	Reaction Vials, 1.5 ml, 100 pcs.

Startup Accessories

75100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
75010	System Check Solution
75015	Tuning Mix 1, Analytes and Internal Standards, 1 ml
75016	Tuning Mix 2, Analytes and Internal Standards, 1 ml
75017	Tuning Mix 3, Analytes and Internal Standards, 1 ml
75018	Tuning Mix 4, Analytes and Internal Standards, 1 ml
75019	Tuning Mix 5, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
55033	PEEK Prefilter, 2 µm, 5 pcs.

Multilevel Calibrator and Controls

75128	3PLUS1® Multilevel Plasma Calibrator Set (lyoph.), 4 x 0.5 ml
0471	***MassCheck***® Amino Acid Analysis Plasma Control, Level I (lyoph.), 5 x 1 ml
0472	***MassCheck***® Amino Acid Analysis Plasma Control, Level II (lyoph.), 5 x 1 ml
0473	***MassCheck***® Amino Acid Analysis Plasma Control, Level III (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 3-fold concentration of calibrator 3
Limit of quantification:	down to 0.2 µmol/l
Intraassay:	CV < 9 % (Full Panel) CV < 9 % (PKU/MSUD Panel)
Interassay:	CV < 11 % (Full Panel) CV < 7 % (PKU/MSUD Panel)
Analysis time:	< 20 min (Full Panel) < 8 min (PKU/MSUD Panel)

Pre-analytic Treatment

Specimens: plasma or serum.

Sample Preparation

→ Pipette 50 µl reconstituted Internal Standard + 25 µl sample/calibrator/***MassCheck***® control + 400 µl Precipitation Reagent into a reaction vial.
→ Mix for 30 s (vortex) and centrifuge for 5 min at 16 000 x g.
→ Transfer supernatant into autosampler vial.
→ Inject 5 µl into the LC-MS/MS system.

LC-MS/MS Parameters

Injection volume:	5 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM

3.1.2 *MassChrom*® Amino Acid Analysis with 96 Deep Well Plates

Parameters Full Panel:
acetyltyrosine, adenosylhomocysteine, alanine, β-alanine, a-aminoadipic acid, a-aminobutyric acid, β-aminobutyric acid, γ-aminobutyric acid, anserine, arginine, argininosuccinic acid, asparagine, aspartic acid, carnosin, citrulline, homocitrulline, cystathionine, cysteine-S-sulfate, cystine, homocystine, ethanolamine, phosphoethanolamine, glutamic acid, glutamine, glycine, histidine, 1-methylhistidine, 3-methylhistidine, **leucine**, **isoleucine**, **allo-isoleucine**, lysine, hydroxylysine, **methionine**, ornithine, **phenylalanine**, pipecolinic acid, proline, 4-hydroxyproline, saccharopine, sarcosine, serine, phosphoserine, taurine, threonine, tryptophan, **tyrosine**, **valine**.

Parameters PKU/MSUD:
leucine, isoleucine, allo-isoleucine, methionine, phenylalanine, tyrosine, valine.

Order no.	Product
75111/ DWP	***MassChrom***® Amino Acid Analysis in Plasma/ Serum with 96 Deep Well Plates For 3 x 96 tests

Components available separately

75001	Mobile Phase A, 950 ml
75002	Mobile Phase B, 950 ml
75009	Rinsing Solution, 500 ml
75146	Internal Standard Set Amino Acid Analysis, consisting of: Internal Standard Mix (lyoph.), 3 x 5 ml Reconstitution Buffer, 3 x 5.5 ml
75105	Precipitation Reagent, 40 ml
75156	96 Deep Well Plates, 4 pcs.
75058	Collection Plates, 4 pcs.
75060	Pierceable Heat Seals, 5 pcs.

Startup Accessories

75100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
75010	System Check Solution
75015	Tuning Mix 1, Analytes and Internal Standards, 1 ml
75016	Tuning Mix 2, Analytes and Internal Standards, 1 ml
75017	Tuning Mix 3, Analytes and Internal Standards, 1 ml
75018	Tuning Mix 4, Analytes and Internal Standards, 1 ml
75019	Tuning Mix 5, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
55033	PEEK Prefilter, 2 µm, 5 pcs.

Multilevel Calibrator and Controls

75128	3PLUS1® Multilevel Plasma Calibrator Set (lyoph.), 4 x 0.5 ml
0471	***MassCheck***® Amino Acid Analysis Plasma Control, Level I (lyoph.), 5 x 1 ml
0472	***MassCheck***® Amino Acid Analysis Plasma Control, Level II (lyoph.), 5 x 1 ml
0473	***MassCheck***® Amino Acid Analysis Plasma Control, Level III (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 3-fold concentration of calibrator 3
Limit of quantification:	down to 0.2 µmol/l
Intraassay:	CV < 9 % (Full Panel) CV < 9 % (PKU/MSUD Panel)
Interassay:	CV < 11 % (Full Panel) CV < 7 % (PKU/MSUD Panel)
Analysis time:	< 20 min (Full Panel) < 8 min (PKU/MSUD Panel)

Pre-analytic Treatment

Specimens: plasma or serum.

Sample Preparation

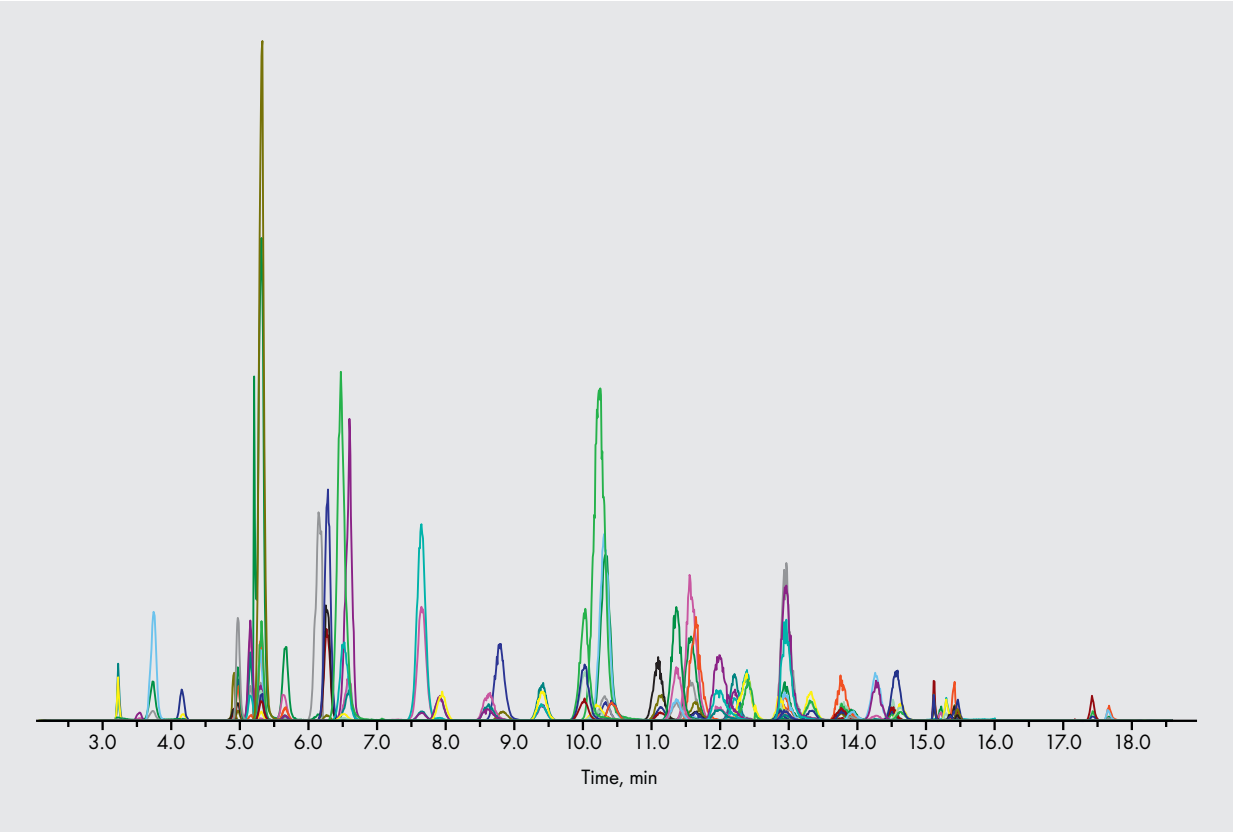
→ Pipette 50 µl reconstituted Internal Standard + 25 µl sample/calibrator/***MassCheck***® control + 400 µl Precipitation Reagent into a 96 deep well plate.
→ Shake for 2 min at 1200 rpm and centrifuge for 5 min at 2000 x g.
→ Transfer supernatant into collection plate and seal with pierceable heat seal.
→ Inject 5 µl into the LC-MS/MS system.

LC-MS/MS Parameters

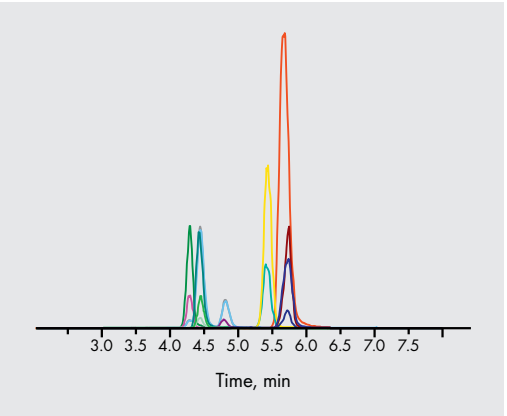
Injection volume:	5 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM

MassChrom® Amino Acid Analysis

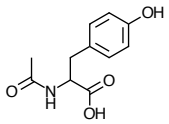
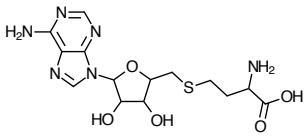
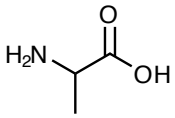
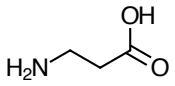
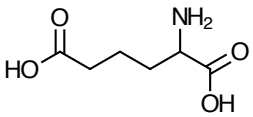
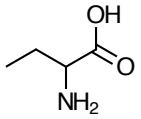
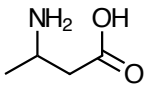
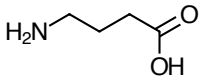
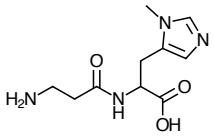
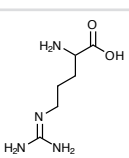
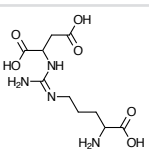
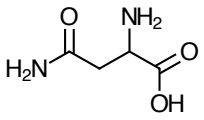
Full Panel



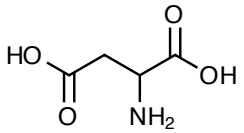
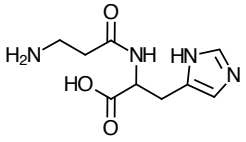
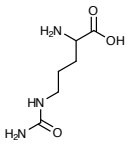
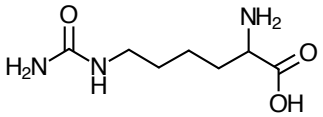
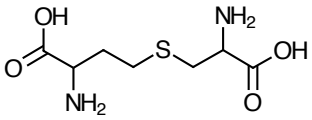
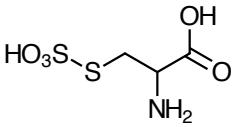
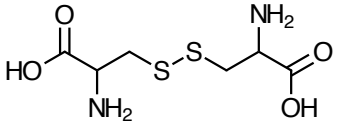
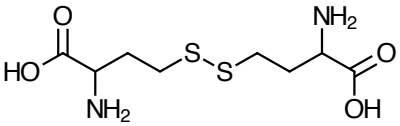
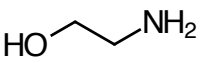
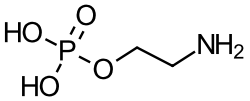
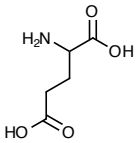
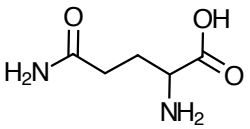
PKU/MSUD Panel



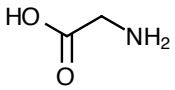
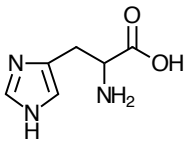
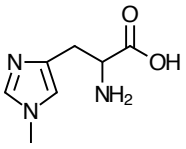
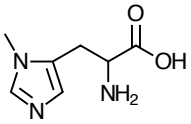
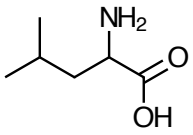
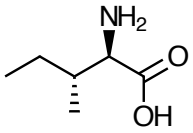
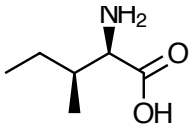
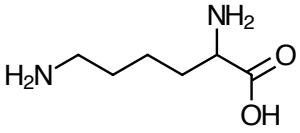
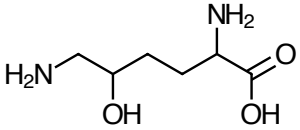
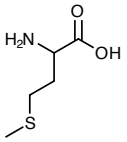
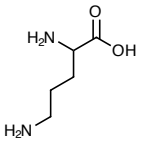
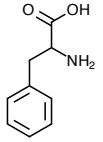
MassChrom® Amino Acid Analysis

Amino Acids	Mw (g/mol)	Formula	Structure
Acetyltyrosine	223.23	$C_{11}H_{13}NO_4$	
Adenosylhomocysteine	384.41	$C_{14}H_{20}N_6O_5S$	
Alanine	89.09	$C_3H_7NO_2$	
β-Alanine	89.09	$C_3H_7NO_2$	
α-Aminoadipic acid	161.16	$C_6H_{11}NO_4$	
α-Aminobutyric acid	103.12	$C_4H_9NO_2$	
β-Aminobutyric acid	103.12	$C_4H_9NO_2$	
γ-Aminobutyric acid	103.12	$C_4H_9NO_2$	
Anserine	240.26	$C_{10}H_{16}N_4O_3$	
Arginine	174.20	$C_6H_{14}N_4O_2$	
Argininosuccinic acid	290.27	$C_{10}H_{18}N_4O_6$	
Asparagine	132.12	$C_4H_8N_2O_3$	

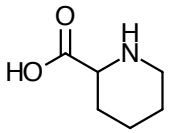
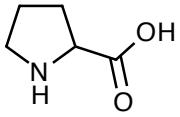
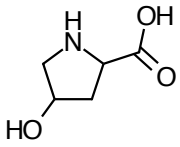
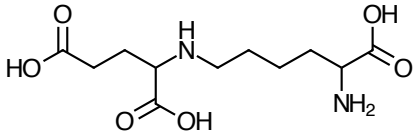
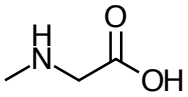
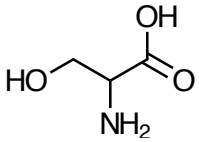
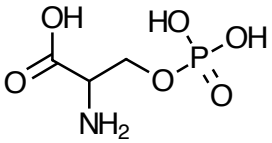
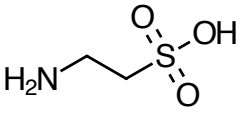
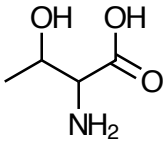
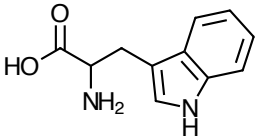
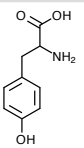
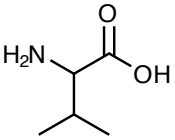
MassChrom® Amino Acid Analysis

Amino Acids	Mw (g/mol)	Formula	Structure
Aspartic acid	133.10	$C_4H_7NO_4$	
Carnosin	226.23	$C_9H_{14}N_4O_3$	
Citrulline	175.19	$C_6H_{13}N_3O_3$	
Homocitrulline	189.21	$C_7H_{15}N_3O_3$	
Cystathionine	222.26	$C_7H_{14}N_2O_4S$	
Cysteine-S-sulfate	201.21	$C_3H_7NO_5S_2$	
Cystine	240.29	$C_6H_{12}N_2O_4S_2$	
Homocystine	268.35	$C_8H_{16}N_2O_4S_2$	
Ethanolamine	61.08	C_2H_7NO	
Phosphoethanolamine	141.06	$C_2H_8NO_4P$	
Glutamic Acid	147.13	$C_5H_9NO_4$	
Glutamine	146.14	$C_5H_{10}N_2O_3$	

MassChrom® Amino Acid Analysis

Amino Acids	Mw (g/mol)	Formula	Structure
Glycine	75.07	$C_2H_5NO_2$	
Histidine	155.15	$C_6H_9N_3O_2$	
1-Methylhistidine	169.18	$C_7H_{11}N_3O_2$	
3-Methylhistidine	169.18	$C_7H_{11}N_3O_2$	
Leucine	131.17	$C_6H_{13}NO_2$	
Isoleucine	131.17	$C_6H_{13}NO_2$	
Allo-Isoleucine	131.17	$C_6H_{13}NO_2$	
Lysine	146.19	$C_6H_{14}N_2O_2$	
Hydroxylysine	162.19	$C_6H_{14}N_2O_3$	
Methionine	149.21	$C_5H_{11}NO_2S$	
Ornithine	132.16	$C_5H_{12}N_2O_2$	
Phenylalanine	165.19	$C_9H_{11}NO_2$	

MassChrom® Amino Acid Analysis

Amino Acids	Mw (g/mol)	Formula	Structure
Pipecolinic acid	129.16	$C_6H_{11}NO_2$	
Proline	115.13	$C_5H_9NO_2$	
4-Hydroxyproline	131.13	$C_5H_9NO_3$	
Saccharopine	276.29	$C_{11}H_{20}N_2O_6$	
Sarcosine	89.09	$C_3H_7NO_2$	
Serine	105.09	$C_3H_7NO_3$	
Phosphoserine	185.07	$C_3H_8NO_6P$	
Taurine	125.14	$C_2H_7NO_3S$	
Threonine	119.12	$C_4H_9NO_3$	
Tryptophan	204.23	$C_{11}H_{12}N_2O_2$	
Tyrosine	181.19	$C_9H_{11}NO_3$	
Valine	117.15	$C_5H_{11}NO_2$	

3PLUS1® Multilevel Plasma Calibrator Set Amino Acid Analysis

Substance	Calibrator 1* (µmol/l)	Calibrator 2* (µmol/l)	Calibrator 3* (µmol/l)	Blank Calibrator (µmol/l)
Acetyltyrosine	2.48	18	100	< LOQ
Adenosylhomocysteine	2.66	11.5	49.5	< LOQ
Alanine	127	475	1500	< LOQ
β-Alanine	7.55	27.8	115	< LOQ
α-Aminoadipic acid	2.99	7.94	22.5	< LOQ
α-Aminobutyric acid	5.49	15.8	115	< LOQ
β-Aminobutyric acid	2.48	4.28	49.8	< LOQ
γ-Aminobutyric acid	2.43	7.12	18.7	< LOQ
Anserine	2.71	7.6	21	< LOQ
Arginine	6.55	100	400	< LOQ
Argininosuccinic acid	1.76	15	116	< LOQ
Asparagine	24	90.6	271	< LOQ
Aspartic acid	21.5	56.4	300	< LOQ
Carnosin	6.61	16.3	64.3	< LOQ
Citrulline	6.34	37	250	< LOQ
Homocitrulline	4.7	23.5	56.7	< LOQ
Cystathionine	2.55	12.8	52	< LOQ
Cysteine-S-sulfate	7.37	28.8	56.6	< LOQ
Cystine	3.9	18.3	180	< LOQ
Homocystine	3.1	14.8	47	< LOQ
Ethanolamine	7.26	38	305	< LOQ
Phosphoethanolamine	5	18.7	158	< LOQ
Glutamic Acid	88.4	265	1000	< LOQ
Glutamine	143	795	1705	< LOQ
Glycine	130	515	1500	< LOQ
Histidine	25.1	120	400	< LOQ
1-Methylhistidine	1.33	8.43	18.3	< LOQ
3-Methylhistidine	3.65	17.3	105	< LOQ
Leucine	53.3	189	750	< LOQ
Isoleucine	25.6	72.6	500	< LOQ
Allo-Isoleucine	2.75	25	220	< LOQ
Lysine	34.9	123	757	< LOQ
Hydroxylysine	2.34	11.7	36.9	< LOQ
Methionine	6.99	26.9	200	< LOQ
Ornithine	15	100	500	< LOQ
Phenylalanine	28.9	250	800	< LOQ
Pipecolinic acid	1.5	10.6	36.4	< LOQ
Proline	58.5	250	800	< LOQ
4-Hydroxyproline	5.15	30.3	216	< LOQ
Saccharopine	2.51	10.5	22.3	< LOQ
Sarcosine	2.64	12.4	38	< LOQ
Serine	50.1	288	835	< LOQ
Phosphoserine	3.76	15.1	100	< LOQ
Taurine	12.9	144	524	< LOQ
Threonine	53.1	135	604	< LOQ
Tryptophan	10.7	45	260	< LOQ
Tyrosine	23.1	94.7	400	< LOQ
Valine	72.8	200	750	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Amino Acid Analysis Plasma Controls

Substance	Target Value Level I * (µmol/l)	Target Value Level II* (µmol/l)	Target Value Level III * (µmol/l)
Acetyltyrosine	4.87	25	40
Adenosylhomocysteine	5.29	21.1	38.9
Alanine	232	609	916
β-Alanine	8.45	48.4	84.6
a-Aminoadipic acid	5.80	10.4	16.5
a-Aminobutyric acid	8.48	46.0	86.0
β-Aminobutyric acid	4.79	22.0	37.9
γ-Aminobutyric acid	4.76	9.39	14.0
Anserine	5.44	10.5	15.7
Arginine	12.3	150	211
Argininosuccinic acid	3.79	22.4	41.2
Asparagine	41.6	117	211
Aspartic acid	41.7	90.8	200
Carnosin	13.1	30.6	48.3
Citrulline	13.9	60	150
Homocitrulline	9.44	19.6	29.1
Cystathionine	5.26	22.1	39.3
Cysteine-S-sulfate	14.3	22.1	42.8
Cystine	7.68	64.4	135
Homocystine	6.12	18.7	32.8
Ethanolamine	9.79	127	232
Phosphoethanolamine	6.10	65.7	112
Glutamic Acid	120	393	604
Glutamine	319	591	1331
Glycine	268	665	1063
Histidine	49.5	93.1	185
1-Methylhistidine	2.58	10.1	14.0
3-Methylhistidine	7.17	39.2	77.6
Leucine	90.4	222	500
Isoleucine	43.9	56.0	250
Allo-Isoleucine	4.97	46.0	91.1
Lysine	56.9	287	686
Hydroxylysine	4.83	16.5	27.4
Methionine	12.7	53.6	120
Ornithine	19.5	150	250
Phenylalanine	52.9	400	600
Pipecolinic acid	4.74	15.2	26.7
Proline	96.9	320	509
4-Hydroxyproline	10.0	86.2	162
Saccharopine	4.99	8.12	6.45
Sarcosine	3.55	17.4	28.8
Serine	110	317	678
Phosphoserine	7.57	30	80
Taurine	21.3	208	398
Threonine	64.6	243	477
Tryptophan	20.3	104	197
Tyrosine	41.5	122	211
Valine	120	250	500

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Amino Acid Analysis Plasma Controls

Order no.	Product
75128	3PLUS1® Multilevel Plasma Calibrator Set ***MassChrom***® Amino Acid Analysis (lyoph.), 4 x 0.5 ml
0471	***MassCheck***® Amino Acid Analysis Plasma Control, Level I (lyoph.), 5 x 1 ml
0472	***MassCheck***® Amino Acid Analysis Plasma Control, Level II (lyoph.), 5 x 1 ml
0473	***MassCheck***® Amino Acid Analysis Plasma Control, Level III (lyoph.), 5 x 1 ml

Stability of Plasma Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to one week at +2 °C to +8 °C

Overview Newborn Screening Assays

Chromsystems provides a range of newborn screening assays that are divided into methods with and without derivatisation. Derivatisation provides highest sensitivity with extremely low interferences, whereas underivatised assays offer a simpler and faster sample preparation. Both methods are available with well plates or alternatively with well filter plates, reducing the sample prep by one pipetting step. An upgrade for the determination of succinylacetone is also available that can be easily integrated into the assays.

Chromsystems bietet eine Reihe an Lösungen für das Neugeborenen-Screening mit und ohne Derivatisierung an. Die Derivatisierung ermöglicht höchste Empfindlichkeit und extrem geringe Interferenzen, während die Bestimmung ohne Derivatisierung die Probenvorbereitung vereinfacht und beschleunigt. Beide Methoden sind mit Well-Platten sowie mit Well-Filterplatten erhältlich, wobei bei letzterer noch ein weiterer Pipettierschritt eingespart werden kann. Ein Upgrade für die Bestimmung von Succinylaceton ist ebenfalls verfügbar und lässt sich einfach in die Kits integrieren.

	With Derivatisation		Without Derivatisation	
Order Number	**55000**	**55000/F**	**57000**	**57000/F**
Method	96 Well Plates	96 Well FilterPlates	96 Well Plates	96 Well FilterPlates
Parameters	Amino Acids and Acylcarnitines	Amino Acids and Acylcarnitines	Amino Acids and Acylcarnitines	Amino Acids and Acylcarnitines
Number of Tests	960	960	960	960
Assay Characteristics	Highest sensitivity and extremely low interferences	Highest sensitivity and extremely low interferences One pipetting step can be saved by using well filter plates	Efficient and timesaving sample preparation	Efficient and timesaving sample preparation One pipetting step can be saved by using well filter plates
SUAC-Screening	55111 Succinylacetone Upgrade Set		55111 Succinylacetone Upgrade Set	57111/F Succinylacetone Upgrade Set
Page	42	42	46	46

3.2 Newborn Screening

CE 0123
IVD

These Chromsystems assays allow the fast and reliable determination of amino acids, acylcarnitines and succinylacetone from dried blood spot samples as part of the newborn screening for amino acid and fatty acid metabolic disorders using tandem mass spectrometry.

The kits with derivatisation combine highest sensitivity with extremely low interferences. The underivatised assays are characterised by a shorter and faster sample preparation. The methods are available with well plates, or alternatively with well filter plates, reducing the sample prep by one pipetting step. Upgrade sets for the determination of succinylacetone can be easily integrated into these assays and are available for both solutions – with and without derivatisation. The underivatised methods use Multi Reaction Monitoring (MRM) for all analytes. In comparison, the methods with derivatisation use Neutral Loss Scan or MRM for amino acids/succinylacetone and Parent Ion Scan for all acylcarnitines.

The use of stable isotope labelled internal standards for calibration and measurement ensures reliable and precise quantification of the analytes.

> Each analyte safeguarded by its own internal standard
> Screening of many metabolic disorders in a single run such as PKU, MSUD and tyrosinemia type I
> Fast and robust sample preparation

Diese Chromsystems Kits erlauben eine schnelle und zuverlässige Bestimmung von Aminosäuren, Acylcarnitinen und Succinylaceton aus Trockenblut im Rahmen des Neugeborenen-Screenings von Aminosäure- und Fettsäurestoffwechselstörungen mit der Tandem-Massenspektrometrie.

Die Kits mit Derivatisierung kombinieren höchste Empfindlichkeit mit extrem geringen Interferenzen. Alternativ stehen Kits ohne Derivatisierung zur Verfügung, die sich durch eine kürzere und schnellere Probenvorbereitung auszeichnen. Die Methoden sind mit Well-Platten sowie mit Well-Filterplatten erhältlich, wobei bei letzterer noch ein weiterer Pipettierschritt eingespart werden kann. Upgrade Sets für die Bestimmung von Succinylaceton lassen sich einfach in unsere Methoden integrieren und stehen für beide Lösungen zur Verfügung – mit und ohne Derivatisierung. Die Methoden ohne Derivatisierung verwenden Multi-Reaction-Monitoring (MRM) für alle Analyten. Im Vergleich dazu verwenden die Methoden mit Derivatisierung Neutral Loss Scan oder MRM für Aminosäuren/Succinylaceton und Parent Ion Scan für alle Acylcarnitine.

Stabile isotopenmarkierte interne Standards für die Kalibration und Messung stellen eine präzise Quantifizierung der Analyten sicher.

> Je ein eigener interner Standard pro Analyt
> Screening vieler Stoffwechselstörungen in einem Lauf wie PKU, MSUD und Tyrosinämie Typ I
> Schnelle und robuste Probenvorbereitung

3.2.1 *MassChrom*® Amino Acids and Acylcarnitines from Dried Blood

Parameters:
alanine, arginine, aspartic acid, carnitnines, citrulline, glutamic acid, glycine, leucine, methionine ornithine, phenylalanine, proline, succinylacetone, tyrosine, valine.

Order no.	Product
55000	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood using 96 Well Plates For 960 tests
55111	Succinylacetone Upgrade Set for 960 tests, consisting of Internal Standard and Reconstitution Buffer
55000/F	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood using 96 Well Filter Plates For 960 tests
	Components available separately
55001	Mobile Phase, 1000 ml
55002	Mobile Phase, 10 x 1000 ml
55004	Internal Standard (lyoph.), 4 x 50 ml
55044	Internal Standard for Succinylacetone, 3 x 50 ml
55005	Derivatisation Reagent, 30 ml
55006	Reconstitution Buffer, 100 ml
55007	Rinsing Solution, 1000 ml
55008	Extraction Buffer, 200 ml
55010	96 Well Plates, 10 pcs.
55010/F	96 Well Plates, 5 pcs.
55011	Protective Sheets for 96 Well Plates, 10 pcs.
55057	96 Well Filter Plates, 5 pcs.
	MassCheck® Amino Acids, Acylcarnitines and Succinylacetone Dried Blood Spot Controls
0192	Level I, 1 x 3 spots
0193	Level II, 1 x 3 spots

	Startup Accessories
55013	Pierceable Adhesive Seals for 96 Well Plates, 10 pcs.
55015	Restrictor Capillary, 1 pc.
55016	Adapter Collar for Centrifugation, 2 pcs.
55098	Tuning Mix for Succinylacetone and Internal Standard, 1 ml
55099	Tuning Mix, Analytes and Internal Standards, 2 ml
55033	PEEK Prefilter, 2 µm, 5 pcs.
15010	PEEK Prefilter Housing, 1 pc.
	MassCheck® Amino Acids, Acylcarnitines and Succinylacetone Dried Blood Spot Controls
0191	Bi-Level (I + II), 2 x 3 spots

MassChrom® Amino Acids and Acylcarnitines from Dried Blood

Specifications

Linearity:
amino acids with SUAC: 250–2500 µmol/l
(acyl-)carnitines: 25–200 µmol/l

Limit of quantification:
amino acids with SUAC: 0.5–5 µmol/l
(acyl-)carnitines: 0.05–0.5 µmol/l

Intraassay: amino acids with SUAC: CV = 4–10 %
(acyl-)carnitines: CV = 5–20 %

Interassay: amino acids with SUAC: CV = 6–9 %
(acyl-)carnitines: CV = 9–28 %

Recovery: amino acids with SUAC: 51–94 %
(acyl-)carnitines: 62–89 %

Analysis time: < 2 min

Cutoff thresholds
amino acids: 22–834 µmol/l
free carnitine: 50–60 µmol/l
acylcarnitines: 0.1–57 µmol/l
SUAC: 1.16 µmol/l

Pre-analytic Treatment

Specimen collection: whole blood from the heel of the newborn taken onto a filter card.
Collection between 24th and 72nd hour of life depending on individual national guideline.

Sample Preparation

→ Punch out 3.2 mm blood spots from the filter cards into a 96 well plate.
→ Add 200 µl Internal Standard, agitate 20 min.
→ Transfer supernatant into a new 96 well plate (or with 55000/F centrifuge for 2 min).
→ Evaporate supernatant.
→ Add 60 µl Derivatisation Reagent and incubate 15 min at 60 °C.
→ Evaporate to dryness.
→ Reconstitute with 100 µl Reconstitution Buffer and agitate for 1 min.
→ Inject 10 µl into the LC-MS/MS system.
Does not apply to succinylacetone analysis.

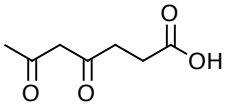
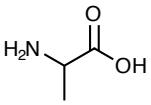
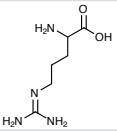
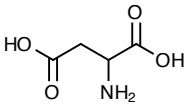
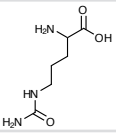
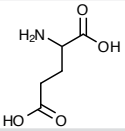
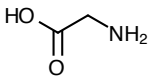
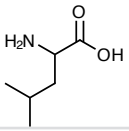
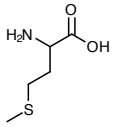
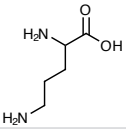
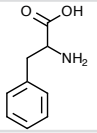
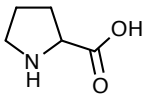
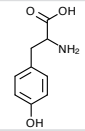
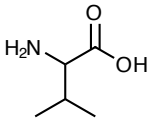
LC-MS/MS Parameters

For newborn screening any LC-MS/MS system with sufficient sensitivity is suitable. No HPLC column is required.

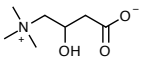
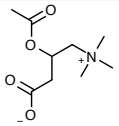
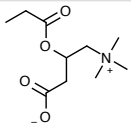
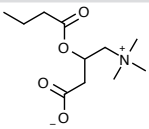
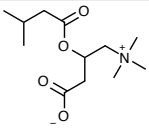
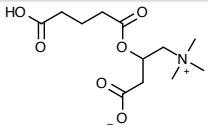
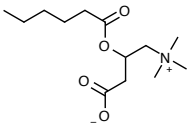
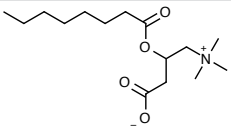
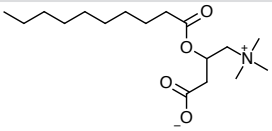
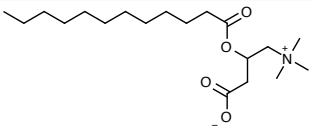
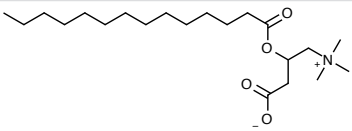
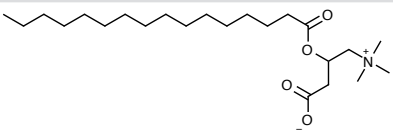
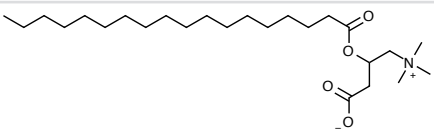
Injection volume: 10 µl
Flow gradient: 20–600 µl/min

MS/MS mode
Amino acids: Neutral Loss Scan/MRM
Acylcarnitines: Parent Ion Scan

MassChrom® Amino Acids and Acylcarnitines from Dried Blood

Succinylacetone and Amino Acids	Mw (g/mol)	Formula	Structure	Internal Standard
Succinylacetone	158.15	$C_7H_{10}O_4$		Succinylacetone-$^{13}C_5$
Alanine	89.09	$C_3H_7NO_2$		Alanine-D4
Arginine	174.20	$C_6H_{14}N_4O_2$		Arginine-D7
Aspartic acid	133.10	$C_4H_7NO_4$		Aspartic acid-D3
Citrulline	175.19	$C_6H_{13}N_3O_3$		Citrulline-D2
Glutamic acid	147.13	$C_5H_9NO_4$		Glutamic acid-D5
Glycine	75.07	$C_2H_5NO_2$		Glycine-$^{13}C_2$-^{15}N
Leucine	131.17	$C_6H_{13}NO_2$		Leucine-D3
Methionine	149.21	$C_5H_{11}NO_2S$		Methionine-D3
Ornithine	132.16	$C_5H_{12}N_2O_2$		Ornithine-D6
Phenylalanine	165.19	$C_9H_{11}NO_2$		Phenylalanine-D5
Proline	115.13	$C_5H_9NO_2$		Proline-D7
Tyrosine	181.19	$C_9H_{11}NO_3$		Tyrosine-D4
Valine	117.15	$C_5H_{11}NO_2$		Valine-D8

MassChrom® Amino Acids and Acylcarnitines from Dried Blood

Free Carnitine and Acylcarnitines	Mw (g/mol)	Formula	Structure	Internal Standard
Carnitine	161.20	$C_7H_{15}NO_3$		Carnitine-D9
C2-Carnitine	203.24	$C_9H_{17}NO_4$		C2-Carnitine-D3
C3-Carnitine	217.26	$C_{10}H_{19}NO_4$		C3-Carnitine-D3
C4-Carnitine	231.29	$C_{11}H_{21}NO_4$		C4-Carnitine-D3
C5-Carnitine	245.32	$C_{12}H_{23}NO_4$		C5-Carnitine-D9
C5DC-Carnitine	275.30	$C_{12}H_{21}NO_6$		C5DC-Carnitine-D6
C6-Carnitine	259.34	$C_{13}H_{25}NO_4$		C6-Carnitine-D3
C8-Carnitine	287.40	$C_{15}H_{29}NO_4$		C8-Carnitine-D3
C10-Carnitine	315.45	$C_{17}H_{33}NO_4$		C10-Carnitine-D3
C12-Carnitine	343.50	$C_{19}H_{37}NO_4$		C12-Carnitine-D3
C14-Carnitine	371.55	$C_{21}H_{41}NO_4$		C14-Carnitine-D3
C16-Carnitine	399.61	$C_{23}H_{45}NO_4$		C16-Carnitine-D3
C18-Carnitine	427.66	$C_{25}H_{49}NO_4$		C18-Carnitine-D3

3.2.2 *MassChrom*® Amino Acids and Acylcarnitines from Dried Blood/Non Derivatised

Parameters:
alanine, arginine, aspartic acid, carnitnines, citrulline, glutamic acid, glycine, leucine, methionine ornithine, phenylalanine, proline, succinylacetone, tyrosine, valine.

Order no.	Product
57000	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood/Non Derivatised using 96 Well Plates For 960 tests
57111	Succinylacetone Upgrade Set for 960 tests, consisting of Internal Standard, Extraction Buffer and Protective Sheets
57000/F	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood/Non Derivatised with 96 Well Filter Plates Kit for 960 tests
57111/F	Succinylacetone Upgrade Set for 960 tests, consisting of Internal Standard, Extraction Buffer, Protective Sheets and Pierceable Adhesive Seals

	Components available separately
57001	Mobile Phase, 1000 ml
57002	Mobile Phase, 10 x 1000 ml
57004	Internal Standard (lyoph.), 4 x 25 ml
57044	Internal Standard–Succinylacetone (non derivatised), 4 x 18 ml
57007	Rinsing Solution, 1000 ml
57008	Extraction Buffer, 100 ml
57012	Extraction Buffer–Succinylacetone (non derivatised), 4 x 18 ml
57010	96 Well Plates, V-bottomed, 5 pcs.
57057	96 Well Filter Plates, 5 pcs.
55011	Protective Sheets for 96 Well Plates, 10 pcs.
55013	Pierceable Adhesive Seals for 96 Well Plates, 10 pcs.
	MassCheck® Amino Acids, Acylcarnitines and Succinylacetone Dried Blood Spot Controls
0192	Level I, 1 x 3 spots
0193	Level II, 1 x 3 spots

	Startup Accessories
57014	Pierceable Heat Seals for 96 Well Plates, 6 pcs.
55015	Restrictor Capillary, 1 pc.
55016	Adapter Collar for Centrifugation, 2 pcs.
57098	Tuning Mix for Succinylacetone and Internal Standard, 1 ml
57099	Tuning Mix, Analytes and Internal Standards, 2 ml
55033	PEEK Prefilter, 2 µm, 5 pcs.
15010	PEEK Prefilter Housing, 1 pc.
42740	Chromsystems Heat Sealer
	MassCheck® Amino Acids, Acylcarnitines and Succinylacetone Dried Blood Spot Controls
0191	Bi-Level (I + II), 2 x 3 spots

MassChrom® Amino Acids and Acylcarnitines from Dried Blood/ Non Derivatised

Specifications

Linearity
amino acids with SUAC: 120–7000 µmol/l
(acyl-)carnitines: 15–400 µmol/l

Limit of quantification
amino acids with SUAC: 0.5–12 µmol/l
(acyl-)carnitines: 0.01–1.9 µmol/l

Intraassay
amino acids with SUAC: CV = 2–10 %
(acyl-)carnitines: CV = 3-8 %
Interassay
amino acids with SUAC: CV = 4.3–10 %
(acyl-)carnitines: CV = 4.3–10.8 %

Recovery
amino acids: 41–119 %
(acyl-)carnitines: 89–103 %

Analysis time: < 2 min

Cutoff thresholds
amino acids: ca. 35 to 1090 µmol/l
free carnitine: ca. 55 µmol/l
acylcarnitines: ca. 0.2 to 73 µmol/l
SUAC: 1.2 µmol/l

Pre-analytic Treatment

Specimen collection: whole blood from the heel of the newborn taken onto a filter card.
Collection between 24th and 72nd hour of life depending on individual national guideline.

Sample Preparation

→ Punch out 3.2 mm blood spots from the filter cards into a 96 well plate.
→ Add 100 µl Internal Standard, agitate 20 min.
→ Transfer supernatant into a new 96 well plate (or with 57000/F centrifuge for 2 min).
→ Inject 10 µl of the extract into the LC-MS/MS system.
Does not apply to succinylacetone analysis.

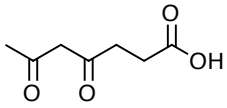
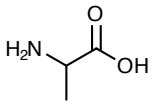
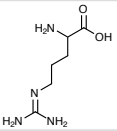
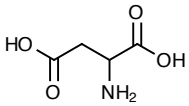
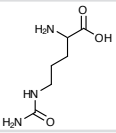
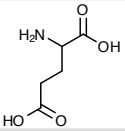
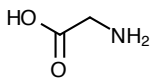
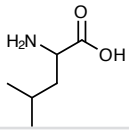
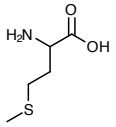
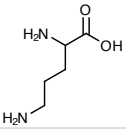
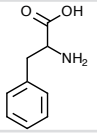
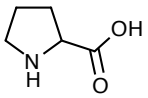
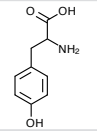
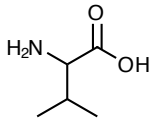
LC-MS/MS Parameters

For newborn screening any LC-MS/MS system with sufficient sensitivity is suitable. No HPLC column is required.

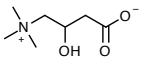
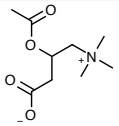
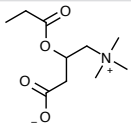
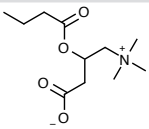
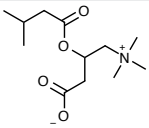
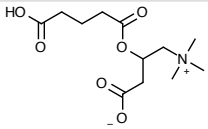
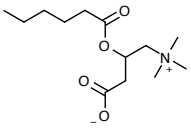
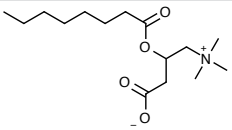
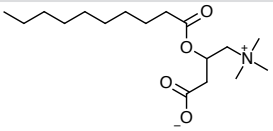
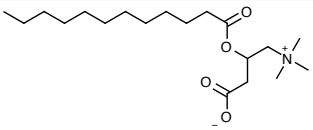
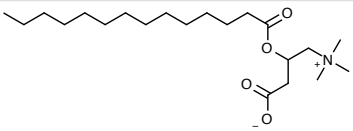
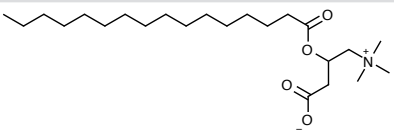
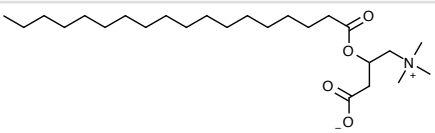
Injection volume: 10 µl
Flow gradient: 20–600 µl/min

MS/MS mode: MRM

MassChrom® Amino Acids and Acylcarnitines from Dried Blood/ Non Derivatised

Succinylacetone and Amino Acids	Mw (g/mol)	Formula	Structure	Internal Standard
Succinylacetone	158.15	$C_7H_{10}O_4$		Succinylacetone-$^{13}C_5$
Alanine	89.09	$C_3H_7NO_2$		Alanine-D4
Arginine	174.20	$C_6H_{14}N_4O_2$		Arginine-D7
Aspartic acid	133.10	$C_4H_7NO_4$		Aspartic acid-D3
Citrulline	175.19	$C_6H_{13}N_3O_3$		Citrulline-D2
Glutamic acid	147.13	$C_5H_9NO_4$		Glutamic acid-D5
Glycine	75.07	$C_2H_5NO_2$		Glycine-$^{13}C_2$-^{15}N
Leucine	131.17	$C_6H_{13}NO_2$		Leucine-D3
Methionine	149.21	$C_5H_{11}NO_2S$		Methionine-D3
Ornithine	132.16	$C_5H_{12}N_2O_2$		Ornithine-D6
Phenylalanine	165.19	$C_9H_{11}NO_2$		Phenylalanine-D5
Proline	115.13	$C_5H_9NO_2$		Proline-D7
Tyrosine	181.19	$C_9H_{11}NO_3$		Tyrosine-D4
Valine	117.15	$C_5H_{11}NO_2$		Valine-D8

MassChrom® Amino Acids and Acylcarnitines from Dried Blood/ Non Derivatised

Free Carnitine and Acylcarnitines	Mw (g/mol)	Formula	Structure	Internal Standard
Carnitine	161.20	$C_7H_{15}NO_3$		Carnitine-D9
C2-Carnitine	203.24	$C_9H_{17}NO_4$		C2-Carnitine-D3
C3-Carnitine	217.26	$C_{10}H_{19}NO_4$		C3-Carnitine-D3
C4-Carnitine	231.29	$C_{11}H_{21}NO_4$		C4-Carnitine-D3
C5-Carnitine	245.32	$C_{12}H_{23}NO_4$		C5-Carnitine-D9
C5DC-Carnitine	275.30	$C_{12}H_{21}NO_6$		C5DC-Carnitine-D6
C6-Carnitine	259.34	$C_{13}H_{25}NO_4$		C6-Carnitine-D3
C8-Carnitine	287.40	$C_{15}H_{29}NO_4$		C8-Carnitine-D3
C10-Carnitine	315.45	$C_{17}H_{33}NO_4$		C10-Carnitine-D3
C12-Carnitine	343.50	$C_{19}H_{37}NO_4$		C12-Carnitine-D3
C14-Carnitine	371.55	$C_{21}H_{41}NO_4$		C14-Carnitine-D3
C16-Carnitine	399.61	$C_{23}H_{45}NO_4$		C16-Carnitine-D3
C18-Carnitine	427.66	$C_{25}H_{49}NO_4$		C18-Carnitine-D3

MassChrom® Amino Acids and Acylcarnitines Dried Blood Spot Controls

Substance	Method	Level I Target Value* (µmol/l)	Level II Target Value* (µmol/l)
Succinylacetone	Succinylacetone	2.39	8.43
Alanine	underivatised derivatised with succinylacetone	411 392 423	752 744 791
Arginine	underivatised derivatised with succinylacetone	80 86 96	167 187 225
Aspartic acid	underivatised derivatised with succinylacetone	231 167 199	461 326 364
Citrulline	underivatised derivatised with succinylacetone	73 70 83	275 282 331
Glutamic acid	underivatised derivatised with succinylacetone	433 378 429	876 754 840
Glycine	underivatised derivatised with succinylacetone	389 433 467	1032 1166 1253
Leucine	underivatised derivatised with succinylacetone	351 267 276	637 543 582
Methionine	underivatised derivatised with succinylacetone	73 58 55	238 193 225
Ornithine	underivatised derivatised with succinylacetone	220 189 292	677 487 737
Phenylalanine	underivatised derivatised with succinylacetone	196 146 160	572 458 501
Proline	underivatised derivatised with succinylacetone	481 517 547	716 782 827
Tyrosine	underivatised derivatised with succinylacetone	192 155 178	585 496 560
Valine	underivatised derivatised with succinylacetone	267 208 219	520 440 455

** Please check packaging leaflet for specific lot concentrations*

MassChrom® Amino Acids and Acylcarnitines Dried Blood Spot Controls

Substance	Method	Level I Target Value* (µmol/l)	Level II Target Value* (µmol/l)
C0-Carnitine	underivatised derivatised with succinylacetone	40.7 40.2 43.3	108 115 120
C2-Carnitine	underivatised derivatised with succinylacetone	28.5 26.3 29.1	75.4 71.0 77.0
C3-Carnitine	underivatised derivatised with succinylacetone	5.84 4.86 5.02	16.7 13.9 14.2
C4-Carnitine	underivatised derivatised with succinylacetone	1.04 0.89 0.98	4.84 4.28 4.68
C5-Carnitine	underivatised derivatised with succinylacetone	0.60 0.55 0.55	2.70 2.20 2.40
C5DC-Carnitine	underivatised derivatised with succinylacetone	0.58 0.50 0.54	2.16 2.12 2.40
C6-Carnitine	underivatised derivatised with succinylacetone	0.49 0.41 0.52	2.43 2.02 2.26
C8-Carnitine	underivatised derivatised with succinylacetone	0.51 0.42 0.48	2.53 2.08 2.34
C10-Carnitine	underivatised derivatised with succinylacetone	0.50 0.43 0.45	2.47 2.14 2.34
C12-Carnitine	underivatised derivatised with succinylacetone	0.47 0.46 0.52	2.36 2.14 2.40
C14-Carnitine	underivatised derivatised with succinylacetone	0.52 0.44 0.51	2.45 2.19 2.34
C16-Carnitine	underivatised derivatised with succinylacetone	4.91 3.76 4.45	14.3 11.4 12.9
C18-Carnitine	underivatised derivatised with succinylacetone	2.54 2.00 2.41	9.38 7.56 9.33

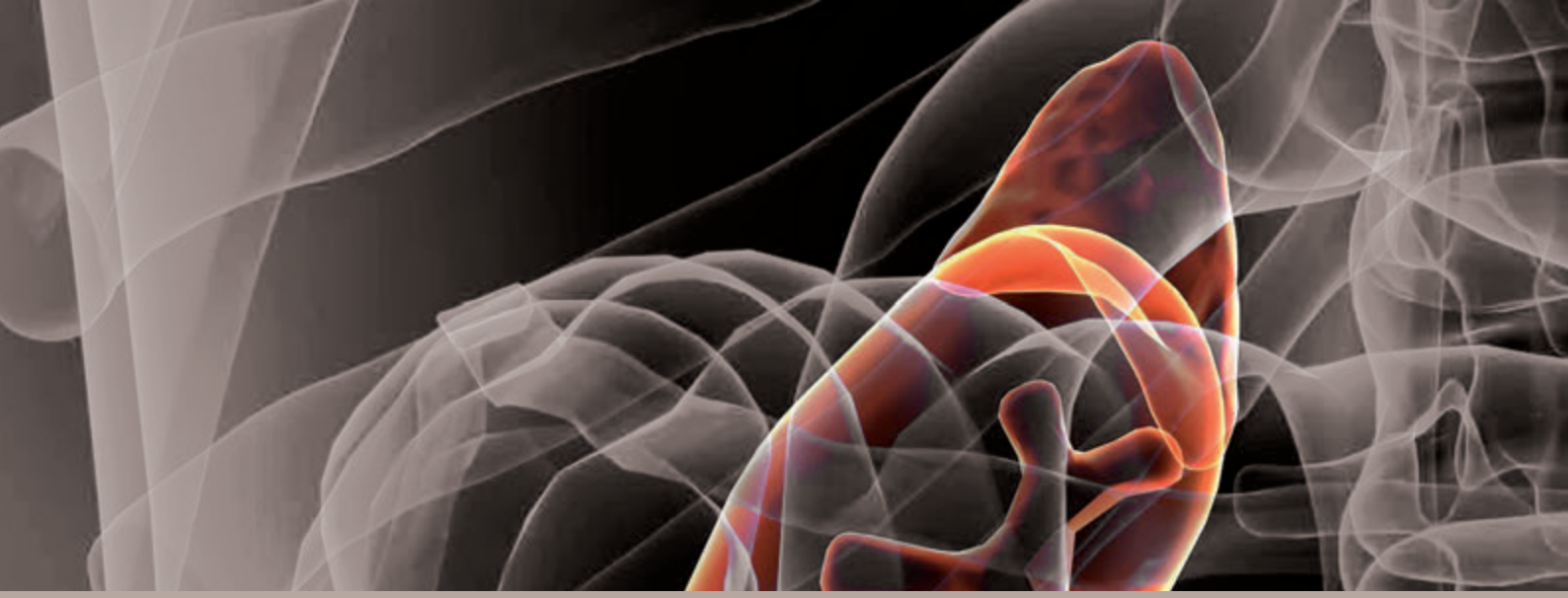
** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
0191	***MassCheck***® Amino Acids, Acylcarnitines Dried Blood Spot Control, Bi-Level (I + II), 2 x 3 spots
0192	***MassCheck***® Amino Acids, Acylcarnitines Dried Blood Spot Control, Level I, 1 x 3 spots
0193	***MassCheck***® Amino Acids, Acylcarnitines Dried Blood Spot Control, Level II, 1 x 3 spots

Stability of Dried Blood Spot Controls

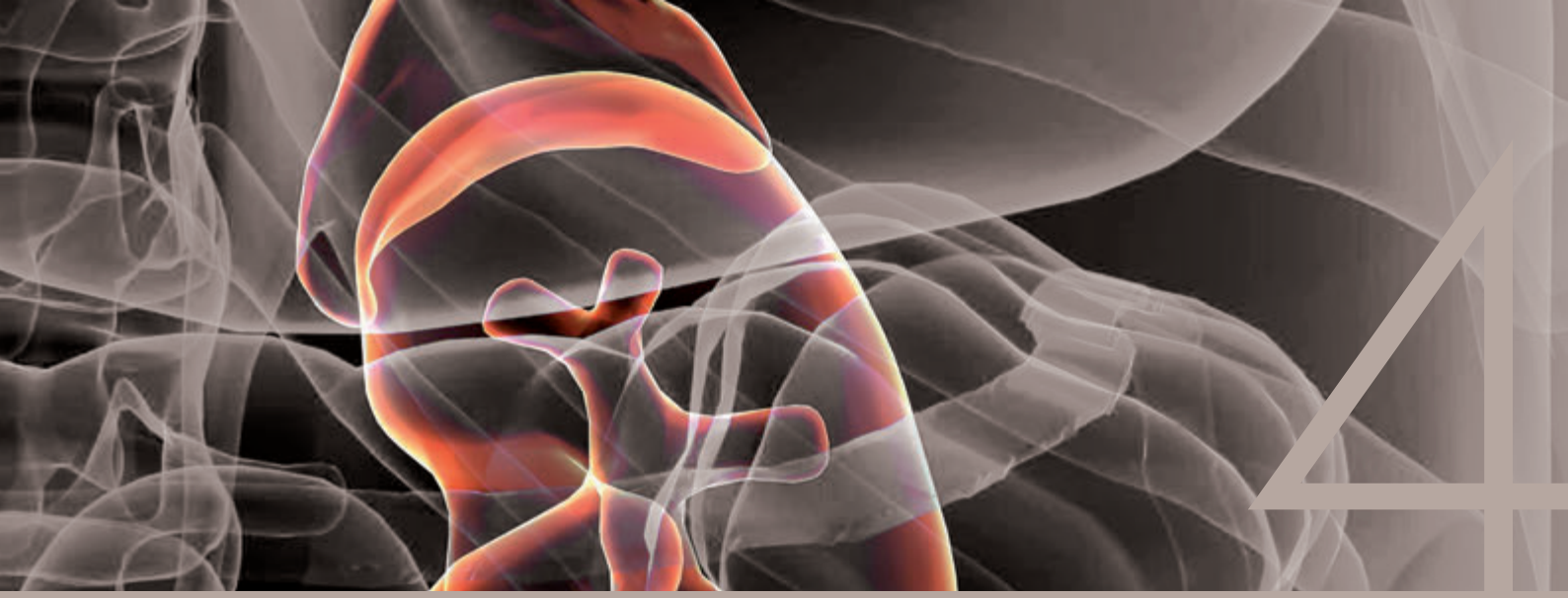
Please check instruction manual for detailed information

> Stable to expiry date below -18 °C



Steroids

Steroids are a group of compounds that are structurally derived from cholesterol. The majority of steroid hormones are secreted by the three steroids glands – the adrenal cortex, testes and ovaries – and during pregnancy by the placenta. They are transported through the bloodstream to the cells of various target organs where they help to regulate a wide range of physiological functions. It is therefore not surprising that the determination of steroids is of clinical significance for the diagnosis of a variety of diseases. The high sensitivity and specificity in comparison to many other methods, as well as the ability to determine several parameters in a single run, makes mass spectrometry the method of choice for the analysis of steroid hormones.



Steroide

Steroide sind eine Gruppe von Verbindungen, die strukturell vom Cholesterin abgeleitet sind. Die Mehrheit der Steroidhormone werden von der Nebennierenrinde, den Hoden und den Eierstöcken produziert sowie während der Schwangerschaft von der Plazenta. Sie werden über den Blutkreislauf zu den Zielzellen transportiert, wo sie eine Vielzahl an physiologischen Prozessen steuern. Daher ist es nicht verwunderlich, dass die Bestimmung von Steroiden bei vielen Krankheiten von klinischer Relevanz sind. Die Methode der Wahl zur Analytik von Steroidhormonen ist die Massenspektrometrie, da sie eine hohe Sensitivität und Spezifität gewährleistet und es ermöglicht, mehrere Parameter in einem Lauf bestimmen zu können.

Overview Steroid Assays

Chromsystems offers CE-IVD validated complete assays, calibrators and controls for the determination of steroids in serum/plasma and of cortisol and cortisone in saliva.

Steroid Profile:
MassChrom® Steroids in Serum/Plasma

> 15 Steroids – 2 panels – 1 analytical column
> One sample preparation for all parameters
> Clinically most relevant steroids covered
> Each parameter safeguarded by its own internal standard
> With 96 SPE well plate or sample clean up columns

Saliva Solution:
MassChrom® Cortisol, Cortisone in Saliva

> Simple and non-invasive sample collection
> Easy sample preparation
> Complete solution from sample to result
> Reliable, robust and proven CE-IVD method

Chromsystems bietet CE-IVD validierte, komplette Kits sowie Kalibratoren und Kontrollen zur Bestimmung von Steroiden im Serum/Plasma und von Cortisol und Cortison im Speichel an.

Steroidbestimmung:
MassChrom® Steroide im Serum/Plasma

> 15 Steroide – 2 Panels – 1 analytische Säule
> Eine Probenvorbereitung für alle Parameter
> Umfasst die klinisch relevantesten Steroide
> Je ein eigener interner Standard pro Parameter
> Wahlweise mit 96-SPE-Well-Platte oder Sample Clean Up Columns

Bestimmung im Speichel:
MassChrom® Cortisol, Cortison im Speichel

> Nicht-invasive und praktische Probenentnahme
> Einfache Probenvorbereitung
> Gesamtlösung von der Probe bis zum Resultat
> Zuverlässige, stabile und validierte CE-IVD-Methode

	Steroid Profile		Saliva
Order number	**72072/96** **72072/480**	**72072/C**	**73000**
Assay name	***MassChrom***® **Steroids in Serum/Plasma**	***MassChrom***® **Steroids in Serum/Plasma**	***MassChrom***® **Cortisol, Cortisone in Saliva**
Sample preparation	96 SPE Well Plate	Sample Clean Up Columns	Clean-Up Tubes
Number of tests	96/480	96	400
Analysis time	Panel 1: 10.0 min Panel 2: 11.7 min	Panel 1: 10.0 min Panel 2: 11.7 min	4.6 min
Parameters	Aldosterone, androstenedione, corticosterone, 11-deoxycorticosterone, cortisol, 11-deoxycortisol, 21-deoxycortisol, cortisone, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), estradiol, progesterone, 17-OH-progesterone, testosterone, dihydrotestosterone (DHT)		Cortisol, cortisone
Page	56	58	66

4.1 *MassChrom*® Steroids in Serum/Plasma

CE IVD

Steroid hormones regulate a number of physiological functions such as lipid and protein metabolism, regulation of reproductive processes and in maintaining water and electrolyte balance. The determination of these parameters is therefore vital for the diagnosis of a number of diseases. By using LC-MS/MS, not only high sensitivity and specificity can be achieved, but also the measurement of multiple analytes in a single run.

The ***MassChrom***® steroid assays include the clinically most important parameters and allow the quantitative determination of 15 steroid hormones that are divided into two panels. Sample preparation is the same for both steroid panels using an optimised and efficient SPE sample clean up procedure in 96 SPE well plates, or with sample clean up columns. The use of stable isotope-labelled internal standards for every single analyte ensures reproducible and reliable quantification of the steroids.

> One single analytical column and one sample preparation for all parameters
> Clinically most relevant steroids covered
> Each parameter safeguarded by its own internal standard

Steroidhormone werden über den Blutstrom zu den Zellen verschiedener Organe transportiert, deren physiologische Prozesse sie beeinflussen und regulieren, wie der Fett- und Proteinstoffwechsel und die Aufrechterhaltung des Wasser- und Elektrolythaushalts. Deshalb ist die Bestimmung dieser Hormone bedeutsam für die Diagnostik vieler Krankheiten. Mittels LC-MS/MS kann nicht nur eine hohe Sensitivität und Spezifität bei der Analytik der Steroidhormone erreicht werden, es wird auch die Messung von mehreren Analyten in einem einzigen Lauf ermöglicht.

Die ***MassChrom***® Steroid Methode erlaubt die quantitative Bestimmung der 15 klinisch relevantesten Steroidhormone, die auf zwei Panels verteilt sind. Die Probenvorbereitung ist für beide Panels identisch und erfolgt über eine Festphasenextraktion mit 96-SPE-Well-Platten oder mit Sample Clean Up Columns. Die Verwendung von isotopenmarkierten stabilen internen Standards für jeden Analyten sichert reproduzierbare und zuverlässige Ergebnisse bei der Quantifizierung der Steroide.

> Eine analytische Säule und eine Probenvorbereitung für alle Parameter
> Umfasst die klinisch relevantesten Steroide
> Je ein eigener interner Standard pro Parameter

4.1.1 *MassChrom*® Steroids with 96 SPE Well Plates

Parameters:
aldosterone, androstenedione, corticosterone, 11-deoxycorticosterone, cortisol, 11-deoxycortisol, 21-deoxycortisol, cortisone, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), estradiol, progesterone, 17-OH-progesterone, testosterone, dihydrotestosterone (DHT).

Order no.	Product
72072/96	***MassChrom***® Steroids in Serum/Plasma with 96 SPE Well Plate For 96 tests
72072/480	***MassChrom***® Steroids in Serum/Plasma with 96 SPE Well Plates For 480 tests

Components available separately

72011	Mobile Phase A, 900 ml
72002	Mobile Phase B, 1000 ml
72033	Elution Buffer, 50 ml
72044	Internal Standard Mix, 5 ml
72005	Extraction Buffer, 45 ml
72006	Reconstitution Buffer, 10 ml
72077	Equilibration Reagent 1, 80 ml
72008	Equilibration Reagent 2, 80 ml
72009	Rinsing Solution, 1000 ml
72012	Wash Buffer, 70 ml
72056	Steroid Collection Plates, 3 pcs.
72057	Steroid 96 SPE Well Plate, 1 pc.
72059	Pierceable Adhesive Seals for 96 SPE Well Plates, 3 pcs.

Startup Accessories

72110	Analytical Column, equilibrated, with test chromatogram, 1 pc.
72019	Tuning Mix ***MassChrom***® Steroid Panel 1, Analytes and Internal Standards, 1 ml
72020	Tuning Mix ***MassChrom***® Steroid Panel 2, Analytes and Internal Standards, 1 ml
72058	Waste Plates, 3 pcs.
72088	System Check Solution ***MassChrom***® Steroid Panel 1, 1 ml
72099	System Check Solution ***MassChrom***® Steroid Panel 2, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
42720	Sample Concentrator for 96 Well Plates, 1 pc.

Multilevel Calibrators and Controls

72038	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 1 (lyoph.), 7 x 3 ml
72039	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 2 (lyoph.), 7 x 3 ml
0341	***MassCheck***® Steroid Panel 1 Serum Control, Level I (lyoph.), 5 x 3 ml
0342	***MassCheck***® Steroid Panel 1 Serum Control, Level II (lyoph.), 5 x 3 ml
0343	***MassCheck***® Steroid Panel 1 Serum Control, Level III (lyoph.), 5 x 3 ml
0345	***MassCheck***® Steroid Panel 2 Serum Control, Level I (lyoph.), 5 x 3 ml
0346	***MassCheck***® Steroid Panel 2 Serum Control, Level II (lyoph.), 5 x 3 ml
0347	***MassCheck***® Steroid Panel 2 Serum Control, Level III (lyoph.), 5 x 3 ml

MassChrom® Steroids with 96 SPE Well Plates

Specifications

Steroid Panel 1
Linearity: covering reference range of each steroid
Limit of quantification: down to 14 ng/l
Intraassay: CV = 1–6 %
Interassay: CV = 3–11 %
Analysis time: 10 min

Steroid Panel 2
Linearity: covering reference range of each steroid
Limit of quantification: down to 5 ng/l
Intraassay: CV = 1–3 %
Interassay: CV = 4–13 %
Analysis time: 11.7 min

Pre-analytic Treatment

Specimen: serum or plasma.
Stability: depending on the specific steroid. Further information can be obtained from the instruction manual.

Sample Preparation

EQUILIBRATION
→ Equilibrate steroid 96 SPE plate with 0.8 ml Equilibration Reagent 1 into each well.
→ Centrifuge 1 min at 400 x g.
→ Repeat with 0.8 ml Equilibration Reagent 2.

SPE CLEAN UP PROCEDURE
→ Pipette 500 µl sample/calibrator/***MassCheck***® control, 50 µl Internal Standard Mix and 450 µl Extraction Buffer into each well of the steroid 96 SPE plate.
→ Vortex for 2 min at 600 rpm.
→ Add 0.7 ml Wash Buffer into each well, centrifuge for 1 min at 400 x g.
→ Add 0.7 ml Wash Buffer into each well, centrifuge for 2 min at 3000 x g to dryness, discard effluent.
→ Place plate onto the steroid collection plate.
→ Add 500 µl Elution Buffer and centrifuge for 1 min at 400 x g.

CONCENTRATION AND INJECTION
→ Place steroid collection plate under nitrogen at 50 °C and evaporate the eluates.
→ Add 100 µl Reconstitution Buffer into each well.
→ Shake collection plate for 2 min at 900 rpm.
→ Seal collection plate with adhesive seal, transfer to autosampler.
→ Inject 5–50 µl eluate into the LC-MS/MS system.

LC-MS/MS Parameters

Injection volume: 5–50 µl
Flowrate: 0.4–0.8 ml/min

Column temperature:
Panel 1: 32 °C
Panel 2: 27 °C

Ionisation:
Panel 1: ESI negative and positive (ESI switch)
Panel 2: ESI positive

MS/MS mode: MRM
Gradient: binary

4.1.2 *MassChrom*® Steroids with Sample Clean Up Columns

Parameters:
aldosterone, androstenedione, corticosterone, 11-deoxycorticosterone, cortisol, 11-deoxycortisol, 21-deoxycortisol, cortisone, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), estradiol, progesterone, 17-OH-progesterone, testosterone, dihydrotestosterone (DHT).

Order no.	Product
72072/C	***MassChrom***® Steroids in Serum/Plasma with Sample Clean Up Columns For 96 tests
	Components available separately
72011	Mobile Phase A, 900 ml
72002	Mobile Phase B, 1000 ml
72033	Elution Buffer, 50 ml
72044	Internal Standard Mix, 5 ml
72005	Extraction Buffer, 45 ml
72006	Reconstitution Buffer, 10 ml
72077	Equilibration Reagent 1, 80 ml
72008	Equilibration Reagent 2, 80 ml
72009	Rinsing Solution, 1000 ml
72012	Wash Buffer, 70 ml
72055	Sample Clean Up Columns, 96 pcs.
J0602	Autosampler Vials, screw neck, 15 µl inner cone, clear glass, 1.1 ml, 100 pcs.
J0410	PP Screw-on Caps, pierceable silicone/ PTFE septa, 1 mm, 100 pcs.
	Startup Accessories
72110	Analytical Column, equilibrated, with test chromatogram, 1 pc.
72019	Tuning Mix ***MassChrom***® Steroid Panel 1, Analytes and Internal Standards, 1 ml
72020	Tuning Mix ***MassChrom***® Steroid Panel 2, Analytes and Internal Standards, 1 ml
33007	Tubes for sample preparation, 50 pcs.
72088	System Check Solution ***MassChrom***® Steroid Panel 1, 1 ml
72099	System Check Solution ***MassChrom***® Steroid Panel 2, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
42730	Sample Concentrator for Autosampler Vials, 1 pc.

	Multilevel Calibrators and Controls
72038	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 1 (lyoph.), 7 x 3 ml
72039	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 2 (lyoph.), 7 x 3 ml
0341	***MassCheck***® Steroid Panel 1 Serum Control, Level I (lyoph.), 5 x 3 ml
0342	***MassCheck***® Steroid Panel 1 Serum Control, Level II (lyoph.), 5 x 3 ml
0343	***MassCheck***® Steroid Panel 1 Serum Control, Level III (lyoph.), 5 x 3 ml
0345	***MassCheck***® Steroid Panel 2 Serum Control, Level I (lyoph.), 5 x 3 ml
0346	***MassCheck***® Steroid Panel 2 Serum Control, Level II (lyoph.), 5 x 3 ml
0347	***MassCheck***® Steroid Panel 2 Serum Control, Level III (lyoph.), 5 x 3 ml

MassChrom® Steroids with Sample Clean Up Columns

Specifications

Steroid Panel 1
Linearity: covering reference range of each steroid
Limit of quantification: down to 14 ng/l
Intraassay: CV = 1–6 %
Interassay: CV = 3–11 %
Analysis time: 10 min

Steroid Panel 2
Linearity: covering reference range of each steroid
Limit of quantification: down to 5 ng/l
Intraassay: CV = 1–3 %
Interassay: CV = 4–13 %
Analysis time: 11.7 min

Pre-analytic Treatment

Specimen: serum or plasma.
Stability: depending on the specific steroid. Further information can be obtained from the instruction manual.

Sample Preparation

EQUILIBRATION
→ Put sample clean up columns into tubes for sample preparation.
→ Pipette 0.8 ml Equilibration Reagent 1 into each sample clean up column.
→ Centrifuge 1 min at 400 x g, check for complete run through, discard effluent.
→ Repeat with 0.8 ml Equilibration Reagent 2.

SAMPLE PREPARATION WITH SAMPLE CLEAN UP COLUMNS
→ Pipette 500 µl of the well homogenised sample/calibrator/*MassCheck*® control into each sample clean up column.
→ Add 50 µl Internal Standard Mix and 450 µl Extraction Buffer and homogenise (vortex slightly for 15 seconds).
→ Centrifuge 1 min at 400 x g, check for complete run through, discard effluent.
→ Add 0.7 ml Wash Buffer and centrifuge 1 min at 400 x g, discard effluent.
→ Add 0.7 ml Wash Buffer and centrifuge 2 min at 3000 x g to dryness, discard effluent.
→ Put labelled autosampler vials with inner cone into tubes for sample preparation, then put sample clean up columns on top.
→ Add 1 ml Elution Buffer and centrifuge 1 min at 400 x g.

CONCENTRATION AND INJECTION
→ Evaporate eluates in the labelled autosampler vials under nitrogen or compressed air at 45 °C to dryness.
→ Reconstitute with 100 µl Reconstitution Buffer in the labelled autosampler vials, then close using crimping pliers and vortex for 15 sec.
→ Centrifuge 5 min at 15 000 x g.
→ Transfer to autosampler.
→ Inject 5–50 µl of eluate into the LC-MS/MS system.

LC-MS/MS Parameters

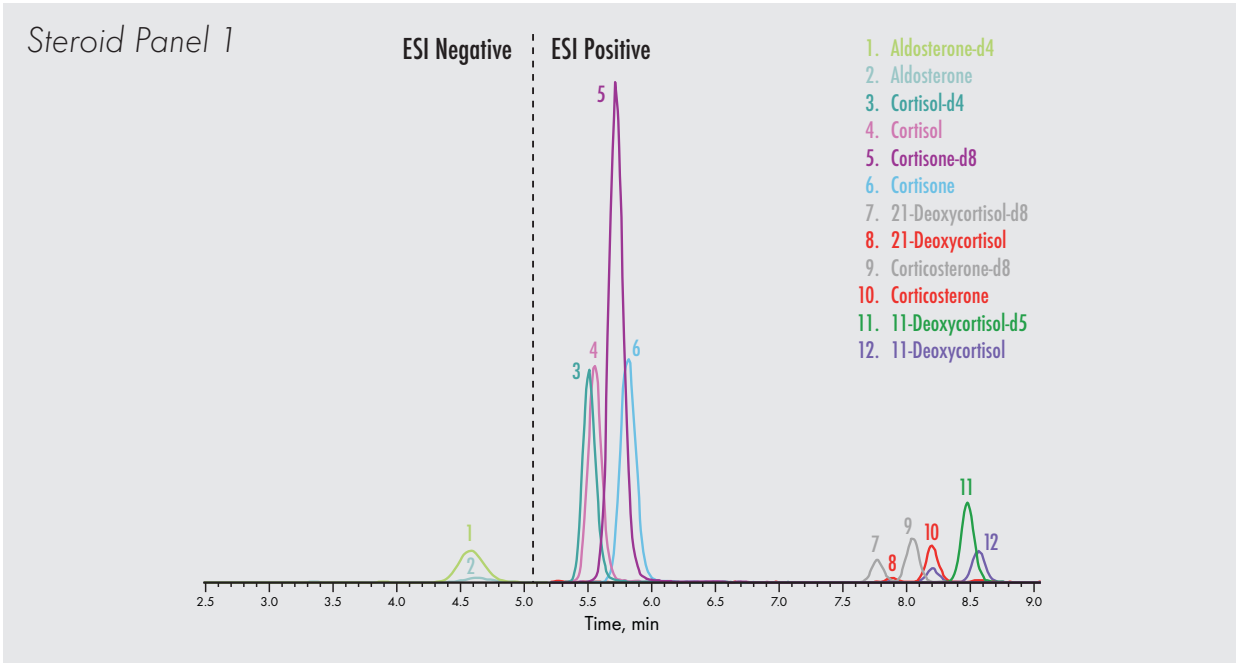
Injection volume: 5–50 µl
Flowrate: 0.4–0.8 ml/min

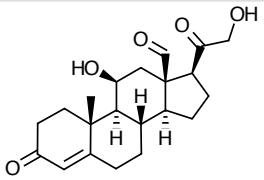
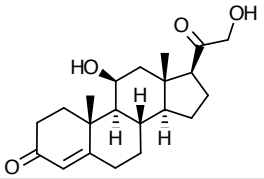
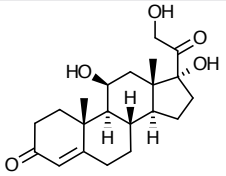
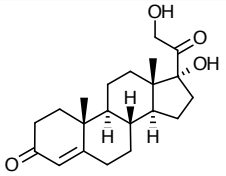
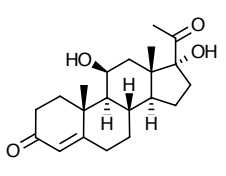
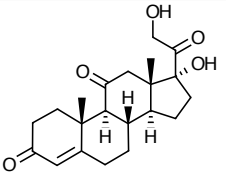
Column temperature:
Panel 1: 32 °C
Panel 2: 27 °C

Ionisation:
Panel 1: ESI negative and positive (ESI switch)
Panel 2: ESI positive

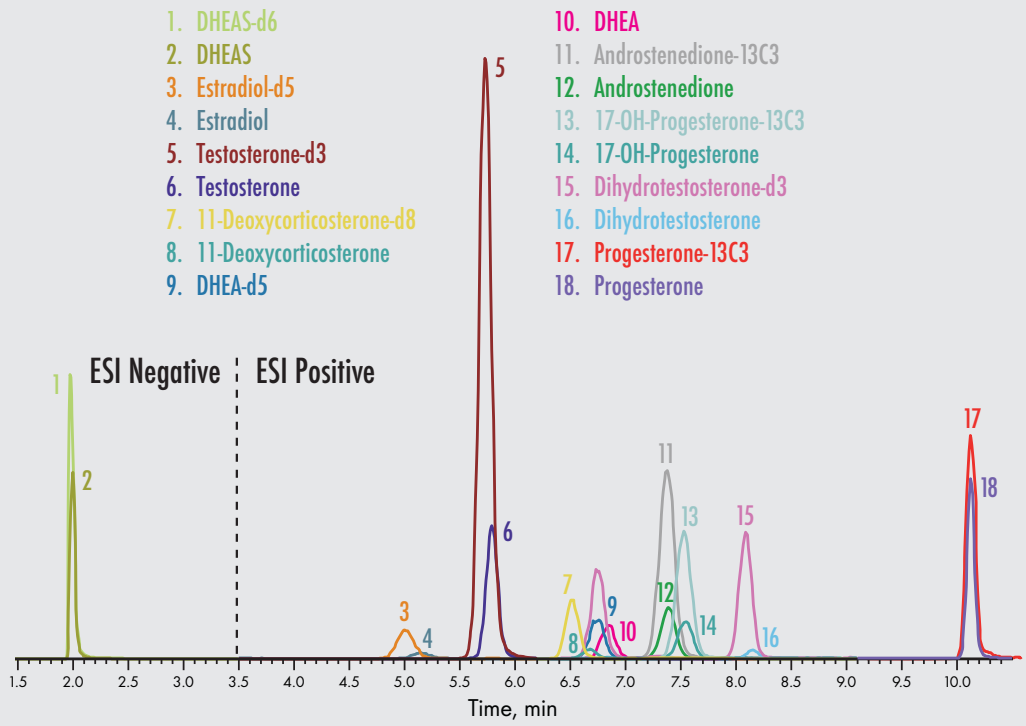
MS/MS mode: MRM
Gradient: binary

MassChrom® Steroids in Serum/Plasma Panel 1

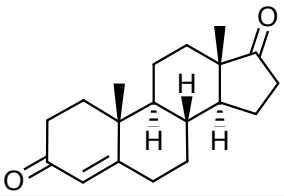
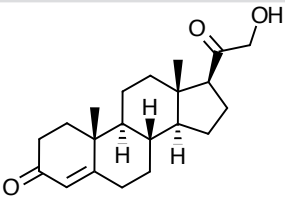
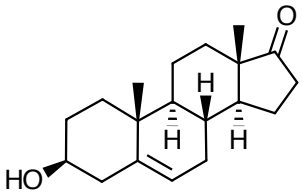
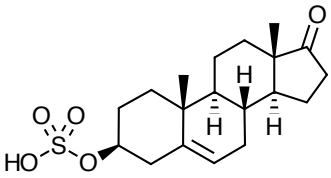
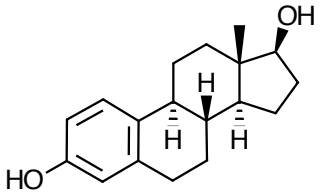
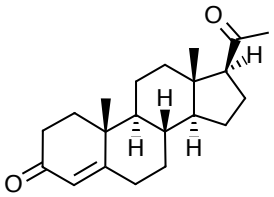
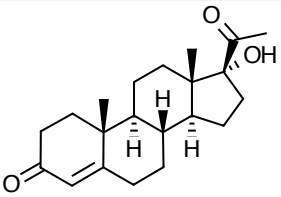
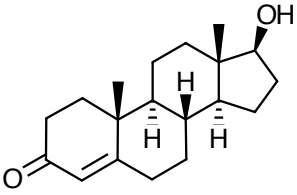
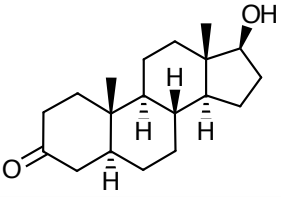


Substance	Mw (g/mol)	Formula	Structure
Aldosterone	360.44	$C_{21}H_{28}O_5$	
Corticosterone	346.46	$C_{21}H_{30}O_4$	
Cortisol	362.46	$C_{21}H_{30}O_5$	
11-Deoxycortisol	346.46	$C_{21}H_{30}O_4$	
21-Deoxycortisol	346.47	$C_{21}H_{30}O_4$	
Cortisone	360.44	$C_{21}H_{28}O_5$	

Steroid Panel 2



MassChrom® Steroids in Serum/Plasma Panel 2

Substance	Mw (g/mol)	Formula	Structure
Androstenedione	286.41	$C_{19}H_{26}O_2$	
11-Deoxycorticosterone	330.46	$C_{21}H_{30}O_3$	
Dehydroepiandrosterone (DHEA)	288.42	$C_{19}H_{28}O_2$	
Dehydroepiandrosterone sulfate (DHEA-S)	368.49	$C_{19}H_{28}O_5S$	
Estradiol	272.36	$C_{18}H_{24}O_2$	
Progesterone	314.46	$C_{21}H_{30}O_2$	
17-OH-progesterone	330.46	$C_{21}H_{30}O_3$	
Testosterone	288.42	$C_{19}H_{28}O_2$	
Dihydrotestosterone (DHT)	290.44	$C_{19}H_{30}O_2$	

6PLUS1® Multilevel Serum Calibrator Set Steroid Panel 1

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Aldosterone	0.030	0.077	0.148	0.294	0.735	2.88	< LOQ
Corticosterone	0.505	0.998	2.59	5.10	15.0	47.6	< LOQ
Cortisol	9.72	20.4	41.1	80.5	149	289	< LOQ
11-Deoxycortisol	0.093	0.492	0.979	1.92	4.60	14.2	< LOQ
21-Deoxycortisol	0.066	0.151	0.238	0.461	1.41	4.57	< LOQ
Cortisone	1.04	2.56	5.04	9.92	19.5	38.2	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

6PLUS1® Multilevel Serum Calibrator Set Steroid Panel 2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Androstenedione	0.200	0.401	0.773	1.42	4.79	14.3	< LOQ
11-Deoxycorticosterone	0.046	0.093	0.137	0.278	0.674	2.71	< LOQ
Dehydroepiandrosterone (DHEA)	1.14	5.49	10.5	15.8	31.8	61.9	< LOQ
Dehydroepiandrosterone sulfate (DHEA-S)	119	542	1044	2045	4016	6012	< LOQ
Estradiol	0.040	0.106	0.261	0.525	1.58	5.25	< LOQ
Progesterone	0.181	0.784	2.00	4.87	10.1	24.7	< LOQ
17-OH-progesterone	0.098	0.487	0.971	1.91	3.84	14.5	< LOQ
Testosterone	0.058	0.261	1.04	2.96	5.91	11.9	< LOQ
Dihydrotestosterone (DHT)	0.058	0.106	0.242	0.465	0.898	1.33	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Steroid Panel 1 Serum Controls

Substance	Target Value Level I* (µg/l)	Target Value Level II* (µg/l)	Target Value Level III* (µg/l)
Aldosterone	0.097	0.247	0.979
Corticosterone	0.814	4.13	29.8
Cortisol	25.3	60.7	178
11-Deoxycortisol	0.286	1.44	9.63
21-Deoxycortisol	0.098	0.370	2.32
Cortisone	2.04	11.8	29.4

MassCheck® Steroid Panel 2 Serum Controls

Substance	Target Value Level I* (µg/l)	Target Value Level II* (µg/l)	Target Value Level III* (µg/l)
Androstenedione	0.297	1.15	9.68
11-Deoxycorticosterone	0.075	0.185	0.936
Dehydroepiandrosterone (DHEA)	2.2	13.1	42.4
Dehydroepiandrosterone sulfate (DHEA-S)	269	1549	5084
Estradiol	0.081	0.414	2.66
Progesterone	0.342	3.12	15.6
17-OH-progesterone	0.289	1.46	8.79
Testosterone	0.208	1.49	8.08
Dihydrotestosterone (DHT)	0.084	0.374	1.09

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
72038	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 1 (lyoph.), 7 x 3 ml
72039	6PLUS1® Multilevel Serum Calibrator Set ***MassChrom***® Steroid Panel 2 (lyoph.), 7 x 3 ml
0341	***MassCheck***® Steroid Panel 1 Serum Control, Level I (lyoph.), 5 x 3 ml
0342	***MassCheck***® Steroid Panel 1 Serum Control, Level II (lyoph.), 5 x 3 ml
0343	***MassCheck***® Steroid Panel 1 Serum Control, Level III (lyoph.), 5 x 3 ml
0345	***MassCheck***® Steroid Panel 2 Serum Control, Level I (lyoph.), 5 x 3 ml
0346	***MassCheck***® Steroid Panel 2 Serum Control, Level II (lyoph.), 5 x 3 ml
0347	***MassCheck***® Steroid Panel 2 Serum Control, Level III (lyoph.), 5 x 3 ml

Stability of Serum Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 10 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

4.2 *MassChrom*® Cortisol, Cortisone in Saliva

CE IVD

The ***MassChrom***® assay Cortisol, Cortisone in Saliva allows the quantitative determination of cortisol and cortisone in patient saliva samples by LC-MS/MS. It encompasses all required components for an efficient and fast sample preparation by filtration with clean-up tubes. The use of stable isotopically labelled internal standards for both analytes ensures reproducible and reliable quantification. The 6PLUS1® Multilevel Calibrator Set and ***MassCheck***® controls ensure high precision of results.

Der ***MassChrom***® Kit Cortisol, Cortison im Speichel ermöglicht die quantitative Bestimmung von Cortisol und Cortison in Patientenspeichelproben mit LC-MS/MS. Die Probenvorbereitung erfolgt über eine einfache Filtration mit Clean-Up Tubes. Die Verwendung von stabilen isotopenmarkierten internen Standards für beide Analyten gewährleistet eine reproduzierbare und zuverlässige Quantifizierung. 6PLUS1® Multilevel Calibrator Set und ***MassCheck***® Kontrollen sorgen zudem für eine hohe Präzision der Ergebnisse.

- **Simple and non-invasive sample collection**
- **Easy sample preparation**
- **Complete solution from sample to result**
- **Reliable, robust and proven CE-IVD method**

- **Nicht-invasive und praktische Probenentnahme**
- **Einfache Probenvorbereitung**
- **Gesamtlösung von der Probe bis zum Resultat**
- **Zuverlässige, stabile und validierte CE-IVD-Methode**

MassChrom® Cortisol, Cortisone in Saliva

Parameters:
cortisol, cortisone

Order no.	Product
73000	***MassChrom***® Cortisol, Cortisone in Saliva For 400 tests
	Components available separately
73001	Mobile Phase A, 500 ml
73002	Mobile Phase B, 450 ml
73004	Internal Standard Mix, 4 x 5 ml
73009	Rinsing Solution, 500 ml
73008	Clean-Up Tubes, 100 pcs.
	Startup Accessories
73100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
73015	Tuning Mix, Analytes and Internal Standards, 1 ml
72088	System Check Solution ***MassChrom***® Steroid Panel 1, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0410	PP Screw-on Caps, pierceable silicone/PTFE septa, 1 mm, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
J0403	Micro-inserts for autosampler vials, 100 pcs.
	Multilevel Calibrators and Controls
73039	6PLUS1® Multilevel Saliva Calibrator Set Cortisol, Cortisone, 7 x 1 ml
0349	***MassCheck***® Cortisol, Cortisone Saliva Control, Level I, 5 x 1 ml
0350	***MassCheck***® Cortisol, Cortisone Saliva Control, Level II, 5 x 1 ml

Specifications

Limit of quantification:	0.3 µg/l
Linearity:	cortisol up to 120 µg/l cortisone up to 180 µg/l
Intraassay:	CV = 2–5 %
Interassay:	CV = 2–7 %
Recovery:	96–105 %
Analysis time:	4.6 min

Pre-analytic Treatment

Specimens: saliva.
Stability: stored cooled at +4 °C samples are stable for 3 months. For longer storage periods keep samples frozen below -18 °C.

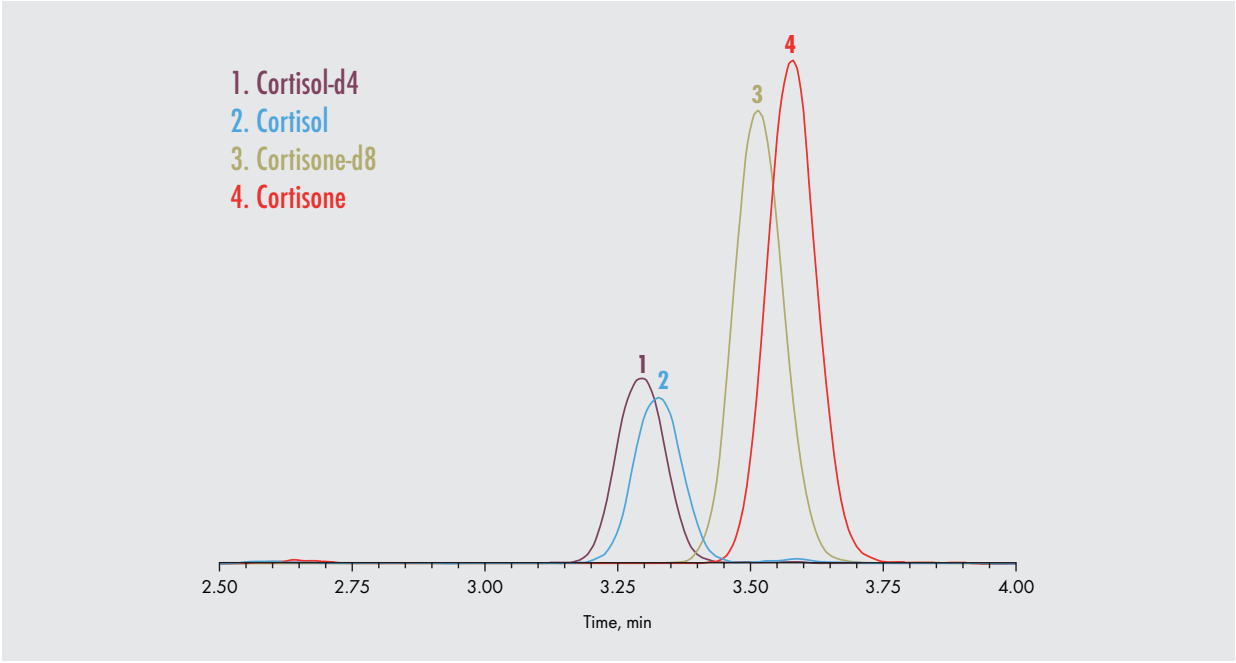
Sample Preparation

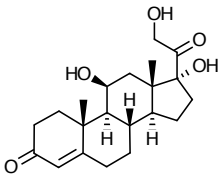
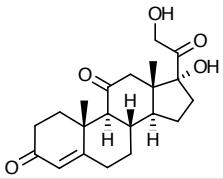
→ Pipette 100 µl sample/calibrator/***MassCheck***® control into a clean-up tube.
→ Add 50 µl Internal Standard Mix.
→ Centrifuge 15 min at 14 000 x g.
→ Transfer each filtrate into a 1.5 ml vial equipped with micro-inserts.
→ Seal each vial and transfer into autosampler.
→ Inject up to 30 µl.

LC-MS/MS Parameters

Injection volume:	≤ 30 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	binary

MassChrom® Cortisol, Cortisone in Saliva



Substance	Mw (g/mol)	Formula	Structure
Cortisol	362.46	$C_{21}H_{30}O_5$	
Cortisone	360.44	$C_{21}H_{28}O_5$	

6PLUS1® Multilevel Saliva Calibrator Set Cortisol, Cortisone

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Cortisol	0.57	1.10	5.36	10.8	21.7	64.6	< LOQ
Cortisone	1.16	5.68	11.3	16.8	34.0	99.2	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Cortisol, Cortisone Saliva Controls

Substance	Target Value Level I* (µg/l)	Target Value Level II* (µg/l)
Cortisol	0.86	7.92
Cortisone	2.22	14.0

** Please check packaging leaflet for specific lot concentrations*

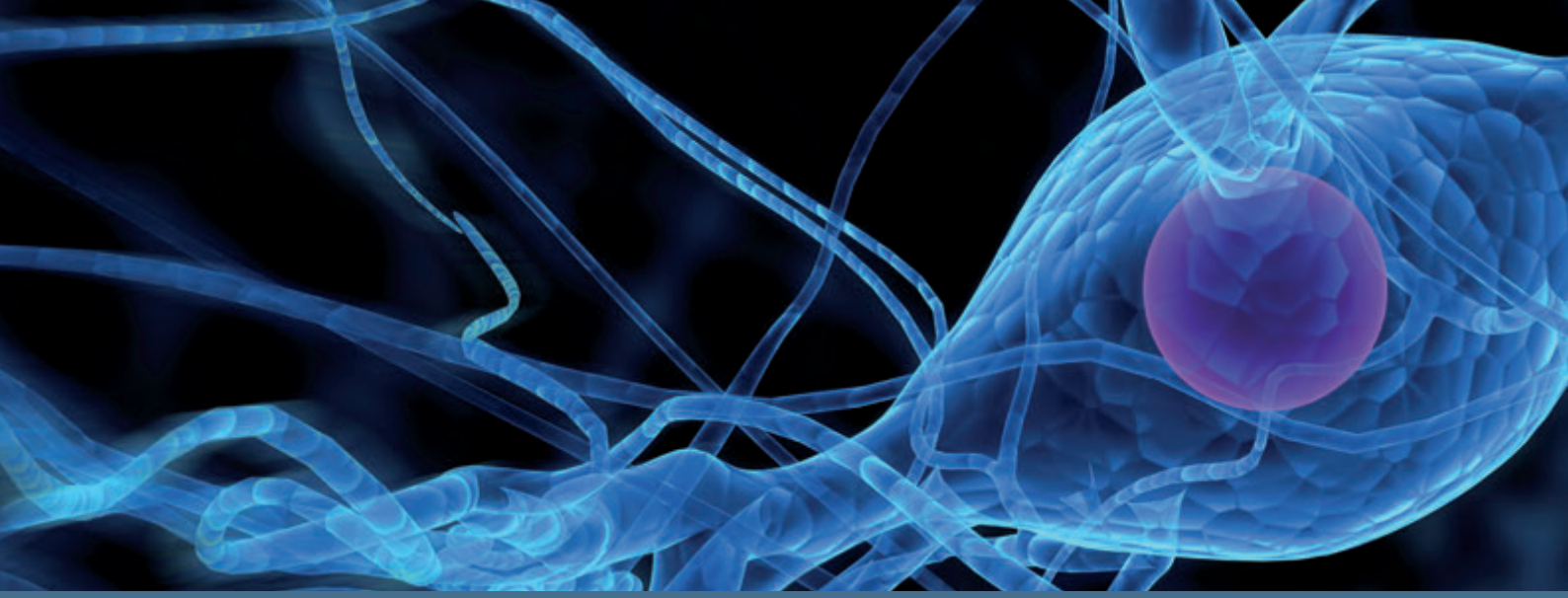
Order no.	Product
73039	6PLUS1® Multilevel Saliva Calibrator Set Cortisol, Cortisone, 7 x 1 ml
0349	***MassCheck***® Cortisol, Cortisone Saliva Control, Level I, 5 x 1 ml
0350	***MassCheck***® Cortisol, Cortisone Saliva Control, Level II, 5 x 1 ml

Stability of Saliva Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C

Notes



Biogenic Amines

Biogenic amines are biologically active compounds that play critical roles in physiological functions, such as brain activity or the regulation of body temperature and stomach pH. They are important parameters for the diagnosis of a number of diseases such as phaeochromocytoma or other tumours of the nervous system. Reliable results in routine diagnostics are therefore of clinical significance.

Biogene Amine sind biologisch aktive Substanzen, die eine wichtige Aufgabe bei physiologischen Prozessen erfüllen, wie zum Beispiel der Hirnaktivität oder der Regulation von Körpertemperatur und pH-Wert des Magens. Sie sind wichtige Parameter für die Diagnose einer Reihe von Krankheiten wie der Phäochromazytome oder anderer Tumore des Nervensystems. Zuverlässige Ergebnisse in der Routinediagnostik haben deshalb eine hohe klinische Bedeutung.

5

Biogene Amine

Overview Biogenic Amine Assays by LC-MS/MS

The system ***MassChrom®*** Biogenic Amines/Metabolites in Urine consists of one Chromatographic Platform and three individual Sample Prep Sets. The Sample Prep Sets represent different analyte groups:
1. Catecholamines, free metanephrines and serotonin
2. Total metanephrines (free + conjugated)
3. VMA, HVA and 5-HIAA.

The single Chromatographic Platform is used for all three Sample Prep Sets and comprises of mobile phases, rinsing solution and analytical column. An exchange of the chromatographic system between analysis of the different analyte groups is therefore not required. The Sample Prep Sets provide everything required for the reliable and equally efficient sample preparation. Furthermore, an assay allows the quantitative determination of free metanephrine, normetanephrine and 3-methoxytyramine in plasma.

> One Chromatographic Platform for all parameters in urine determination
> Automated assay also available
> Determination of free metanephrines in plasma
> Fast and efficient sample prep and analysis
> 6PLUS1® Multilevel Calibrator Sets and *MassCheck®* controls

Das System ***MassChrom®*** Biogene Amine/Metaboliten im Urin besteht aus einer chromatographischen Plattform (Chromatographic Platform) und drei individuellen Sample Prep Sets. In den Sample Prep Sets sind die verschiedenen Analytgruppen zusammengefasst:
1. Katecholamine, freie Metanephrine und Serotonin
2. Gesamt-Metanephrine (frei + konjugiert)
3. VMA, HVA, 5-HIAA.

Die chromatographische Plattform ist für alle Sample Prep Sets gleich und besteht aus mobilen Phasen, Rinsing Solution und analytischer Säule. Ein Austausch des chromatographischen Systems ist somit zwischen den Analysen der einzelnen Analytgruppen nicht erforderlich. Die Sample Prep Sets bieten alles, was für die zuverlässige und effiziente Probenvorbereitung notwendig ist. Weiterhin ermöglicht ein Assay die quantitative Bestimmung von freiem Metanephrin, Normetanephrin und 3-Methoxytyramin im Plasma.

> Eine chromatographische Plattform für alle Parameter bei der Bestimmung im Urin
> Automatisierte Methoden verfügbar
> Freie Metanephrine im Plasma bestimmbar
> Schnelle und effiziente Probenvorbereitung und Analytik
> 6PLUS1® Multilevel Kalibrator Sets und *MassCheck®* Kontrollen

MassChrom® Biogenic Amines/Metabolites in Urine

Chromatographic Platform Starter Set	No. 80000 ***MassChrom*® Biogenic Amines/Metabolites in Urine** consisting of Mobile Phases, Rinsing Solution and Analytical Column		
Sample Prep Sets	No. 80600 **Catecholamines** **Free Metanephrines** **Serotonin** *Adrenaline (epinephrine)* *Noradrenaline (norepinephrine)* *Dopamine* *Free metanephrine* *Free normetanephrine* *Free 3-methoxytyramine* *Serotonin*	No. 80700 **Total Metanephrines** (free + conjugated) *Total metanephrine* *Total normetanephrine* *Total 3-methoxytyramine*	No. 80800 **VMA, HVA, 5-HIAA** *Vanillylmandelic acid (VMA)* *Homovanillic acid (HVA)* *5-Hydroxyindoleacetic acid (5-HIAA)*
Calibrators	No. 80639 **6PLUS1® Catecholamines** **Free Metanephrines** **Serotonin**	No. 80739 **6PLUS1® Total Metanephrines**	No. 80839 **6PLUS1® VMA, HVA, 5-HIAA**
Controls	No. 0372/0373 ***MassCheck*® Controls** **Catecholamines** **Free Metanephrines** **Serotonin, Level I + II**	No. 0376/0377 ***MassCheck*® Controls** **Total Metanephrines** **Level I + II**	No. 0381/0382 ***MassCheck*® Controls** **VMA, HVA, 5-HIAA** **Level I + II**

MassChrom® Biogenic Amines in Plasma

Assay	***MassChrom*® Free Metanephrines in Plasma**	
Kits	No. 81000 **Free Metanephrines** **with 96 SPE Well Plates** *Free metanephrine* *Free normetanephrine* *Free 3-methoxytyramine*	No. 81000/C **Free Metanephrines** **with Sample Clean Up Columns** *Free metanephrine* *Free normetanephrine* *Free 3-methoxytyramine*
Calibrators	No. 81039 **6PLUS1® Free Metanephrines**	No. 81039 **6PLUS1® Free Metanephrines**
Controls	No. 0384/0385/0386 ***MassCheck*® Controls** **Free Metanephrines** **Level I + II + III**	No. 0384/0385/0386 ***MassCheck*® Controls** **Free Metanephrines** **Level I + II + III**

The Multilevel Calibrators cover the whole concentration range from the LLOQ through to the cut-off value and pathological ranges.
Die Multilevel Kalibratoren decken den gesamten Konzentrationsbereich von der LLOQ bis zum Cut-off-Wert und den pathologischen Bereich ab.

5.1 *MassChrom*® Biogenic Amines/Metabolites in Urine Catecholamines, free Metanephrines, Serotonin

CE IVD

The Sample Prep Set Catecholamines, free Metanephrines and Serotonin in Urine allows the quantitative determination of adrenaline, noradrenaline, dopamine, metanephrine, normetanephrine and serotonin in patient urine samples by LC-MS/MS. One typical application for this test is the analysis of patient samples with suspected catecholamine or serotonine secreting tumors.

The Sample Prep Set encompasses all required components for an efficient and fast sample preparation. The correct pH, required for a precise analysis, is verified quickly and conveniently by a colour indicator and can be adjusted with a specific reagent. The 6PLUS1® Multilevel Calibrator Set and ***MassCheck***® controls ensure high precision of results.

- **Identical Chromatographic Platform for all Sample Prep Sets**
- **7 parameters with one Sample Prep Set**
- **Isotopically labelled internal standards**
- **6PLUS1® Multilevel Calibrator Set and *MassCheck*® controls**
- **Automated version available**

Das Sample Prep Set Katecholamine, freie Metanephrine und Serotonin im Urin erlaubt die quantitative Bestimmung von Adrenalin, Noradrenalin, Dopamin, Metanephrin, Normetanephrin und Serotonin in Patienten-Urinproben mit LC-MS/MS. Eine typische Anwendung des Tests ist die Analytik von Patientenproben mit Verdacht auf katecholamin- oder serotoninbildende Tumore.

Das Sample Prep Set umfasst alle Komponenten, die für die effiziente und schnelle Probenvorbereitung notwendig sind. Der für eine präzise Analytik erforderliche korrekte pH-Wert wird schnell und einfach mittels eines Farbindikators geprüft und bei Bedarf mit einem speziellen Reagenz angepasst. Das 6PLUS1® Multilevel Calibrator Set und die ***MassCheck***® Kontrollen gewährleisten eine hohe Genauigkeit der Ergebnisse.

- **Identische chromatographische Plattform für alle Sample Prep Sets**
- **7 Parameter mit einem Sample Prep Set**
- **Isotopenmarkierte interne Standards**
- **6PLUS1® Multilevel Calibrator Set und *MassCheck*® Kontrollen**
- **Automatisierte Methode verfügbar**

5.1.1 Sample Prep Set Catecholamines, free Metanephrines, Serotonin in Urine with 96 SPE Well Plates

Parameters:
adrenaline (epinephrine), noradrenaline (norepinephrine), dopamine, free metanephrine, free normetanephrine, free 3-methoxytyramine, serotonin.

Order no.	Product
80000	***Mass**Chrom*® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80600/96	***Mass**Chrom*® Biogenic Amines/Metabolites in Urine: Catecholamines, free Metanephrines, Serotonin with 96 SPE Well Plate Sample Prep Set for 96 tests
	Components available separately
80604	Internal Standard Mix , 5 ml
80605	Neutralisation Buffer, 60 ml
80606	Wash Buffer 1, 90 ml
80607	Wash Buffer 2, 90 ml
80608	Elution Buffer, 50 ml
80609	Dilution Buffer, 50 ml
80056	Collection Plates, 3 pcs.
80057	96 SPE Well Plate, 1 pc.
80059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
80600/480	***Mass**Chrom*® Biogenic Amines/Metabolites in Urine: Catecholamines, free Metanephrines, Serotonin with 96 SPE Well Plates Sample Prep Set for 480 tests
	Components available separately
80604/5	Internal Standard Mix, 5 x 5 ml
80675	Neutralisation Buffer, 300 ml
80676	Wash Buffer 1, 450 ml
80677	Wash Buffer 2, 500 ml
80678	Elution Buffer, 250 ml
80679	Dilution Buffer, 250 ml
80056	Collection Plates, 3 pcs.
80057	96 SPE Well Plate, 1 pc.
80059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
	Startup Accessories
80615	Tuning Mix, Internal Standards and Analytes, 1 ml
80610	System Check Solution, 1 ml
80603	Adjustment Reagent, 10 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
80639	6PLUS1® Multilevel Urine Calibrator Set, Catecholamines, free Metanephrines, Serotonin (lyoph.), 7 x 2 ml
0372	***Mass**Check*® Catecholamines, free Metanephrines, Serotonin Urine Control, Level I (lyoph.), 5 x 2 ml
0373	***Mass**Check*® Catecholamines, free Metanephrines, Serotonin Urine Control, Level II (lyoph.), 5 x 2 ml

Sample Prep Catecholamines, free Metanephrines, Serotonin in Urine with SPE 96 Well Plates

Specifications

Linearity:	1600–5000 µg/l
Limit of quantification:	1.0–13.5 µg/l
Intraassay:	CV = 1.5–8.7 %
Interassay:	CV = 3.1–10.7 %
Analysis time:	4 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl. Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ 200 µl sample + 50 µl Internal Standard Mix + 600 µl Neutralisation Buffer.
→ Check for correct colour.
→ Centrifuge 5 min at 150 x g, discard effluent.
→ Wash 3 times and centrifuge each time, discard effluent.
→ Elute with 500 µl Elution Buffer and centrifuge.
→ Add 500 µl Dilution Buffer and vortex.
→ Inject ≤ 10 µl.

LC-MS/MS Parameters

Injection volume:	≤ 10 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

5.1.2 Sample Prep Set Catecholamines, free Metanephrines, Serotonin in Urine with Sample Clean Up Columns

Parameters:
adrenaline (epinephrine), noradrenaline (norepinephrine), dopamine, free metanephrine, free normetanephrine, free 3-methoxytyramine, serotonin.

Order no.	Product
80000	***MassChrom***® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80600/C	***MassChrom***® Biogenic Amines/Metabolites in Urine: Catecholamines, free Metanephrines, Serotonin with Sample Clean Up Columns Sample Prep Set for 96 tests
	Components available separately
80604	Internal Standard Mix , 5 ml
80605	Neutralisation Buffer, 60 ml
80606	Wash Buffer 1, 90 ml
80607	Wash Buffer 2, 90 ml
80608	Elution Buffer, 50 ml
80609	Dilution Buffer, 50 ml
80055	Sample Clean Up Columns, 96 pcs.
	Startup Accessories
80615	Tuning Mix, Internal Standards and Analytes, 1 ml
80610	System Check Solution, 1 ml
80603	Adjustment Reagent, 10 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
33007	Tubes for sample preparation, 50 pcs.
	Multilevel Calibrator and Controls
80639	6PLUS1® Multilevel Urine Calibrator Set, Catecholamines, free Metanephrines, Serotonin (lyoph.), 7 x 2 ml
0372	***MassCheck***® Catecholamines, free Metanephrines, Serotonin Urine Control, Level I (lyoph.), 5 x 2 ml
0373	***MassCheck***® Catecholamines, free Metanephrines, Serotonin Urine Control, Level II (lyoph.), 5 x 2 ml

Specifications

Linearity:	1600–5000 µg/l
Limit of quantification:	1.0–13.5 µg/l
Intraassay:	CV = 1.5–8.7 %
Interassay:	CV = 3.1–10.7 %
Analysis time:	4 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl. Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

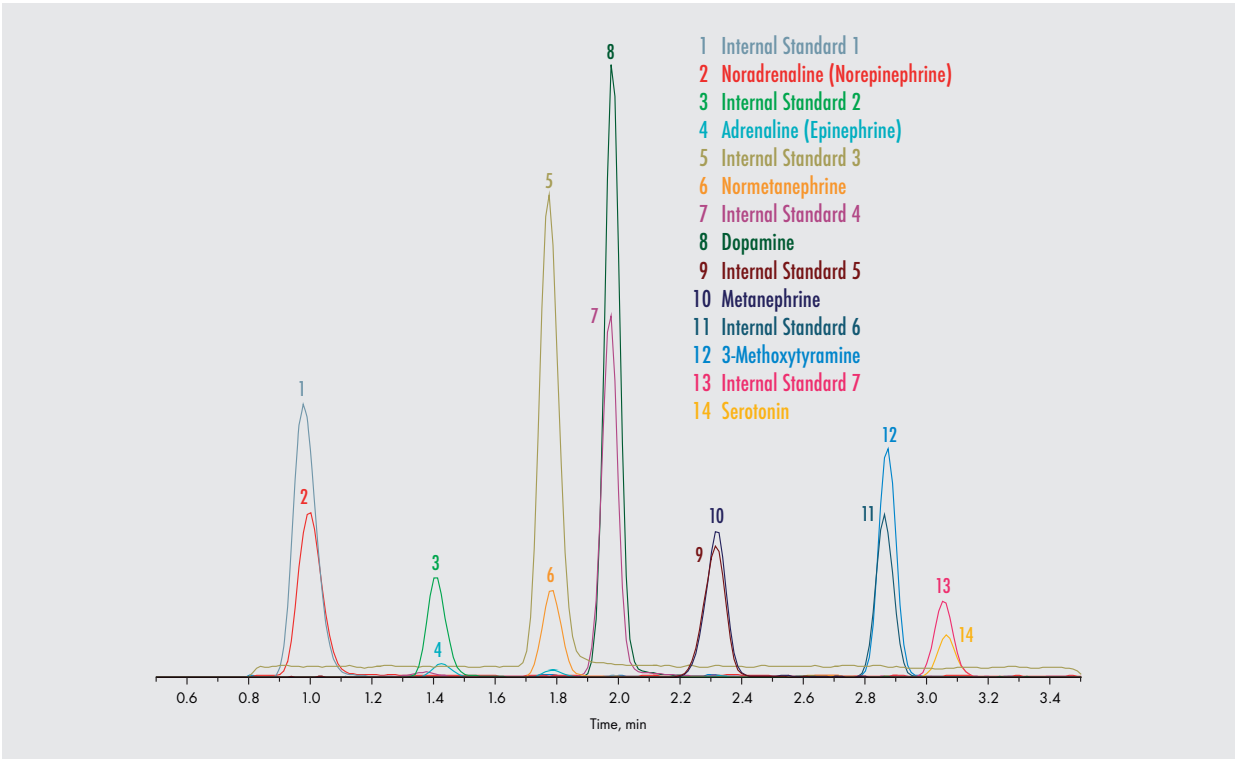
Sample Preparation

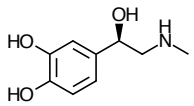
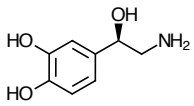
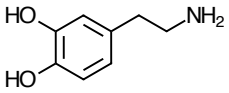
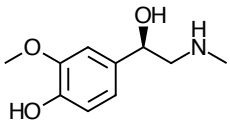
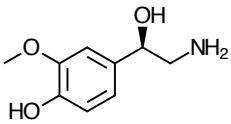
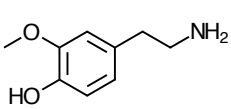
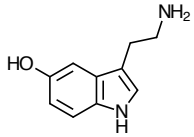
→ 200 µl sample + 50 µl Internal Standard Mix + 600 µl Neutralisation Buffer.
→ Check for correct colour.
→ Centrifuge 5 min at 150 x g, discard effluent.
→ Wash 3 times and centrifuge each time, discard effluent.
→ Elute with 500 µl Elution Buffer and centrifuge.
→ Add 500 µl Dilution Buffer and vortex.
→ Inject ≤ 10 µl.

LC-MS/MS Parameters

Injection volume:	≤ 10 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

MassChrom® Biogenic Amines/Metabolites in Urine
Catecholamines, free Metanephrines, Serotonin



Substance	Mw (g/mol)	Formula	Structure
Adrenaline (epinephrine)	183.20	$C_9H_{13}NO_3$	
Noradrenaline (norepinephrine)	169.18	$C_8H_{11}NO_3$	
Dopamine	153.18	$C_8H_{11}NO_2$	
Free metanephrine	197.23	$C_{10}H_{15}NO_3$	
Free normetanephrine	183.20	$C_9H_{13}NO_3$	
Free 3-methoxytyramine	167.21	$C_9H_{13}NO_2$	
Serotonin	176.22	$C_{10}H_{12}N_2O$	

6PLUS1® Multilevel Urine Calibrator Set Catecholamines, free Metanephrines, Serotonin

Substance	Calibrator 1* µg/l nmol/l	Calibrator 2* µg/l nmol/l	Calibrator 3* µg/l nmol/l	Calibrator 4* µg/l nmol/l	Calibrator 5* µg/l nmol/l	Calibrator 6* µg/l nmol/l	Blank Calibrator µg/l nmol/l
Adrenaline (epinephrine)	4.96 27.1	11.4 62.2	17.7 96.6	24.1 132	298 1627	570 3111	< LOQ < LOQ
Noradrenaline (norepinephrine)	4.56 27.0	34.3 203	66.3 392	95.6 565	423 2500	751 4439	< LOQ < LOQ
Dopamine	31.5 206	180 1175	326 2128	477 3114	1036 6762	1579 10307	< LOQ < LOQ
Free metanephrine	2.18 11.1	35.3 179	67.2 341	98.6 500	1280 6491	2424 12292	< LOQ < LOQ
Free normetanephrine	3.31 18.1	36.5 199	68.5 374	99.1 541	1054 5753	2001 10922	< LOQ < LOQ
Free 3-methoxytyramine	7.46 44.6	38.0 227	69.3 414	100 598	712 4258	1313 7853	< LOQ < LOQ
Serotonin	28.7 163	83.0 471	137 777	190 1078	1276 7241	2347 13319	< LOQ < LOQ

** Please check packaging leaflet for specific lot concentrations, LOQ = limit of quantification*

MassCheck® Catecholamines, free Metanephrines, Serotonin Urine Controls

Substance	Unit	Target Value Level I*	Target Value Level II*
Adrenaline (epinephrine)	µg/l nmol/l	19.1 104	161 879
Noradrenaline (norepinephrine)	µg/l nmol/l	75.8 448	268 1584
Dopamine	µg/l nmol/l	374 2441	752 4909
Free metanephrine	µg/l nmol/l	77.6 394	684 3469
Free normetanephrine	µg/l nmol/l	78.6 429	572 3122
Free 3-methoxytyramine	µg/l nmol/l	79.2 474	406 2428
Serotonin	µg/l nmol/l	152 863	726 4120

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
80639	6PLUS1® Multilevel Urine Calibrator Set, Catecholamines, free Metanephrines, Serotonin (lyoph.), 7 x 2 ml
0372	*MassCheck*® Catecholamines, free Metanephrines, Serotonin Urine Control, Level I (lyoph.), 5 x 2 ml
0373	*MassCheck*® Catecholamines, free Metanephrines, Serotonin Urine Control, Level II (lyoph.), 5 x 2 ml

Stability of Urine Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

5.2 *MassChrom*® Biogenic Amines/Metabolites in Urine Total Metanephrines (free + conjugated)

CE IVD

Total Metanephrines (free + conjugated)

This Sample Prep Set allows the quantitative determination of total metanephrine, normetanephrine and 3-methoxytyramine in patient urine samples by LC-MS/MS. The conjugated metanephrines are released by hydrolysis and are determined as sum together with the free forms. One typical application of this kit is the analysis of patient samples with a suspicion of catecholamine-secreting tumours.

The Sample Prep Set encompasses all components required for an efficient and fast sample preparation. After hydrolysis of the conjugated metanephrines, the sample is purified by solid phase extraction (SPE) with sample clean up columns or 96 SPE well plates, and the concentration of the total metanephrines is determined. The 6PLUS1® Multilevel Calibrator Set and ***MassCheck***® controls ensure high precision of results. An automated workflow is also available.

- **Identical Chromatographic Platform for all Sample Prep Sets**
- **Isotopically labelled internal standards for each analyte**
- **6PLUS1® Multilevel Calibrator Set and *MassCheck*® controls**
- **Automated method available**

Dieses Sample Prep Set erlaubt die quantitative Bestimmung von Gesamt-Metanephrin, Normetanephrin und 3-Methoxytyramin im Urin mit LC-MS/MS. Die konjugierten Metanephrine werden durch Hydrolyse freigesetzt und als Summe mit den freien Formen quantifiziert. Eine typische Anwendung ist die Diagnostik von Patientenproben mit Verdacht auf Katecholamin-sezernierende Tumore.

In diesem Sample Prep Set sind alle erforderlichen Komponenten für eine effiziente und schnelle Probenvorbereitung enthalten. Nach der Hydrolyse der konjugierten Metanephrine wird die Probe durch Festphasenextraktion (SPE) mit Sample Clean Up Columns oder mit 96-SPE-Well-Platten gereinigt und die Konzentration der Gesamt-Metanephrine bestimmt. Eine automatisierte Workflow-Lösung ist ebenfalls verfügbar.

- **Eine gemeinsame chromatographische Plattform für alle Sample Prep Sets**
- **Isotopenmarkierter interner Standard für jeden Analyten**
- **6PLUS1® Multilevel Calibrator Set und *MassCheck*® Kontrollen**
- **Automatisierte Methode verfügbar**

5.2.1 Sample Prep Set Total Metanephrines (free + conjugated) in Urine with 96 SPE Well Plate

Parameters:
total metanephrine (free + conjugated), total normetanephrine (free + conjugated), total 3-methoxytyramine (free + conjugated).

Order no.	Product
80000	***MassChrom***® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80700/96	***MassChrom***® Biogenic Amines/Metabolites in Urine: Total Metanephrines (free + conjugated) with 96 SPE Well Plate Sample Prep Set for 96 tests
	Components available separately
80703	Hydrolysis Buffer, 3 ml
80704	Internal Standard Mix , 5 ml
80605	Neutralisation Buffer, 60 ml
80606	Wash Buffer 1, 90 ml
80607	Wash Buffer 2, 90 ml
80608	Elution Buffer, 50 ml
80609	Dilution Buffer, 50 ml
80056	Collection Plates, 3 pcs.
80057	96 SPE Well Plate, 1 pc.
80058	Hydrolysis Plates, 3 pcs.
80059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
	Startup Accessories
80615	Tuning Mix, Internal Standards and Analytes, 1 ml
80610	System Check Solution, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
80739	6PLUS1® Multilevel Urine Calibrator Set, Total Metanephrines (free + conjugated) (lyoph.), 7 x 2 ml
0376	***MassCheck***® Total Metanephrines (free + conjugated) Urine Control, Level I (lyoph.), 5 x 2 ml
0377	***MassCheck***® Total Metanephrines (free + conjugated) Urine Control, Level II (lyoph.), 5 x 2 ml

Specifications

Linearity:	metanephrine, normetanephrine up to 20 mg/l 3-methoxytyramine up to 10 mg/l
Limit of quantification:	4.0–5.5 µg/l
Intraassay:	CV = 2.5–5.6 %
Interassay:	CV = 3.2–4.9 %
Recovery:	92–107 %
Analysis time:	4 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl. Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ 200 µl urine + 50 µl Internal Standard Mix + 25 µl Hydrolysis Buffer.
→ Hydrolyse in the oven for 45 min at 120 °C.
→ Cool for at least 10 min at +2 to +8 °C.
→ 50 µl hydrolysed sample + 600 µl Neutralisation Buffer.
→ Centrifuge 5 min at 150 x g, discard effluent.
→ Wash 3 times and centrifuge each time, discard effluent.
→ Centrifuge 1 min at 2000 x g to dryness, discard effluent.
→ Elute with 500 µl Elution Buffer and centrifuge 2 min at 100 x g.
→ Add 500 µl Dilution Buffer and vortex.
→ Inject ≤ 20 µl.

LC-MS/MS Parameters

Injection volume:	≤ 20 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

5.2.2 Sample Prep Set Total Metanephrines (free + conjugated) in Urine with Sample Clean Up Columns

Parameters:
total metanephrine (free + conjugated), total normetanephrine (free + conjugated), total 3-methoxytyramine (free + conjugated).

Order no.	Product
80000	***Mass**Chrom*® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80700/C	***Mass**Chrom*® Biogenic Amines/Metabolites in Urine: Total Metanephrines (free + conjugated) with Sample Clean Up Columns Sample Prep Set for 96 tests
	Components available separately
80703	Hydrolysis Buffer, 3 ml
80704	Internal Standard Mix , 5 ml
80605	Neutralisation Buffer, 60 ml
80606	Wash Buffer 1, 90 ml
80607	Wash Buffer 2, 90 ml
80608	Elution Buffer, 50 ml
80609	Dilution Buffer, 50 ml
80055	Sample Clean Up Columns, 96 pcs.
33006	Reaction Vials, 100 pcs.
	Startup Accessories
80615	Tuning Mix, Internal Standards and Analytes, 1 ml
80610	System Check Solution, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
80739	6PLUS1® Multilevel Urine Calibrator Set, Total Metanephrines (free + conjugated) (lyoph.), 7 x 2 ml
0376	***Mass**Check*® Total Metanephrines (free + conjugated) Urine Control, Level I (lyoph.), 5 x 2 ml
0377	***Mass**Check*® Total Metanephrines (free + conjugated) Urine Control, Level II (lyoph.), 5 x 2 ml

Specifications

Limit of quantification:	4.0–5.5 µg/l
Linearity:	Metanephrine, Normetanephrine up to 20 mg/l 3-Methoxytyramine up to 10 mg/l
Recovery:	92–107 %
Intraassay:	CV = 2.5–5.6 %
Interassay:	CV = 3.2–4.9 %
Analysis time:	4 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl. Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

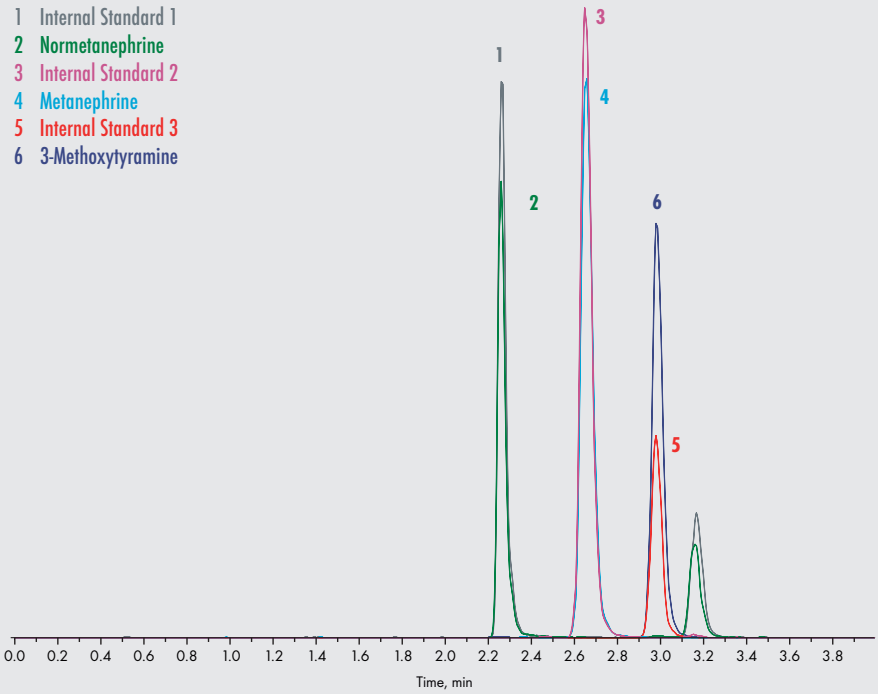
Sample Preparation

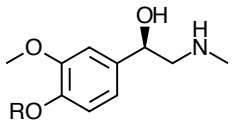
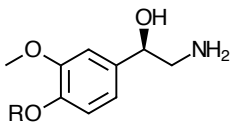
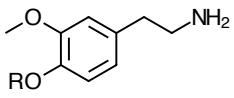
→ 200 µl urine + 50 µl Internal Standard Mix + 25 µl Hydrolysis Buffer.
→ Hydrolyse in the waterbath for 30 min at 95 °C.
→ Cool for at least 10 min at +2 to +8 °C.
→ 50 µl hydrolysed sample + 600 µl Neutralisation Buffer.
→ Centrifuge 5 min at 150 x g, discard effluent.
→ Wash 3 times and centrifuge each time, discard effluent.
→ Centrifuge 1 min at 2000 x g to dryness, discard effluent.
→ Elute with 500 µl Elution Buffer and centrifuge 2 min at 100 x g.
→ Add 500 µl Dilution Buffer and vortex.
→ Inject ≤ 20 µl.

LC-MS/MS Parameters

Injection volume:	≤ 20 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

MassChrom® Biogenic Amines/Metabolites in Urine
Total Metanephrines (free + conjugated)



Substance	Mw (g/mol)	Formula	Structure
Total metanephrine (free + conjugated)	197.23 (free)	$C_{10}H_{15}NO_3$ (free)	 Free metanephrine R = H Conjugated metanephrine mainly as R = SO_3 R = glucuronide
Total normetanephrine (free + conjugated)	183.20 (free)	$C_9H_{13}NO_3$ (free)	 Free normetanephrine R = H Conjugated normetanephrine mainly as R = SO_3 R = glucuronide
Total 3-methoxytyramine (free + conjugated)	167.21 (free)	$C_9H_{13}NO_2$ (free)	 Free 3-methoxytyramine R = H Conjugated 3-methoxytyramine mainly as R = SO_3 R = glucuronide

6PLUS1® Multilevel Urine Calibrator Set
MassChrom® Total Metanephrines (free + conjugated)

Substance	Calibrator 1* µg/l	Calibrator 2* µg/l	Calibrator 3* µg/l	Calibrator 4* µg/l	Calibrator 5* µg/l	Calibrator 6* µg/l	Blank Calibrator µg/l
Total metanephrine (free + conjugated)	10.5	197	370	557	2686	4875	< LOQ
Total normetanephrine (free + conjugated)	15.6	319	607	883	4770	8582	< LOQ
Total 3-methoxytyramine (free + conjugated)	15.9	134	239	345	2501	4723	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Total Metanephrines (free + conjugated) Urine Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Total metanephrine (free + conjugated)	138	953
Total normetanephrine (free + conjugated)	224	1633
Total 3-methoxytyramine (free + conjugated)	129	778

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
80739	6PLUS1® Multilevel Urine Calibrator Set, Total Metanephrines (free + conjugated) (lyoph.), 7 x 2 ml
0376	*MassCheck*® Total Metanephrines (free + conjugated) Urine Control, Level I (lyoph.), 5 x 2 ml
0377	*MassCheck*® Total Metanephrines (free + conjugated) Urine Control, Level II (lyoph.), 5 x 2 ml

Stability of Urine Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

5.3 *MassChrom*® Biogenic Amines/Metabolites in Urine VMA, HVA, 5-HIAA

CE IVD

This Sample Prep Set in urine allows the quantitative determination of vanillylmandelic acid (VMA), homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) in patient urine samples by LC-MS/MS. It is used for the diagnostics of neuroblastoma and carcinoid tumours.

The Sample Prep Set includes all components for an efficient and fast sample preparation, which consists of just 3 simple pipetting steps: addition of the Internal Standard Mix and Stabilisation Buffer to the urine sample and following injection into the LC-MS/MS instrument.

You have the choice between autosampler vials or a method with collection plates, to which there is also an automated workflow available.

> Simple and fast sample preparation
> Isotopically labelled internal standards for each analyte
> Identical Chromatographic Platform for all Sample Prep Sets
> 6PLUS1® Multilevel Calibrator Set and *MassCheck*® controls
> Automated version available

Dieses Sample Prep Set erlaubt die quantitative Bestimmung von Vanillinmandelsäure (VMA), Homovanillinsäure (HVA), 5-Hydroxyindolessigsäure (5-HIAA) im Urin mit LC-MS/MS. Es wird für die Diagnostik von Neuroblastomen und karzinoiden Tumoren eingesetzt.

Dieses Sample Prep Set enthält alle erforderlichen Komponenten für eine effiziente und schnelle Probenvorbereitung, die lediglich 3 Pipettierschritte umfasst: Zugabe des Internal Standard Mix und des Stabilisation Buffers zur Urinprobe mit anschließender Injektion in das LC-MS/MS Gerät.

Sie haben die Wahl zwischen Autosampler Vials oder einer Methode mit Auffangplatten, zu der es auch eine automatisierte Workflow-Lösung gibt.

> Einfache und schnelle Probenvorbereitung: Injektion nach nur 3 Pipettierschritten
> Isotopenmarkierter interner Standard für jeden Analyten
> Eine gemeinsame Chromatographische Plattform für alle Sample Prep Sets
> 6PLUS1® Multilevel Calibrator Set und *MassCheck*® Kontrollen
> Automatisierte Methode verfügbar

5.3.1 Sample Prep Set VMA, HVA, 5-HIAA in Urine with Autosampler Vials

Parameters:
vanillylmandelic acid (VMA), homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA).

Order no.	Product
80000	***MassChrom***® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80200	Analytical Column, equilibrated, with test chromatogram (allows the use of higher injection volumes), 1 pc.
80800	***MassChrom***® Biogenic Amines/Metabolites in Urine: VMA, HVA, 5-HIAA with Autosampler Vials, Sample Prep Set for 96 tests
	Components available separately
80804	Internal Standard Mix, 2.5 ml
80805	Stabilisation Buffer, 45 ml
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
	Startup Accessories
80815	Tuning Mix, Internal Standards and Analytes, 1 ml
80810	System Check Solution Set, consisting of: System Check Solution, 1 ml Dilution Buffer, 2 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
80839	6PLUS1® Multilevel Urine Calibrator Set, VMA, HVA, 5-HIAA (lyoph.), 7 x 1 ml
0381	***MassCheck***® VMA, HVA, 5-HIAA Urine Control, Level I (lyoph.), 5 x 1 ml
0382	***MassCheck***® VMA, HVA, 5-HIAA Urine Control, Level II (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 150–250 mg/l
Limit of quantification:	down to 0.2 mg/l
Intraassay:	CV = 2.5–6.7 %
Interassay:	CV = 3.7–7.7 %
Recovery:	95–113 %
Analysis time:	3 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl (VMA, HVA) or 10 ml glacial acetic acid (5-HIAA). Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ 50 µl urine + 25 µl Internal Standard Mix + 425 µl Stabilisation Buffer.
→ Mix briefly (vortex).
→ Inject ≤ 2 µl.

LC-MS/MS Parameters

Injection volume:	≤ 2 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

5.3.2 Sample Prep Set VMA, HVA, 5-HIAA in Urine with Collection Plates

Parameters:
vanillylmandelic acid (VMA), homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA).

Order no.	Product
80000	***MassChrom***® Biogenic Amines/Metabolites in Urine, Chromatographic Platform Starter Set
	Components available separately
80001	Mobile Phase A, 1000 ml
80002	Mobile Phase B, 500 ml
80009	Rinsing Solution, 1000 ml
80100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
80200	Analytical Column, equilibrated, with test chromatogram (allows the use of higher injection volumes), 1 pc.
80800/96	***MassChrom***® Biogenic Amines/Metabolites in Urine: VMA, HVA, 5-HIAA with Collection Plates Sample Prep Set for 96 tests
	Components available separately
80804	Internal Standard Mix, 2.5 ml
80805	Stabilisation Buffer, 45 ml
80056	Collection Plates, 3 pcs.
80059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
80800/480	***MassChrom***® Biogenic Amines/Metabolites in Urine: VMA, HVA, 5-HIAA with Collection Plates Sample Prep Set for 480 tests
	Components available separately
80804/5	Internal Standard Mix, 5 x 2.5 ml
80875	Stabilisation Buffer, 105 ml
80056	Collection Plates, 3 pcs.
80059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
	Startup Accessories
80815	Tuning Mix, Internal Standards and Analytes, 1 ml
80810	System Check Solution Set, consisting of: System Check Solution, 1 ml Dilution Buffer, 2 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
80839	6PLUS1® Multilevel Urine Calibrator Set, VMA, HVA, 5-HIAA (lyoph.), 7 x 1 ml
0381	***MassCheck***® VMA, HVA, 5-HIAA Urine Control, Level I (lyoph.), 5 x 1 ml
0382	***MassCheck***® VMA, HVA, 5-HIAA Urine Control, Level II (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 150–250 mg/l
Limit of quantification:	down to 0.2 mg/l
Intraassay:	CV = 2.5–6.7 %
Interassay:	CV = 3.7–7.7 %
Recovery:	95–113 %
Analysis time:	3 min

Pre-analytic Treatment

Specimens: 24 h urine collected in a suitable container with 10 ml of 10–25 % HCl (VMA, HVA) or 10 ml glacial acetic acid (5-HIAA). Spontaneous urine can be also analysed (see instruction manual).
Stability: protected from light, patient specimens are stable for up to 7 days at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

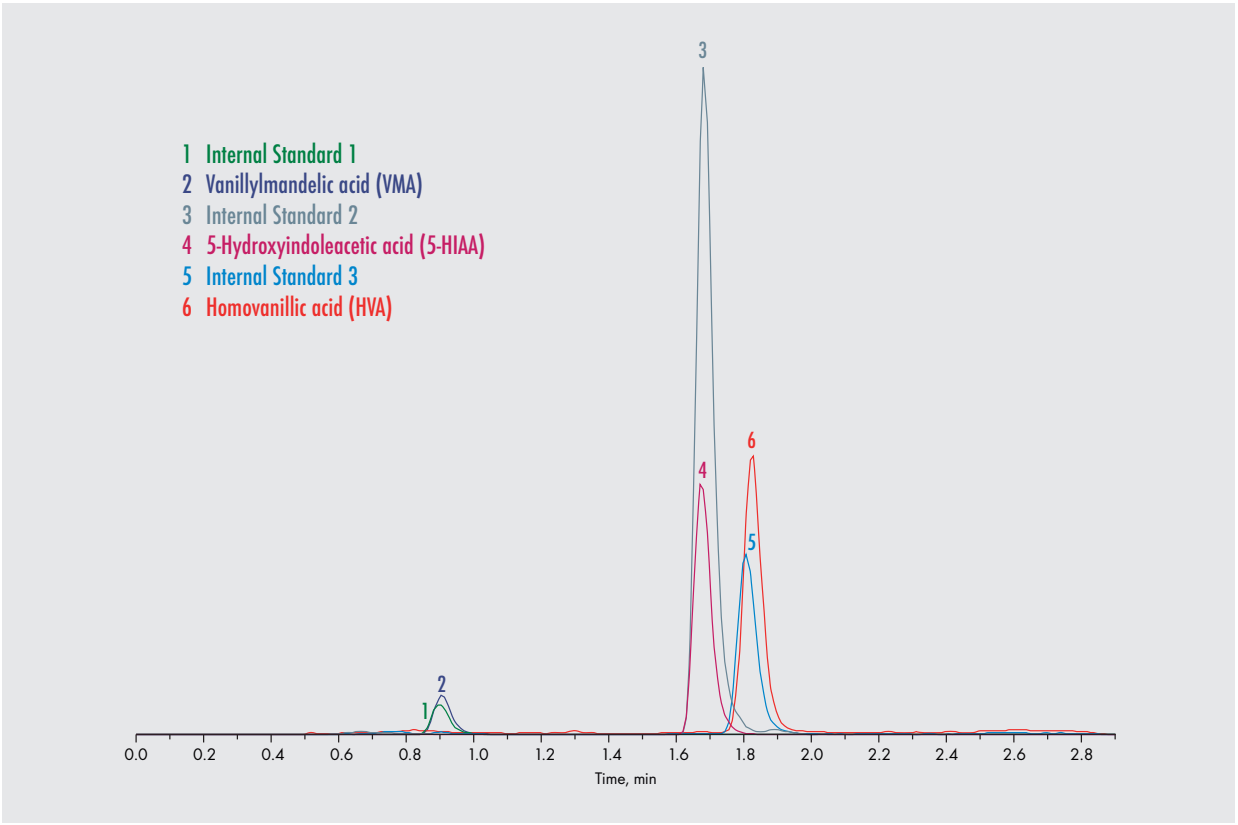
Sample Preparation

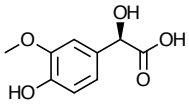
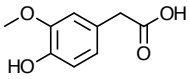
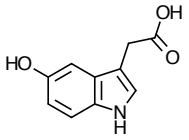
→ 50 µl urine + 25 µl Internal Standard Mix + 425 µl Stabilisation Buffer.
→ Seal and agitate collection plate for 2 min at 1200 rpm (orbit 2 mm) and transfer to autosampler.
→ Inject ≤ 2 µl.

LC-MS/MS Parameters

Injection volume:	≤ 2 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

MassChrom® Biogenic Amines/Metabolites in Urine
VMA, HVA, 5-HIAA



Substance	Mw (g/mol)	Formula	Structure
Vanillylmandelic acid (VMA)	198.17	$C_9H_{10}O_5$	
Homovanillic acid (HVA)	182.18	$C_9H_{10}O_4$	
5-Hydroxyindoleacetic acid (5-HIAA)	191.19	$C_{10}H_9NO_3$	

6PLUS1® Multilevel Urine Calibrator Set VMA, HVA, 5-HIAA

Substance	Calibrator 1* mg/l µmol/l	Calibrator 2* mg/l µmol/l	Calibrator 3* mg/l µmol/l	Calibrator 4* mg/l µmol/l	Calibrator 5* mg/l µmol/l	Calibrator 6* mg/l µmol/l	Blank Calibrator mg/l µmol/l
Vanillylmandelic acid (VMA)	1.19 6.00	9.37 47.3	17.4 87.8	25.4 128	51.1 258	77.3 390	< LOQ < LOQ
Homovanillic acid (HVA)	0.869 4.77	11.8 64.8	23.4 128	34.7 190	79.9 439	119 653	< LOQ < LOQ
5-Hydroxyindoleacetic acid (5-HIAA)	0.699 3.66	2.51 13.1	4.55 23.8	6.44 33.7	37.2 195	68.0 356	< LOQ < LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® VMA, HVA, 5-HIAA Urine Controls

Substance	Unit	Target Value Level I*	Target Value Level II*
Vanillylmandelic acid (VMA)	mg/l µmol/l	20.3 102	38.4 194
Homovanillic acid (HVA)	mg/l µmol/l	27.9 153	57.4 315
5-Hydroxyindoleacetic acid (5-HIAA)	mg/l µmol/l	5.36 28	22.0 115

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
80839	6PLUS1® Multilevel Urine Calibrator Set, VMA, HVA, 5-HIAA (lyoph.), 7 x 1 ml
0381	*MassCheck®* VMA, HVA, 5-HIAA Urine Control, Level I (lyoph.), 5 x 1 ml
0382	*MassCheck®* VMA, HVA, 5-HIAA Urine Control, Level II (lyoph.), 5 x 1 ml

Stability of Urine Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

5.4 *MassChrom*® Free Metanephrines in Plasma

CE IVD

Free Metanephrines in Plasma

Pheochromocytomas and other neural crest tumours (e.g. paragangliomas and neuroblastomas) secrete metanephrine, normetanephrine and 3-methoxytyramine. These plasma free metanephrines are more stable and secreted more evenly than catecholamines (epinephrine, norepinephrine, and dopamine). Some studies show that the analysis of plasma free metanephrines has the highest sensitivity and specificity in pheochromocytoma diagnostics compared to plasma free catecholamines and metanephrines in urine.

This assay allows the quantitative determination of metanephrine, normetanephrine and 3-methoxytyramine in plasma by LC-MS/MS. It encompasses all required components and allows a simple and fast sample preparation: solid phase extraction (SPE) without equilibration/conditioning steps, analyte enrichment without evaporation step, only one elution step. The analytes are chromatographically separated to avoid co-elution and to minimise risks of interferences. The use of stable isotope-labelled internal standards for every single analyte ensures reproducible and reliable quantification.

- **6PLUS1® Multilevel Calibrator Set and *MassCheck*® controls based on human plasma**
- **Simple sample prep in just a few steps**
- **Chromatographic separation of analytes, no co-elution**
- **Isotopically labelled internal standards for all analytes**

Phäochromozytome und andere neuroendokrine Tumore (z. B. Paragangliome und Neuroblastome) sezernieren Metanephrin, Normetanephrin und 3-Methoxytyramin. Diese freien Plasma-Metanephrine sind stabiler und werden gleichmäßiger ausgeschieden als Katecholamine (Epinephrin, Norepinephrin und Dopamin). Einige Studien zeigen, dass die Analytik von freien Plasma Metanephrinen die höchste Sensitivität und Spezifität bei der Phäochromozytom-Diagnostik im Vergleich zu freien Plasma-Katecholaminen und Metanephrinen im Urin aufweist.

Dieser Kit ermöglicht die quantitative Bestimmung von Metanephrin, Normetanephrin und 3-Methoxytyramin im Plasma mit LC-MS/MS. Er umfasst alle benötigten Komponenten und zeichnet sich durch eine einfache und schnelle Probenvorbereitung aus: Festphasenextraktion (SPE) ohne Äquilibrierungs-/Konditionierungsschritte, Analyt-Anreicherung ohne Verdampfungsschritt, nur ein Elutionsschritt. Die Analyten werden chromatographisch getrennt, um eine Co-Elution zu vermeiden und Risiken von Interferenzen zu minimieren. Die Verwendung von stabilen isotopenmarkierten internen Standards für jeden einzelnen Analyten gewährleistet eine reproduzierbare und zuverlässige Quantifizierung.

- **6PLUS1® Multilevel Calibrator Set und *MassCheck*® Kontrollen aus Humanplasma**
- **Einfache Probenvorbereitung in nur wenigen Schritten**
- **Chromatographische Trennung der Analyten, keine Co-Elution**
- **Isotopenmarkierte interne Standards für alle Analyten**

5.4.1 Free Metanephrines in Plasma with 96 SPE Well Plates

Parameters:
free metanephrine, free normetanephrine, free 3-methoxytyramine.

Order no.	Product
81000	***MassChrom***® Free Metanephrines in Plasma with 96 SPE Well Plates For 2 x 96 tests
	Components available separately
81001	Mobile Phase A, 750 ml
81002	Mobile Phase B, 450 ml
81003	Dilution Buffer, 50 ml
81004	Internal Standard Mix, 2 x 2.5 ml
81005	Wash Buffer 1, 90 ml
81006	Wash Buffer 2, 90 ml
81007	Elution Buffer, 25 ml
81009	Rinsing Solution, 500 ml
81057	96 SPE Well Plate, 1 pc.
81058	Collection Plates, 3 pcs.
81059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
	Startup Accessories
81100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
81015	Tuning Mix, Analytes and Internal Standards, 1 ml
81010	System Check Solution, 1 ml
81056	Waste Plates, 3 pcs.
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Multilevel Calibrator and Controls
81039	6PLUS1® Multilevel Plasma Calibrator Set Free Metanephrines, 7 x 3 ml
0384	***MassCheck***® Free Metanephrines Plasma Control, Level I, 5 x 3 ml
0385	***MassCheck***® Free Metanephrines Plasma Control, Level II, 5 x 3 ml
0386	***MassCheck***® Free Metanephrines Plasma Control, Level III, 5 x 3 ml

Specifications

Linearity: free metanephrine up to 5650 ng/l
free normetanephrine up to 8500 ng/l
free 3-methoxytyramine up to 5800 ng/l

Limit of quantification: free metanephrine 15 ng/l
free normetanephrine 7 ng/l
free 3-methoxytyramine 11 ng/l

Intraassay:	CV = 2.7–6.9 %
Interassay:	CV = 3.3–8.6 %
Recovery:	89–100 %
Analysis time:	5 min

Pre-analytic Treatment

Specimens: plasma.
Stability: samples are stable for 3 days at +4 °C. For longer storage, temperatures of ≤ -20 °C are required.

Sample Preparation

→ Pipette 500 µl Dilution Buffer and 25 µl Internal Standard Mix into each well of the 96 SPE well plate.
→ Add 500 µl of the sample/calibrator/***MassCheck***® control, centrifuge, discard effluent.
→ Add 0.9 ml Wash Buffer 1, centrifuge, discard effluent.
→ Add 2 x 0.9 ml Wash Buffer 2, centrifuge, discard effluent.
→ Add 250 µl Elution Buffer into each well and centrifuge.
→ Inject up to 25 µl.

LC-MS/MS Parameters

Injection volume:	≤ 25 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	binary

5.4.2 Free Metanephrines in Plasma with Sample Clean Up Columns

Parameters:
free metanephrine, free normetanephrine, free 3-methoxytyramine.

Order no.	Product
81000/C	***Mass**Chrom*® Free Metanephrines in Plasma with Sample Clean Up Columns For 2 x 96 tests
	Components available separately
81001	Mobile Phase A, 750 ml
81002	Mobile Phase B, 450 ml
81003	Dilution Buffer, 50 ml
81004	Internal Standard Mix, 2 x 2.5 ml
81005	Wash Buffer 1, 90 ml
81006	Wash Buffer 2, 90 ml
81007	Elution Buffer, 25 ml
81009	Rinsing Solution, 500 ml
81055	Sample Clean Up Columns, 96 pcs.
	Startup Accessories
81100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
81015	Tuning Mix, Analytes and Internal Standards, 1 ml
81010	System Check Solution, 1 ml
33007	Tubes for sample preparation, 50 pcs.
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
J0602	Autosampler Vials, screw neck, 15 µl inner cone, clear glass, 1.1 ml, 100 pcs.
J0410	PP Screw-on Caps, silicone/pierceable PTFE septa, 1.0 mm, 100 pcs.
	Multilevel Calibrator and Controls
81039	6PLUS1® Multilevel Plasma Calibrator Set Free Metanephrines, 7 x 3 ml
0384	***Mass**Check*® Free Metanephrines Plasma Control, Level I, 5 x 3 ml
0385	***Mass**Check*® Free Metanephrines Plasma Control, Level II, 5 x 3 ml
0386	***Mass**Check*® Free Metanephrines Plasma Control, Level III, 5 x 3 ml

Specifications

Linearity: free metanephrine up to 5650 ng/l
free normetanephrine up to 8500 ng/l
free 3-methoxytyramine up to 5800 ng/l

Limit of quantification: free metanephrine 15 ng/l
free normetanephrine 7 ng/l
free 3-methoxytyramine 11 ng/l

Intraassay:	CV = 2.7–6.9 %
Interassay:	CV = 3.3–8.6 %
Recovery:	89–100 %
Analysis time:	5 min

Pre-analytic Treatment

Specimens: plasma.
Stability: samples are stable for 3 days at +4 °C. For longer storage, temperatures of ≤ -20 °C are required.

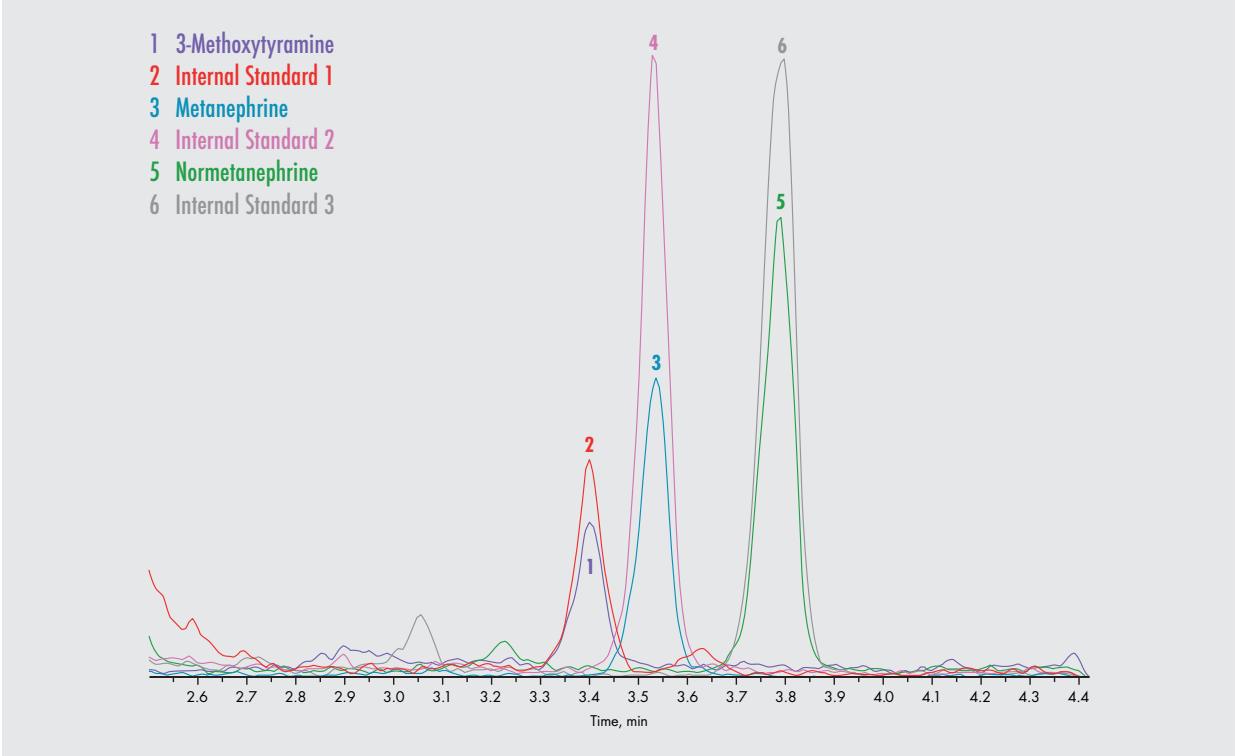
Sample Preparation

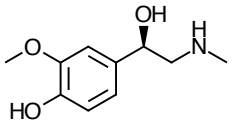
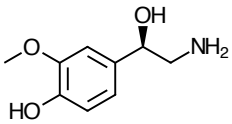
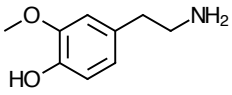
→ Pipette 500 µl Dilution Buffer and 25 µl Internal Standard Mix into each sample clean up column.
→ Add 500 µl of the sample/calibrator/***Mass**Check*® control, centrifuge, discard effluent.
→ Add 0.9 ml Wash Buffer 1, centrifuge, discard effluent.
→ Add 2 x 0.9 ml Wash Buffer 2, centrifuge, discard effluent.
→ Add 250 µl Elution Buffer into each well and centrifuge.
→ Inject up to 25 µl.

LC-MS/MS Parameters

Injection volume:	≤ 25 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	binary

MassChrom® Free Metanephrines in Plasma



Substance	Mw (g/mol)	Formula	Structure
Free metanephrine	197.23	$C_{10}H_{15}NO_3$	
Free normetanephrine	183.20	$C_9H_{13}NO_3$	
Free 3-methoxytyramine	167.21	$C_9H_{13}NO_2$	

6PLUS1® Multilevel Plasma Calibrator Set Free Metanephrines

Substance	Calibrator 1* ng/l	Calibrator 2* ng/l	Calibrator 3* ng/l	Calibrator 4* ng/l	Calibrator 5* ng/l	Calibrator 6* ng/l	Blank Calibrator ng/l
Free metanephrine	24.7	123	225	331	1528	2717	< LOQ
Free normetanephrine	24.5	176	320	473	2239	4010	< LOQ
Free 3-methoxytyramine	13.8	70.7	125	191	1481	2783	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Free Metanephrines in Plasma Controls

Substance	Level I Target Value* (ng/l)	Level II Target Value* (ng/l)	Level III Target Value* (ng/l)
Free metanephrine	52.7	169	988
Free normetanephrine	119	255	1355
Free 3-methoxytyramine	24.6	96.9	841

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
81039	6PLUS1® Multilevel Plasma Calibrator Set Free Metanephrines (lyoph.), 7 x 3 ml
0384	*MassCheck®* Free Metanephrines Plasma Control, Level I (lyoph.), 5 x 3 ml
0385	*MassCheck®* Free Metanephrines Plasma Control, Level II (lyoph.), 5 x 3 ml
0386	*MassCheck®* Free Metanephrines Plasma Control, Level III (lyoph.), 5 x 3 ml

Stability of Plasma Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

Notes

Therapeutic Drug Monitoring

Therapeutic drug monitoring (TDM) provides valuable information on the actual blood concentration of a specific drug. This ensures sufficient levels of the drug, while at the same time avoiding overdoses with potentially harmful side effects. TDM is also employed to assess patient compliance to a certain therapy regimen.

With our complete solutions in therapeutic drug monitoring covering assays through to controls and calibrators, we support you in getting reliable results efficiently. Our methods are validated and comply with relevant regulatory rules, thereby ensuring confident results in your laboratory.

Therapeutisches Drug Monitoring

Das Therapeutische Drug Monitoring (TDM) liefert wertvolle Informationen über den aktuellen Blutspiegel eines bestimmten Arzneistoffes. Damit ist sichergestellt, dass das Therapeutikum in ausreichenden Mengen im Körper vorhanden ist, während gleichzeitig Überdosierungen mit potentiell gefährlichen Nebenwirkungen ausgeschlossen werden. TDM ermöglicht weiterhin die Patientenkontrolle therapeutischer Maßnahmen.

Unsere Komplettlösungen beim Therapeutischen Drug Monitoring umfassen sowohl Kits als auch Qualitätskontrollen und Kalibratoren. Damit unterstützen wir Sie zuverlässige Ergebnisse auf effiziente Weise zu erzielen. Unsere Methoden sind validiert, erfüllen relevante regulatorische Anforderungen und liefern somit zuverlässige Daten in Ihrem Labor.

MassTox® TDM Series A

Overview *MassTox*® TDM Series A

The ***MassTox***® TDM Series A from Chromsystems allows the fast and efficient monitoring of a broad range of therapeutic drugs. Substances include antidepressants, antiepileptic drugs, benzodiazepines, neuroleptics and psychostimulants. All sets have been comprehensively validated and provide everything that is required for the analysis.

The modular system allows the determination of nearly 200 parameters without column switching or changes to the mobile phases, thereby helping to minimise the workload in the laboratory. Reagents can be combined to meet the individual needs of laboratories.

Available *MassTox*® TDM Parameter Sets	Order no.
Antiarrhythmic Drugs	92923
Antidepressants 1/*EXTENDED*	92913/XT
Antidepressants 2/Psychostimulants/*EXTENDED*	92915/XT
Antiepileptic Drugs	92921
Antiepileptic Drugs All-in-One	92921/XT
Anti-HIV Drugs	92924
Antimycotic Drugs	92922
Benzodiazepines 1	92917
Benzodiazepines 2	92918
Mycophenolic Acid	92916
Neuroleptics 1/*EXTENDED*	92912/XT
Neuroleptics 2/*EXTENDED 2*	92914/XT2
Tricyclic Antidepressants TCA 1	92919
Tricyclic Antidepressants TCA 2	92920

Die ***MassTox***® TDM Serie A von Chromsystems ermöglicht die schnelle und effiziente Überwachung von Arzneimittelspiegeln einer großen Bandbreite an Medikamenten aus unterschiedlichen Wirkstoffgruppen, wie beispielsweise Antidepressiva, Antiepileptika, Benzodiazepine, Neuroleptika und Psychostimulantien. Alle Sets sind umfassend validiert und beinhalten sämtliche Komponenten, die zur Analytik benötigt werden.

Das Baukastensystem ermöglicht die Überwachung von fast 200 Parametern ohne Säulentausch oder Auswechseln der mobilen Phasen und minimiert damit den Arbeitsaufwand im Labor. Reagenzien können nach den individuellen Anforderungen im Labor zusammengestellt werden.

Verfügbare *MassTox*® TDM Parameter-Sets	Bestell-Nr.
Antiarrhythmika	92923
Antidepressiva 1/*EXTENDED*	92913/XT
Antidepressiva 2/Psychostimulantien/*EXTENDED*	92915/XT
Antiepileptika	92921
Antiepileptika All-in-One	92921/XT
Anti-HIV-Medikamente	92924
Antimykotika	92922
Benzodiazepine 1	92917
Benzodiazepine 2	92918
Mycophenolsäure	92916
Neuroleptika 1/*EXTENDED*	92912/XT
Neuroleptika 2/*EXTENDED 2*	92914/XT2
Tricyclische Antidepressiva TCA 1	92919
Tricyclische Antidepressiva TCA 2	92920

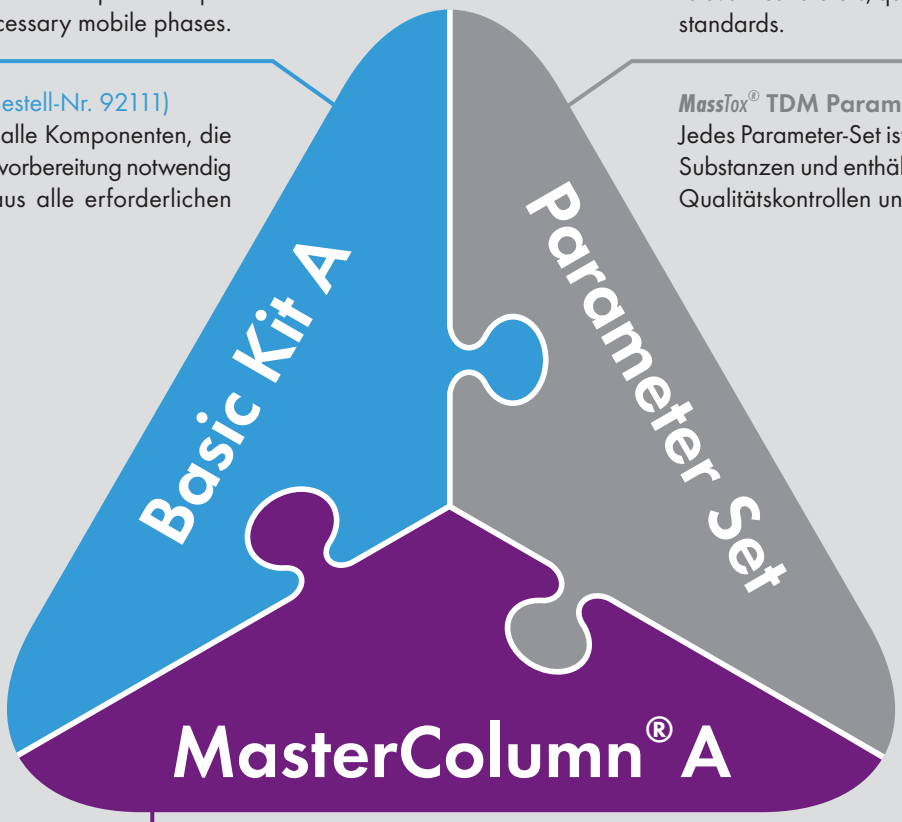
MassTox® TDM Series A consists of three major components.
Die *MassTox*® TDM Serie A besteht aus drei Hauptkomponenten.

***MassTox*® Basic Kit A** (Order no. 92111)
Is used for all determinations and contains all components required for a complete sample preparation and all necessary mobile phases.

***MassTox*® Basic-Kit A** (Bestell-Nr. 92111)
Der Basic-Kit A enthält alle Komponenten, die für die komplette Probenvorbereitung notwendig sind und darüber hinaus alle erforderlichen Mobilen Phasen.

***MassTox*® TDM Parameter Sets**
Each Parameter Set is optimised for the analysis of the particular substances and contains all relevant calibrators, quality controls and internal standards.

***MassTox*® TDM Parameter-Sets**
Jedes Parameter-Set ist spezifisch für bestimmte Substanzen und enthält passende Kalibratoren, Qualitätskontrollen und interne Standards.



***MassTox*® MasterColumn® A** (Order no. 92110)
The analytical column enables the determination of nearly 200 parameters of the TDM Series A. No column switching or changes in the setup of the mass spectrometer are required.

***MassTox*® MasterColumn® A** (Bestell-Nr. 92110)
Die analytische Säule ermöglicht die Bestimmung von fast 200 Parametern der TDM Serie A. Ein Säulentausch oder Änderungen im Setup des Massenspektrometers sind nicht erforderlich.

MassTox® TDM Series A Parameter Menu

Antiarrhythmic Drugs

Acebutolol
Ajmaline
Amiodarone → Desethylamiodarone
Aprindine
Atenolol
Bisoprolol
Diltiazem
Disopyramide
Dronedarone → Debutyldronedarone
Flecainide
Flunarizine
Gallopamil
Lidocaine
Metoprolol
Mexiletine
Propafenone
Propranolol
Quinidine → Hydroquinidine
Sotalol
Tocainide
Verapamil → Norverapamil

Order no. 92923 Page 105

Antidepressants 1/*EXTENDED*

Citalopram → N-Desmethylcitalopram
Duloxetine
Fluoxetine → Desmethylfluoxetine
Fluvoxamine
Mirtazapine → N-Desmethylmirtazepine
Paroxetine
Sertraline → N-Desmethylsertraline
Venlafaxine → O-Desmethylvenlafaxine

Order no. 92913/XT Page 113

Antidepressants 2/Psychostimulants/*EXTENDED*

Atomoxetine
Bupropion → Erythro-dihydrobupropion
→ Threo-dihydrobupropion
→ Hydroxybupropion
Clomethiazole
Dosulepin → N-Desmethyldosulepin
Methylphenidate
Mianserin
Milnacipran
Moclobemide
Opipramol
Reboxetine
Ritalinic acid
Tianeptine
Tranylcypromine
Trazodone
Vilazodone
Vortioxetine

Order no. 92915/XT Page 117

Antiepileptic Drugs All-in-One-Method

Brivaracetam
Carbamazepine → Carbamazepine-10,11-epoxide
→ 10-OH-carbamazepine
→ 10,11-Dihydroxycarbamazepine (Carbamazepine-diol)
Desmethylmesuximide
Ethosuximide
Felbamate
Gabapentin
Lacosamide
Lamotrigine
Levetiracetam
Oxcarbazepine
Perampanel
Phenobarbital
Phenylethylmalonamide (PEMA)
Phenytoin
Pregabalin
Primidone
Retigabine
Rufinamide
Stiripentol
Sultiame
Tiagabine
Theophylline
Topiramate
Valproic acid
Vigabatrin
Zonisamide

Order no. 92921/XT Page 129

Anti-HIV Drugs

Amprenavir
Atazanavir
Darunavir
Delavirdine
Efavirenz
Elvitegravir
Etravirine
Indinavir
Lopinavir
Maraviroc
Nelfinavir → Nelfinavir-M8
Nevirapine
Raltegravir
Rilpivirine
Ritonavir
Saquinavir
Tipranavir

Order no. 92924 Page 136

Antimycotic Drugs

Fluconazole
5-Flucytosine
Itraconazole → OH-itraconazole
Ketoconazole
Posaconazole
Voriconazole

Order no. 92922 Page 143

Benzodiazepines 1

Chlordiazepoxide
Clobazam → Norclobazam
Demoxepam
Diazepam → Nordiazepam
Medazepam
Midazolam → 1-OH-midazolam
Oxazepam
Prazepam
Temazepam
Tetrazepam

Order no. 92917 Page 148

Benzodiazepines 2

Alprazolam
Bromazepam
Clonazepam
Flurazepam → Desalkylflurazepam
Flunitrazepam
Lorazepam
Lormetazepam
Nitrazepam
Triazolam

Order no. 92918 Page 152

Mycophenolic Acid

Mycophenolic acid
Mycophenolic acid glucuronide

Order no. 92916 Page 157

Neuroleptics 1/*EXTENDED*

Aripiprazole → Dehydroaripiprazole
Clozapine → N-Desmethylclozapine
Haloperidol
Olanzapine → N-Desmethylolanzapine
Quetiapine → Norquetiapine
Risperidone → 9-OH-risperidone

Order no. 92912/XT Page 163

Neuroleptics 2/*EXTENDED 2*

Amisulpride
Benperidol
Brexpiprazole
Bromperidol
Cariprazine
Chlorpromazine
Chlorprothixene
Flupentixol
Fluphenazine
Guanfacine
Iloperidone
Levomepromazine
Loxapine
Lurasidone
Melperone
Mesoridazine
Perazine
Perphenazine
Pimozide
Pipamperone
Promethazine
Prothipendyl
Sertindole
Sulforidazine
Sulpiride
Thioridazine
Ziprasidone
Zotepine
Zuclopenthixol

Order no. 92914/XT2 Page 167

Tricyclic Antidepressants TCA 1

Amitriptyline
Desipramine
Doxepin → Nordoxepin
Imipramine
Nortriptyline

Order no. 92919 Page 174

Tricyclic Antidepressants TCA 2

Clomipramine → Norclomipramine
Maprotiline → Normaprotiline
Protriptyline
Trimipramine → Nortrimipramine

Order no. 92920 Page 177

Continuously extended.
Please refer to our website.

6.1 *MassTox*® Antiarrhythmic Drugs

CE IVD

Antiarrhythmic drugs are used for the treatment of cardiac arrhythmias in order to reduce their frequency or intensity. The severity of ventricular and supraventricular rhythm disturbances ranges from harmless extra beats through to complex multiple blows and life-threatening tachycardia. By using antiarrhythmic agents, it is possible to restore a normal electrical cardiac activity. Since antiarrhythmic drugs are in their chemistry and mechanisms of action an inhomogeneous group, various side effects and drug interactions have to be considered. Their use should be monitored by echocardiography (ECG) as well as electrolyte and plasma level determinations, in particular when starting new drug regimens. Each antiarrhythmic drug possesses a pro-arrhythmic potential, which means that it can also cause heart arrhythmia. Additionally, there are drug-drug interactions between the different antiarrhythmics, and therefore, combinations should be taken with extreme caution as well as with due attention to the side-effects and interaction profiles.

The modular system ***MassTox***® TDM Basic Kit A in combination with the ***MassTox***® TDM Parameter Set Antiarrhythmic Drugs allows the rapid and reliable quantitative determination of antiarrhythmic drugs using LC-MS/MS. Careful optimisation of all reagents and the chromatographic separation minimise matrix effects and increase the robustness of the method. Deuterated stable isotopes, co-eluting internal standards and a multilevel calibrator ensure a reproducible and dependable quantification of the analytes. Just as for all Parameter Sets of the ***MassTox***® Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 25 antiarrhythmic drugs
> Deuterated, co-eluting and stable internal standards
> 3PLUS1® Multilevel Calibrator Set

Antiarrhythmika sind Arzneistoffe, die zur Behandlung von Herzrhythmusstörungen eingesetzt werden, um diese in der Häufigkeit oder der Intensität zu senken. Die Ausprägung ventrikulärer und supraventrikulärer Rhythmusstörungen reicht von harmlosen Extraschlägen über komplexe Mehrfachschläge bis hin zu lebensgefährlichen Tachykardien. Mit Antiarrhythmika ist es möglich, wieder eine normale elektrische Herztätigkeit zu erreichen. Da es sich bei den Antiarrhythmika um eine chemisch sehr inhomogene Gruppe mit unterschiedlichen Wirkmechanismen handelt, müssen verschiedene Nebenwirkungen und Arzneimittelinteraktionen beachtet werden. Ihr Einsatz sollte besonders bei einer Neueinstellung mittels EKG-Kontrolle, Elektrolyt- und Plasmaspiegelbestimmungen überwacht werden. So hat jedes Antiarrhythmikum auch ein proarrhythmisches Potential, d. h. es kann auch Herzrhythmusstörungen auslösen. Zudem gibt es zahlreiche Wechselwirkungen zwischen den Antiarrhythmika untereinander, weshalb Kombinationen nur unter größter Vorsicht und Beachtung der Nebenwirkungs- und Wechselwirkungsprofile eingenommen werden sollten.

Mit dem Baukastensystem ***MassTox***® TDM Basic-Kit A und ***MassTox***® TDM Parameter-Set für die LC-MS/MS-Analytik von Antiarrhythmika können die einzelnen Wirkstoffe schnell und effektiv gemessen werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methode erhöht. Die Verwendung von stabilen isotopenmarkierten und co-eluierenden internen Standards sowie eines Multilevel-Kalibrators gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. Die Probenvorbereitung basiert, so wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> Methode umfasst 25 Antiarrhythmika
> Deuterierte, co-eluierende und stabile interne Standards
> 3PLUS1® Multilevel Calibrator Set

MassTox® Antiarrhythmic Drugs

Parameters:
acebutolol, ajmaline, amiodarone, desethylamiodarone, aprindine, atenolol, bisoprolol, diltiazem, disopyramide, dronedarone, debutyldronedarone, flecainide, flunarizine, gallopamil, lidocaine, metoprolol, mexiletine, propafenone, propranolol, quinidine, hydroquinidine, sotalol, tocainide, verapamil, norverapamil.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92923	***MassTox*® TDM Parameter Set Antiarrhythmic Drugs**
	Components available separately
92052	3PLUS1® Multilevel Plasma Calibrator Set Antiarrhythmic Drugs (lyoph.), 4 x 1 ml
0265	***MassCheck*® Antiarrhythmic Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml**
0266	***MassCheck*® Antiarrhythmic Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml**
92746	Internal Standard Set Antiarrhythmic Drugs, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92041	Tuning Mix Antiarrhythmic Drugs, Analytes and Internal Standards, 1 ml
0264	***MassCheck*® Antiarrhythmic Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml**
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 30 000 µg/l
Limit of quantification:	1.5–80 µg/l
Intraassay:	CV = 2–9 %
Interassay:	CV = 3–8.5 %
Analysis time:	1.2–3.5 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable up to 3 weeks at +2 to +8 °C.
For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/*MassCheck*® control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

LC-MS/MS Parameters

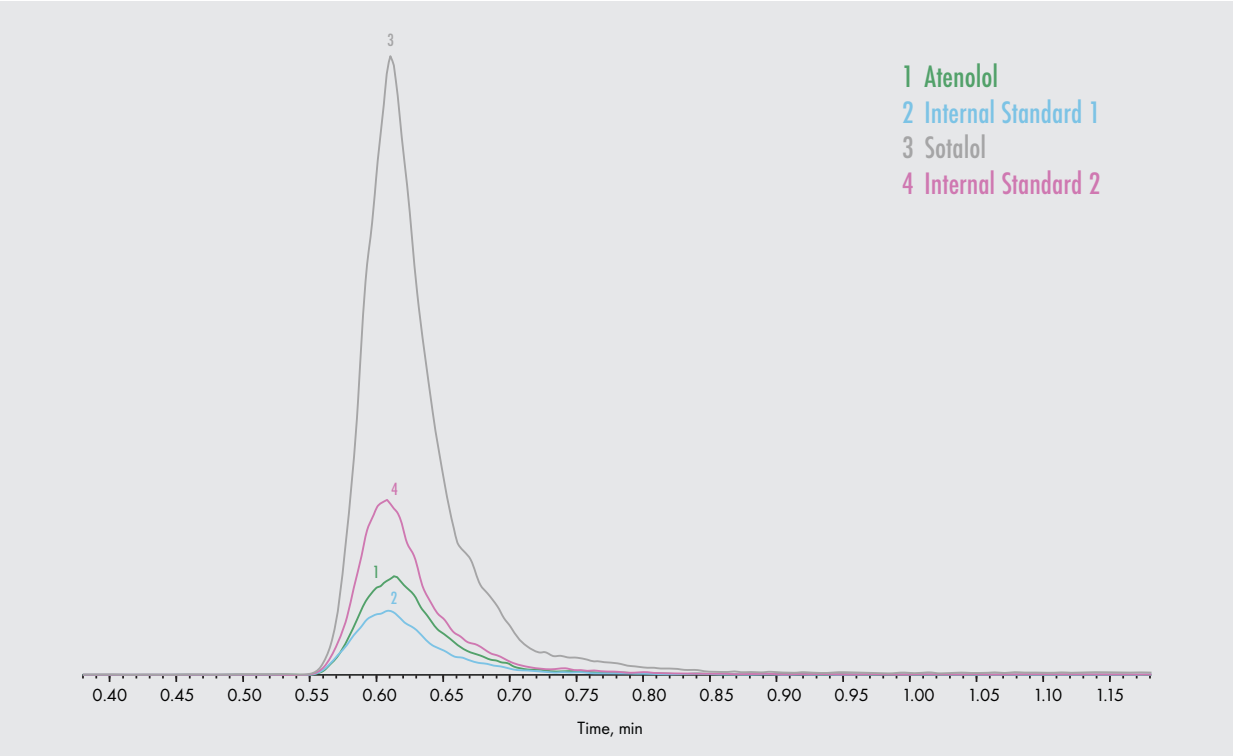
Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

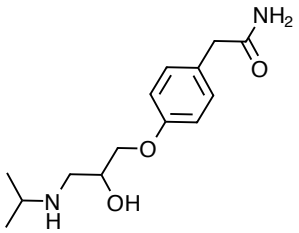
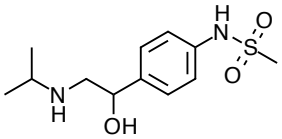
Gradient:

Group 1:	isocratic 25 % Mobile Phase 2
Group 2:	isocratic 43 % Mobile Phase 2
Group 3:	isocratic 65 % Mobile Phase 2
Group 4:	0.00–0.40 min, 0 % Mobile Phase 2
	0.41–1.00 min, 80 % Mobile Phase 2
	1.01–2.90 min, 100 % Mobile Phase 2
	2.91–3.50 min, 0 % Mobile Phase 2

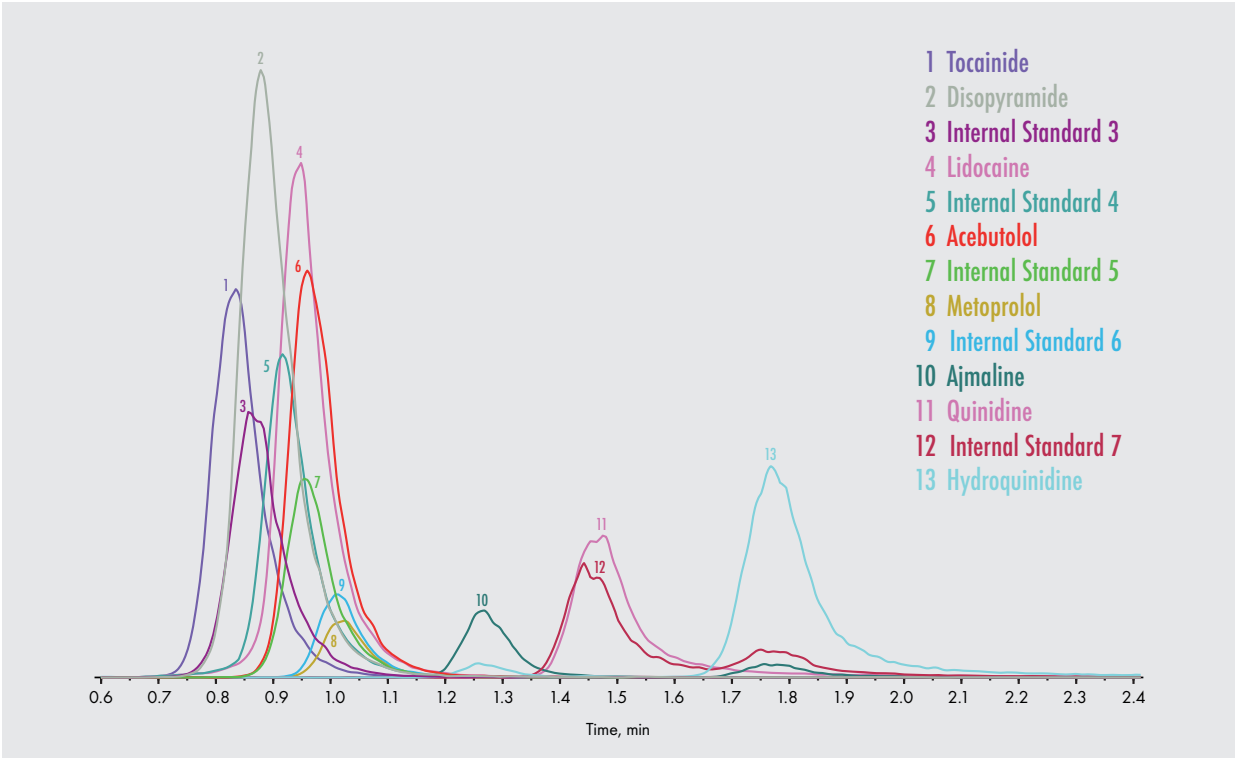
We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

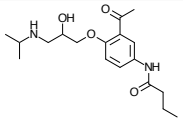
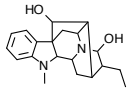
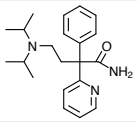
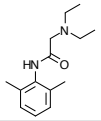
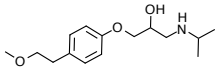
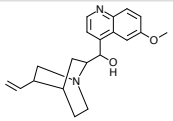
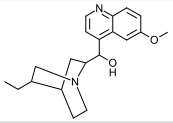
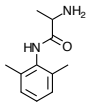
MassTox® Antiarrhythmic Drugs Group 1



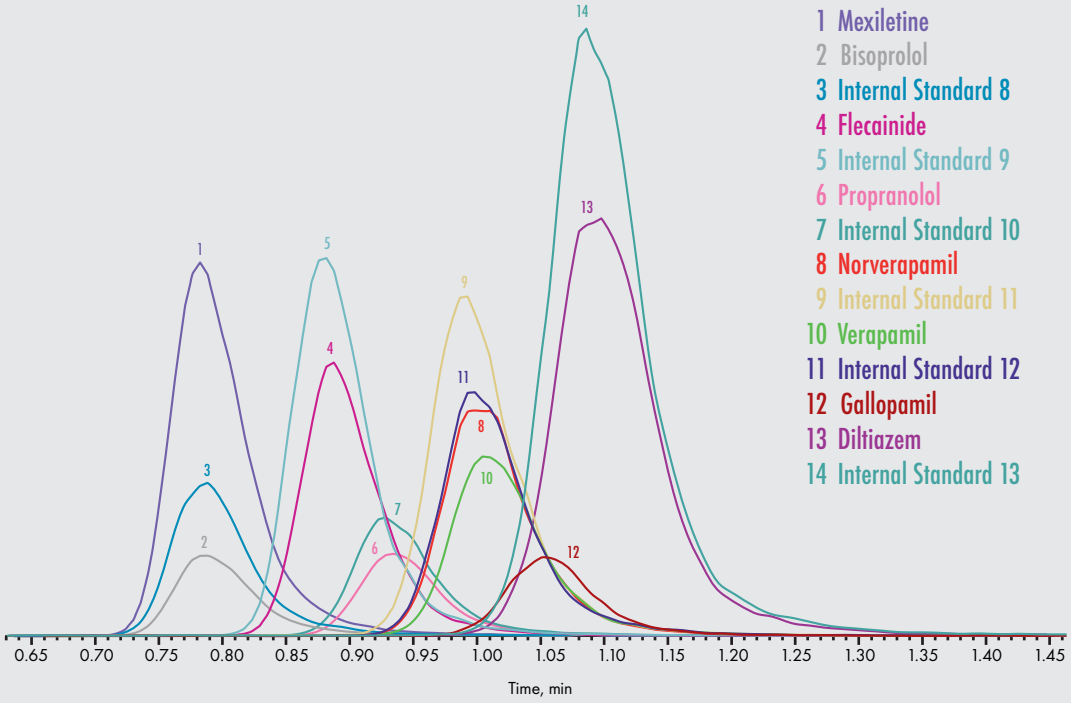
Substance	Published Reference Ranges[3–5] (mg/l)	Mw (g/mol)	Formula	Structure
Atenolol	0.1–2	266.34	$C_{14}H_{22}N_2O_3$	
Sotalol	0.5–5	272.36	$C_{12}H_{20}N_2O_3S$	

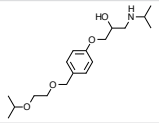
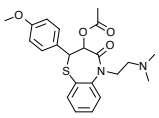
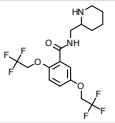
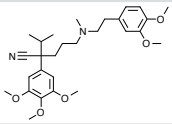
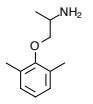
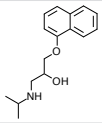
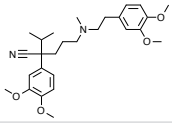
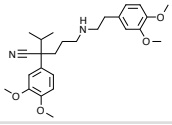
MassTox® Antiarrhythmic Drugs Group 2



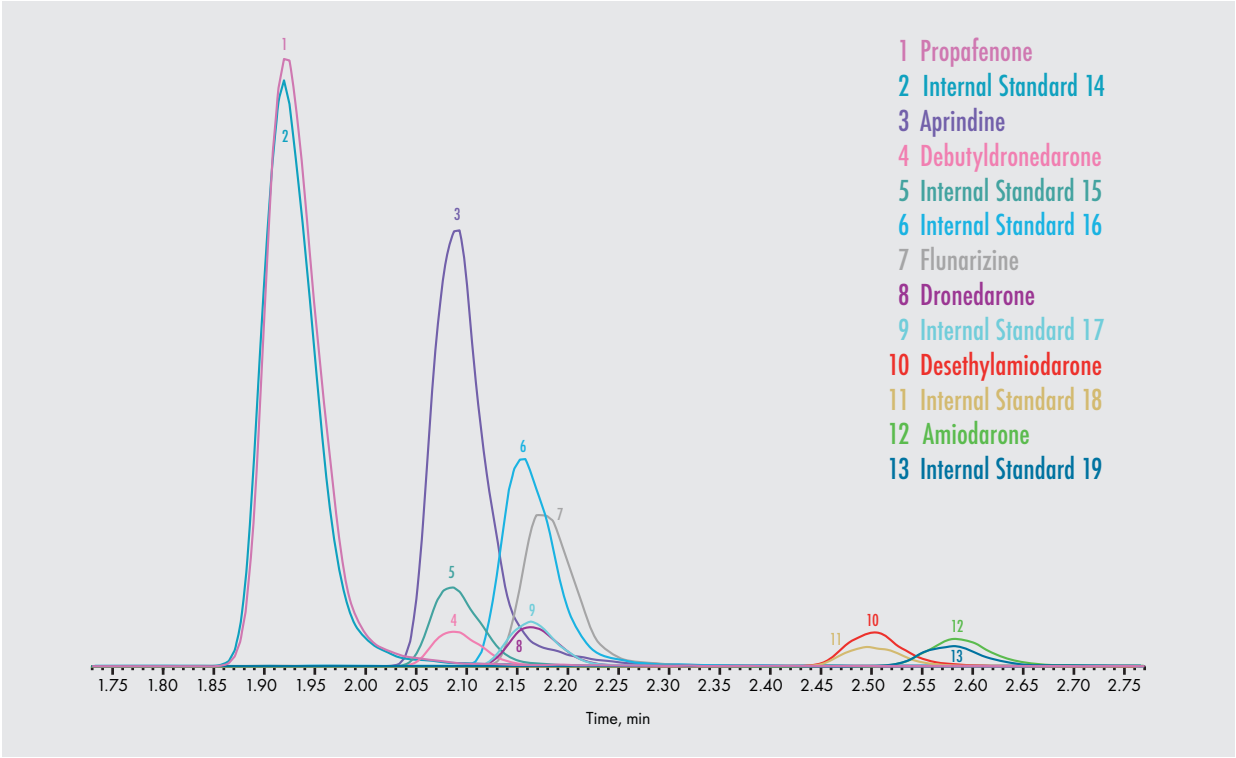
Substance	Published Reference Ranges [3-5] (mg/l)	Mw (g/mol)	Formula	Structure
Acebutolol	0.2–2	336.43	$C_{18}H_{28}N_2O_4$	
Ajmaline	0.01–2.21	326.43	$C_{20}H_{26}N_2O_2$	
Disopyramide	2–8	339.47	$C_{21}H_{29}N_3O$	
Lidocaine	1–6	234.34	$C_{14}H_{22}N_2O$	
Metoprolol	0.02–0.5	267.36	$C_{15}H_{25}NO_3$	
Quinidine	1–6	324.42	$C_{20}H_{24}N_2O_2$	
Hydroquinidine	–	326.43	$C_{20}H_{26}N_2O_2$	
Tocainide	4–12	192.26	$C_{11}H_{16}N_2O$	

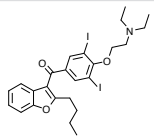
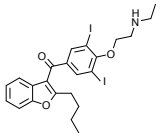
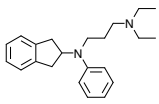
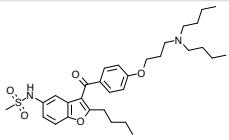
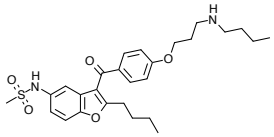
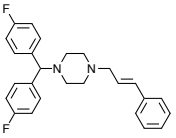
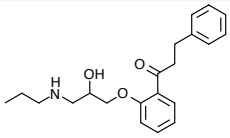
MassTox® Antiarrhythmic Drugs Group 3



Substance	Published Reference Ranges [3–5] (mg/l)	Mw (g/mol)	Formula	Structure
Bisoprolol	0.01–0.1	325.44	$C_{18}H_{31}NO_4$	
Diltiazem	0.05–0.4	414.52	$C_{22}H_{26}N_2O_4S$	
Flecainide	0.2–1	414.34	$C_{17}H_{20}F_6N_2O_3$	
Gallopamil	0.02–0.1	484.63	$C_{28}H_{40}N_2O_5$	
Mexiletine	0.5–2	179.26	$C_{11}H_{17}NO$	
Propranolol	0.02–0.3	259.34	$C_{16}H_{21}NO_2$	
Verapamil	0.01–0.5	454.60	$C_{27}H_{38}N_2O_4$	
Norverapamil	0.05–0.6	440.58	$C_{26}H_{36}N_2O_4$	

MassTox® Antiarrhythmic Drugs Group 4



Substance	Published Reference Ranges [3–5] (mg/l)	Mw (g/mol)	Formula	Structure
Amiodarone	0.5–2.5	645.31	$C_{25}H_{29}I_2NO_3$	
Desethylamiodarone	1–5	617.26	$C_{23}H_{25}I_2NO_3$	
Aprindine	0.7–2.5	322.49	$C_{22}H_{30}N_2$	
Dronedarone	–	556.76	$C_{31}H_{44}N_2O_5S$	
Debutyldronedarone	–	500.65	$C_{27}H_{36}N_2O_5S$	
Flunarizine	0.025–0.2	404.49	$C_{26}H_{26}F_2N_2$	
Propafenone	0.4–3	341.44	$C_{21}H_{27}NO_3$	

3PLUS1® Multilevel Plasma Calibrator Set
Antiarrhythmic Drugs

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Group 1				
Atenolol	71.1	1233	2423	< LOQ
Sotalol	331	2933	5537	< LOQ
Group 2				
Acebutolol	156	1259	2413	< LOQ
Ajmaline	6.51	540	1114	< LOQ
Disopyramide	1406	5277	9076	< LOQ
Lidocaine	641	3586	6537	< LOQ
Metoprolol	14.9	356	705	< LOQ
Quinidine	196	3437	6778	< LOQ
Hydroquinidine	178	5582	10941	< LOQ
Tocainide	700	6854	12778	< LOQ
Group 3				
Bisoprolol	6.85	56.7	109	< LOQ
Diltiazem	20.5	226	439	< LOQ
Flecainide	137	771	1535	< LOQ
Gallopamil	13.3	60.9	111	< LOQ
Mexiletine	66.8	1164	2266	< LOQ
Propranolol	14.7	180	354	< LOQ
Verapamil	34.7	433	847	< LOQ
Norverapamil	33.4	238	452	< LOQ
Group 4				
Amiodarone	363	1651	2950	< LOQ
Desethylamiodarone	419	2238	4160	< LOQ
Aprindine	506	1955	3184	< LOQ
Dronedarone	25.9	104	184	< LOQ
Debutyldronedarone	29.1	118	214	< LOQ
Flunarizine	18.4	121	233	< LOQ
Propafenone	35.1	1632	3277	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Antiarrhythmic Drugs Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Group 1		
Atenolol	280	1756
Sotalol	845	4053
Group 2		
Acebutolol	363	1753
Ajmaline	95.1	795
Disopyramide	2396	6769
Lidocaine	1277	4643
Metoprolol	72.4	515
Quinidine	770	4900
Hydroquinidine	1117	7953
Tocainide	1901	9393
Group 3		
Bisoprolol	16.5	80.2
Diltiazem	57.9	320
Flecainide	283	1073
Gallopamil	25	82.3
Mexiletine	267	1657
Propranolol	45	260
Verapamil	108	620
Norverapamil	78.4	336
Group 4		
Amiodarone	667	2183
Desethylamiodarone	824	3085
Aprindine	866	2433
Dronedarone	46	138
Debutyldronedarone	51.2	156
Flunarizine	38.9	169
Propafenone	307	2347

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92052	3PLUS1® Multilevel Plasma Calibrator Set Antiarrhythmic Drugs (lyoph.), 4 x 1 ml
0264	***MassCheck***® Antiarrhythmic Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0265	***MassCheck***® Antiarrhythmic Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml
0266	***MassCheck***® Antiarrhythmic Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Calibrators and Plasma Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 2 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.2 *MassTox*® Antidepressants and Psychostimulants

CE IVD

The ***MassTox***® TDM Parameter Set Antidepressants 1/*EXTENDED* encompasses a number of drugs for the treatment of depression. In addition to classical tricyclic antidepressant drugs, there are several new generation drugs called „Selective Serotonin Re-uptake Inhibitors" (SSRI) as well as „Selective Serotonin and Noradrenaline Re-uptake Inhibitors" (SSNRI) included. Some of the SSRIs inhibit the re-uptake of the messenger substance serotonin into neurons. These drugs help combat fear and improve mood. They predominantly prevent the cellular re-uptake of serotonin. Other SSNRIs also affect mood and motivation positively. Similar to SSRI, SSNRI not only influence intracellular serotonin levels but also block the re-uptake of noradrenaline.

The ***MassTox***® TDM Parameter Set Antidepressants 2/Psychostimulants/*EXTENDED* covers antidepressants as well as several psychostimulants, such as methylphenidate (Ritalin®). It is related to amphetamines and is prescribed mainly for attention deficit hyperactivity disorder (ADHD).

Both Parameter Sets allow the rapid and reliable quantitative determination of every individual parameter. Careful optimisation of al reagents and the chromatographic separation minimises matrix effects and warrants the robustness of the methods. Using deuterated stable isotopes, co-eluting internal standards and multilevel calibrators ensures a reliable and reproducible quantification of the analytes. Just as for all Parameter Sets of the ***MassTox***® TDM Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 33 analytes divided in 2 Parameter Sets
> Isotopically labelled internal standards
> 3PLUS1® Multilevel Calibrator Sets

Im ***MassTox***® TDM Parameter-Set Antidepressants 1/*EXTENDED* sind eine Reihe von Medikamenten zur Behandlung von Depressionen zusammengefasst. Dazu gehören neben den klassischen tricyclischen Antidepressiva auch selektive Serotonin-Wiederaufnahmehemmer (SSRI), und selektive Serotonin-Noradrenalin-Wiederaufnahmehemmer (SSNRI) als Antidepressiva der zweiten Generation. Einige der SSRIs hemmen vor allem die Wiederaufnahme des Botenstoffes Serotonin in die Nervenzelle. SSRIs besitzen angstlösende Eigenschaften und wirken stimmungsaufhellend. Sie verhindern vor allem, dass die Zellspeicher das Serotonin wieder aufnehmen. Einige SSNRIs sind stimmungsaufhellend und antriebssteigernd. Diese wirken ähnlich wie SSRIs, beeinflussen jedoch zusätzlich den Noradrenalinspeicher. SSNRIs blockieren die Wiederaufnahme von Serotonin und Noradrenalin.

Neben mehreren Antidepressiva finden sich im erweiterten Parameter-Set Antidepressiva 2/Psychostimulants/*EXTENDED* auch so genannte Psychostimulantien wie zum Beispiel das Methylphenidat (Ritalin®). Die den Amphetaminen verwandte Substanz wird hauptsächlich bei der Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (ADHS) eingesetzt.

Mit den beiden Parameter-Sets können die einzelnen Wirkstoffe im Serum/Plasma schnell und effektiv bestimmt werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methoden sichergestellt. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. So wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, basiert die Probenvorbereitung auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> 2 Parameter-Sets mit insgesamt 33 Analyten
> Isotopenmarkierte interne Standards
> 3PLUS1® Multilevel Calibrator Sets

6.2.1 *MassTox*® Antidepressants 1/*EXTENDED*

Parameters:
citalopram, N-desmethylcitalopram, duloxetine, fluoxetine, desmethylfluoxetine, fluvoxamine, mirtazapine, N-desmethylmirtazapine, paroxetine, sertraline, N-desmethylsertraline, venlafaxine, O-desmethylvenlafaxine.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92913/XT	***MassTox*® TDM Parameter Set Antidepressants 1/*EXTENDED***
	Components available separately
92029/XT	3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 1/*EXTENDED* (lyoph.), 4 x 1 ml
0214/XT	***MassCheck*®** Antidepressants 1/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0215/XT	***MassCheck*®** Antidepressants 1/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92046/AN1/XT	Internal Standard Set Antidepressants 1/*EXTENDED* and Neuroleptics 1/*EXTENDED*, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92016/A1/XT	Tuning Mix Antidepressants 1/*EXTENDED*, Analytes and Internal Standards, 1 ml
0213/XT	***MassCheck*®** Antidepressants 1/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	at least twice the therapeutic range
Limit of quantification:	0.5–30 µg/l
Intraassay:	CV < 9 %
Interassay:	CV < 9 %
Analysis time:	3.0 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable at least 24h when stored in the dark at +4 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

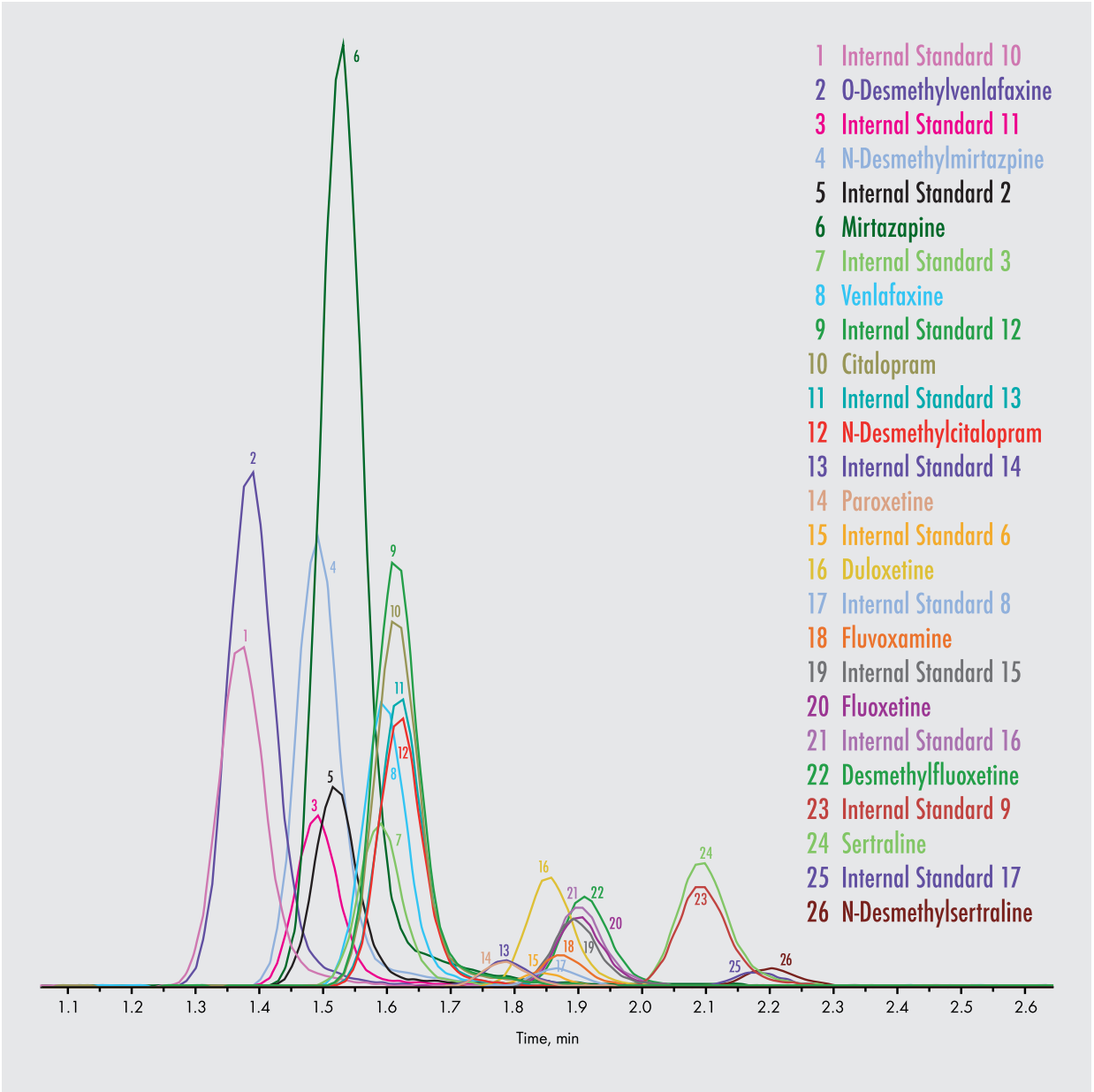
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

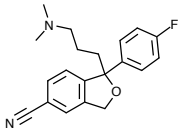
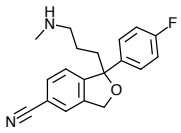
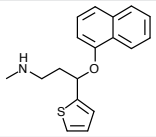
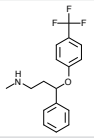
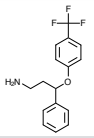
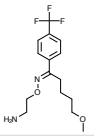
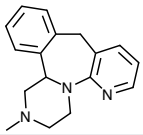
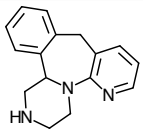
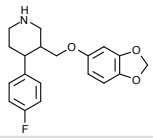
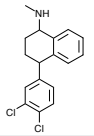
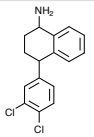
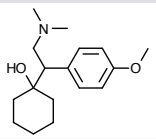
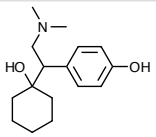
Gradient:
0.00–0.20 min, 0 % Mobile Phase 2
0.21–0.70 min, 50 % Mobile Phase 2
0.71–2.40 min, 80 % Mobile Phase 2
2.41–3.00 min, 0 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassTox® Antidepressants 1/*EXTENDED*



MassTox® Antidepressants 1/EXTENDED

Substance	Published Reference Ranges [3,5,6] (µg/l)	Mw (g/mol)	Formula	Structure
Citalopram	10–200	324.39	$C_{20}H_{21}FN_2O$	
N-Desmethylcitalopram	0.31–0.6 x Citalopram	310.15	$C_{19}H_{19}FN_2O$	
Duloxetine	3–120	297.41	$C_{18}H_{19}NOS$	
Fluoxetine	100–500*	309.33	$C_{17}H_{18}F_3NO$	
Desmethylfluoxetine	100–500*	295.30	$C_{16}H_{16}F_3NO$	
Fluvoxamine	50–230	318.33	$C_{15}H_{21}F_3N_2O_2$	
Mirtazapine	10–300	265.35	$C_{17}H_{19}N_3$	
N-Desmethylmirtazapine	0.2–1.2 x Mirtazapine	251.33	$C_{16}H_{17}N_3$	
Paroxetine	10–120	329.37	$C_{19}H_{20}FNO_3$	
Sertraline	5–250	306.23	$C_{17}H_{17}Cl_2N$	
N-Desmethylsertraline	1.7–3.4 x Sertraline	292.20	$C_{16}H_{15}Cl_2N$	
Venlafaxine	70–500*	277.40	$C_{17}H_{27}NO_2$	
O-Desmethylvenlafaxine	70–500*	263.38	$C_{16}H_{25}NO_2$	

** Sum of drug and metabolite*

3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 1/*EXTENDED*

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Citalopram	8.16	104	292	< LOQ
N-Desmethylcitalopram	9.00	114	315	< LOQ
Duloxetine	2.17	85.4	164	< LOQ
Fluoxetine	76.4	295	720	< LOQ
Desmethylfluoxetine	117	347	774	< LOQ
Fluvoxamine	39.7	160	381	< LOQ
Mirtazapine	7.75	155	445	< LOQ
N-Desmethylmirtazapine	8.40	162	452	< LOQ
Paroxetine	23.0	67.5	146	< LOQ
Sertraline	4.26	81.1	228	< LOQ
N-Desmethylsertraline	11.6	132	364	< LOQ
Venlafaxine	22.9	107	269	< LOQ
O-Desmethylvenlafaxine	54.8	295	736	< LOQ

** Please check packaging leaflet for specific lot concentrations, LOQ = limit of quantification*

MassCheck® Antidepressants 1/*EXTENDED* Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Citalopram	70.8	133
N-Desmethylcitalopram	78.6	146
Duloxetine	16.5	120
Fluoxetine	228	360
Desmethylfluoxetine	280	403
Fluvoxamine	122	192
Mirtazapine	107	201
N-Desmethylmirtazapine	108	211
Paroxetine	53.3	77.5
Sertraline	54.1	104
N-Desmethylsertraline	90.9	167
Venlafaxine	82.3	131
O-Desmethylvenlafaxine	209	349

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92029/XT	3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 1/*EXTENDED* (lyoph.), 4 x 1 ml
0213/XT	***MassCheck®*** Antidepressants 1/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0214/XT	***MassCheck®*** Antidepressants 1/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0215/XT	***MassCheck®*** Antidepressants 1/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 2 weeks at +2 °C to +8 °C
> For longer storage keep below -18 °C

6.2.2 *MassTox*® Antidepressants 2/Psychostimulants/*EXTENDED*

Parameters:
atomoxetine, bupropion, erythro-dihydrobupropion, threo-dihydrobupropion, hydroxybupropion, clomethiazole, dosulepin, N-desmethyldosulepin, methylphenidate, mianserin, milnacipran, moclobemide, opipramol, reboxetine, ritalinic acid, tianeptine, tranylcypromine, trazodone, vilazodone, vortioxetine.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92915/XT	***MassTox*® TDM Parameter Set Antidepressants 2/Psychostimulants/*EXTENDED* Components available separately**
92027/XT	3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 2/Psychostimulants/*EXTENDED* (lyoph.), 4 x 1 ml
0231/XT	***MassCheck*®** Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0232/XT	***MassCheck*®** Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92146/XT	Internal Standard Mix Antidepressants 2/Psychostimulants/*EXTENDED*, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92018/XT	Tuning Mix Antidepressants 2/Psychostimulants/*EXTENDED*, Analytes and Internal Standards, 1 ml
0230/XT	***MassCheck*®** Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 150–12 500 µg/l
Limit of quantification:	1.01–115 µg/l
Intraassay:	CV = 2–13.7 %
Interassay:	CV = 5.3–13.2 %
Analysis time:	Group 1 = 2.8 min
	Group 2 = 6 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: depending on the specific analyte. Further information can be obtained from the instruction manual.
It is mandatory to ship and keep samples frozen when samples have to be measured for methylphenidate and bupropion.

Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

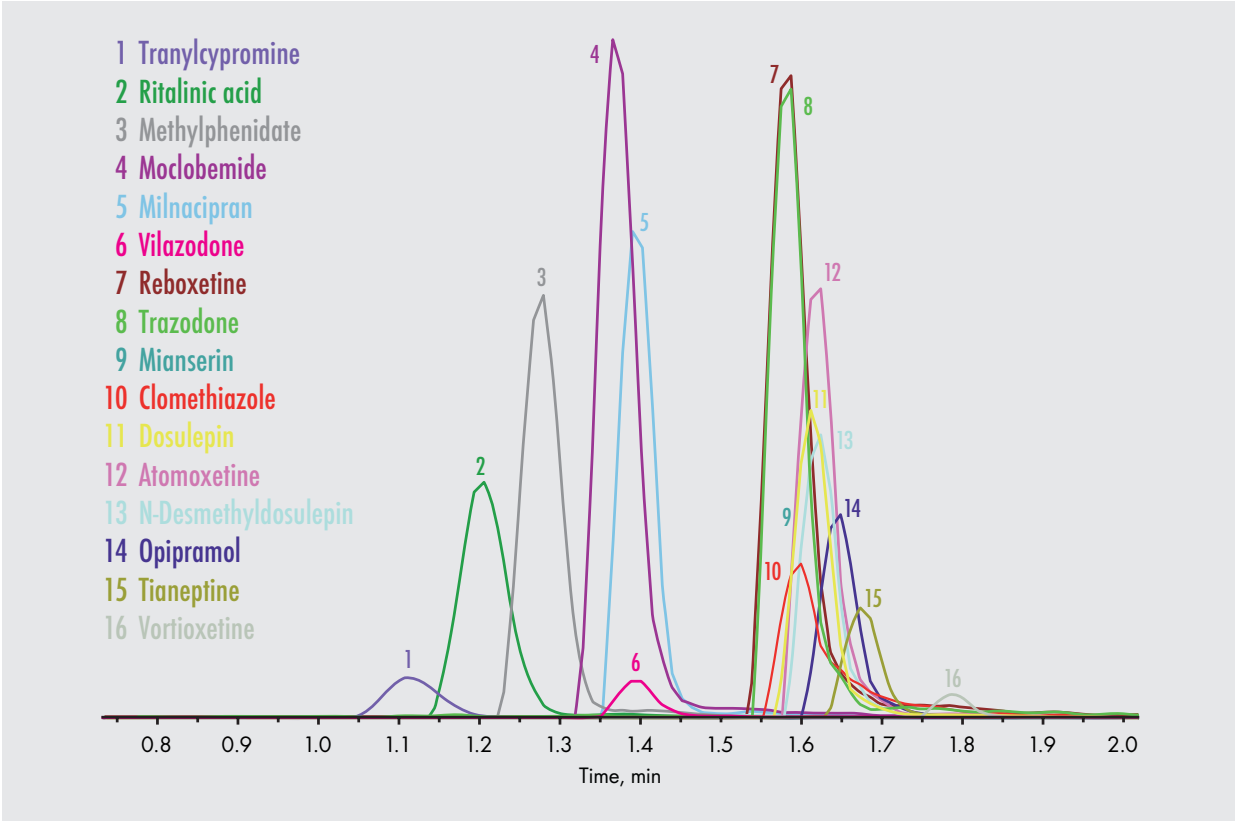
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	Group 1 sMRM
	Group 2 MRM

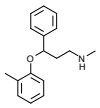
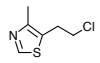
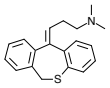
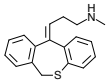
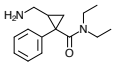
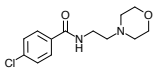
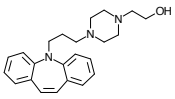
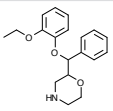
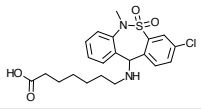
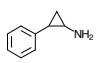
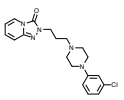
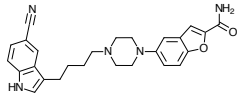
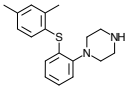
Gradient:
Group 1 binary
Group 2 isocratic

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

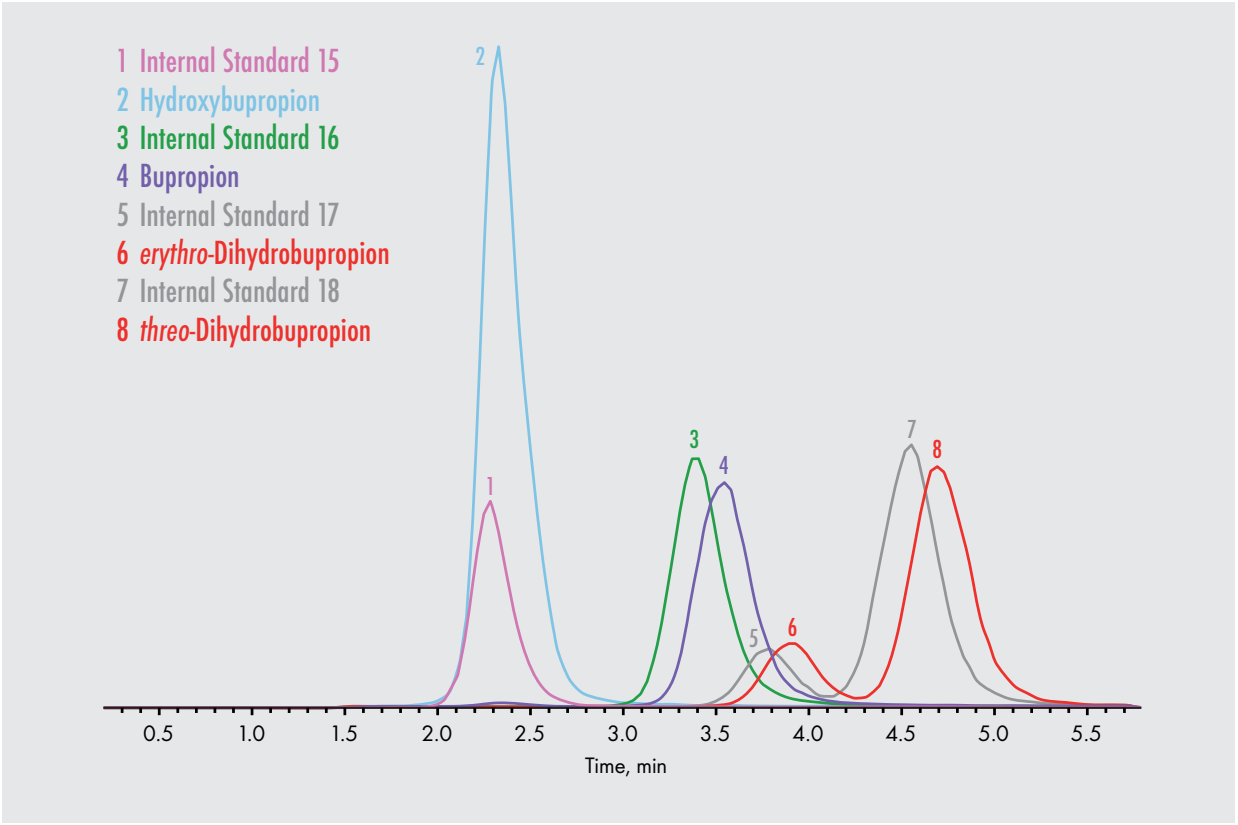
MassTox® Antidepressants 2/Psychostimulants/*EXTENDED Group 1*

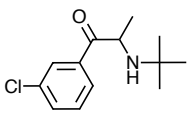
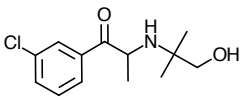
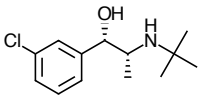
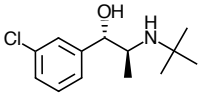


MassTox® Antidepressants 2/Psychostimulants/*EXTENDED Group 1*

Substance	Published Reference Ranges [4,7,8] (µg/l)	Mw (g/mol)	Formula	Structure
Atomoxetine	30–1000	255.35	$C_{17}H_{21}NO$	
Clomethiazole	100–5000	161.65	C_6H_8ClNS	
Dosulepin	20–300	295.44	$C_{19}H_{21}NS$	
N-Desmethyldosulepin	–	281.42	$C_{18}H_{19}NS$	
Methylphenidate	5–60	233.31	$C_{14}H_{19}NO_2$	
Mianserin	10–150	264.36	$C_{18}H_{20}N_2$	
Milnacipran	100–150	246.35	$C_{15}H_{22}N_2O$	
Moclobemide	300–1500	268.74	$C_{13}H_{17}ClN_2O_2$	
Opipramol	50–500	363.51	$C_{23}H_{29}N_3O$	
Reboxetine	30–350	313.39	$C_{19}H_{23}NO_3$	
Ritalinic acid	–	219.28	$C_{13}H_{17}NO_2$	
Tianeptine	30–300	436.95	$C_{21}H_{25}ClN_2O_4S$	
Tranylcypromine	< 500	133.19	$C_9H_{11}N$	
Trazodone	300–1600	371.86	$C_{19}H_{22}ClN_5O$	
Vilazodone	30–70	441.52	$C_{26}H_{27}N_5O_2$	
Vortioxetine	10–40	298.45	$C_{18}H_{22}N_2S$	

MassTox® Antidepressants 2/Psychostimulants/*EXTENDED Group 2*



Substance	Published Reference Ranges [4,7,8] (µg/l)	Mw (g/mol)	Formula	Structure
Bupropion	10–100	239.74	$C_{13}H_{18}ClNO$	
Hydroxybupropion	850–1500	255.74	$C_{13}H_{18}ClNO_2$	
Erythro-dihydrobupropion	–	241.76	$C_{13}H_{20}ClNO$	
Threo-dihydrobupropion	–	241.76	$C_{13}H_{20}ClNO$	

3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 2/ Psychostimulants/*EXTENDED*

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Atomoxetine	21.5	632	1215	< LOQ
Clomethiazol	61.3	2684	5309	< LOQ
N-Desmethyldosulepin	71.2	148	226	< LOQ
Dosulepin	13.7	189	366	< LOQ
Methylphenidate	3.25	41.3	78.7	< LOQ
Mianserin	6.97	94.0	174	< LOQ
Milnacipran	19.7	205	369	< LOQ
Moclobemide	148	1355	2517	< LOQ
Opipramol	34.2	317	592	< LOQ
Reboxetine	20.6	217	413	< LOQ
Ritalinic acid	27.4	186	344	< LOQ
Tianeptine	20.7	186	351	< LOQ
Tranylcypromine	7.43	306	616	< LOQ
Trazodone	220	1650	2979	< LOQ
Vilazodone	23.0	56.0	89.8	< LOQ
Vortioxetine	6.31	48.9	94.5	< LOQ
Bupropion	6.51	146	293	< LOQ
Erythro-Dihydrobupropion	6.93	148	288	< LOQ
Hydroxybupropion	29.0	1058	2085	< LOQ
Threo-Dihydrobupropion	35.0	740	1393	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Atomoxetine	125	897
Clomethiazol	582	4769
N-Desmethyldosulepin	84.5	212
Dosulepin	47.6	336
Methylphenidate	10.2	57.7
Mianserin	22.4	131
Milnacipran	57.8	344
Moclobemide	390	2300
Opipramol	90.6	546
Reboxetine	57.1	297
Ritalinic acid	59.6	252
Tianeptine	52.9	317
Tranylcypromine	67.5	570
Trazodone	515	2175
Vilazodone	30.1	84.8
Vortioxetine	14.6	85.8
Bupropion	34.1	263
Erythro-Dihydrobupropion	35.1	261
Hydroxybupropion	230	1887
Threo-Dihydrobupropion	178	1273

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92027/XT	3PLUS1® Multilevel Plasma Calibrator Set Antidepressants 2/Psychostimulants/*EXTENDED* (lyoph.), 4 x 1 ml
0230/XT	***MassCheck***® Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0231/XT	***MassCheck***® Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0232/XT	***MassCheck***® Antidepressants 2/Psychostimulants/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 7 days at +2 °C to +8 °C (bupropion up to 3 days)
> Reconstituted aliquots up to 3 months below -18 °C (bupropion up to 2 months)

6.3 *MassTox*® Antiepileptic Drugs

CE IVD

Epileptic seizures are the result of synchronous discharges of neurons in the brain, leading to sudden and involuntary stereotypical behaviour or mood disorders. For the majority of patients, however, treatment with anticonvulsive medication can reduce the incidence of, or even achieve freedom from fits. The therapeutic effects of antiepileptic drugs are dependent on the compliance of the patient, hence the regular use of medication according to the doctor's prescription.

The ***MassTox***® TDM Parameter Set Antiepileptic Drugs allows a rapid and reliable quantitative determination of nearly 30 antiepileptic drugs by LC-MS/MS. The assay is available in two options: the standard method divides the analytes in 5 groups. Alternatively, the all-in-one method allows the determination of all parameters in a single run of less than 5 minutes. The use of deuterated stable isotopes, co-eluting internal standards, and multilevel calibrators ensures reproducible and dependable quantification of the analytes. For large batches of samples automated sample preparation can save considerable amounts of time.

> Part of the modular system of *MassTox*® TDM Series A
> Isotopically labelled internal standard
> 3PLUS1® Multilevel Calibrator Set
> Automated method available
> All-in-one method: all parameters in a run of 5 min

Epileptische Anfälle sind die Folge synchroner Entladungen von Neuronengruppen im Gehirn, die zu plötzlichen und unwillkürlichen stereotypen Verhaltens- oder Befindlichkeitstörungen führen. Mit der Gabe antikonvulsiver Medikamente kann eine Reduktion der Anfälle oder sogar Anfallsfreiheit erreicht werden. Die Voraussetzung für die Wirksamkeit der Antiepileptika ist in der Regel die Compliance des Patienten, d. h. die regelmäßige Einnahme der Medikamente entsprechend ärztlicher Verordnung.

Das ***MassTox***® TDM Parameter-Set Antiepileptika im Serum/Plasma ermöglicht die schnelle und effektive Messung von nahezu 30 Antiepileptika mittels LC-MS/MS. Wahlweise stehen zwei Assay-Varianten zur Verfügung: mit der Standardmethode sind die Analyte in 5 Gruppen aufgeteilt. Alternativ bietet die All-in-One-Methode die Bestimmung aller Parameter in einem einzigen Lauf von unter 5 Minuten. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare sowie verlässliche Quantifizierung der Analyte. Mit der automatisierten Probenvorbereitung kann bei großen Probenserien deutlich Zeit gespart werden.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> Isotopenmarkierter interner Standard
> 3PLUS1® Multilevel Calibrator Set
> Automatisierte Methode verfügbar
> All-in-One-Methode: alle Parameter in weniger als 5 Minuten

6.3.1 *MassTox*® Antiepileptic Drugs Standard Method

Parameters:
carbamazepine, carbamazepine-10,11-epoxide, 10-OH-carbamazepine, 10,11-dihydroxycarbamazepine (carbamazepine-diol), N-desmethylmesuximide, ethosuximide, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, PEMA, phenobarbital, phenytoin, pregabalin, primidone, rufinamide, stiripentol, sultiame, theophylline, tiagabine, topiramate, valproic acid, vigabatrin, zonisamide.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests

	Basic Kit A ***Components available separately***
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.

92921	***MassTox*® TDM Parameter Set Antiepileptic Drugs Components available separately**
92025/XT	3PLUS1® Multilevel Plasma Calibrator Set Antiepileptic Drugs/*EXTENDED* (lyoph.), 4 x 1 ml
0250/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0251/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92546	Internal Standard Mix Antiepileptic Drugs, 3.8 ml

	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92034/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 1, Analytes and Internal Standards, 1 ml
92035/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 2, Analytes and Internal Standards, 1 ml
92036/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 3, Analytes and Internal Standards, 1 ml
92037/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 4, Analytes and Internal Standards, 1 ml
92038/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 5, Analytes and Internal Standards, 1 ml
0249/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 1–300 mg/l
Limit of quantification:	0.1–7 mg/l
Intraassay:	CV = 2–8 %
Interassay:	CV = 4–9 %
Analysis time:	< 3.5 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: stored in the dark and cooled at +4 °C samples are stable for at least 24 hours. For longer storage periods keep samples frozen at approx. -20 °C.

Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive and negative
MS/MS mode:	MRM

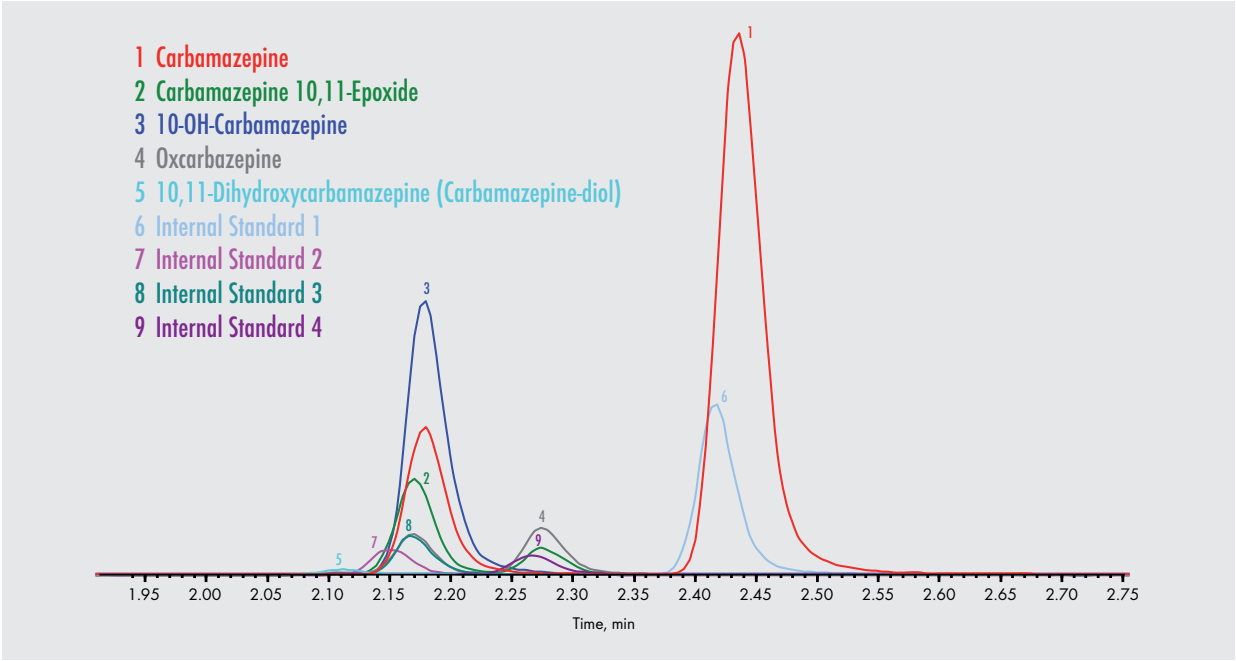
Gradient:
Starting point: 0% Mobile Phase 2
Group 1
0.00 → 2.00 min, 100 % Mobile Phase 2
2.00–2.60 min, 100 % Mobile Phase 2
2.61–3.50 min, 0 % Mobile Phase 2

Group 2 and 3
0.00 → 1.00 min, 100 % Mobile Phase 2
1.00–1.60 min, 100 % Mobile Phase 2
1.61–2.50 min, 0 % Mobile Phase 2

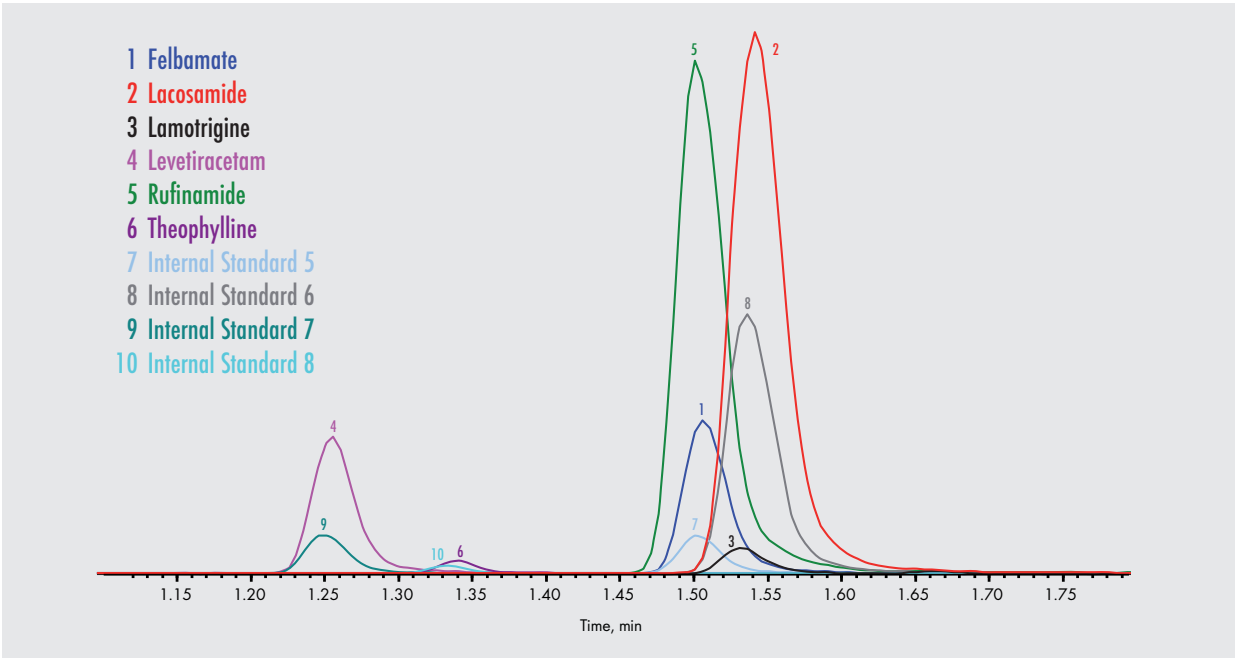
Group 4 and 5
0.00 → 1.00 min, 100 % Mobile Phase 2
1.00–1.80 min, 100 % Mobile Phase 2
1.81–2.70 min, 0 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

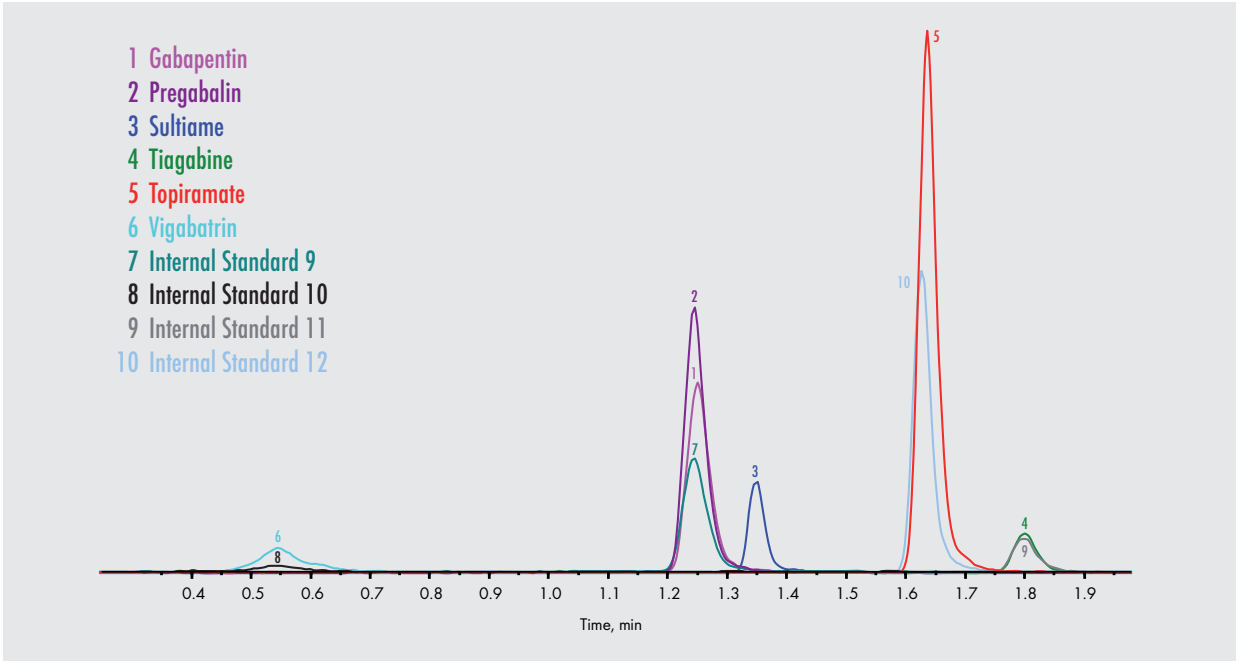
MassTox® Antiepileptic Drugs Group 1



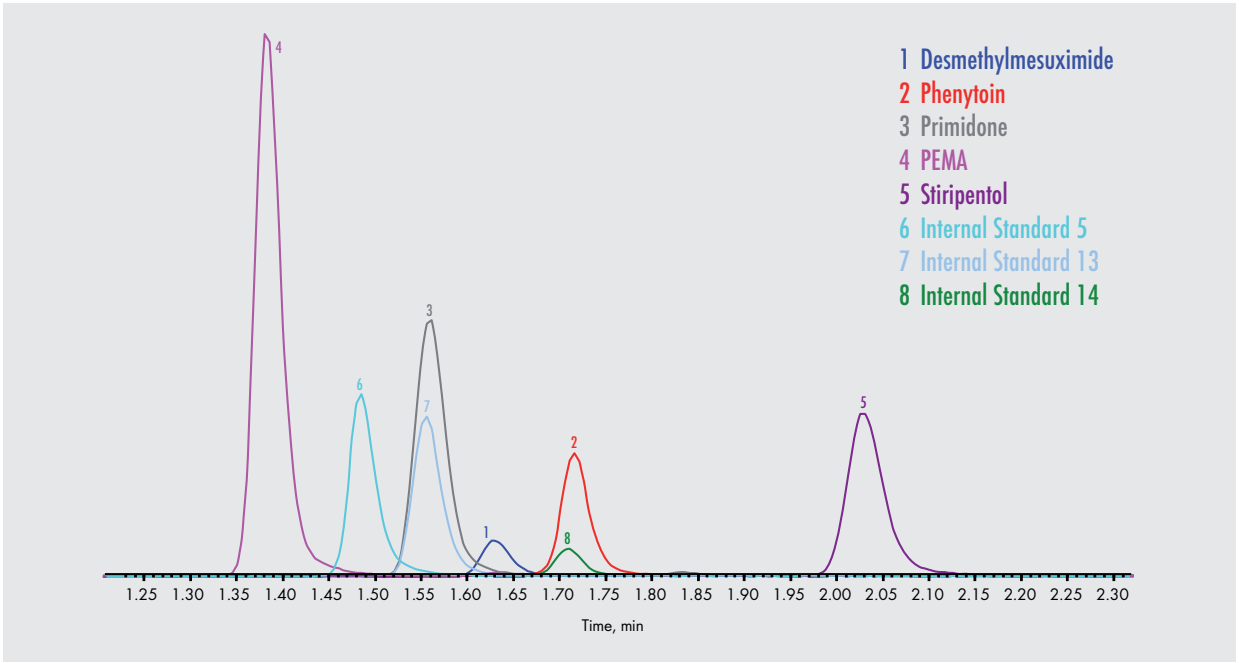
MassTox® Antiepileptic Drugs Group 2



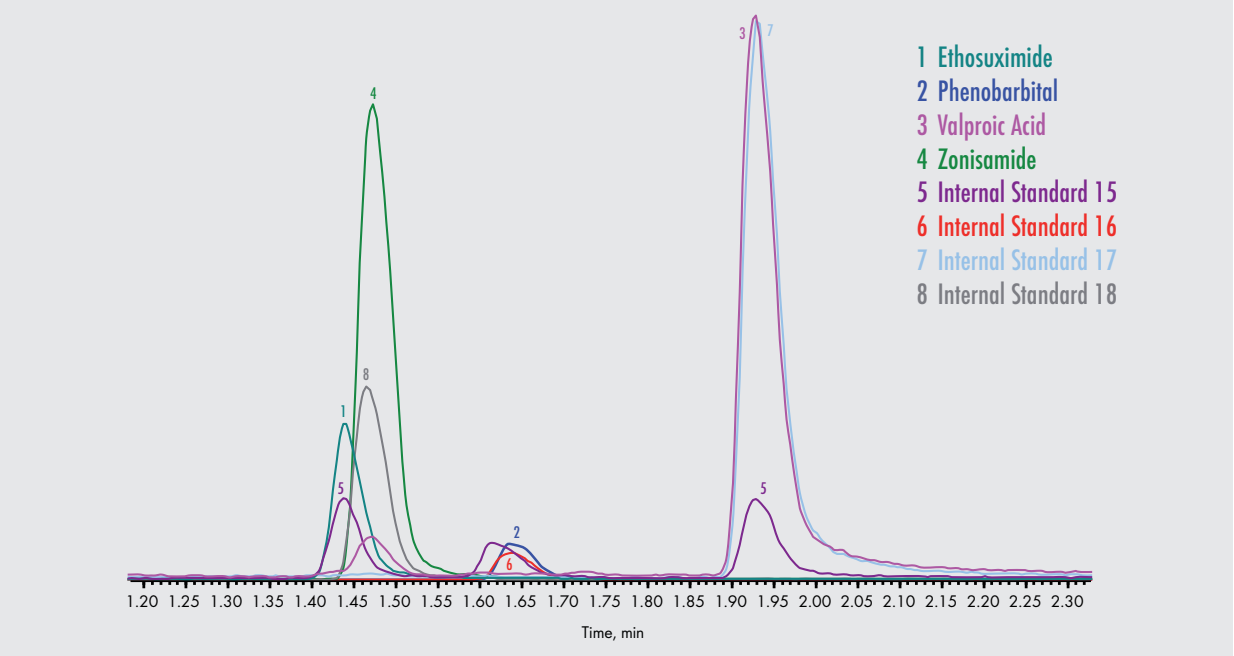
MassTox® Antiepileptic Drugs Group 3



MassTox® Antiepileptic Drugs Group 4



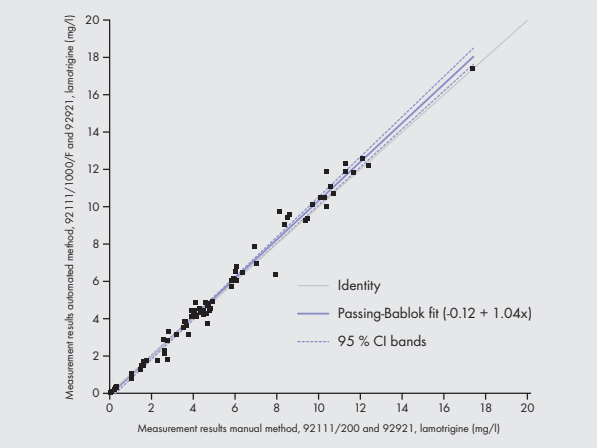
MassTox® Antiepileptic Drugs Group 5

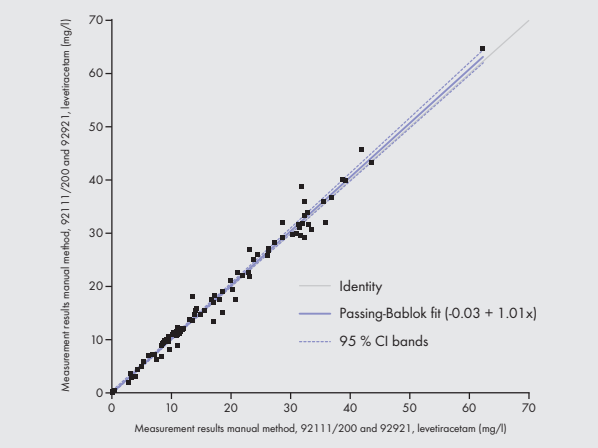


For more details on these substances see page 131–132.

6.3.2 *MassTox*® Antiepileptic Drugs Automated Method

Automated with 96 Well Filter Plates





Comparison of human samples prepared manually and with automation (Tecan Freedom EVO 100). The analysis was performed with the ***MassTox***® *TDM Series A Parameter Set Antiepileptic Drugs in Serum/Plasma (order no. 92921) on an ABSciex API 4000 mass spectrometer.*

Order no.	Product
92111/ 1000/F	***MassTox*® *TDM Basic Kit A*** Automated with 96 Well Filter Plates For 1000 tests
	Basic Kit A ***Components available separately***
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
92012	Precipitation Reagent, for automated sample preparation, 250 ml
92057	96 Well Filter Plates, 3 pcs.
92058	Collection Plates, 3 pcs.
92059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
92921	***MassTox*® *TDM Parameter Set Antiepileptic Drugs*** ***Components available separately***
92025/XT	3PLUS1® Multilevel Plasma Calibrator Set Antiepileptic Drugs/*EXTENDED* (lyoph.), 4 x 1 ml
0250/XT	***MassCheck***® Antiepileptic Drugs/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0251/XT	***MassCheck***® Antiepileptic Drugs/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92546	Internal Standard Mix Antiepileptic Drugs, 3.8 ml

	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92034/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 1, Analytes and Internal Standards, 1 ml
92035/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 2, Analytes and Internal Standards, 1 ml
92036/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 3, Analytes and Internal Standards, 1 ml
92037/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 4, Analytes and Internal Standards, 1 ml
92038/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 5, Analytes and Internal Standards, 1 ml
0249/XT	***MassCheck***® Antiepileptic Drugs/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml

Automated Workflow

→ Load liquid handling device with samples, reagents, 96 well filter plate and collection plate.
→ Start the **automation routine***.
→ After completion remove collection plate from the liquid handling device, seal with an adhesive seal and transfer to autosampler.
→ Inject 0.2–50 µl eluate into LC-MS/MS system.

* *Ready to use automation routine provided with the installation by Chromsystems.*

6.3.3 *MassTox*® Antiepileptic Drugs All-in-One Method

Parameters:
brivaracetam, carbamazepine, carbamazepine-10,11-epoxide, 10-OH-carbamazepine, 10,11-dihydroxycarbamazepine (carbamazepine-diol), N-desmethylmesuximide, ethosuximide, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenobarbital, phenylethylmalonamide (PEMA), phenytoin, pregabalin, primidone, retigabine, rufinamide, stiripentol, sultiame, theophylline, tiagabine, topiramate, valproic acid, vigabatrin, zonisamide.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92921/XT	***MassTox*® TDM Parameter Set Antiepileptic Drugs All-in-One Method Components available separately**
92025/XT	3PLUS1® Multilevel Plasma Calibrator Set Antiepileptic Drugs/*EXTENDED* (lyoph.), 4 x 1 ml
0250/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0251/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92546/XT	Internal Standard Mix Antiepileptic Drugs/*EXTENDED*, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92034/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 1, Analytes and Internal Standards, 1 ml
92035/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 2, Analytes and Internal Standards, 1 ml
92036/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 3, Analytes and Internal Standards, 1 ml
92037/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 4, Analytes and Internal Standards, 1 ml
92038/XT	Tuning Mix Antiepileptic Drugs/*EXTENDED* 5, Analytes and Internal Standards, 1 ml
0249/XT	***MassCheck*®** Antiepileptic Drugs/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 0.5–250 mg/l
Limit of quantification:	0.004–9 mg/l
Intraassay:	CV < 10 %
Interassay:	CV < 13 %
Analysis time:	4.9 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: stored in the dark and cooled at +4 °C samples are stable for at least 24 hours. For longer storage periods keep samples frozen below -18 °C.

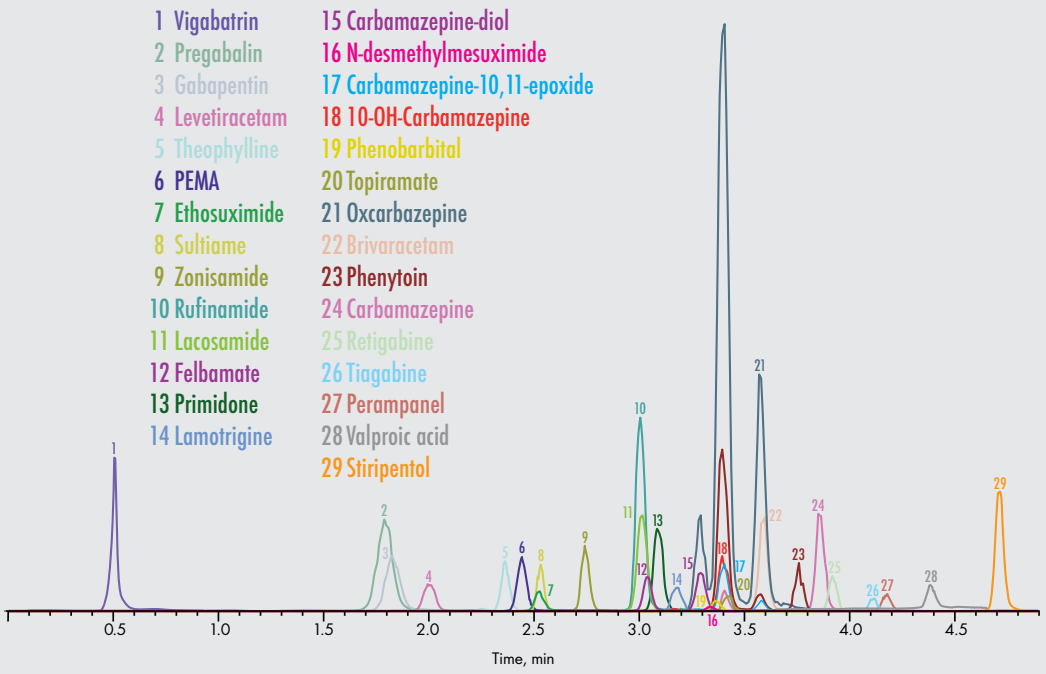
Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

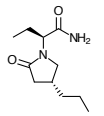
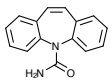
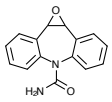
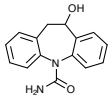
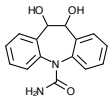
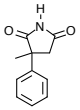
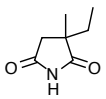
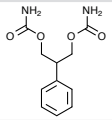
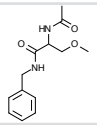
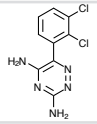
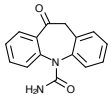
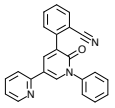
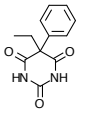
LC-MS/MS Parameters

Injection volume: 0.2–50 µl
Ionisation: ESI positive and negative
MS/MS mode: MRM
Gradient: 0.00–0.20 min, 0 % Mobile Phase 2
0.20 → 3.75 min, 100 % Mobile Phase 2
3.75–4.25 min, 100 % Mobile Phase 2
4.26–4.90 min, 0 % Mobile Phase 2
We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width. Using ESI polarity switching, all parameters can be measured in a single run.

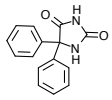
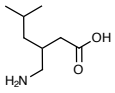
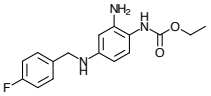
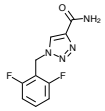
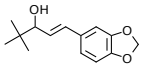
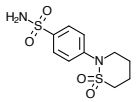
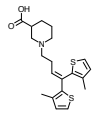
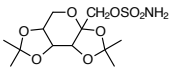
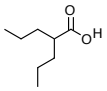
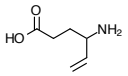
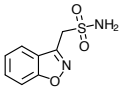
MassTox® Antiepileptic Drugs All-in-One Method



MassTox® Antiepileptic Drugs

Substance	Published Reference Ranges [7–10] (µg/l)	Mw (g/mol)	Formula	Structure
Brivaracetam	0.5–0.9	212.15	$C_{11}H_{20}N_2O_2$	
Carbamazepine	4–12	236.27	$C_{15}H_{12}N_2O$	
Carbamazepine-10,11-epoxide	0.2–9	252.27	$C_{15}H_{12}N_2O_2$	
10-OH-Carbamazepine	3–40	254.28	$C_{15}H_{14}N_2O_2$	
10,11-Dihydroxycarbamazepine (Carbamazepine-Diol)	–	270.28	$C_{15}H_{14}N_2O_3$	
N-Desmethylmesuximide	10–40	189.21	$C_{11}H_{11}NO_2$	
Ethosuximide	30–100	141.17	$C_7H_{11}NO_2$	
Felbamate	3–110	238.24	$C_{11}H_{14}N_2O_4$	
Gabapentin	0.5–20	171.24	$C_9H_{17}NO_2$	
Lacosamide	1–10	250.29	$C_{13}H_{18}N_2O_3$	
Lamotrigine	3–15	256.09	$C_9H_7Cl_2N_5$	
Levetiracetam	10–43	170.21	$C_8H_{14}N_2O_2$	
Oxcarbazepine	0.4–2	252.27	$C_{15}H_{12}N_2O_2$	
Perampanel	0.05–1.5	349.38	$C_{23}H_{15}N_3O$	
Phenobarbital	10–40	232.24	$C_{12}H_{12}N_2O_3$	

MassTox® Antiepileptic Drugs

Substance	Published Reference Ranges [7–10] (µg/l)	Mw (g/mol)	Formula	Structure
Phenylethylmalonamide (PEMA)	7–10	206.24	$C_{11}H_{14}N_2O_2$	
Phenytoin	5–20	252.27	$C_{15}H_{12}N_2O_2$	
Pregabalin	2–5	159.23	$C_8H_{17}NO_2$	
Primidone	4–12	218.25	$C_{12}H_{14}N_2O_2$	
Retigabine	0.15–0.9	330.33	$C_{16}H_{18}FN_3O_2$	
Rufinamide	5–30**	238.19	$C_{10}H_8F_2N_4O$	
Stiripentol	1–10	234.29	$C_{14}H_{18}O_3$	
Sultiame	0.5–12.5	290.36	$C_{10}H_{14}N_2O_4S_2$	
Theophylline	5–20	180.16	$C_7H_8N_4O_2$	
Tiagabine	0.01–0.2	375.55	$C_{20}H_{25}NO_2S_2$	
Topiramate	1–25	339.36	$C_{12}H_{21}NO_8S$	
Valproic acid	40–100	144.21	$C_8H_{16}O_2$	
Vigabatrin	1–36	129.16	$C_6H_{11}NO_2$	
Zonisamide	5–40	212.23	$C_8H_8N_2O_3S$	

** *preliminary*

3PLUS1® Multilevel Plasma Calibrator Set Antiepileptic Drugs

Substance	Calibrator 1* (mg/l)	Calibrator 2* (mg/l)	Calibrator 3* (mg/l)	Blank Calibrator (mg/l)
Brivaracetam	0.618	2.42	4.19	< LOQ
10-OH-Carbamazepine	3.43	25.1	45.7	< LOQ
Carbamazepine	1.62	8.35	14.0	< LOQ
Carbamazepine-10,11-epoxide	0.158	5.64	10.3	< LOQ
Carbamazepine-Diol	0.137	5.60	12.2	< LOQ
Ethosuximide	20.3	66.4	110	< LOQ
Felbamate	12.9	68.1	121	< LOQ
Gabapentin	1.58	14.5	25.5	< LOQ
Lacosamide	0.735	6.25	11.2	< LOQ
Lamotrigine	1.51	9.66	17.0	< LOQ
Levetiracetam	5.06	30.5	88.2	< LOQ
N-Desmethylmesuximide	6.99	27.5	47.3	< LOQ
Oxcarbazepine	0.137	1.83	3.60	< LOQ
PEMA	0.997	6.31	11.2	< LOQ
Perampanel	0.0357	0.883	1.780	< LOQ
Phenobarbital	6.34	30.8	55.1	< LOQ
Phenytoin	3.45	13.9	23.4	< LOQ
Pregabalin	0.146	6.35	12.2	< LOQ
Primidone	3.06	11.4	18.7	< LOQ
Retigabine	0.0487	1.058	2.050	< LOQ
Rufinamide	3.99	20.5	34.1	< LOQ
Stiripentol	2.80	14.4	24.1	< LOQ
Sultiame	0.371	8.10	15.0	< LOQ
Theophylline	6.22	15.7	24.7	< LOQ
Tiagabine	0.0135	0.126	0.230	< LOQ
Topiramate	0.642	15.6	29.4	< LOQ
Valproic acid	28.4	73.4	120	< LOQ
Vigabatrin	1.48	22.7	41.2	< LOQ
Zonisamide	3.73	27.6	49.1	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Antiepileptic Drugs Plasma Controls

Substance	Level I Target Value* (mg/l)	Level II Target Value* (mg/l)
Brivaracetam	0.973	3.80
10-OH-Carbamazepine	7.80	33.9
Carbamazepine	3.17	10.6
Carbamazepine-10,11-epoxide	1.14	7.68
Carbamazepine-Diol	0.978	8.34
Ethosuximide	33.2	81.6
Felbamate	25.1	89.3
Gabapentin	4.13	19.4
Lacosamide	1.84	8.28
Lamotrigine	3.21	12.7
Levetiracetam	16.6	68.3
N-Desmethylmesuximide	12.6	35.0
Oxcarbazepine	0.402	2.81
PEMA	2.09	8.28
Perampanel	0.175	1.213
Phenobarbital	12.0	40.5
Phenytoin	6.00	17.4
Pregabalin	1.15	8.91
Primidone	5.19	14.1
Retigabine	0.243	1.786
Rufinamide	7.83	25.8
Stiripentol	5.57	18.2
Sultiame	1.71	11.1
Theophylline	9.38	18.8
Tiagabine	0.0349	0.170
Topiramate	3.04	21.4
Valproic acid	43.3	87.7
Vigabatrin	5.35	30.7
Zonisamide	8.53	36.9

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92025/XT	3PLUS1® Multilevel Plasma Calibrator Set Antiepileptic Drugs/*EXTENDED* (lyoph.), 4 x 1 ml
0250/XT	***MassCheck***® Antiepileptic Drugs/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0251/XT	***MassCheck***® Antiepileptic Drugs/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 2 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.4 *MassTox*® Anti-HIV Drugs

CE IVD

According to estimates from UNAIDS there are about 36.9 million people worldwide living with HIV, of which approximately 3 mill. are children under the age of 15 years. Even though the number of globally registered new infections is decreasing, it was still at approximately 2 mill. in 2014. Medications currently available as part of HAART (highly active antiretroviral therapy), interfere with or inhibit the development of the virus at different stages of virus reproduction. The individual plasma level of the administered antiretroviral agents may vary for a variety of reasons (absorption, compliance, metabolism), thus diminishing the efficacy of therapy. Therefore the measurement of the drug concentration in serum or plasma is essential for therapy control.

The ***MassTox***® TDM Parameter Set Anti-HIV Drugs allows a rapid and reliable quantitative determination of the analytes using LC-MS/MS. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and increases the robustness of the method. The use of stable isotope-labelled (deuterated), co-eluting internal standards, and the multilevel calibrators ensures reproducible and dependable quantification of the analytes. Just as for all Parameter Sets of Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 18 analytes
> Deuterated, co-eluting and stable internal standards
> 6PLUS1® Multilevel Calibrator Set

Nach Schätzungen der UNAIDS leben weltweit etwa 36,9 Mio. Menschen mit HIV, davon etwa 3 Mio. Kinder unter 15 Jahren. Auch wenn die Zahl der weltweit registrierten Neuinfektionen abnimmt, lag sie dennoch im Jahr 2014 bei ca. 2 Mio. Die zurzeit verfügbaren Medikamente, die im Rahmen der HAART (hochaktive antiretrovirale Therapie) gegeben werden, stören oder unterbinden die Entwicklung des Virus in den verschiedenen Phasen der Vermehrung oder der Zellinfektion. Der individuelle Plasmaspiegel der verabreichten antiretroviralen Arzneimittel kann aus verschiedenen Gründen (Aufnahme, Compliance, Stoffwechsel) stark variieren und damit den Therapieerfolg beeinträchtigen. Daher ist die Messung der Arzneimittelkonzentration im Serum oder Plasma für die Optimierung der Therapie unbedingt notwendig.

Mit diesem Parameter-Set für die LC-MS/MS Analytik von Anti-HIV-Medikamenten im Serum/Plasma können die einzelnen Wirkstoffe schnell und effektiv gemessen werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methode erhöht. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. Die Probenvorbereitung basiert, so wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> Umfasst 18 Anti-HIV-Wirkstoffe
> Deuterierte, co-eluierende und stabile interne Standards
> 6PLUS1® Multilevel Calibrator Set

MassTox® Anti-HIV Drugs

Parameters:
amprenavir, atazanavir, darunavir, delavirdine, efavirenz, elvitegravir, etravirine, indinavir, lopinavir, maraviroc, nelfinavir, nelfinavir-M8, nevirapine, raltegravir, rilpivirine, ritonavir, saquinavir, tipranavir.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92924	***MassTox*® TDM Parameter Set Anti-HIV Drugs**
	Components available separately
92053	6PLUS1® Multilevel Plasma Calibrator Set Anti-HIV Drugs (lyoph.), 7 x 1 ml
0262	***MassCheck*®** Anti-HIV Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml
0263	***MassCheck*®** Anti-HIV Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml
92844	Internal Standard, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92042	Tuning Mix Anti-HIV Drugs, Analytes and Internal Standards, 1 ml
0261	***MassCheck*®** Anti-HIV Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Limit of quantification:	1.0–65 µl
Linearity:	up to 168 mg/l
Intraassay:	CV 0.9–6.7 %
Interassay:	CV 1.5–8.1 %
Analysis time:	3.0–3.5 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: protected from light samples are stable up to 7 days at ambient temperature (~ 25 °C) and up to 2 weeks at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

LC-MS/MS Parameters

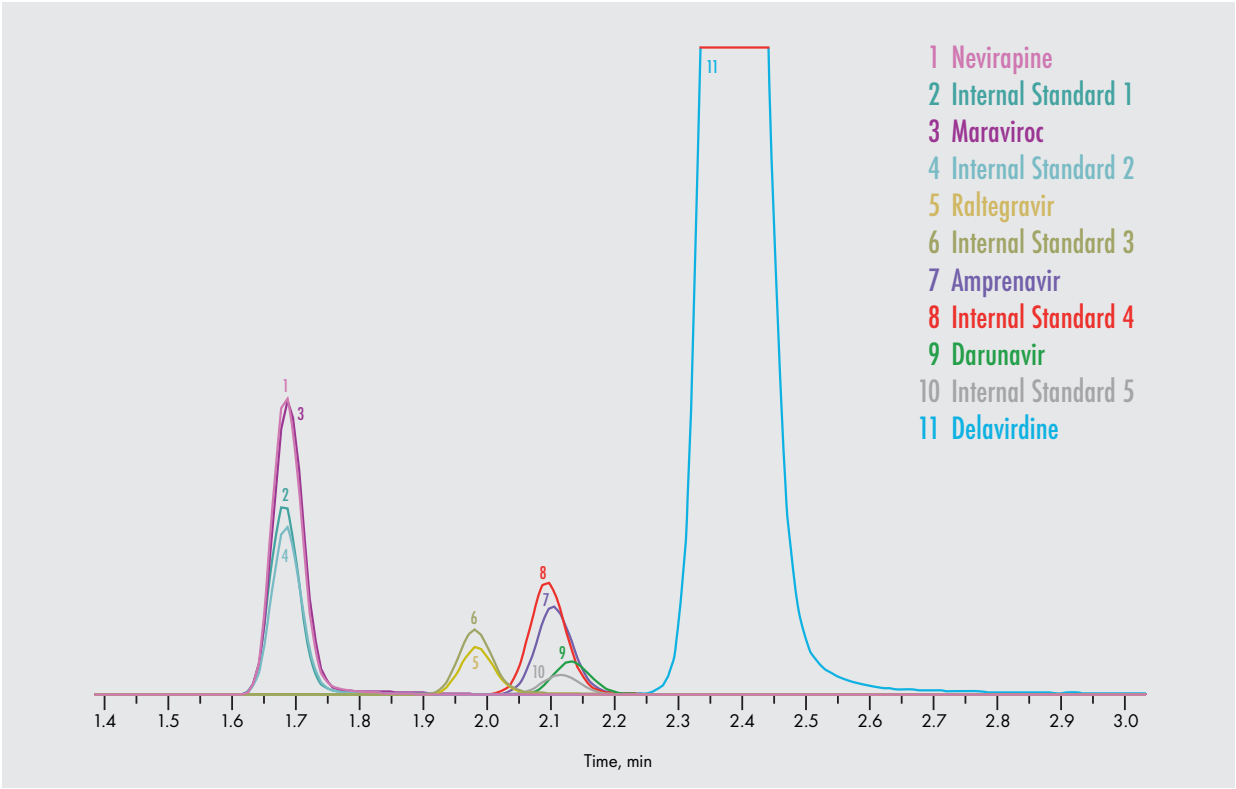
Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

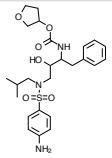
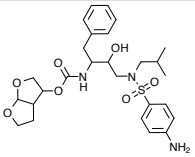
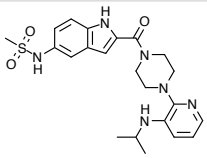
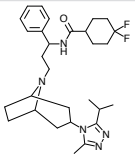
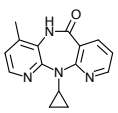
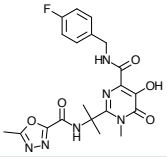
Gradient:

Group 1:	0.00 – 0.20 min,	0 % Mobile Phase 2
	0.21 – 2.00 min,	70 % Mobile Phase 2
	2.01 – 2.90 min,	100 % Mobile Phase 2
	2.91 – 3.50 min,	0 % Mobile Phase 2
Group 2:	0.00 – 0.20 min,	0 % Mobile Phase 2
	0.21 – 0.60 min,	50 % Mobile Phase 2
	0.61 – 2.40 min,	90 % Mobile Phase 2
	2.41 – 3.00 min,	0 % Mobile Phase 2
Group 3:	0.00 – 0.20 min,	0 % Mobile Phase 2
	0.21 – 2.30 min,	90 % Mobile Phase 2
	2.31 – 3.10 min,	0 % Mobile Phase 2

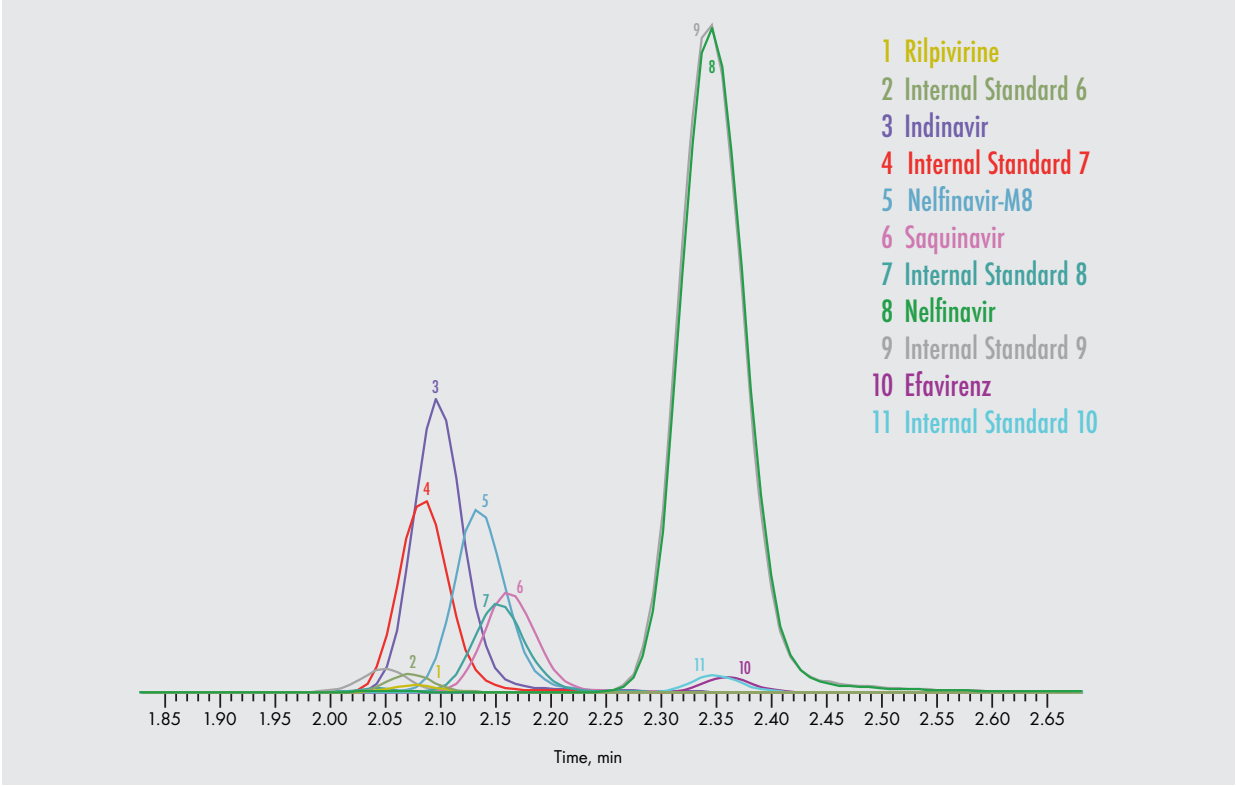
We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

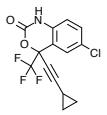
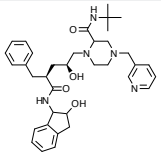
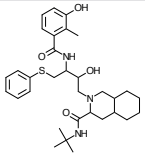
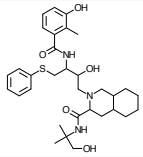
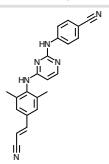
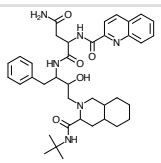
MassTox® Anti-HIV Drugs Group 1



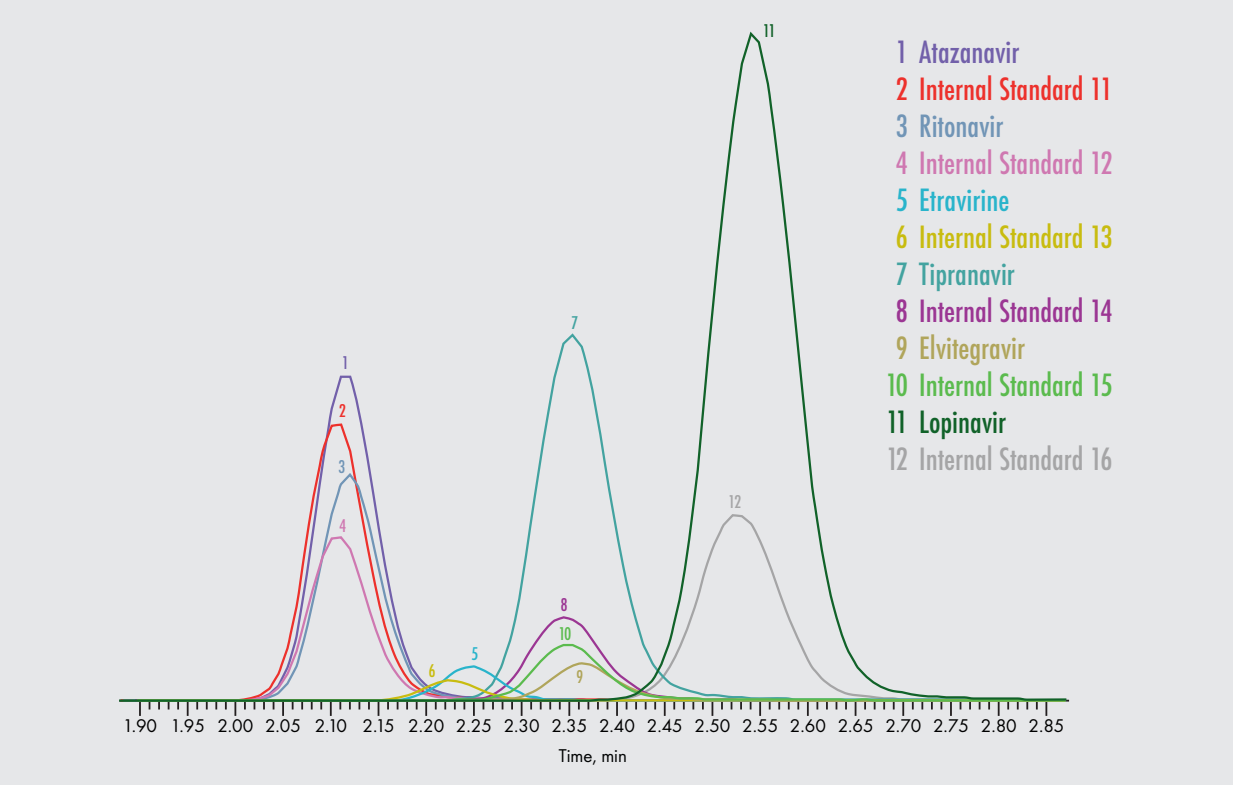
Substance	Published Reference Ranges [3,11–13] (µg/l)	Mw (g/mol)	Formula	Structure
Amprenavir	300–10000	505.63	$C_{25}H_{35}N_3O_6S$	
Darunavir	400–7200	547.66	$C_{27}H_{37}N_3O_7S$	
Delavirdine	–	456.56	$C_{22}H_{28}N_6O_3S$	
Maraviroc	400	513.67	$C_{29}H_{41}F_2N_5O$	
Nevirapine	2600–6400	266.30	$C_{15}H_{14}N_4O$	
Raltegravir	40–100	444.42	$C_{20}H_{21}FN_6O_5$	

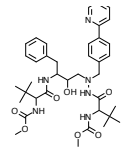
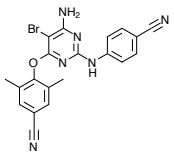
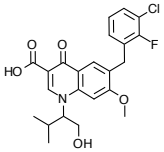
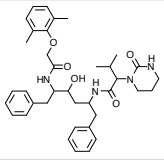
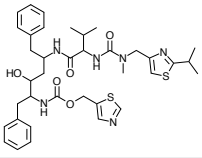
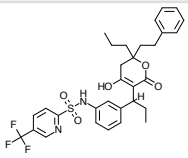
MassTox® Anti-HIV Drugs Group 2



Substance	Published Reference Ranges [3,11–13] (µg/l)	Mw (g/mol)	Formula	Structure
Efavirenz	700–4000	315.67	$C_{14}H_9ClF_3NO_2$	
Indinavir	50–3000	613.79	$C_{36}H_{47}N_5O_4$	
Nelfinavir	750–2500	567.78	$C_{32}H_{45}N_3O_4S$	
Nelfinavir-M8	–	583.78	$C_{32}H_{45}N_3O_5S$	
Rilpivirine	–	366.42	$C_{22}H_{18}N_6$	
Saquinavir	170–800	670.84	$C_{38}H_{50}N_6O_5$	

MassTox® Anti-HIV Drugs Group 3



Substance	Published Reference Ranges [3,11–13] (µg/l)	Mw (g/mol)	Formula	Structure
Atazanavir	20–6000	704.86	$C_{38}H_{52}N_6O_7$	
Etravirine	100–3000	435.28	$C_{20}H_{15}BrN_6O$	
Elvitegravir	190–710	447.88	$C_{23}H_{23}ClFNO_5$	
Lopinavir	1000–10000	628.80	$C_{37}H_{48}N_4O_5$	
Ritonavir	1100–11000	720.94	$C_{37}H_{48}N_6O_5S_2$	
Tipranavir	11000–45000	602.66	$C_{31}H_{33}F_3N_2O_5S$	

6PLUS1® Multilevel Plasma Calibrator Set
Anti-HIV Drugs

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
Amprenavir	221	623	1291	1836	2465	2881	< LOQ
Atazanavir	66.5	626	1286	1853	2515	3110	< LOQ
Darunavir	50.7	1068	2186	3268	4456	5646	< LOQ
Delavirdine	503	1830	3518	6454	8721	9798	< LOQ
Efavirenz	616	1068	2135	3191	4343	4833	< LOQ
Elvitegravir	135	252	523	755	1064	1230	< LOQ
Etravirine	73.0	742	1499	2171	2944	3374	< LOQ
Indinavir	11.2	717	1453	3191	2833	3514	< LOQ
Lopinavir	773	2536	5098	7270	9729	11088	< LOQ
Maraviroc	25.0	239	494	722	968	1221	< LOQ
Nelfinavir	552	704	1405	2005	2680	2934	< LOQ
Nelfinavir-M8	156	376	774	1135	1535	1803	< LOQ
Nevirapine	1970	2945	3968	5729	7725	8901	< LOQ
Raltegravir	28.1	116	254	366	497	609	< LOQ
Rilpivirine	35.5	76.6	158	239	333	372	< LOQ
Ritonavir	232	2826	5696	8151	10838	13563	< LOQ
Saquinavir	35.2	192	391	568	794	956	< LOQ
Tipranavir	8643	13088	26800	37400	50100	54650	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Anti-HIV Drugs Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Amprenavir	469	2051
Atazanavir	325	2185
Darunavir	504	4054
Delavirdine	1193	7270
Efavirenz	1181	3476
Elvitegravir	244	845
Etravirine	366	2623
Indinavir	299	2526
Lopinavir	1838	8256
Maraviroc	121	866
Nelfinavir	876	2113
Nelfinavir-M8	321	1289
Nevirapine	2888	5925
Raltegravir	82.1	435
Rilpivirine	69.9	263
Ritonavir	1373	9563
Saquinavir	116	678
Tipranavir	14375	40663

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92053	6PLUS1® Multilevel Plasma Calibrator Set Anti-HIV Drugs (lyoph.), 7 x 1 ml
0261	***MassCheck***® Anti-HIV Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0262	***MassCheck***® Anti-HIV Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml
0263	***MassCheck***® Anti-HIV Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 2 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.5 *MassTox*® Antimycotic Drugs

CE IVD

Due to the increasing number of immunocompromised patients, invasive fungal infections have been growing steadily in recent years. Usually the immune deficiencies are the result of an infectious disease such as AIDS, or are caused by the increased use of highly effective drugs such as immunosuppressants and chemotherapeutics, or during radiation treatments. Most fungal infections are caused by Candida and Aspergillus species, which enter the body either from the air (spores of moulds) or via skin injuries. Here they can affect different internal organs or entire organ systems (e.g. the gastrointestinal tract), hence they are also known as systemic mycoses. Through improved diagnostic methods rare mycoses such as fusarium, scedosporium and zygomycosis have also become recognised and are accessible for therapy. These infections can be treated with modern antifungal agents such as posaconazole or voriconazole from the new group of echinocandins. Older agents such as fluconazole or 5-flucytosine, which are both listed in the "WHO Model List of Essential Medicines", are still used in the treatment of fungal infections.

The ***MassTox***® TDM Parameter Set Antimycotic Drugs allows a rapid and reliable quantitative determination of the analytes using LC-MS/MS. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and increases the robustness of the method The use of stable isotope-labelled (deuterated), co-eluting internal standards, and the multilevel calibrators ensures reproducible and dependable quantification of the analytes. Just as for all Parameter Sets of Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 8 analytes
> Isotopically labelled internal standards
> 3PLUS1® Multilevel Calibrator Set

Aufgrund der steigenden Zahl immungeschwächter Patienten haben invasive Mykosen in den letzten Jahren kontinuierlich zugenommen. Dabei ist die Immunschwäche meist Folge einer Infektionskrankheit wie AIDS oder wird durch den vermehrten Einsatz hochwirksamer Medikamente wie Immunsuppressiva, Chemotherapeutika sowie während Strahlentherapien hervorgerufen. Die meisten Pilzerkrankungen werden durch Candida- und Aspergillus-Arten hervorgerufen, die entweder über die Luft (Sporen von Schimmelpilzen) oder durch Verletzungen der Haut in den Körper gelangen. Hier können sie verschiedene innere Organe oder ganze Organsysteme (z. B. Magen-Darm-Trakt) befallen, weshalb sie auch als Systemmykosen bezeichnet werden. Durch verbesserte diagnostische Methoden werden zunehmend auch seltene Mykosen wie Fusariosen, Scedosporium- oder Zygomykosen erkannt und für die Therapie zugänglich. Behandeln lassen sich diese Infektionen mit modernen Antimykotika wie Posaconazol oder Voriconazol aus der neuen Gruppe der Echinocandine. Aber auch ältere Vertreter wie Fluconazol oder 5-Flucytosin, die beide in der „WHO Model List of Essential Medicines" gelistet sind, finden noch Verwendung bei der Behandlung von Pilzinfektionen.

Mit diesem Parameter-Set für die LC-MS/MS Analytik von Antimykotika im Serum/Plasma können die einzelnen Wirkstoffe schnell und effektiv gemessen werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methode erhöht. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. Die Probenvorbereitung basiert, so wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> Methode umfasst 8 Analyte
> Isotopenmarkierte interne Standards
> 3PLUS1® Multilevel Calibrator Set

MassTox® Antimycotic Drugs

Parameters:
fluconazole, 5-flucytosine, itraconazole, hydroxyitraconazole, ketoconazole, posaconazole, voriconazole.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92922	***MassTox*® TDM Parameter Set Antimycotic Drugs**
	Components available separately
92051	3PLUS1® Multilevel Plasma Calibrator Set Antimycotic Drugs (lyoph.), 4 x 1 ml
0253	***MassCheck*®** Antimycotic Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml
0254	***MassCheck*®** Antimycotic Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml
92644	Internal Standard Mix, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92039	Tuning Mix Antimycotic Drugs, Analytes and Internal Standards, 1 ml
0252	***MassCheck*®** Antimycotic Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 250 mg/l
Limit of quantification:	0.01–2.00 mg/l
Intraassay:	CV = 1.7–4.9 %
Interassay:	CV = 3.6–5.3 %
Recovery:	95–111 %
Analysis time:	3.2 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable up to 2 weeks at ambient temperature and up to 4 weeks at +2 to +8 °C. For longer storage periods (max. up to 3 months) keep samples frozen below -18 °C.

Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

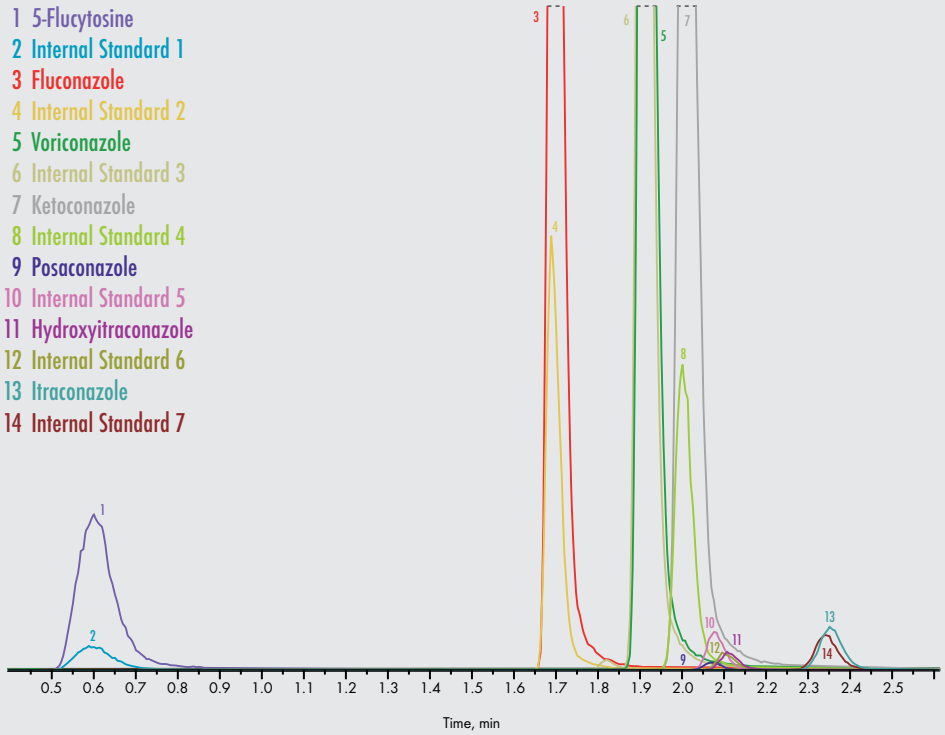
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

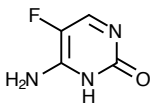
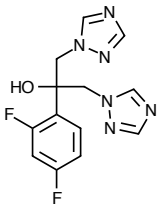
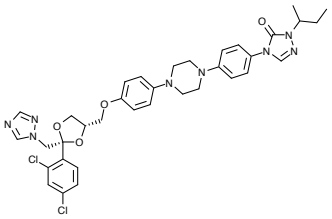
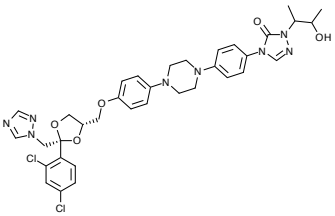
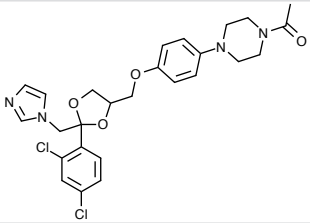
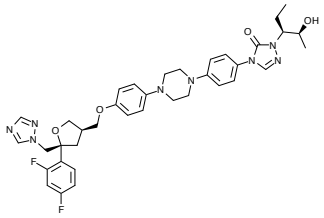
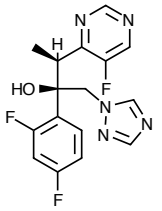
Gradient:
0.00–0.50 min, 30 % Mobile Phase 2
0.51–2.80 min, 100 % Mobile Phase 2
2.81–3.20 min, 30 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassTox® Antimycotic Drugs



MassTox® Antimycotic Drugs

Substance	Published Reference Ranges [3–5,14] (mg/l)	Mw (g/mol)	Formula	Structure
5-Flucytosine	20–75	129.09	$C_4H_4FN_3O$	
Fluconazole	1–15	306.27	$C_{13}H_{12}F_2N_6O$	
Itraconazole	0.4–4	705.63	$C_{35}H_{38}Cl_2N_8O_4$	
Hydroxyitraconazole	0.4–4	721.63	$C_{35}H_{38}Cl_2N_8O_5$	
Ketoconazole	0.3–6	531.43	$C_{26}H_{28}Cl_2N_4O_4$	
Posaconazole	0.5–1.5	700.78	$C_{37}H_{42}F_2N_8O_4$	
Voriconazole	0.5–6	349.31	$C_{16}H_{14}F_3N_5O$	

3PLUS1® Multilevel Plasma Calibrator Set Antimycotic Drugs

Substance	Calibrator 1* (mg/l)	Calibrator 2* (mg/l)	Calibrator 3* (mg/l)	Blank Calibrator (mg/l)
Fluconazole	0.674	9.10	17.8	< LOQ
5-Flucytosine	7.04	63.6	122	< LOQ
Itraconazole	0.184	1.03	1.86	< LOQ
Hydroxyitraconazole	0.239	1.36	2.43	< LOQ
Ketoconazole	0.190	5.69	11.8	< LOQ
Posaconazole	0.221	2.39	4.55	< LOQ
Voriconazole	0.342	2.98	5.92	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Antimycotic Drugs Plasma Controls

Substance	Level I Target Value* (mg/l)	Level II Target Value* (mg/l)
Fluconazole	2.23	13.0
5-Flucytosine	19.2	89.0
Itraconazole	0.365	1.36
Hydroxyitraconazole	0.477	1.82
Ketoconazole	1.06	8.46
Posaconazole	0.634	3.33
Voriconazole	0.849	4.30

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92051	3PLUS1® Multilevel Plasma Calibrator Set Antimycotic Drugs (lyoph.), 4 x 1 ml
0252	*MassCheck®* Antimycotic Drugs Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0253	*MassCheck®* Antimycotic Drugs Plasma Control, Level I (lyoph.), 5 x 1 ml
0254	*MassCheck®* Antimycotic Drugs Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 3 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.6 *MassTox*® Benzodiazepines

CE IVD

Benzodiazepines (BZD) are a large group of psychoactive drugs with similar chemical structure that are also classified as tranquilizers. By virtue of their high lipophilicity they penetrate the blood-brain barrier readily and, soon after reaching their receptors in the central nervous system, enhance the impact of the inhibiting neurotransmitter GABA (γ-amino-butyric acid). Besides anxiolytic and sedative effects, benzodiazepines have anti-aggressive, hypnotic, muscle relaxant and anticonvulsive properties. The predominance of the individual effects varies with the individual agent and the administered dose. Chronic administration (several weeks) can lead to the development of dependency, especially when high doses are employed.

The benzodiazepines are grouped into two Parameter Sets as part of the Series A modular system. Both sets allow the rapid and reliable quantitative determination of every individual parameter. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and warrants the robustness of the methods. Using deuterated stable isotopes, co-eluting internal standards and multilevel calibrators ensures a reliable and reproducible quantification of the analytes. Just as for all Parameter Sets of the ***MassTox***® TDM Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 23 analytes divided in 2 Parameter Sets
> Isotopically labelled internal standards
> 3PLUS1® Multilevel Calibrator Sets

Als Benzodiazepine (BZD) bezeichnet man eine große Gruppe chemisch ähnlich aufgebauter Psychopharmaka, die auch als Tranquilizer klassifiziert werden. Aufgrund ihrer lipophilen chemischen Struktur überwinden sie sehr leicht die Blut-Hirn-Schranke und gelangen nach der Resorption rasch ins zentrale Nervensystem, wo sie die Wirkung des hemmenden Neurotransmitters GABA (γ-Aminobuttersäure) verstärken. So besitzen Benzodiazepine neben angstlösender und sedierender Wirkung auch antiaggressive, hypnotische, muskelrelaxierende und antikonvulsive Eigenschaften. Die Ausprägung individueller Effekte variiert je nach struktureller Besonderheit des Benzodiazepins und der verabreichten Dosis. Bereits eine Anwendungsdauer von wenigen Wochen kann aber zu einer Abhängigkeitsentwicklung führen, vor allem wenn höhere Dosen verabreicht wurden.

Die Benzopdiazepine sind in 2 Parameter-Sets unterteilt, die Bestandteil des Serie A Baukastensystems sind. Mit den beiden Parameter-Sets können die einzelnen Wirkstoffe im Serum/Plasma schnell und effektiv bestimmt werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methoden sichergestellt. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. So wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, basiert die Probenvorbereitung auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> 2 Parameter-Sets mit insgesamt 23 Analyten
> Isotopenmarkierte interne Standards
> 3PLUS1® Multilevel Calibrator Sets

6.6.1 *MassTox*® Benzodiazepines 1

Parameters:
chlordiazepoxide, clobazam, norclobazam, demoxepam, diazepam, nordiazepam, medazepam, midazolam, 1-OH-midazolam, oxazepam, prazepam, temazepam, tetrazepam.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92917	***MassTox*® TDM Parameter Set Benzodiazepines 1 Components available separately**
92030	3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 1 (lyoph.), 4 x 1 ml
0238	***MassCheck*®** Benzodiazepines 1 Plasma Control, Level I (lyoph.), 5 x 1 ml
0239	***MassCheck*®** Benzodiazepines 1 Plasma Control, Level II (lyoph.), 5 x 1 ml
92346	Internal Standard Mix Benzodiazepines, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92020	Tuning Mix Benzodiazepines 1, Analytes and Internal Standards 1 ml
0237	***MassCheck*®** Benzodiazepines 1 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 1000–5050 µg/l
Limit of quantification:	3–40 µg/l
Intraassay:	CV = 2–5 %
Interassay:	CV = 2–7 %
Recovery:	87–107 %
Analysis time:	< 3 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: stored in the dark and cooled (+4 °C) samples are stable for at least 24 hours. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

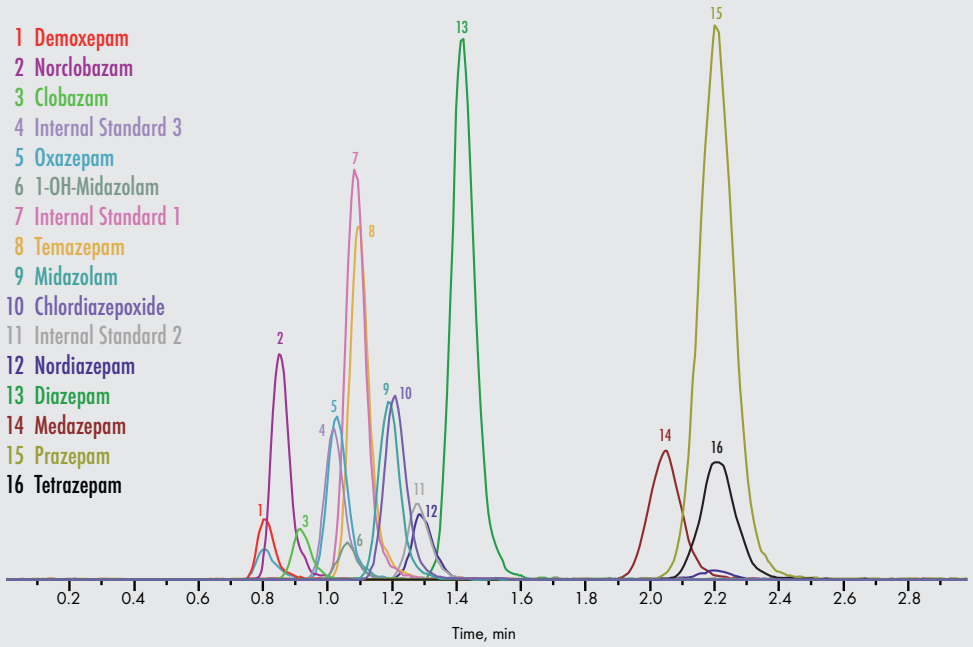
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

LC-MS/MS Parameters

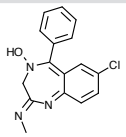
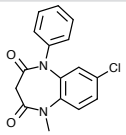
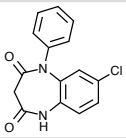
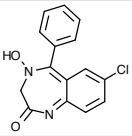
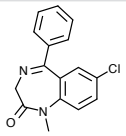
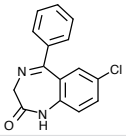
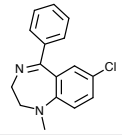
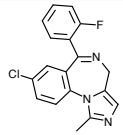
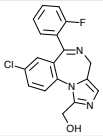
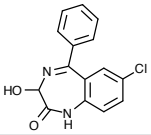
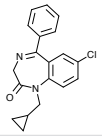
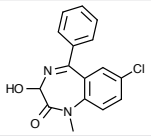
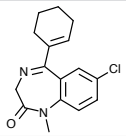
Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	isocratic 25 % Mobile Phase 1 75 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassTox® Benzodiazepines 1



MassTox® Benzodiazepines 1

Substance	Published Reference Ranges [3,6,15] (µg/l)	Mw (g/mol)	Formula	Structure
Chlordiazepoxide	400–3000	299.75	$C_{16}H_{14}ClN_3O$	
Clobazam	30–600	300.74	$C_{16}H_{13}ClN_2O_2$	
Norclobazam	300–4000	286.71	$C_{15}H_{11}ClN_2O_2$	
Demoxepam	500–740	286.71	$C_{15}H_{11}ClN_2O_2$	
Diazepam	125–2500	284.74	$C_{16}H_{13}ClN_2O$	
Nordiazepam	20–800	270.71	$C_{15}H_{11}ClN_2O$	
Medazepam	100–500	270.76	$C_{16}H_{15}ClN_2$	
Midazolam	6– 250	325.77	$C_{18}H_{13}ClFN_3$	
1-OH-midazolam	–	341.77	$C_{18}H_{13}ClFN_3O$	
Oxazepam	200–1500	286.71	$C_{15}H_{11}ClN_2O_2$	
Prazepam	200–700	324.80	$C_{19}H_{17}ClN_2O$	
Temazepam	20–1000	300.74	$C_{16}H_{13}ClN_2O_2$	
Tetrazepam	50–1000	288.77	$C_{16}H_{17}ClN_2O$	

3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 1

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Chlordiazepoxide	236	1110	1992	< LOQ
Clobazam	57.0	283	518	< LOQ
Norclobazam	582	2388	4299	< LOQ
Demoxepam	261	1268	2290	< LOQ
Diazepam	72.3	892	1703	< LOQ
Nordiazepam	13.5	864	1759	< LOQ
Medazepam	62.8	289	534	< LOQ
Midazolam	15.1	132	249	< LOQ
1-OH-midazolam	12.2	117	219	< LOQ
Oxazepam	134	1183	2292	< LOQ
Prazepam	124	421	689	< LOQ
Temazepam	12.8	557	1150	< LOQ
Tetrazepam	34.9	471	912	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Benzodiazepines 1 Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Chlordiazepoxide	473	1569
Clobazam	111	398
Norclobazam	1112	3212
Demoxepam	508	1703
Diazepam	226	1240
Nordiazepam	153	1258
Medazepam	115	382
Midazolam	30.1	157
1-OH-midazolam	33.1	168
Oxazepam	346	1686
Prazepam	208	569
Temazepam	105	857
Tetrazepam	115	662

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92030	3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 1 (lyoph.), 4 x 1 ml
0237	*MassCheck®* Benzodiazepines 1 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0238	*MassCheck®* Benzodiazepines 1 Plasma Control, Level I (lyoph.), 5 x 1 ml
0239	*MassCheck®* Benzodiazepines 1 Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 1 week at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.6.2 *MassTox*® Benzodiazepines 2

Parameters:
alprazolam, bromazepam, clonazepam, flunitrazepam, flurazepam, desalkylflurazepam, lorazepam, lormetazepam, nitrazepam, triazolam.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92918	***MassTox*® TDM Parameter Set Benzodiazepines 2 Components available separately**
92031	3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 2 (lyoph.), 4 x 1 ml
0241	***MassCheck*®** Benzodiazepines 2 Plasma Control, Level I (lyoph.), 5 x 1 ml
0242	***MassCheck*®** Benzodiazepines 2 Plasma Control, Level II (lyoph.), 5 x 1 ml
92346	Internal Standard Mix Benzodiazepines, 3.8 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92021	Tuning Mix Benzodiazepines 2, Analytes and Internal Standards, 1 ml
0240	***MassCheck*®** Benzodiazepines 2 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	up to 50–750 µg/l
Limit of quantification:	1–10 µg/l
Intraassay:	CV = 2–9 %
Interassay:	CV = 6–14 %
Recovery:	90–109 %
Analysis time:	< 3 min

Pre-analytic Treatment

Specimens: serum or plasma
Stability: stored in the dark and cooled (+4 °C) samples are stable for at least 24 hours. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

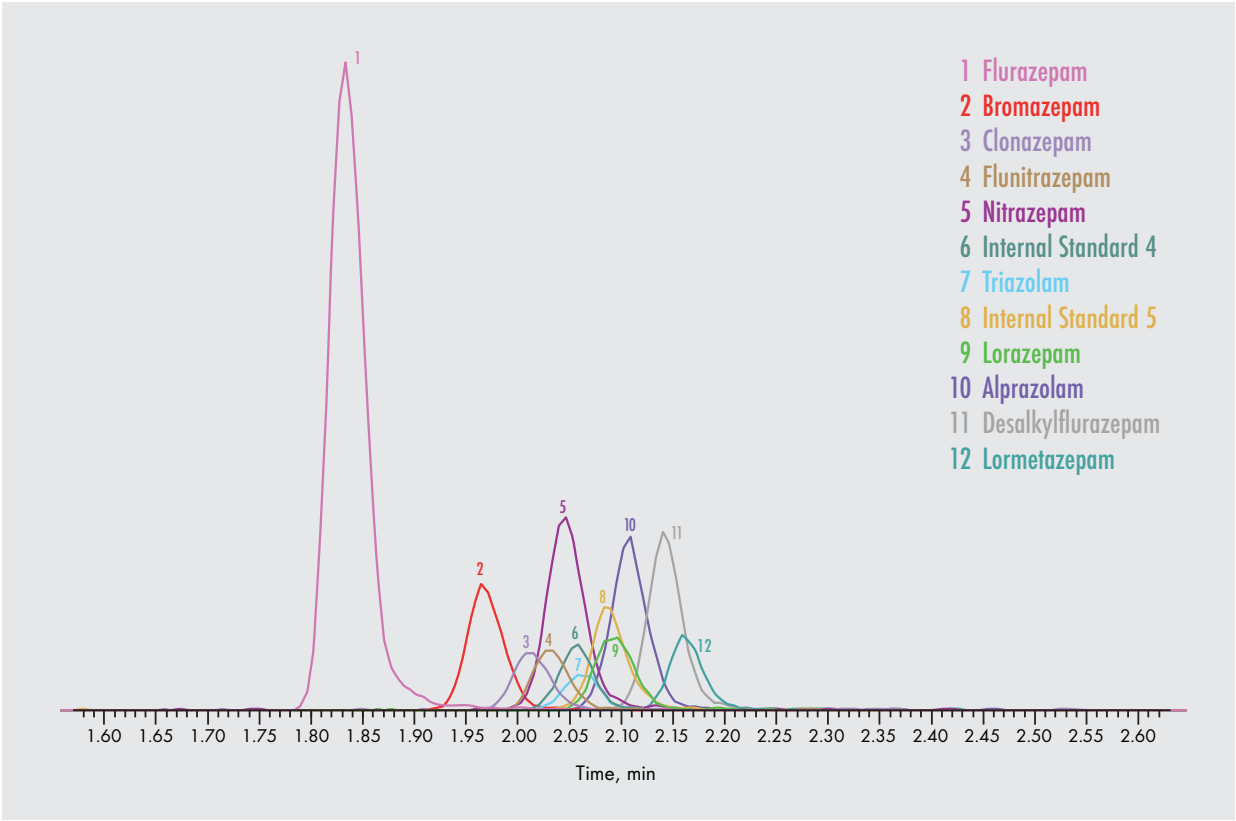
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

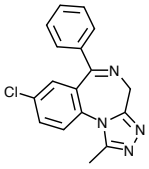
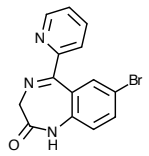
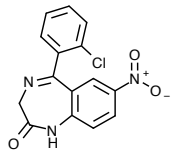
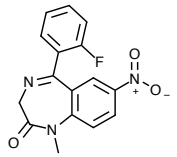
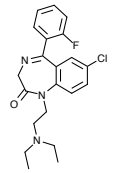
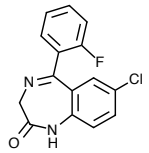
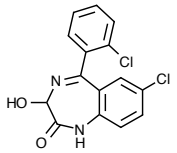
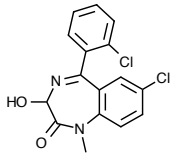
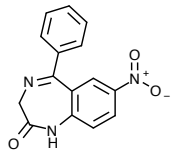
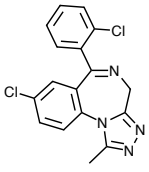
Gradient:
0.00–0.30 min, 20 % Mobile Phase 2
0.31–0.60 min, 50 % Mobile Phase 2
0.61–1.10 min, 80 % Mobile Phase 2
1.11–2.00 min, 100 % Mobile Phase 2
2.01–2.21 min, 100 % → 20 % Mobile Phase 2
2.21–2.80 min, 20 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassTox® Benzodiazepines 2



MassTox® Benzodiazepines 2

Substance	Published Reference Ranges [3,6,15] (µg/l)	Mw (g/mol)	Formula	Structure
Alprazolam	5–50	308.76	$C_{17}H_{13}ClN_4$	
Bromazepam	50–200	316.15	$C_{14}H_{10}BrN_3O$	
Clonazepam	4–80	315.71	$C_{15}H_{10}ClN_3O_3$	
Flunitrazepam	5–15	313.28	$C_{16}H_{12}FN_3O_3$	
Flurazepam	5–100	387.88	$C_{21}H_{23}ClFN_3O$	
Desalkylflurazepam	10–150	288.70	$C_{15}H_{10}ClFN_2O$	
Lorazepam	10–250	321.16	$C_{15}H_{10}Cl_2N_2O_2$	
Lormetazepam	2–25	335.18	$C_{16}H_{12}Cl_2N_2O_2$	
Nitrazepam	30–180	281.27	$C_{15}H_{11}N_3O_3$	
Triazolam	2–20	343.21	$C_{17}H_{12}Cl_2N_4$	

MassTox® Benzodiazepines 2

3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Alprazolam	3.30	30.1	56.5	< LOQ
Bromazepam	38.3	153	266	< LOQ
Clonazepam	7.84	56.2	101	< LOQ
Flunitrazepam	3.35	19.2	33.2	< LOQ
Flurazepam	4.29	23.4	41.8	< LOQ
Desalkylflurazepam	6.24	81.1	161	< LOQ
Lorazepam	14.9	153	287	< LOQ
Lormetazepam	3.06	14.7	27.1	< LOQ
Nitrazepam	19.3	112	190	< LOQ
Triazolam	2.02	17.5	32.1	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Benzodiazepines 2 Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Alprazolam	8.54	44.9
Bromazepam	66.9	209
Clonazepam	17.4	76.5
Flunitrazepam	6.35	25.8
Flurazepam	8.29	30.6
Desalkylflurazepam	19.8	129
Lorazepam	40.8	216
Lormetazepam	5.90	20.1
Nitrazepam	37.1	145
Triazolam	4.71	25.1

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92031	3PLUS1® Multilevel Plasma Calibrator Set Benzodiazepines 2 (lyoph.), 4 x 1 ml
0240	*MassCheck*® Benzodiazepines 2 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0241	*MassCheck*® Benzodiazepines 2 Plasma Control, Level I (lyoph.), 5 x 1 ml
0242	*MassCheck*® Benzodiazepines 2 Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 1 week at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.7 *MassTox*® Mycophenolic Acid

CE IVD

Mycophenolic acid (MPA) is used as an immunosuppressant agent to prevent organ transplant rejection. MPA selectively inhibits the synthesis of purins and specifically reduces growth of B- and T-lymphocytes. Moreover, MPA is also utilised to treat autoimmune diseases such as psoriasis, systemic lupus erythematosus and scleroderma. Therapeutic drug monitoring of MPA is required to adjust blood concentrations within the therapeutic window and to achieve a favourable ratio between therapeutic effects and side effects. Currently available drugs contain mycophenolate mofetil or mycophenolate sodium which are both completely metabolised into MPA. To support its elimination, MPA is further metabolised into mycophenolate glucuronide (MPAG). Since this step is reversible, it is advisable to analyse MPAG as well.

The ***MassTox***® TDM Parameter Set Mycophenolic Acid allows a rapid and reliable quantitative determination of the analytes using LC-MS/MS. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and increases the robustness of the method The use of stable isotope-labelled (deuterated), co-eluting internal standards, and the multilevel calibrators ensures reproducible and dependable quantification of the analytes. Just as for all Parameter Sets of ***MassTox***® Series A, sample preparation relies on protein precipitation. For large batches of samples automated sample preparation can save considerable amounts of time.

> Part of the modular system of *MassTox*® TDM Series A
> For the analysis of MPA and MPAG
> Isotopically labelled internal standard
> 3PLUS1® and 6PLUS1® Multilevel Calibrator Sets
> Automated method also available

Mycophenolsäure (MPA) wird als immunsuppressives Präparat zur Unterdrückung von Abstoßungsreaktionen nach Organtransplantationen eingesetzt. MPA hemmt gezielt die Neusynthese von Purinen und reduziert damit das Wachstum von B- und T-Lymphozyten. Darüber hinaus findet MPA auch in der Behandlung von Autoimmunerkrankungen wie beispielsweise Psoriasis, systemischem Lupus erythematodes oder Sclerodermie Anwendung. Das therapeutische Monitoring von MPA ist notwendig, um die individuelle Blutkonzentration im therapeutischen Fenster einzustellen und so ein günstiges Wirkungs-/Nebenwirkungsverhältnis zu erzielen. Die aktuell verfügbaren Medikamente enthalten Mycophenolat-Mofetil oder Natriummycophenolat. Beides wird komplett zur aktiven Substanz MPA metabolisiert. Zur Ausscheidung wird MPA in Mycophenolat-Glucuronid (MPAG) umgewandelt. Da dieser Prozess reversibel ist, sollte das MPAG ebenfalls analysiert werden.

Mit diesem Parameter-Set für die LC-MS/MS Analytik von Mycophenolsäure im Serum/Plasma können die einzelnen Wirkstoffe schnell und effektiv gemessen werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methode erhöht. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. Die Probenvorbereitung basiert, so wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, auf einer Proteinfällung. Bei großen Probensequenzen kann mit der automatisierten Probenvorbereitung deutlich Zeit gespart werden.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> Für die Analyse von MPA und MPAG
> Isotopenmarkierter interner Standard
> 3PLUS1® und 6PLUS1® Multilevel Calibrator Sets
> Automatisierte Methode verfügbar

6.7.1 *MassTox®* Mycophenolic Acid Standard Method

Parameters:
mycophenolic acid, mycophenolic acid glucuronide.

Order no.	Product
	MassTox® TDM Basic Kit A
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92916	***MassTox® TDM Parameter Set Mycophenolic Acid***
	Components available separately
46029	3PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 4 x 1 ml
0235	***MassCheck®*** Mycophenolic Acid/Glucuronide Plasma Control, Level I (lyoph.), 5 x 1 ml
0236	***MassCheck®*** Mycophenolic Acid/Glucuronide Plasma Control, Level II (lyoph.), 5 x 1 ml
92246	Internal Standard Set Mycophenolic Acid/Glucuronide, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml, Reconstitution Buffer, 5 ml
	Multilevel Calibrators and Startup Accessories
46039	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
46039/XL	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
92110	***MassTox®* TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92019	Tuning Mix Mycophenolic Acid, Analytes and Internal Standards, 1 ml
0234	***MassCheck®*** Mycophenolic Acid/Glucuronide Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	MPA up to 20 mg/l MPAG up to 500 mg/l
Limit of quantification:	MPA < 0.1 mg/l MPAG < 0.5 mg/l
Intraassay:	CV < 4 %
Interassay:	CV < 5.5 %
Recovery:	105–119 %
Analysis time:	1.5 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable up to 4 weeks at +2 to +8 °C. For longer storage periods (at least three months) keep samples frozen below -18 °C.

Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck®*** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

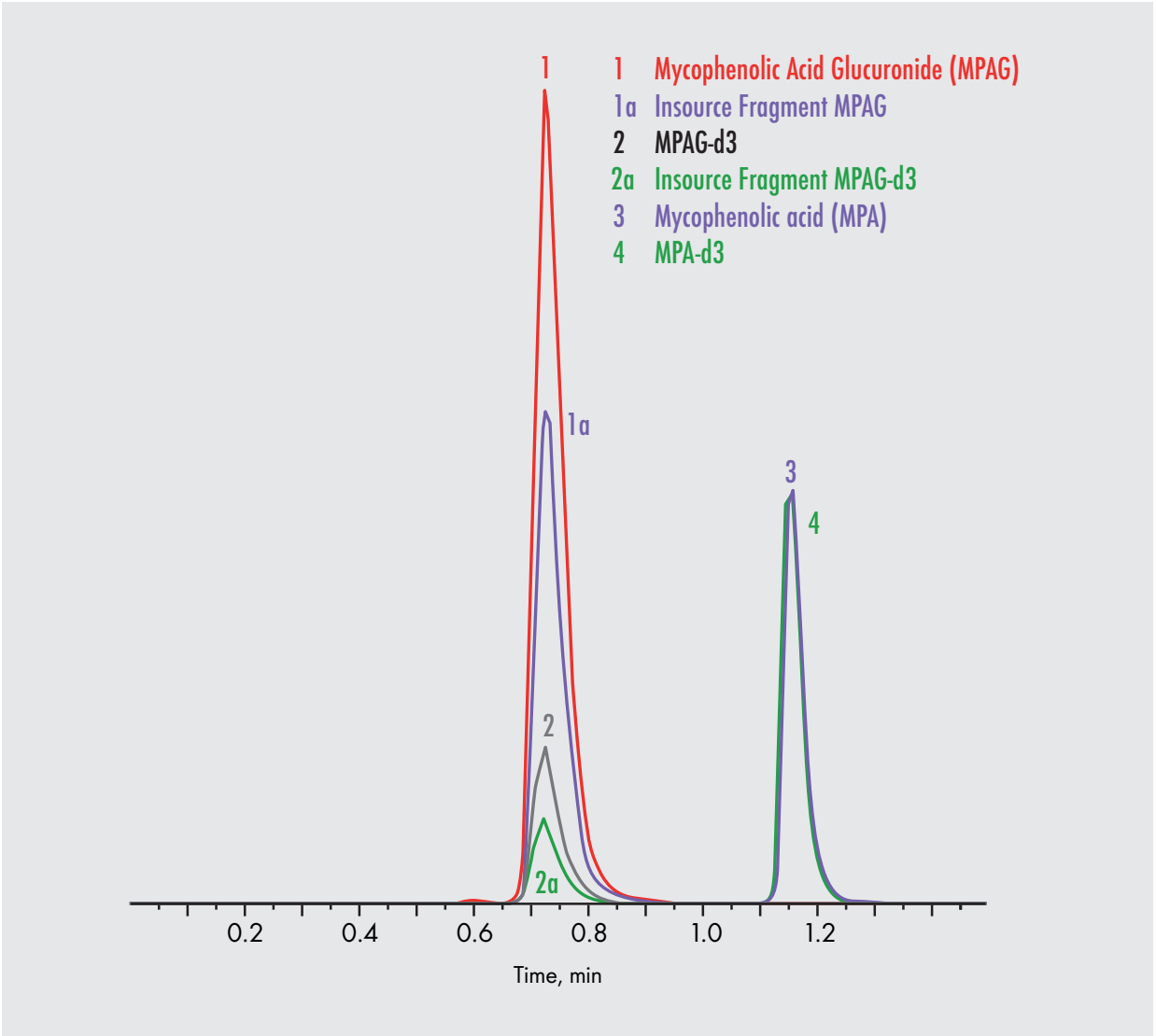
LC-MS/MS Parameters

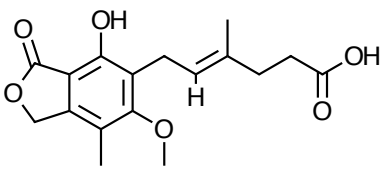
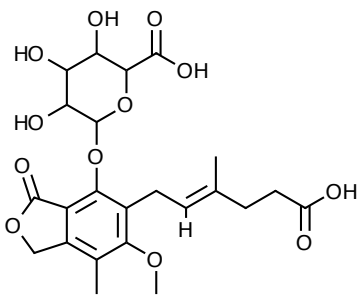
Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

Gradient:
starting point: 60 % Mobile Phase 2
0.00–0.50 min, 100 % Mobile Phase 2
0.51–1.00 min, 100 % Mobile Phase 2
1.01–1.10 min, 60 % Mobile Phase 2
1.11–1.81 min, 60 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

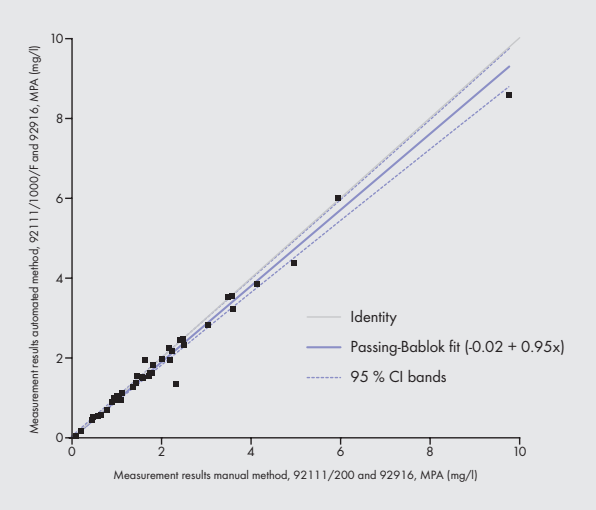
Mycophenolic Acid Standard Method

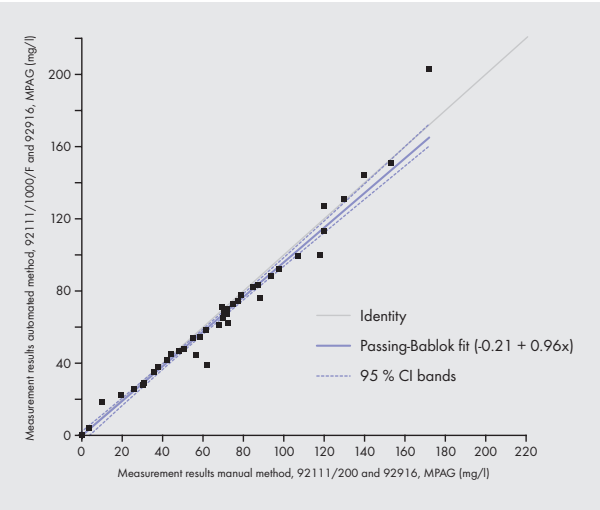


Substance	Published Reference Ranges [3,16,17] (mg/l)	Mw (g/mol)	Formula	Structure
Mycophenolic acid	1–5	320.34	$C_{17}H_{20}O_6$	
Mycophenolic acid glucuronide	–	496.46	$C_{23}H_{28}O_{12}$	

6.7.2 *MassTox*® Mycophenolic Acid Automated Method

Automated with 96 Well Filter Plates





Comparison of human samples prepared manually and with automation (Tecan Freedom EVO 100). The analysis was performed with the ***MassTox***® *TDM Series A Parameter Set Mycophenolic Acid in Serum/Plasma (order no. 92916) on an ABSciex API 3200 mass spectrometer.*

MassTox® Mycophenolic Acid Automated Method

Order no.	Product
92111/ 1000/F	***MassTox*® TDM Basic Kit A** Automated with 96 Well Filter Plates For 1000 tests
	Basic Kit A ***Components available separately***
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
92012	Precipitation Reagent, for automated sample preparation, 250 ml
92057	96 Well Filter Plates, 3 pcs.
92058	Collection Plates, 3 pcs.
92059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
92916	***MassTox*® TDM Parameter Set Mycophenolic Acid** ***Components available separately***
46029	3PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 4 x 1 ml
0235	***MassCheck*®** Mycophenolic Acid/Glucuronide Plasma Control, Level I (lyoph.), 5 x 1 ml
0236	***MassCheck*®** Mycophenolic Acid/Glucuronide Plasma Control, Level II (lyoph.), 5 x 1 ml
92246	Internal Standard Set Mycophenolic Acid/ Glucuronide, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml

	Multilevel Calibrators and Startup Accessories
46039	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
46039/XL	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92019	Tuning Mix Mycophenolic Acid, Analytes and Internal Standards, 1 ml
0234	***MassCheck*®** Mycophenolic Acid/Glucuronide Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Automated Workflow

→ Load liquid handling device with samples, reagents, 96 well filter plate and collection plate.
→ Start the **automation routine***.
→ After completion remove collection plate from the liquid handling device, seal with an adhesive seal and transfer to autosampler.
→ Inject 0.2–50 µl eluate into LC-MS/MS system.

* *Ready to use automation routine provided with the installation by Chromsystems.*

3PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid

Substance	Calibrator 1* (mg/l)	Calibrator 2* (mg/l)	Calibrator 3* (mg/l)	Blank Calibrator (mg/l)
Mycophenolic acid	0.96	3.86	9.40	< LOQ
Mycophenolic acid glucuronide	16.6	84.5	215	< LOQ

** Please check packaging leaflet for specific lot concentrations, LOQ = limit of quantification*

6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid

46039

Substance	Unit	Calibrator 1*	Calibrator 2*	Calibrator 3*	Calibrator 4*	Calibrator 5*	Calibrator 6*	Blank Calibrator
Mycophenolic acid	mg/l	0.96	1.58	3.18	3.86	6.68	9.4	< LOQ
Mycophenolic acid glucuronide	mg/l	16.6	32.7	67.7	84.5	151	215	< LOQ

46039/XL

Substance	Unit	Calibrator 1*	Calibrator 2*	Calibrator 3*	Calibrator 4*	Calibrator 5*	Calibrator 6*	Blank Calibrator
Mycophenolic acid	mg/l	0.93	1.57	3.65	9.02	23.6	60.4	< LOQ
Mycophenolic acid glucuronide	mg/l	16.2	32.4	78.8	197	244	316	< LOQ

** Please check packaging leaflet for specific lot concentrations, LOQ = limit of quantification*

MassCheck® Mycophenolic Acid Standard Method Plasma Controls

Substance	Level I Target Value* (mg/l)	Level II Target Value* (mg/l)
Mycophenolic acid	1.96	5.79
Mycophenolic acid glucuronide	43.0	123

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
46029	3PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 4 x 1 ml
46039	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
46039/XL	6PLUS1® Multilevel Plasma Calibrator Set Mycophenolic Acid/Glucuronide (lyoph.), 7 x 1 ml
0234	***MassCheck***® Mycophenolic Acid/Glucuronide Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0235	***MassCheck***® Mycophenolic Acid/Glucuronide Plasma Control, Level I (lyoph.), 5 x 1 ml
0236	***MassCheck***® Mycophenolic Acid/Glucuronide Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.8 *MassTox*® Neuroleptics

CE IVD

Neuroleptics

Neuroleptic agents, also known as antipsychotics, are used to treat psychosis and other psychological disorders such as manic-depressive conditions accompanied by delusions and hallucinations. Atypical neuroleptics such as clozapine, risperidone, quetiapine and olanzapine block serotonin receptors and binding sites for other neurotransmitters in addition to dopamine receptors, and show considerably fewer side effects compared to typical neuroleptics. In particular, instances of motor disturbance and fatigue occur considerably less frequently.

To avoid interferences and enable an accurate analysis, the neuroleptics are divided into two groups:
Neuroleptics 1/*EXTENDED* and Neuroleptics 2/*EXTENDED* 2. The latter has been extended by 16 additional analytes as part of the continuous expansion of the ***MassTox***® TDM Series A. Both Parameter Sets allow the rapid and reliable quantitative determination of every individual parameter. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and warrants the robustness of the methods. Using deuterated stable isotopes, co-eluting internal standards and multilevel calibrators ensures a reliable and reproducible quantification of the analytes. Just as for all Parameter Sets of the ***MassTox***® TDM Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 40 analytes divided into 2 Parameter Sets
> Isotopically labelled internal standards
> 3PLUS1® Multilevel Calibrator Sets

Neuroleptika werden zur Behandlung von Psychosen und anderen psychischen Störungen wie manisch-depressiven Zuständen mit Wahnvorstellungen und Halluzinationen eingesetzt. Atypische Neuroleptika wie Clozapin, Risperidon, Quetiapin und Olanzapin zeigen meist noch hemmende Wirkungen auf Serotonin-Rezeptoren und Bindungsstellen anderer Botenstoffe. Es kommt zu wesentlich weniger Nebenwirkungen als bei den typischen Neuroleptika. Insbesondere Bewegungsstörungen und Müdigkeit treten deutlich seltener auf.

Um Interferenzen zu vermeiden und eine einwandfreie Analytik zu gewährleisten, wurden die Neuroleptika in zwei Gruppen unterteilt:
Neuroleptika 1/*EXTENDED* und Neuroleptika 2/*EXTENDED* 2. Letztere wurde um 16 Parameter erweitert und ist Teil der kontinuierlichen Weiterentwicklung der ***MassTox***® TDM Serie A. Mit den beiden Parameter-Sets können die einzelnen Wirkstoffe im Serum/Plasma schnell und effektiv bestimmt werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methoden sichergestellt Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. So wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, basiert die Probenvorbereitung auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> 2 Parameter-Sets mit insgesamt 40 Analyten
> Isotopenmarkierte interne Standards
> 3PLUS1® Multilevel Calibrator Sets

6.8.1 *MassTox*® Neuroleptics 1/*EXTENDED*

Parameters:
aripiprazole, dehydroaripiprazole, clozapine, N-desmethylclozapine, haloperidol, olanzapine, N-desmethylolanzapine, quetiapine, norquetiapine, risperidone, 9-OH-risperidone.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92912/XT	***MassTox*® TDM Parameter Set Neuroleptics 1/*EXTENDED***
	Components available separately
92028/XT	3PLUS1® Multilevel Plasma Calibrator Set Neuroleptics 1/*EXTENDED* (lyoph.), 4 x 1 ml
0211/XT	***MassCheck*®** Neuroleptics 1/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0212/XT	***MassCheck*®** Neuroleptics 1/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml
92046/AN1/XT	Internal Standard Set Antidepressants 1/*EXTENDED* and Neuroleptics 1/*EXTENDED*, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram
92015/N1/XT	Tuning Mix Neuroleptics 1/*EXTENDED*, Analytes and Internal Standards, 1 ml
0210/XT	***MassCheck*®** Neuroleptics 1/*EXTENDED*, Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	at least twice the therapeutic range
Limit of quantification:	0.5–35 µg/l
Intraassay:	CV < 7 %
Interassay:	CV < 8 %
Analysis time:	3.0 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable for at least 24h when stored in the dark at +4 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

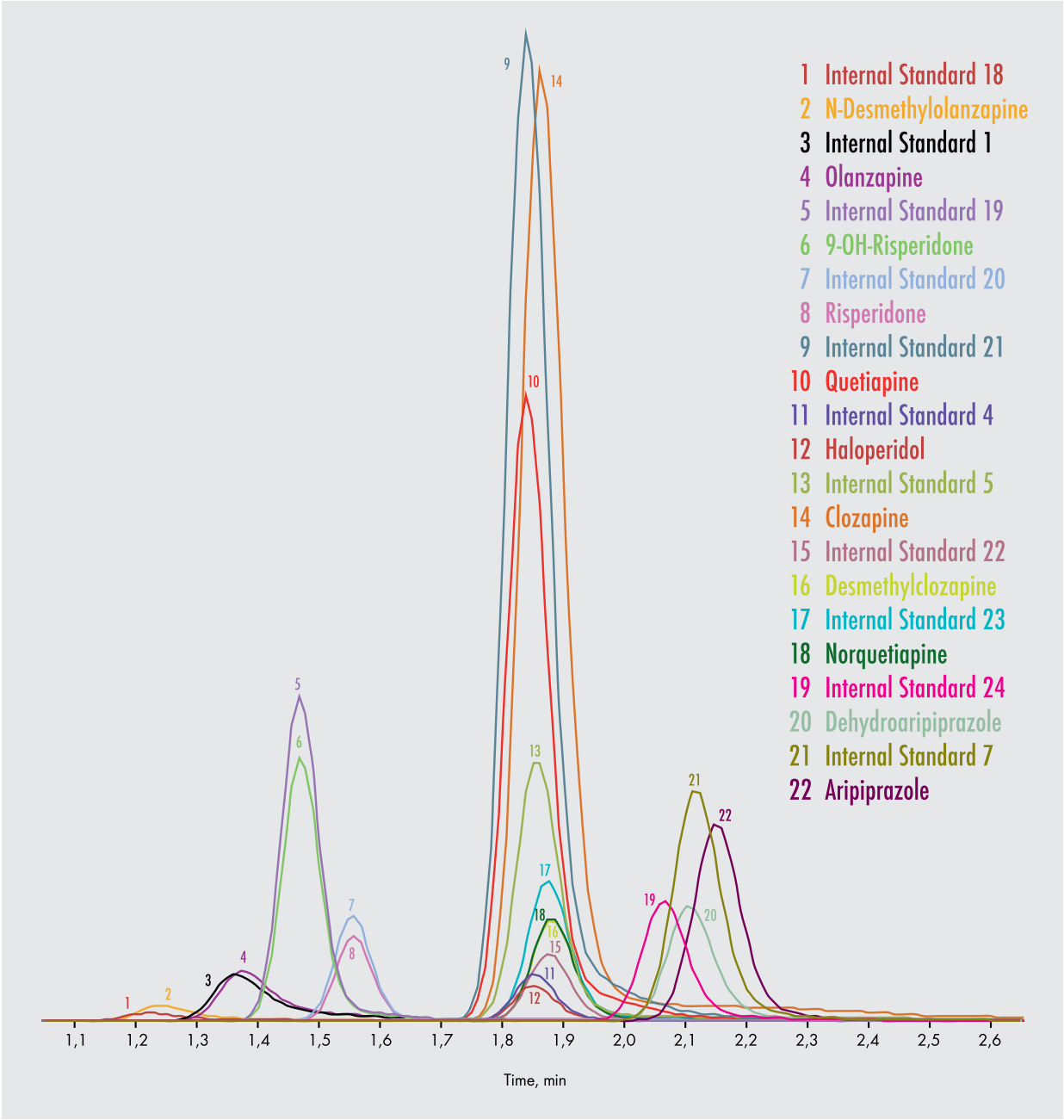
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

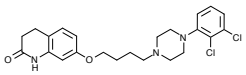
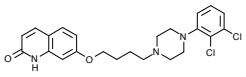
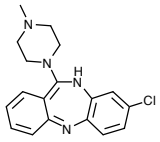
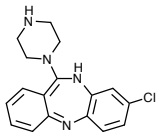
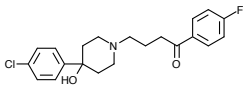
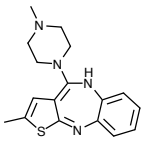
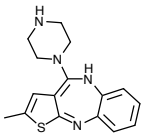
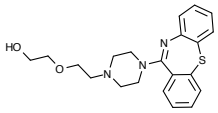
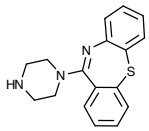
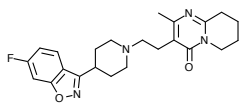
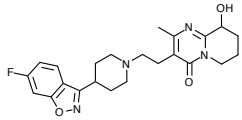
Gradient:
0.00–0.20 min, 20 % Mobile Phase 2
0.21–0.70 min, 50 % Mobile Phase 2
0.71–2.30 min, 70 % Mobile Phase 2
2.31–3.00 min, 20 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassTox® Neuroleptics 1/EXTENDED



MassTox® Neuroleptics 1/EXTENDED

Substance	Published Reference Ranges [5,7,8] (µg/l)	Mw (g/mol)	Formula	Structure
Aripiprazole	15–500	448.39	$C_{23}H_{27}Cl_2N_3O_2$	
Dehydroaripiprazole	0.3–0.5 x Arpipirazole	446.37	$C_{23}H_{25}Cl_2N_3O_2$	
Clozapine	100–800	326.82	$C_{18}H_{19}ClN_4$	
N-Desmethylclozapine	0.4–1.0 x Clozapine 100–300	312.80	$C_{17}H_{17}ClN_4$	
Haloperidol	1–20	375.86	$C_{21}H_{23}ClFNO_2$	
Olanzapine	20–100	312.43	$C_{17}H_{20}N_4S$	
N-Desmethylolanzapine	0.1–0.3 x Olanzapine	298.41	$C_{16}H_{18}N_4S$	
Quetiapine	10–600	383.51	$C_{21}H_{25}N_3O_2S$	
Norquetiapine	100–250	295.40	$C_{17}H_{17}N_3S$	
Risperidone	2–60	410.48	$C_{23}H_{27}FN_4O_2$	
9-OH-risperidone	5–100	426.48	$C_{23}H_{27}FN_4O_3$	

3PLUS1® Multilevel Plasma Calibrator Set Neuroleptics 1/*EXTENDED*

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Aripiprazole	20.4	246	701	< LOQ
Dehydroaripiprazole	7.87	91.8	256	< LOQ
Clozapine	76.0	453	1226	< LOQ
N-Desmethylclozapine	77.0	202	464	< LOQ
Haloperidol	1.82	14.1	27.0	< LOQ
Olanzapine	3.83	50.3	142	< LOQ
N-Desmethylolanzapine	3.42	48.6	141	< LOQ
Quetiapine	27.0	203	556	< LOQ
Norquetiapine	10.3	74.7	206	< LOQ
Risperidone	2.07	12.4	30.9	< LOQ
9-OH-risperidone	3.90	51.6	142	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Neuroleptics 1/*EXTENDED* Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Aripiprazole	172	314
Dehydroaripiprazole	64.2	116
Clozapine	337	567
N-Desmethylclozapine	171	234
Haloperidol	3.70	15.7
Olanzapine	34.9	63.6
N-Desmethylolanzapine	35.9	61.6
Quetiapine	147	256
Norquetiapine	53.4	93.6
Risperidone	9.17	14.3
9-OH-risperidone	35.8	64.2

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92028/XT	3PLUS1® Multilevel Plasma Calibrator Set Neuroleptics 1/*EXTENDED* (lyoph.), 4 x 1 ml
0210/XT	***MassCheck***® Neuroleptics 1/*EXTENDED* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0211/XT	***MassCheck***® Neuroleptics 1/*EXTENDED* Plasma Control, Level I (lyoph.), 5 x 1 ml
0212/XT	***MassCheck***® Neuroleptics 1/*EXTENDED* Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 3 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.8.2 *MassTox*® Neuroleptics 2/*EXTENDED 2*

PREVIEW
Coming Soon
www.chromsystems.com
for more info

Parameters:
amisulpride, benperidol, brexpiprazole, bromperidol, cariprazine, chlorpromazine, chlorprothixene, flupentixol, fluphenazine, guanfacine, iloperidone, levomepromazine, loxapine, lurasidone, melperone, mesoridazine, perazine, perphenazine, pimozide, pipamperone, promethazine, prothipendyl, sertindole, sulforidazine, sulpiride, thioridazine, ziprasidone, zotepine, zuclopenthixol.

Order no.	Product
	***MassTox*® TDM Basic Kit A**
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A
	Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92914/XT2	***MassTox*® TDM Parameter Set Neuroleptics 2/*EXTENDED 2***
	Components available separately
92026/XT2	3PLUS1® Multilevel Plasma Calibrator Set Neuroleptics 2/*EXTENDED 2* (lyoph.), 4 x 1 ml
0228/XT2	***MassCheck*®** Neuroleptics 2/*EXTENDED 2* Plasma Control, Level I (lyoph.), 5 x 1 ml
0229/XT2	***MassCheck*®** Neuroleptics 2/*EXTENDED 2* Plasma Control, Level II (lyoph.), 5 x 1 ml
92046/N2/XT2	Internal Standard Set Neuroleptics 2/*EXTENDED 2*, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox*® TDM MasterColumn® A** Analytical Column, equilibrated, with test chromatogram, 1 pc.
92017/XT2	Tuning Mix Neuroleptics 2/*EXTENDED 2*, Analytes and Internal Standards, 1 ml
0227/XT2	***MassCheck*®** Neuroleptics 2/*EXTENDED 2* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml

Specifications

Linearity:	up to 2500 µg/l
Limit of quantification:	0.6 µg/l
Intraassay:	CV = 2.2–11.5 %
Interassay:	CV = 4.9–14.8 %
Analysis time:	4.5 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: depending on the specific analyte. Further information can be obtained from the instruction manual.

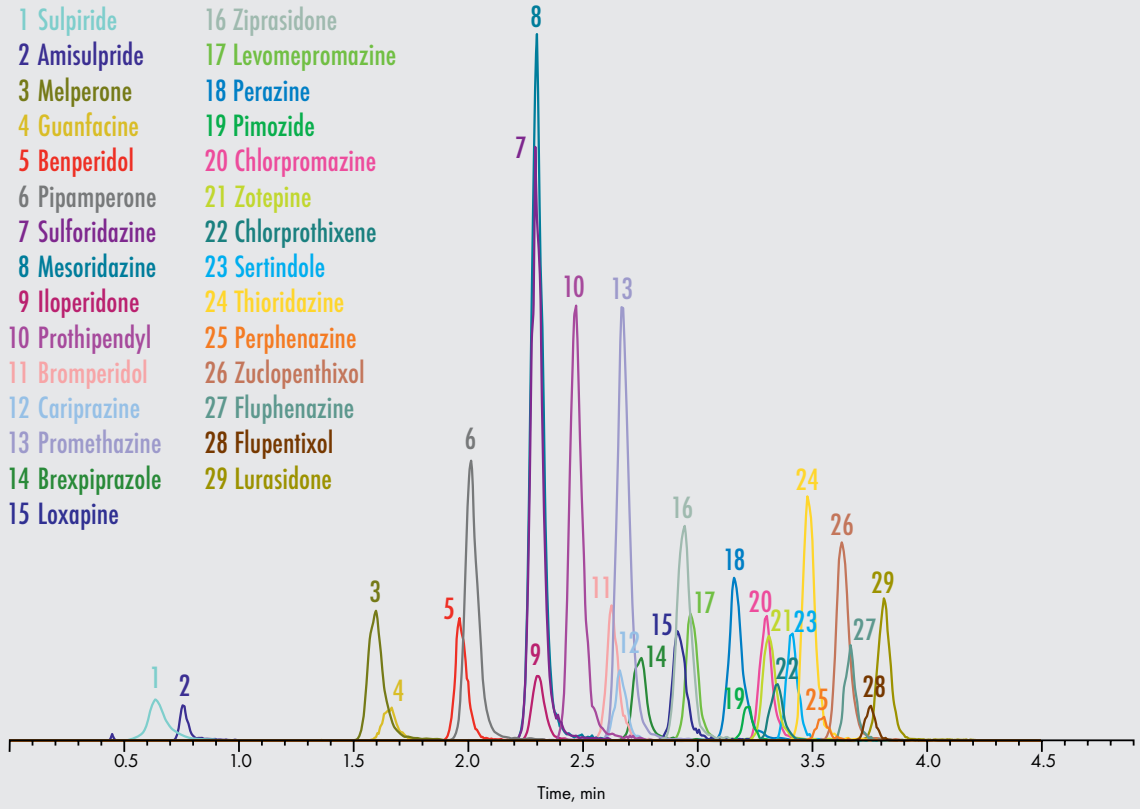
Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck*®** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

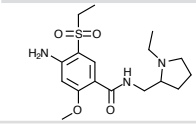
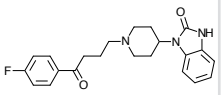
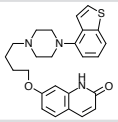
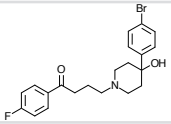
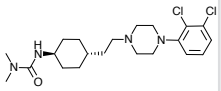
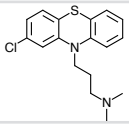
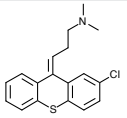
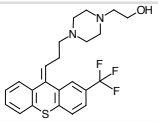
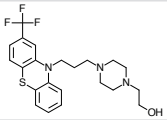
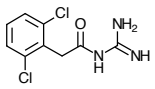
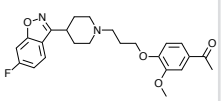
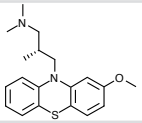
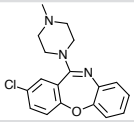
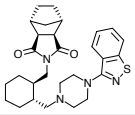
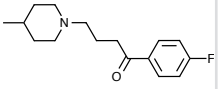
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	binary

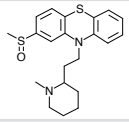
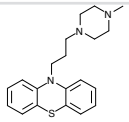
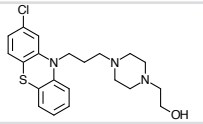
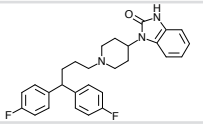
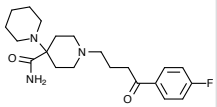
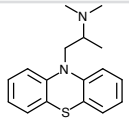
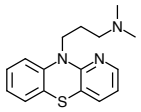
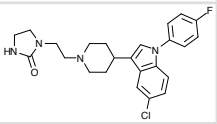
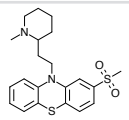
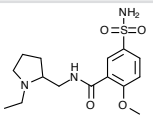
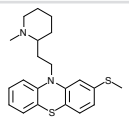
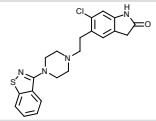
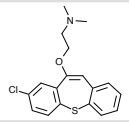
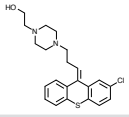
MassTox® Neuroleptics 2/*EXTENDED 2*



MassTox® Neuroleptics 2/EXTENDED 2

Substance	Published Reference Ranges [7,8,18] (µg/l)	Mw (g/mol)	Formula	Structure
Amisulpride	50–500	369.48	$C_{17}H_{27}N_3O_4S$	
Benperidol	1–10	381.44	$C_{22}H_{24}FN_3O_2$	
Brexpiprazole	40–140	433.57	$C_{25}H_{27}N_3O_2S$	
Bromperidol	12–15	420.32	$C_{21}H_{23}BrFNO_2$	
Cariprazine	10–20	427.41	$C_{21}H_{32}Cl_2N_4O$	
Chlorpromazine	30–500	318.86	$C_{17}H_{19}ClN_2S$	
Chlorprothixene	20–300	315.86	$C_{18}H_{18}ClNS$	
Flupentixol	1–15	434.52	$C_{23}H_{25}F_3N_2OS$	
Fluphenazine	1–17	437.52	$C_{22}H_{26}F_3N_3OS$	
Guanfacine	1–15	246.09	$C_9H_9Cl_2N_3O$	
Iloperidone	5–10	426.48	$C_{24}H_{27}FN_2O_4$	
Levomepromazine	5–250	328.47	$C_{19}H_{24}N_2OS$	
Loxapine	5–10	327.81	$C_{18}H_{18}ClN_3O$	
Lurasidone	15–40	492.68	$C_{28}H_{36}N_4O_2S$	
Melperone	30–1000	263.35	$C_{16}H_{22}FNO$	

MassTox® Neuroleptics 2/EXTENDED 2

Substance	Published Reference Ranges [7,8,18] (µg/l)	Mw (g/mol)	Formula	Structure
Mesoridazine	200–1600	386.58	$C_{21}H_{26}N_2OS_2$	
Perazine	20–400	339.50	$C_{20}H_{25}N_3S$	
Perphenazine	0.6–2.4	403.97	$C_{21}H_{26}ClN_3OS$	
Pimozide	15–20	461.56	$C_{28}H_{29}F_2N_3O$	
Pipamperone	100–400	375.48	$C_{21}H_{30}FN_3O_2$	
Promethazine	50–400	284.42	$C_{17}H_{20}N_2S$	
Prothipendyl	5–200	285.41	$C_{16}H_{19}N_3S$	
Sertindole	1–100	440.94	$C_{24}H_{26}ClFN_4O$	
Sulforidazine	< 600	402.58	$C_{21}H_{26}N_2O_2S_2$	
Sulpiride	40–1000	341.43	$C_{15}H_{23}N_3O_4S$	
Thioridazine	100–2000	370.57	$C_{21}H_{26}N_2S_2$	
Ziprasidone	20–200	412.94	$C_{21}H_{21}ClN_4OS$	
Zotepine	10–150	331.86	$C_{18}H_{18}ClNOS$	
Zuclopenthixol	4–100	400.96	$C_{22}H_{25}ClN_2OS$	

3PLUS1® Multilevel Plasma Calibrator Set
Neuroleptics 2/*EXTENDED 2*

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Amisulpride	28.4	283	578	
Benperidol	0.98	5.33	10.2	< LOQ
Brexpiprazole	30.3	80.0	131	< LOQ
Bromperidol	7.97	13.9	18.5	< LOQ
Cariprazine	8.79	14.0	20.6	< LOQ
Chlorpromazine	26.4	190	386	< LOQ
Chlorprothixene	14.2	130	261	< LOQ
Flupentixol	1.130	7.55	14.9	< LOQ
Fluphenazine	1.040	8.39	16.8	< LOQ
Guanfacine	0.954	5.21	11.1	< LOQ
Iloperidone	4.11	7.66	11.6	< LOQ
Levomepromazine	3.96	67.6	137	< LOQ
Loxapine	4.48	7.41	11.4	< LOQ
Lurasidone	11.5	19.9	30.6	< LOQ
Melperone	21.2	425	878	< LOQ
Mesoridazine	75.2	464	852	< LOQ
Perazine	13.0	155	323	< LOQ
Perphenazine	0.67	2.28	4.71	< LOQ
Pimozide	2.94	12.5	22.2	< LOQ
Pipamperone	14.7	200	387	< LOQ
Promethazine	33.70	280	732	< LOQ
Prothipendyl	4.19	221	466	< LOQ
Sertindole	10.53	36.9	84.7	< LOQ
Sulforidazine	26.3	280	523	< LOQ
Sulpiride	31.2	471	886	< LOQ
Thioridazine	70.6	882	1733	< LOQ
Ziprasidone	14.0	95	177	< LOQ
Zotepine	7.83	68.2	132	< LOQ
Zuclopenthixol	3.05	45.6	89	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Neuroleptics 2/*EXTENDED 2*

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Amisulpride	55.6	436
Benperidol	1.77	7.48
Brexpiprazole	32.8	99
Bromperidol	10.4	15.7
Cariprazine	8.33	15.7
Chlorpromazine	35.1	286
Chlorprothixene	31.8	184
Flupentixol	1.49	11.0
Fluphenazine	1.56	12.5
Guanfacine	1.13	6.85
Iloperidone	4.37	8.69
Levomepromazine	14.3	97
Loxapine	4.34	8.27
Lurasidone	10.5	24.2
Melperone	90.2	628
Mesoridazine	95	662
Perazine	37.4	229
Perphenazine	1.80	3.79
Pimozide	4.84	16.7
Pipamperone	45.6	287
Promethazine	80.8	594
Prothipendyl	30.6	343
Sertindole	16.4	63.0
Sulforidazine	45.4	413
Sulpiride	99	644
Thioridazine	199	1274
Ziprasidone	27.5	130
Zotepine	17.1	95
Zuclopenthixol	10.1	65.6

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92026/XT2	3PLUS1® Multilevel Plasma Calibrator Set Neuroleptics 2/*EXTENDED 2* (lyoph.), 4 x 1 ml
0227/XT2	***MassCheck***® Neuroleptics 2/*EXTENDED 2* Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0228/XT2	***MassCheck***® Neuroleptics 2/*EXTENDED 2* Plasma Control, Level I (lyoph.), 5 x 1 ml
0229/XT2	***MassCheck***® Neuroleptics 2/*EXTENDED 2* Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to one week at + 2°C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.9 *MassTox*® Tricyclic Antidepressants TCA

CE IVD

The tricyclic antidepressants (TCA) are used for the treatment of mental disorders such as states of anxiety, pain syndromes and phobias. They inhibit the uptake of the neurotransmitters serotonin, noradrenaline and dopamine, thereby boosting the synaptic transmission. TCAs are highly lipophilic and are absorbed rapidly from the gastrointestinal tract after oral administration. Even before they reach their site of action in the brain, a fraction is already metabolised in the liver (first-pass effect). Important steps are N-dealkylation and hydroxylation. Regular determinations of the plasma levels of TCAs can reduce the risks of over-dosage and allow better control of side-effects. In addition, they allow monitoring and maintenance of patient compliance, thus assuring an optimal therapy.

The tricyclic antidepressants are divided into two groups: TCA 1 and TCA 2. Both Parameter Sets allow the rapid and reliable quantitative determination of every individual Parameter. Careful optimisation of all reagents and the chromatographic separation minimises matrix effects and warrants the robustness of the methods. Using deuterated stable isotopes, co-eluting internal standards and multilevel calibrators ensures a reliable and reproducible quantification of the analytes. Just as for all Parameter Sets of the ***MassTox***® TDM Series A, sample preparation relies on protein precipitation.

> Part of the modular system of *MassTox*® TDM Series A
> Covers 13 analytes divided in 2 Parameter Sets
> Isotopically labelled internal standards
> 3PLUS1® Multilevel Calibrator Sets

Tricyclische Antidepressiva (TCA) werden zur Behandlung von psychischen Erkrankungen wie Angstzuständen, Schmerzsyndromen und Phobien eingesetzt. Sie hemmen die Aufnahme der Neurotransmitter Serotonin, Noradrenalin und Dopamin, sodass die synaptische Übertragung verstärkt wird. TCAs sind sehr lipophile Substanzen und werden nach oraler Applikation rasch im Magen-Darm-Trakt resorbiert. Noch bevor sie im Gehirn wirksam werden können, wird ein Teil in der Leber metabolisiert (First-Pass-Effekt). Wichtige Schritte sind dabei v. a. die N-Desalkylierung und die Hydroxylierung. Die regelmäßige Bestimmung der Plasmaspiegel minimiert das Risiko von Nebenwirkungen in Folge von zum Beispiel Überdosierung. Darüber hinaus wird die Compliance des Patienten überprüft und sichergestellt, so dass ein optimaler Therapieerfolg erzielt werden kann.

Die Tricyclischen Antidepressiva sind in zwei Gruppen unterteilt, TCA 1 und TCA 2. Mit den beiden Parameter-Sets können die einzelnen Wirkstoffe im Serum/Plasma schnell und effektiv bestimmt werden. Durch sorgfältige Optimierung aller Reagenzien sowie der chromatographischen Trennung werden Matrixeffekte minimiert und die Robustheit der Methoden sichergestellt. Die Verwendung von stabilen isotopenmarkierten (deuterierten) und co-eluierenden internen Standards sowie von Multilevel-Kalibratoren gewährleistet eine reproduzierbare und verlässliche Quantifizierung der Analyte. So wie für alle Parameter-Sets der ***MassTox***® TDM Serie A, basiert die Probenvorbereitung auf einer Proteinfällung.

> Bestandteil des Baukastensystems der *MassTox*® TDM Serie A
> 2 Parameter-Sets mit insgesamt 13 Analyten
> Isotopenmarkierte interne Standards
> 3PLUS1® Multilevel Calibrator Sets

6.9.1 Tricyclic Antidepressants TCA 1

Parameters:
amitriptyline, desipramine, doxepin, nordoxepin, imipramine, nortriptyline.

Order no.	Product
	MassTox® TDM Basic Kit A
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92919	***MassTox® TDM Parameter Set Tricyclic Antidepressants TCA 1 Components available separately***
92032	3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 1 (lyoph.), 4 x 1 ml
0244	***MassCheck®*** Tricyclic Antidepressants TCA 1 Plasma Control, Level I (lyoph.), 5 x 1 ml
0245	***MassCheck®*** Tricyclic Antidepressants TCA 1 Plasma Control, Level II (lyoph.), 5 x 1 ml
92446	Internal Standard Set Tricyclic Antidepressants TCA, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox® TDM MasterColumn® A*** Analytical Column, equilibrated, with test chromatogram
92022	Tuning Mix Tricyclic Antidepressants TCA 1, Analytes and Internal Standards, 1 ml
0243	***MassCheck®*** Tricyclic Antidepressants TCA 1 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity:	at least twice the therapeutic range
Limit of quantification:	1–2 µg/l
Intraassay:	CV = 2.2–4.4 %
Interassay:	CV = 3.8–5.3 %
Analysis time:	2.5 min

Pre-analytic Treatment

Specimen: serum or plasma.
Stability: samples are stable up to 1 week at +2 to +8 °C.
For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

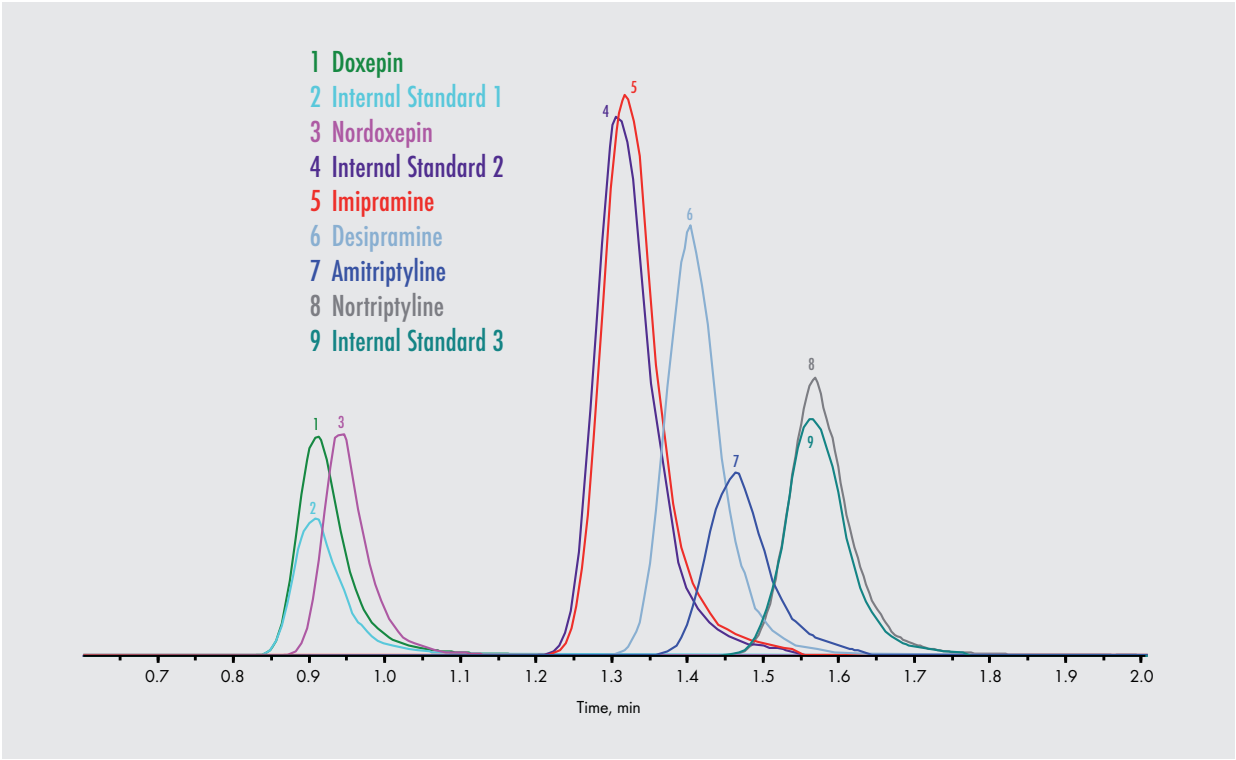
→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck®*** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

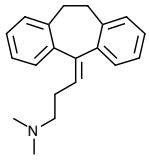
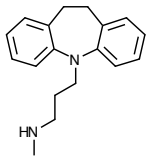
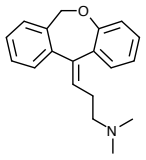
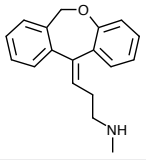
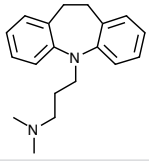
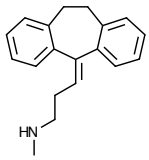
LC-MS/MS Parameters

Injection volume:	0.2–50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM
Gradient:	isocratic 35 % Mobile Phase 1 65 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

Tricyclic Antidepressants TCA 1



Substance	Published Reference Ranges [3,5,6] (µg/l)	Mw (g/mol)	Formula	Structure
Amitriptyline	50–300	277.40	$C_{20}H_{23}N$	
Desipramine	10–500 0.6–3.2 x Imipramine	266.38	$C_{18}H_{22}N_2$	
Doxepin	10–200	279.38	$C_{19}H_{21}NO$	
Nordoxepin	0.6–1.6 x Doxepin	265.35	$C_{18}H_{19}NO$	
Imipramine	50–350	280.41	$C_{19}H_{24}N_2$	
Nortriptyline	20–200	263.38	$C_{19}H_{21}N$	

3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 1

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Amitriptyline	25.9	196	362	< LOQ
Desipramine	13.3	178	348	< LOQ
Doxepin	7.13	150	298	< LOQ
Nordoxepin	6.20	153	299	< LOQ
Imipramine	31.4	193	355	< LOQ
Nortriptyline	23.6	198	352	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Tricyclic Antidepressants TCA 1 Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Amitriptyline	59.6	263
Desipramine	46.0	260
Doxepin	33.5	216
Nordoxepin	32.9	218
Imipramine	68.7	259
Nortriptyline	59.1	257

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92032	3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 1 (lyoph.), 4 x 1 ml
0243	*MassCheck®* Tricyclic Antidepressants TCA 1 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0244	*MassCheck®* Tricyclic Antidepressants TCA 1 Plasma Control, Level I (lyoph.), 5 x 1 ml
0245	*MassCheck®* Tricyclic Antidepressants TCA 1 Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 1 week at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

6.9.2 Tricyclic Antidepressants TCA 2

Parameters:
clomipramine, norclomipramine, maprotiline, normaprotiline, protriptyline, trimipramine, nortrimipramine.

Order no.	Product
	MassTox® TDM Basic Kit A
92111/200	Basic Kit A for 200 tests
92111/1000	Basic Kit A for 1000 tests
	Basic Kit A Components available separately
92001	Mobile Phase 1, 1000 ml
92002	Mobile Phase 2, 1000 ml
92003	Precipitation Reagent, 50 ml
92005	Extraction Buffer, 5 ml
92007	Dilution Buffer 1, 50 ml
92008	Dilution Buffer 2, 50 ml
92009	Rinsing Solution, 1000 ml
33006	Reaction Vials, 100 pcs.
92920	***MassTox® TDM Parameter Set Tricyclic Antidepressants TCA 2 Components available separately***
92033	3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 2 (lyoph.), 4 x 1 ml
0247	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Level I (lyoph.), 5 x 1 ml
0248	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Level II (lyoph.), 5 x 1 ml
92446	Internal Standard Set Tricyclic Antidepressants TCA, consisting of: Internal Standard Mix (lyoph.), 4 x 1 ml Reconstitution Buffer, 5 ml
	Startup Accessories
92110	***MassTox® TDM MasterColumn® A*** Analytical Column, equilibrated, with test chromatogram
92023	Tuning Mix Tricyclic Antidepressants TCA 2, Analytes and Internal Standards, 1 ml
0246	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Specifications

Linearity: at least twice the therapeutic range
Limit of quantification: 1.5–10 µg/l
Intraassay: CV = 1.7–4.3 %
Interassay: CV = 3.8–6.3 %
Analysis time: 3.5 min

Pre-analytic Treatment

Specimen: serum or plasma.
Stability: samples are stable up to 1 week at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Reconstitute the Internal Standard Mix.
→ Add 800 µl Internal Standard Mix to 12 ml Precipitation Reagent (= mixture A).
→ Pipette 50 µl sample/calibrator/***MassCheck®*** control into a 1.5 ml reaction vial.
→ Add 25 µl Extraction Buffer, mix briefly (vortex) and incubate 2 min.
→ Add 250 µl of mixture A, mix 30 s (vortex) and centrifuge 5 min.
→ Dilute supernatant with Dilution Buffer (depending on instrument sensitivity) and inject into LC-MS/MS system.

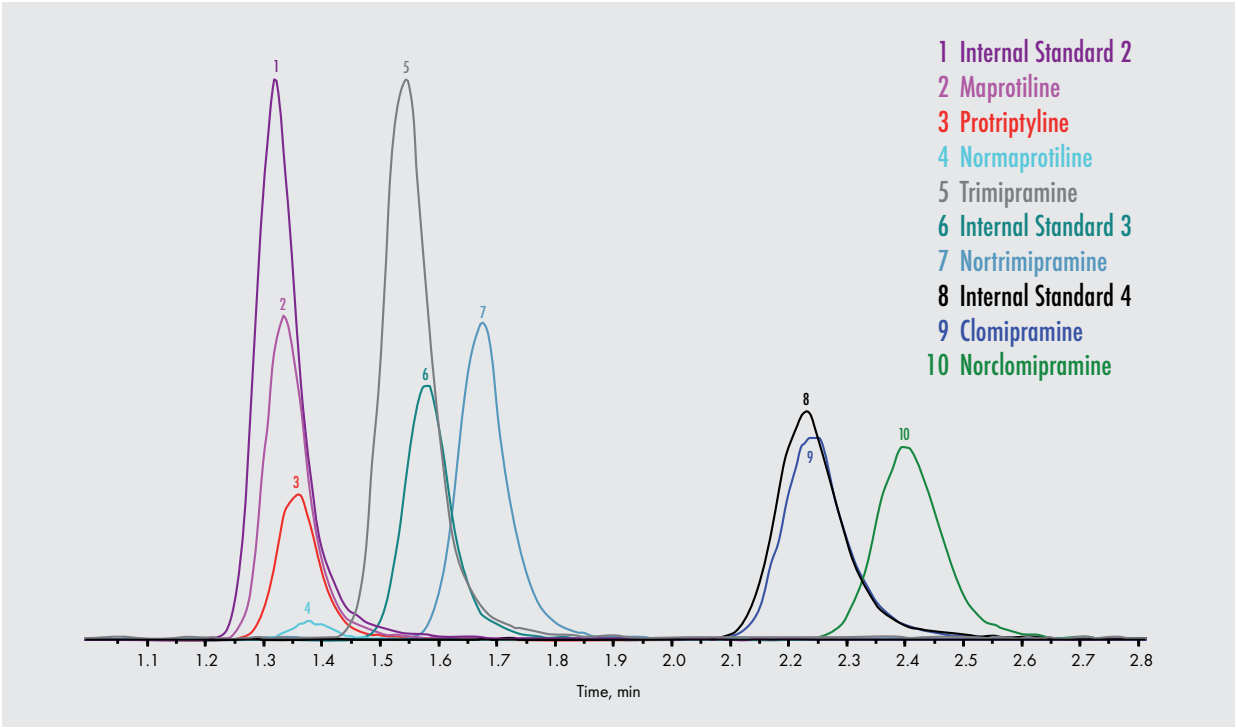
LC-MS/MS Parameters

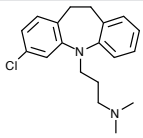
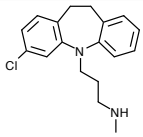
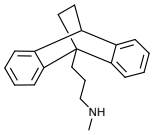
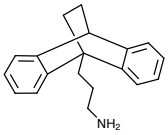
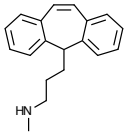
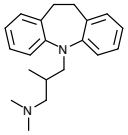
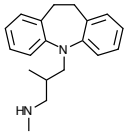
Injection volume: 0.2–50 µl
Ionisation: ESI positive
MS/MS mode: MRM

Gradient: isocratic
35 % Mobile Phase 1
65 % Mobile Phase 2

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

Tricyclic Antidepressants TCA 2



Substance	Published Reference Ranges [3,5,6] (µg/l)	Mw (g/mol)	Formula	Structure
Clomipramine	20–450	314.85	$C_{19}H_{23}ClN_2$	
Norclomipramine	150–350 0.8–2.6 x Clomipramine	300.83	$C_{18}H_{21}ClN_2$	
Maprotiline	75–250	277.40	$C_{20}H_{23}N$	
Normaprotiline	100–400*	263.38	$C_{19}H_{21}N$	
Protriptyline	50–300	263.38	$C_{19}H_{21}N$	
Trimipramine	10–300	294.43	$C_{20}H_{26}N_2$	
Nortrimipramine	0–12 x Trimipramine	280.41	$C_{19}H_{24}N_2$	

** Sum of drug and metabolite*

3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
Clomipramine	12.9	187	361	< LOQ
Norclomipramine	12.8	190	365	< LOQ
Maprotiline	35.4	198	365	< LOQ
Normaprotiline	70.3	219	365	< LOQ
Protriptyline	33.3	193	359	< LOQ
Trimipramine	6.55	182	361	< LOQ
Nortrimipramine	6.27	182	363	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Tricyclic Antidepressants TCA 2 Plasma Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
Clomipramine	47.5	265
Norclomipramine	45.8	260
Maprotiline	73.0	273
Normaprotiline	98.9	272
Protriptyline	68.3	268
Trimipramine	37.0	260
Nortrimipramine	36.9	260

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
92033	3PLUS1® Multilevel Plasma Calibrator Set Tricyclic Antidepressants TCA 2 (lyoph.), 4 x 1 ml
0246	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0247	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Level I (lyoph.), 5 x 1 ml
0248	***MassCheck®*** Tricyclic Antidepressants TCA 2 Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 1 week at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

Immunosuppressants

6.10 *MassTox*® Immunosuppressants in Whole Blood

CE IVD

Therapeutic drug monitoring of immunosuppressants is indispensable for therapy following organ transplantation. Cyclosporin A, tacrolimus, sirolimus and everolimus are mainly prescribed for avoiding organ rejection. All four drugs reduce an immune response by gradually inhibiting signal transduction. When analysing these immunosuppressants in whole blood significant matrix effects have been reported. Hence, for accurate and reliable quantification of all four analytes, a drastic reduction of these interferences is essential.

The sample preparation of the ***MassTox***® Immunosuppressants assay reduces matrix effects significantly. Isotopically labelled internal standards ensure the effective compensation of remaining ion suppression. The analysis produces robust, precise and reproducible results. Analytes are concentrated online in the trap column and potentially interfering matrix effects are eliminated. Alternatively, ***MassTox***® **ONE*MINUTE*** method can be employed that provides the same robust, accurate and reproducible results, but with a very short analysis times of 1–2 min depending on the system. High precision is ensured for all methods through multi-point calibration and the use of controls, which is demonstrated repeatedly in proficiency tests. Large batches of samples can be processed by automated sample preparation that reduces hands-on time and increases throughput. We also offer a solution that combines our validated kits with liquid handler and software in one complete CE-IVD workflow.

> Matrix effects are compensated by
– Online sample preparation using the trap column technique
– Deuterated internal standards
> High selectivity and sensitivity
> 6PLUS1® Multilevel Calibrator Sets and *MassCheck*® Controls
> ONE*MINUTE* method with very short run times
> Complete CE-IVD automated workflow also available

Das Therapeutische Drug Monitoring ist nach Organtransplantationen unverzichtbar. Zur Vermeidung von Abstoßungsreaktionen werden am häufigsten Cyclosporin A, Tacrolimus, Sirolimus und Everolimus eingesetzt. Alle vier Wirkstoffe unterdrücken die Aktivität des Immunsystems, indem sie die erforderliche Signaltransduktion graduell unterbinden. Bei der Analytik dieser Immunsuppressiva spielt die Kompensation von Matrixeffekten eine entscheidende Rolle für die diagnostische Bestimmung aus Vollblut, einer komplexen Matrix. Demzufolge ist zur genauen und sicheren Quantifizierung der vier Analyte eine deutliche Reduzierung dieser Störungen unbedingt erforderlich.

Der ***MassTox***® Immunosuppressants Test gewährleistet durch die Probenvorbereitung eine deutliche Minimierung von Matrixeffekten und sichert durch isotopenmarkierte Standards eine effektive Kompensation verbleibender Ionensuppression. Die Analytik ist robust, präzise und reproduzierbar. Die Analyte werden online auf der Trap-Säule angereichert und so störende Matrixeffekte eliminiert. Alternativ steht der ***MassTox***® **ONE*MINUTE*** Test zur Verfügung, der robuste, präzise und reproduzierbare Ergebnisse innerhalb kürzester Analysenzeiten liefert, die in der Regel systemabhängig zwischen 1–2 min betragen. Die hohe Präzision aller Methoden wird durch Mehrpunktkalibrierung und die Verwendung von Kontrollen gewährleistet, was regelmäßig bei Ringversuchen bestätigt wird. Hohe Probenzahlen können mittels automatisierter Probenvorbereitung verarbeitet werden, was den Arbeitsaufwand reduziert und den Durchsatz im Labor erhöht. Darüber hinaus bieten wir eine Lösung an, die die validierten Kits mit Laborroboter und Software zu einem kompletten CE-IVD-Workflow kombiniert.

> Matrixeffekte werden kompensiert durch:
– Online Probenvorbereitung mit Trap-Säulen-Technologie
– Deuterierte interne Standards
> Hohe Selektivität und Sensitivität
> 6PLUS1® Multilevel Calibrator Sets und *MassCheck*® Controls
> ONE*MINUTE* Methode mit sehr kurzen Laufzeiten
> Auch als vollständiger automatisierter CE-IVD-Workflow verfügbar

6.10.1 *MassTox*® Immunosuppressants in Whole Blood Standard Method

Parameters:
cyclosporin A, everolimus, sirolimus, tacrolimus.

Order no.	Product
93000	***MassTox***® Immunosuppressants in Whole Blood For 400 tests
93000/ 1200	***MassTox***® Immunosuppressants in Whole Blood For 1200 tests
	Components available separately
93001	Mobile Phase A, 1000 ml
93002	Mobile Phase B, 1000 ml
93003	Precipitation Reagent, 100 ml
93005	Extraction Buffer, 40 ml
93009	Rinsing Solution, 1000 ml
93046	Internal Standard Set, consisting of: Internal Standard Mix (lyoph.), 4 x 2.5 ml Reconstitution Buffer, 10 ml
33005	Reaction Vials, amber coloured (light protection), 100 pcs.
	Startup Accessories
93110	Trap Column, equilibrated, with test chromatogramm, 1 pc.
93100	Analytical Column, equilibrated, with test chromatogramm, 1 pc.
93015	Tuning Mix, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
	Multilevel Calibrator and Controls
28039	6PLUS1® Multilevel Whole Blood Calibrator Set Immunosuppressants (lyoph.), 7 x 2 ml
	MassCheck® Immunosuppressants Whole Blood Controls (lyoph.)
0081	Four-Level, 4 x 2 x 2 ml
0082	Level I, 5 x 2 ml
0083	Level II, 5 x 2 ml
0084	Level III, 5 x 2 ml
0085	Level IV, 5 x 2 ml
0089	Blank Control, 5 x 2 ml

Specifications

Linearity:

cyclosporin A	2000 µg/l
everolimus	80 µg/l
sirolimus	80 µg/l
tacrolimus	80 µg/l

Limit of quantification:

cyclosporin A	5.0 µg/l
everolimus	0.5 µg/l
sirolimus	0.5 µg/l
tacrolimus	0.5 µg/l

Analysis time: 4.5 min

Pre-analytic Treatment

Specimens: EDTA whole blood.
Stability: up to 7 days at +2 to 8 °C.

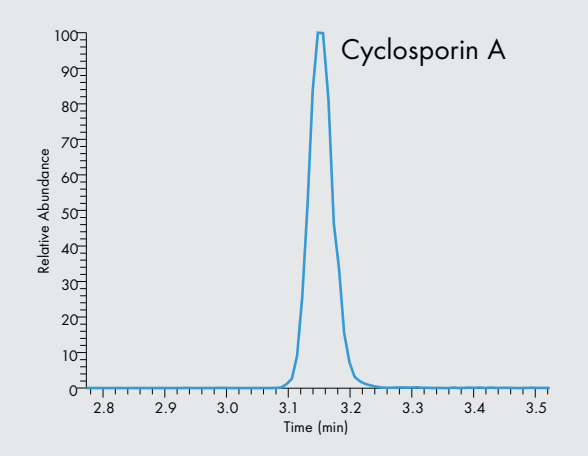
Sample Preparation

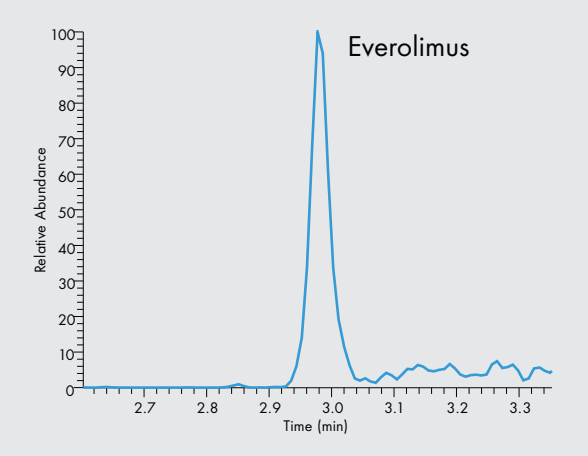
→ Place 50 µl sample into a reaction vial.
→ Add 100 µl Extraction Buffer.
→ Add 25 µl ISTD-solution, vortex 10 s and incubate for 2 min at room temperature.
→ Add 250 µl Precipitation Reagent, vortex 60 s and incubate for 2 min at room temperature.
→ Centrifuge 5 min at 15 000 x g.
→ Inject up to 25 µl of the supernatant for analysis.

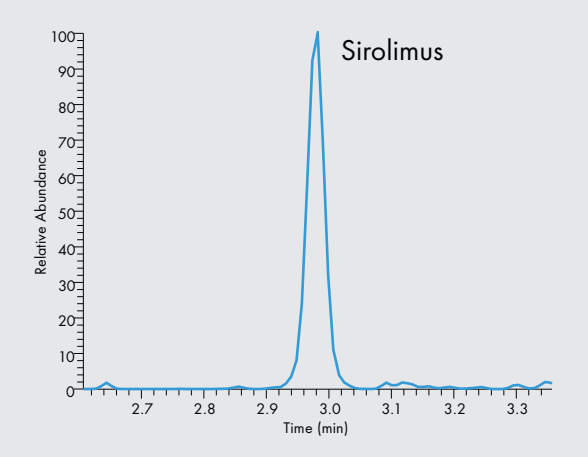
LC-MS/MS Parameters

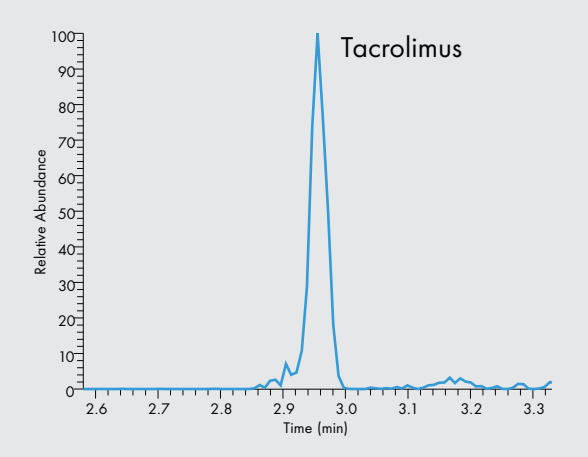
Injection volume:	up to 25 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

MassTox® Immunosuppressants in Whole Blood
Standard Method



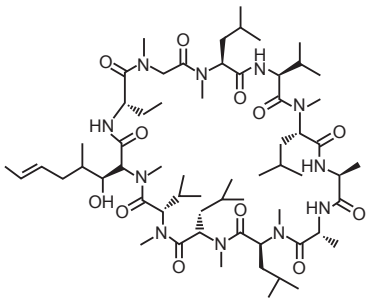






MassTox® Immunosuppressants in Whole Blood

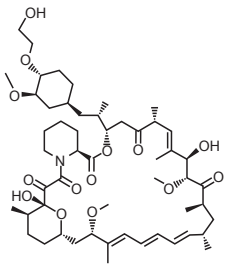
Cyclosporin A: therapeutic range for whole blood [16,19]



$C_{62}H_{111}N_{11}O_{12}$
Mw 1202.61 g/mol

	Initial Therapy (µg/l)	Maintenance Therapy (µg/l)
Kidney transplant	150–225	100–150
Liver transplant	225–300	100–150
Heart transplant	250–350	150–250

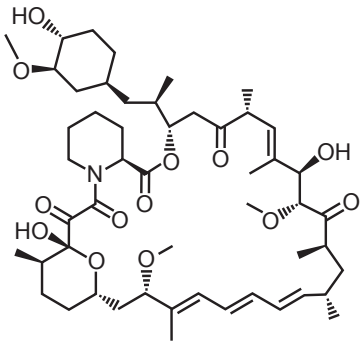
Everolimus: therapeutic range for whole blood [16,19]



$C_{53}H_{83}NO_{14}$
Mw 958.22 g/mol

	Minimum (µg/l)
Kidney transplant patient – triple therapy with cyclosporin A, corticosteroids, and everolimus	3–8

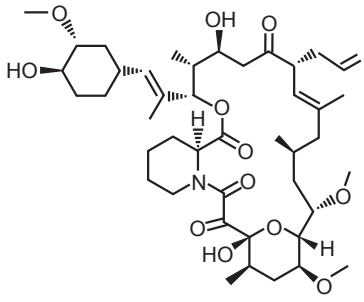
Sirolimus: therapeutic range for whole blood [16,19]



$C_{51}H_{79}NO_{13}$
Mw 914.17 g/mol

		Minimum (µg/l)
Kidney transplant	Combination with steroids and mycophenolate mofetil	5–10
	Combination with steroids and without mycophenolate mofetil	8–12
Kidney transplant	Triple therapy with cyclosporin A, corticosteroids and sirolimus	4–12
	Dual therapy with corticosteroids and sirolimus	12–20
Liver transplant	Therapy with cyclosporin A or tacrolimus, sirolimus and, where appropriate, corticosteroids	3–6
	Therapy with sirolimus and, where appropriate, corticosteroids	5–8

Tacrolimus: therapeutic range for whole blood [16,19]



$C_{44}H_{69}NO_{12}$
Mw 804.02 g/mol

	Initial Therapy (µg/l)	Maintenance Therapy (µg/l)
Kidney transplant	9–15	4–10
Liver transplant	9–15	4–10
Heart transplant	9–18	8–15

All therapeutic ranges listed here are taken from published literature. There are however no universally established therapeutic ranges for cyclosporin A, everolimus, sirolimus or tacrolimus in whole blood. Values obtained with different assay methods cannot be used interchangeably. Laboratories should include identification of the method used for the assay in order to aid in interpretation of results.

6.10.2 *MassTox*® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test

Up to 800 samples per day

Order no.	Product
93900/ 400	***MassTox***® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test For 400 tests
93900/ 1200	***MassTox***® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test For 1200 tests, complete with analytical column, trap column and 6PLUS1® calibrators

Components available separately

93911	Mobile Phase A, 900 ml
93922	Mobile Phase B, 450 ml
93003	Precipitation Reagent, 100 ml
93005	Extraction Buffer, 40 ml
93909	Rinsing Solution, 1000 ml
93946	Internal Standard Set, consisting of: Internal Standard Mix (lyoph.), 4 x 2.5 ml Reconstitution Buffer, 10 ml
33006	Reaction Vials, 100 pcs.

Startup Accessories

93122	Trap Column, equilibrated, with test chromatogramm, 1 pc.
93100	Analytical Column, equilibrated, with test chromatogramm, 1 pc.
93915	Tuning Mix, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.

Multilevel Calibrator and Controls

28039/XL	6PLUS1® Multilevel Whole Blood Calibrator Set Immunosuppressants (lyoph.), 7 x 2 ml
	MassCheck® Immunosuppressants Whole Blood Controls (lyoph.)
0081	Four-Level, 4 x 2 x 2 ml
0082	Level I, 5 x 2 ml
0083	Level II, 5 x 2 ml
0084	Level III, 5 x 2 ml
0085	Level IV, 5 x 2 ml
0089	Blank Control, 5 x 2 ml

Specifications

Linearity:

cyclosporin A	2000 µg/l
everolimus	100 µg/l
sirolimus	100 µg/l
tacrolimus	100 µg/l

Limit of quantification:

cyclosporin A	5.0 µg/l
everolimus	0.5 µg/l
sirolimus	0.5 µg/l
tacrolimus	0.5 µg/l

Analysis time: 1–2 min (mass spectrometer dependent)

Pre-analytic Treatment

Specimens: EDTA whole blood.
Stability: up to 7 days at +2 to 8 °C.

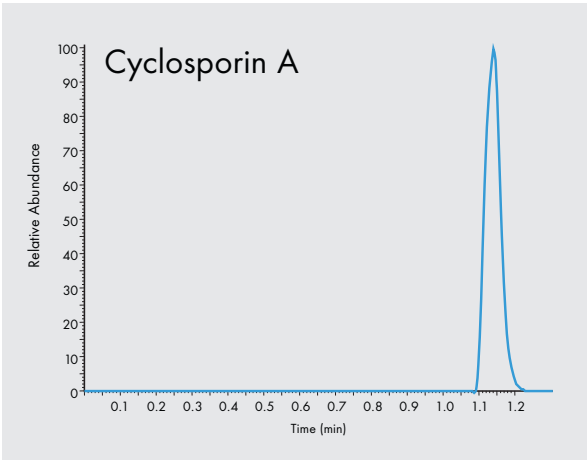
Sample Preparation

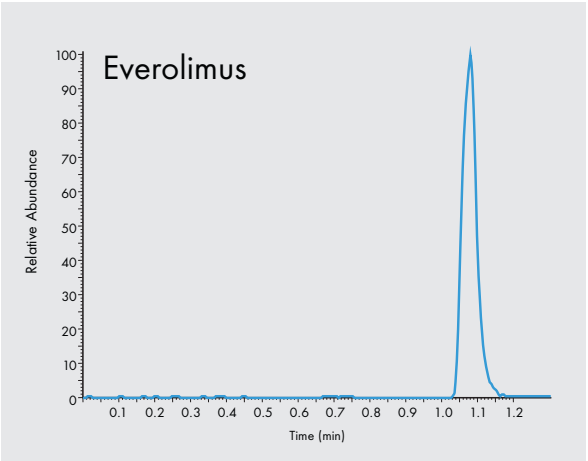
→ Place 50 µl sample/calibrator/***MassCheck***® control into a reaction vial.
→ Add 25 µl reconstituted Internal Standard Mix.
→ Add 100 µl Extraction Buffer and 250 µl Precipitation Reagent, vortex for 1 min and incubate for 2 min at room temperature.
→ Centrifuge 5 min at 15 000 x g.
→ Transfer the supernatant to an autosampler vial and inject 5 to 50 µl into the LC-MS/MS system.

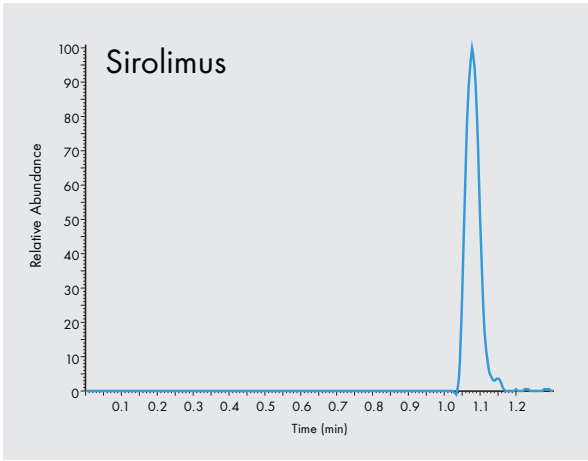
LC-MS/MS Parameters

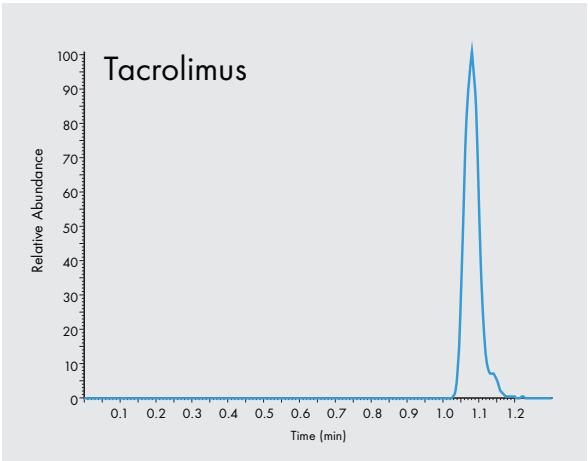
Injection volume:	up to 50 µl
Ionisation:	ESI positive
MS/MS mode:	MRM

MassTox® Immunosuppressants in Whole Blood
ONE*MINUTE* Test



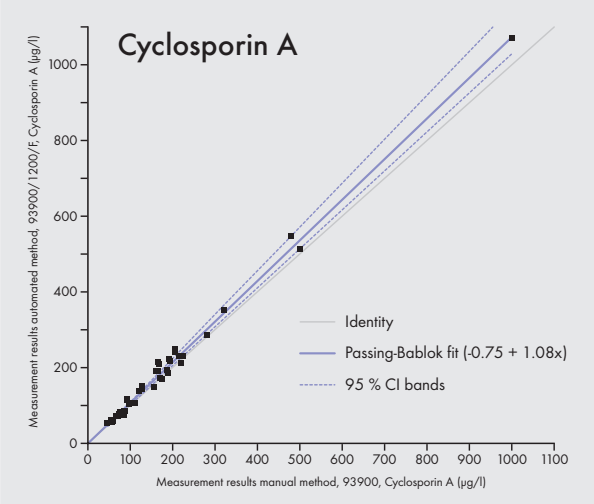


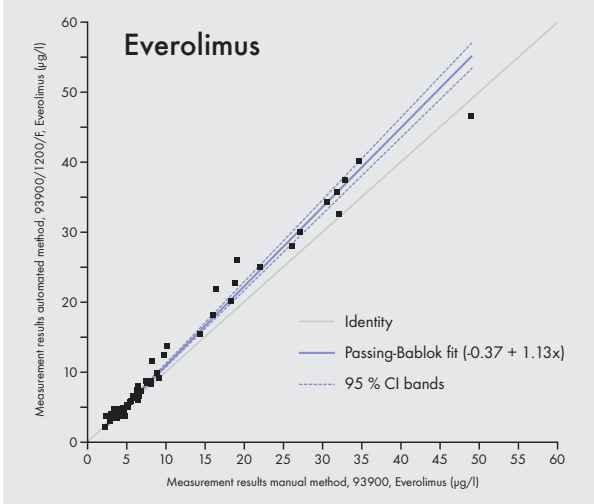


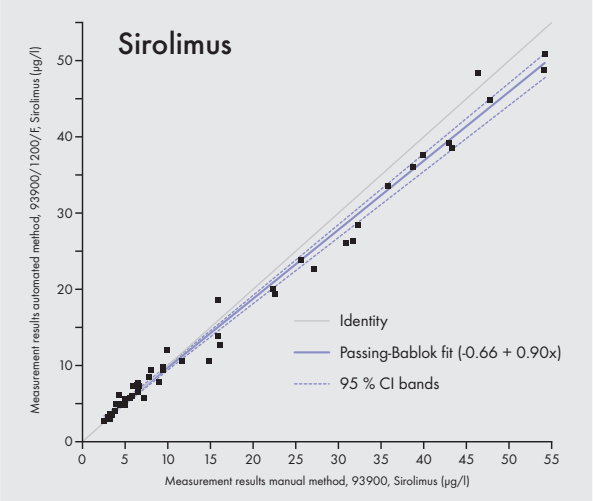


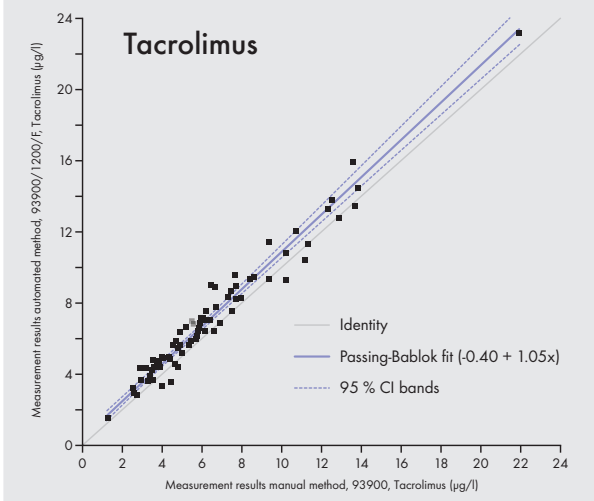
6.10.3 *MassTox*® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test Automated Method

Automated with 96 Deep Well Filter Plates









*Comparison of human samples containing cyclosporin A, tacrolimus, sirolimus and everolimus, prepared manually and with automation (Tecan Freedom EVO 100). The analysis was performed with the **MassTox**® Immunosuppressants in Whole Blood **ONEMINUTE** Test on an ABSciex API 4500 mass spectrometer.*

MassTox® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test Automated Method

Order no.	Product
93900/ 1200/F	***MassTox***® Immunosuppressants in Whole Blood **ONE*MINUTE*** Test Automated with 96 Deep Well Filter Plates For 1200 tests, complete with analytical column, trap column and 6PLUS1® calibrators.

Components available separately

93911	Mobile Phase A, 900 ml
93922	Mobile Phase B, 450 ml
93003	Precipitation Reagent, 100 ml
93909	Rinsing Solution, 1000 ml
93946	Internal Standard Set, consisting of: Internal Standard Mix (lyoph.), 4 x 2.5 ml and Reconstitution Buffer, 10 ml
93005	Extraction Buffer, 40 ml
93957	96 Deep Well Filter Plates, 5 pcs.
93058	Collection Plates, 5 pcs.
93059	Pierceable Adhesive Seals for 96 Well Plates, 5 pcs.
93100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
93122	Trap Column, equilibrated, with test chromatogram, 1 pc.
28039/XL	6PLUS1® Multilevel Calibrator Set Immunosuppressants in Whole Blood (lyoph.), 7 x 2 ml

Controls and Startup Accessories

	MassCheck® Immunosuppressants Whole Blood Controls (lyoph.)
0081	Four-Level, 4 x 2 x 2 ml
0082	Level I, 5 x 2 ml
0083	Level II, 5 x 2 ml
0084	Level III, 5 x 2 ml
0085	Level IV, 5 x 2 ml
0089	Blank Control, 5 x 2 ml
93915	Tuning Mix Immunosuppressants, Analytes and Internal Standards, 1 ml
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
93060	Pierceable Heat Seals for 96 Well Plates, 6 pcs.

Automated Workflow

→ Load liquid handling device with samples, reagents, 96 deep well filter plate and collection plate.
→ Start the **automation routine***.
→ After completion remove collection plate from the liquid handling device, seal with an adhesive or heat seal and transfer to autosampler.
→ Inject 5–50 µl eluate into LC-MS/MS system.

* *Ready to use automation routine provided with the installation by Chromsystems.*

6PLUS1® Multilevel Whole Blood Calibrator Sets Immunosuppressants

Calibrator Level	Substance	Value (µg/l)*
Calibrator 1	Cyclosporin A	23.3
	Everolimus	2.2
	Rapamycin (Sirolimus)	2.3
	Tacrolimus (FK 506)	2.1
Calibrator 2	Cyclosporin A	122
	Everolimus	5.7
	Rapamycin (Sirolimus)	6.2
	Tacrolimus (FK 506)	5.5
Calibrator 3	Cyclosporin A	291
	Everolimus	11.2
	Rapamycin (Sirolimus)	12.1
	Tacrolimus (FK 506)	10.8
Calibrator 4	Cyclosporin A	476
	Everolimus	16.4
	Rapamycin (Sirolimus)	18.9
	Tacrolimus (FK 506)	16.0
Calibrator 5	Cyclosporin A	762
	Everolimus	23.4
	Rapamycin (Sirolimus)	28.5
	Tacrolimus (FK 506)	22.3
Calibrator 6 → for 28039	Cyclosporin A	919
	Everolimus	41.1
	Rapamycin (Sirolimus)	46.1
	Tacrolimus (FK 506)	38.5
Calibrator 6/XL → for 28039/XL	Cyclosporin A	1745
	Everolimus	41.7
	Rapamycin (Sirolimus)	46.5
	Tacrolimus (FK 506)	39.0
Blank Calibrator	Cyclosporin A	< LOQ
	Everolimus	< LOQ
	Rapamycin (Sirolimus)	< LOQ
	Tacrolimus (FK 506)	< LOQ

** Please check packaging leaflet for specific lot concentrations*

LOQ = limit of quantification

MassCheck® Immunosuppressants Whole Blood Controls

Control Level	Substance	Target Value (µg/l)*
Level I	Cyclosporin A	49.7
	Everolimus**	2.7
	Rapamycin (Sirolimus)	2.7
	Tacrolimus (FK 506)	2.7
Level II	Cyclosporin A	249
	Everolimus**	4.8
	Rapamycin (Sirolimus)	9.7
	Tacrolimus (FK 506)	7.4
Level III	Cyclosporin A	484
	Everolimus**	9.4
	Rapamycin (Sirolimus)	18.5
	Tacrolimus (FK 506)	15.3
Level IV	Cyclosporin A	1116
	Everolimus**	33.1
	Rapamycin (Sirolimus)	37.6
	Tacrolimus (FK 506)	32.2
Blank Control	Cyclosporin A	< LOQ
	Everolimus**	< LOQ
	Rapamycin (Sirolimus)	< LOQ
	Tacrolimus (FK 506)	< LOQ

** Please check packaging leaflet for specific lot concentrations*

*** This product is not suitable for the analysis of everolimus by immunoassay, because of possible cross-reaction with sirolimus*

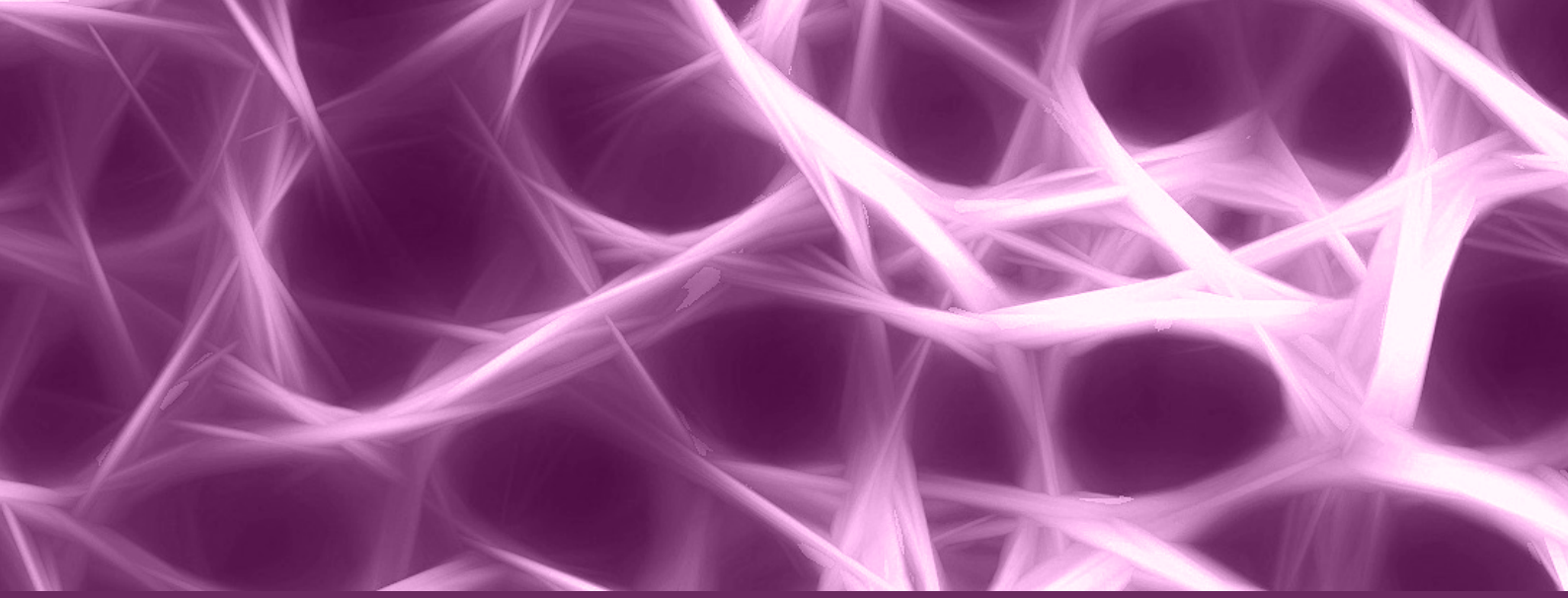
LOQ = limit of quantification

Order no.	Product
28039	6PLUS1® Multilevel Whole Blood Calibrator Set Immunosuppressants, 7 x 2 ml
28039/XL	6PLUS1® Multilevel Whole Blood Calibrator Set Immunosuppressants, 7 x 2 ml
	MassCheck® Immunosuppressants Whole Blood Controls
0081	Four-Level, 4 x 2 x 2 ml
0082	Level I, 5 x 2 ml
0083	Level II, 5 x 2 ml
0084	Level III, 5 x 2 ml
0085	Level IV, 5 x 2 ml
0089	Blank Control, 5 x 2 ml

Stability of Whole Blood Calibrators and Controls

Please check instruction manual for detailed information

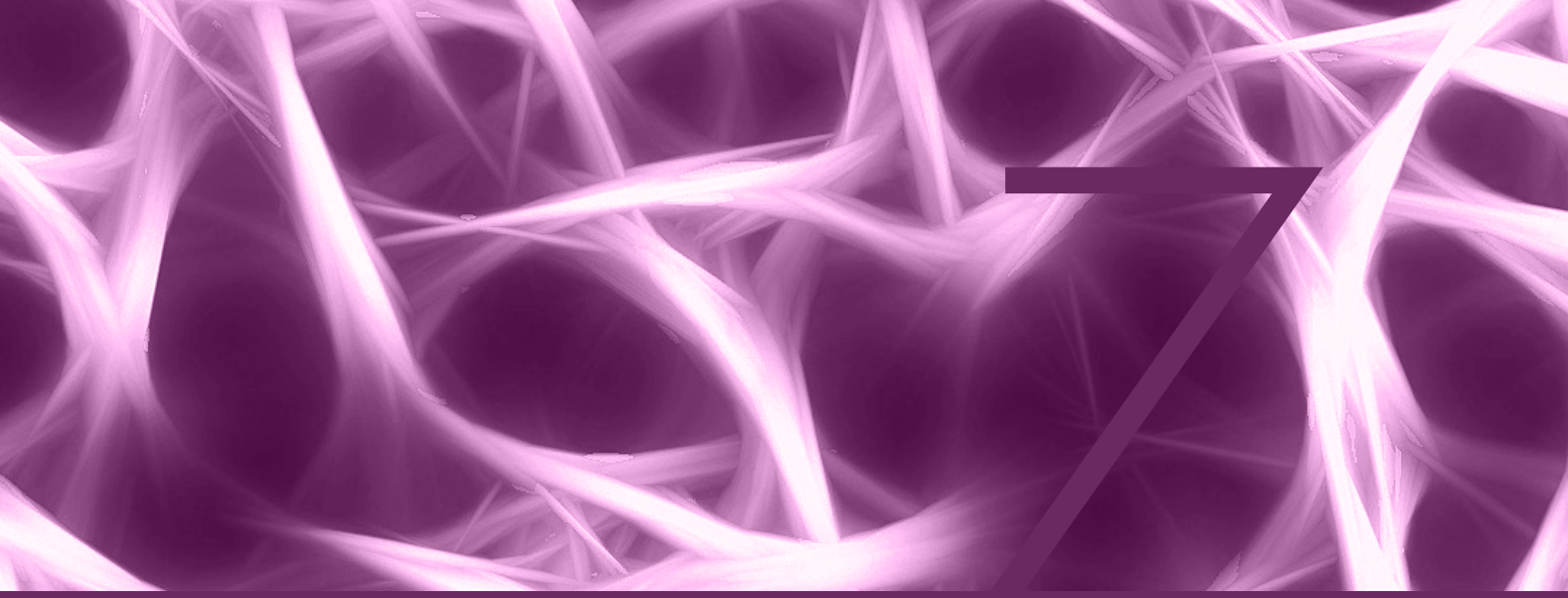
> Stable to expiry date below -18 °C
> Reconstituted up to 7 days at +2 °C to +8 °C
> Reconstituted aliquots up to 9 months below -18 °C



Osteoporosis Diagnosis

Osteoporosis is a disease that leads to low bone mass and deterioration of bone tissue, thereby increasing the risk of fractures. Bone density decreases after 35 years of age, and bone loss occurs more rapidly in women after menopause. Some of the risk factors are a genetic disposition, lack of calcium and vitamin D, smoking and excessive alcohol consumption. A deficiency of this vitamin leads to a decrease of the calcium level and to disturbances in bone mineralisation. Associated symptoms are rickets (children) and osteoporosis (adults). Patients with vitamin D deficiency show increased excretion of collagen crosslinks, which is indicative of a bone resorption process.

25-OH-vitamin D_3 constitutes the principal diagnostic target and is the main vitamin D metabolite in humans. Vitamin D deficiency is treated with vitamin D_3 or vitamin D_2 supplementation.



Knochenstoffwechselmarker

Osteoporose ist eine Krankheit, die zu einer reduzierten Knochenmasse und Verschlechterung des Knochengewebes führt, was das Risiko von Knochenbrüchen erhöht. Die Knochendichte vermindert sich ab einem Alter von 35 Jahren, und Knochenschwund erfolgt bei Frauen nach der Menopause schneller. Risikofaktoren sind neben genetischer Disposition ein Mangel an Calcium und Vitamin D, Rauchen sowie übermäßiger Alkoholkonsum. Vitamin D-Mangelzustände führen zu Hypocalcämie und einer gestörten Knochenmineralisierung, wie Rachitis (Kinder) und Osteoporose (Erwachsene). Dieser Zusammenhang lässt sich durch erhöhte Ausscheidung von Kollagen-Crosslinks nachweisen.

Im menschlichen Organismus wird der Hauptmetabolit 25-OH-Vitamin D_3 gemessen. Vitamin-D-Mangel wird in erster Linie durch Nahrungsergänzung mit Vitamin D_3 oder D_2 therapiert.

Overview Vitamin D Assays

Chromsystems provides a broad range of CE-IVD validated vitamin D assays fulfilling different requirements on speed, throughput and depth of analysis. All assays include an on-line sample preparation that removes potential interferences efficiently. The use of APCI (atmospheric pressure chemical ionisation) and deuterated internal standards ensure precision and robustness and minimises ion suppression effects for all our methods. Manual as well as automated assays are also available.

Chromsystems verfügt über ein breites Portfolio an CE-IVD validierten Vitamin D-Assays, welche verschiedene Anforderungen im Labor an Geschwindigkeit, Probendurchsatz und Parameter erfüllen. Alle Tests umfassen eine Online Probenvorbereitung, die potentielle Interferenzen effizient entfernt. Die Verwendung von APCI (atmospheric pressure chemical ionisation) sowie deuterierte interne Standards stellen die Präzision und Robustheit der Methode sicher und minimieren Ionsuppressionseffekte bei allen unseren Methoden. Manuelle sowie automatisierte Assays sind ebenfalls verfügbar.

MassChrom® Vitamin D (No. 62062)

> Updated method with short run time
> High chromatographic separation

	Parameters: 25-OH-vitamin D_3, 3-*epi*-25-OH-vitamin D_3 25-OH-vitamin D_2, (3-*epi*-25-OH-vitamin D_2*) *separation only, no quantitative measurement			
Order no.	Assay	Sample prep	Analysis time	Page
62062	*MassChrom*® 25-OH-Vitamin D_3/D_2 and 3-*epi*-Vitamin D_3	Manual	3.25–3.9 min	196
62062/1000/F	*MassChrom*® 25-OH-Vitamin D_3/D_2 and 3-*epi*-Vitamin D_3	Automated	3.25–3.9 min	198

MassChrom® Vitamin D (No. 62000)

> Standard method for vitamin D_3/D_2
> Upgrade available for the determination of 3-*epi*-25-OH-vitamin D_3/D_2

Parameters: sum of 25-OH-vitamin D_3 and its C3-epimer sum of 25-OH-vitamin D_2 and its C3-epimer		Epimer upgrade: 25-OH-vitamin D_3, 3-*epi*-25-OH-vitamin D_3 25-OH-vitamin D_2, 3-*epi*-25-OH-vitamin D_2		
Order no.	Assay	Sample prep	Analysis time	Page
62000	*MassChrom*® 25-OH-Vitamin D_3/D_2	Manual	5–6 min	200
62000/1000/F	*MassChrom*® 25-OH-Vitamin D_3/D_2	Automated	5–6 min	202
Epimer upgrade	Upgrade set for separate determination of epimers	Manual	8.5–10 min	204

7.1 *MassChrom*® 25-OH-Vitamin D_3/D_2 in Serum/Plasma

CE IVD

Our vitamin D assays are available for different requirements in the laboratory and are based on a sample preparation that is minimised to a simple and effective protein precipitation. The subsequent online trap column concentrates the analytes and separates interfering substances. The updated method (62062) allows the determination of 25-OH-vitamin D_3, its epimeric form and 25-OH-vitamin D_2 in less than 4 minutes. Our standard method (order. No 62000) offers the determination of 25-OH-vitamin D_3/D_2. An epimer upgrade set is also available that allows to determine both epimeric forms.

The automated assays are aimed at laboratories with a higher sample throughput. They reduce the sample prep time by up to 80 % for large sample series. We also offer an assay that can be integrated with liquid handler and software in one complete CE-IVD workflow.

- **Broad range of assays**
- **Suitable for every tandem-MS with sufficient sensitivity**
- **Manual and automated methods**
- **Determination of epimeric forms possible**
- **Online sample preparation**
- **6PLUS1® and 3PLUS1® Multilevel Calibrator Sets with blank calibrators**

Unsere Vitamin D-Assays sind für verschiedene Bedürfnisse im Labor ausgelegt und verfügen über eine Probenvorbereitung, die auf eine einfache und effektive Proteinfällung beschränkt ist. Danach werden die Analyten mit Hilfe einer Trap-Säule online angereichert und störende Matrixbestandteile abgetrennt. Die aktualisierte Methode (Best.-Nr. 62062) ermöglicht die Bestimmung von 25-OH-Vitamin D_3, seiner epimeren Form sowie das 25-OH-Vitamin D_2 in weniger als 4 Minuten. Unsere Standardmethode (Best.-Nr. 62000) dient der Bestimmung von 25-OH-Vitamin D_3/D_2. Ein Epimer Upgrade-Set steht ebenfalls zur Verfügung, das die separate Bestimmung beider epimeren Formen zusätzlich ermöglicht.

Für Laboratorien mit höherem Probendurchsatz stehen automatisierte Kits zur Verfügung, die bei großen Probenserien die Probenvorbereitungszeit um bis zu 80 % reduzieren können. Darüber hinaus bieten wir einen Assay an, der mit Kit, Laborroboter und Software zu einem kompletten CE-IVD-Workflow kombiniert werden kann.

- **Breites Spektrum an Vitamin-D-Kits**
- **Geeignet für jedes Tandem-MS-Gerät mit ausreichender Sensitivität**
- **Manuelle und automatisierte Methoden**
- **Bestimmung von epimeren Formen möglich**
- **Online Probenvorbereitung**
- **6PLUS1® und 3PLUS1® Multilevel Calibrator Sets mit Blank-Kalibratoren**

7.1.1 *MassChrom*® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 Updated Method

Parameters:
25-OH-vitamin D_3, 3-*epi*-25-OH-vitamin D_3, 25-OH-vitamin D_2.

Order no.	Product
62062	***MassChrom***® 25-OH-Vitamins D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 in Serum/Plasma For 200 tests
62062/ 1000	***MassChrom***® 25-OH-Vitamins D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 in Serum/Plasma For 1000 tests

Components available separately

62011	Mobile Phase A, 1000 ml
62022	Mobile Phase B, 1000 ml
62003	Precipitation Reagent, 5 ml
62044	Internal Standard Mix, 40 ml
62009	Rinsing Solution, 1000 ml

Startup Accessories

62130	Analytical Column, equilibrated, with test chromatogram, 1 pc.
62110/Epi	Trap Column, equilibrated, with test chromatogram, 1 pc.
62016	Tuning Mix, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
3006	Reaction Vials, 1.5 ml, 100 pcs.

Multilevel Calibrator and Controls

62029	3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0310	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0311	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 250 µg/l
Limit of quantification:	1.5 µg/l
Intraassay:	CV < 4 %
Interassay:	CV < 10 %
Analysis time:	3.25–3.9 min

Pre-analytic Treatment

Specimens: serum or plasma.
Stability: samples are stable up to 3 days at ambient temperature and up to 1 week at +2 to +8 °C. For longer storage (maximum 1 month) deep-freeze the samples below -18 °C.

Sample Preparation

→ Pipette 100 µl specimen/calibrator/***MassCheck***® control into a 1.5 ml reaction vial.
→ Add 25 µl Precipitation Reagent.
→ Add 200 µl Internal Standard and mix 20 s (vortex).
→ Incubate 10 min at +4 °C.
→ Centrifuge 5 min at 15 000 x g.
→ Transfer 200 µl supernatant into an autosampler vial.
→ Inject up to 50 µl of the supernatant into the LC-MS/MS system.

HPLC Parameters

Injection volume:	≤ 50 µl
Column temperature:	40 °C

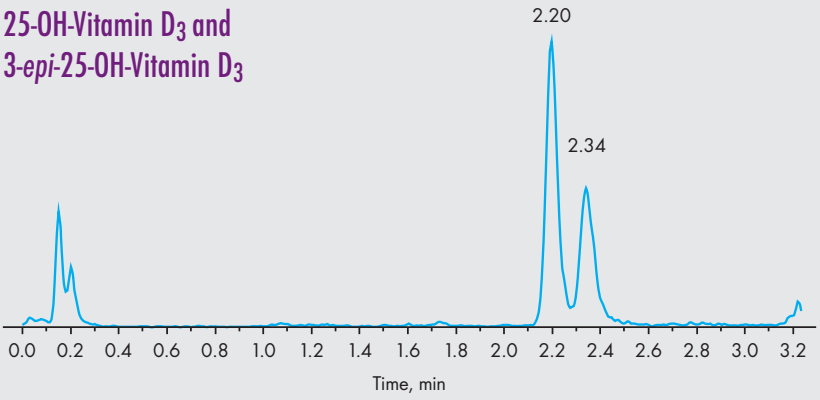
The sample extracts are purified through a trap column and the analytes are subsequently separated on a high resolution analytical column. A binary gradient pump, a 2-position 6-port valve and a column oven are required (run time 3.9 min). Through the use of an additional isocratic pump, the analysis time can be reduced to 3.25 min.

MS/MS Parameters

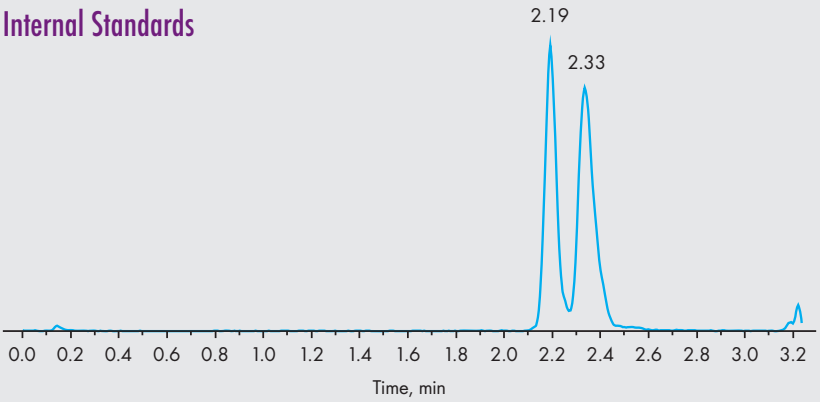
Ionisation:	APCI positive
MS/MS mode:	MRM

MassChrom® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 Updated Method

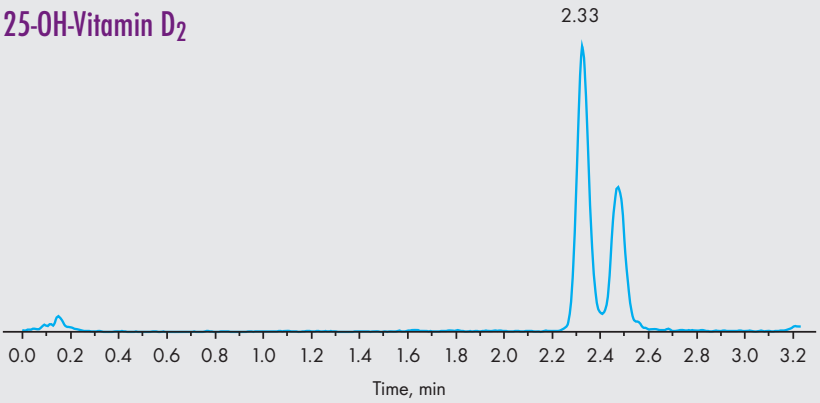
25-OH-Vitamin D_3 and
3-*epi*-25-OH-Vitamin D_3

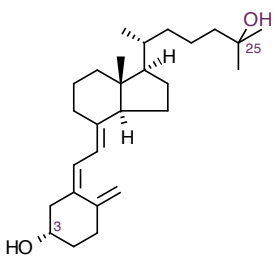


Internal Standards

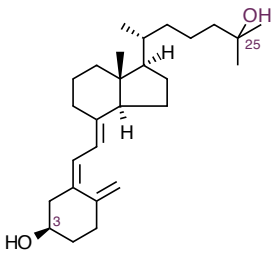


25-OH-Vitamin D_2

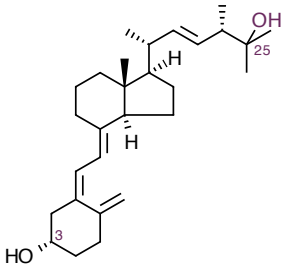




25-OH-Vitamin D_3
$C_{27}H_{44}O_2$
Mw 400.64 g/mol



3-*epi*-25-OH-Vitamin D_3
$C_{27}H_{44}O_2$
Mw 400.64 g/mol



25-OH-Vitamin D_2
$C_{28}H_{44}O_2$
Mw 412.65 g/mol

7.1.2 *MassChrom*® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 Automated Method

Automated with 96 Well Filter Plates

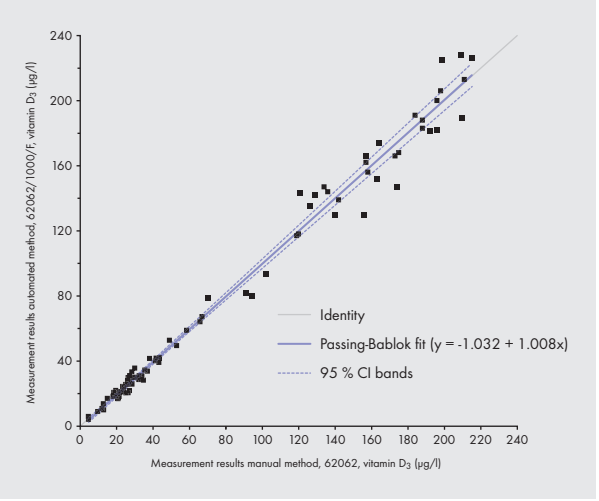
Order no.	Product
62062/ 1000/F	***MassChrom***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 in Serum/Plasma Automated with 96 Well Filter Plates For 1000 tests, complete with analytical column, trap column, 3PLUS1® calibrators and ***MassCheck***® controls

Components available separately

62011	Mobile Phase A, 1000 ml
62022	Mobile Phase B, 1000 ml
62003	Precipitation Reagent, 5 ml
62044	Internal Standard Mix, 40 ml
62009	Rinsing Solution, 1000 ml
62057	96 Well Filter Plates, 3 pcs.
62058	Collection Plates, 3 pcs.
62059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
62130	Analytical Column, equilibrated, with test chromatogram, 1 pc.
62110/Epi	Trap Column, equilibrated, with test chromatogram, 1 pc.
62029	3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0311	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml

Startup Accessories

62016	Tuning Mix, Analytes and Internal Standards, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
0310	***MassCheck***® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml



Automated Workflow

→ Load liquid handling device with samples, reagents, 96 well filter plate and collection plate.
→ Start the **automation routine***.
→ After completion remove collection plate from the liquid handling device, seal with an adhesive seal and transfer to autosampler.
→ Inject up to 50 µl eluate into LC-MS/MS system.

* *Ready to use automation routine provided with the installation by Chromsystems.*

3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
25-OH-vitamin D_3	19.0	33.0	67.2	< LOQ
3-*epi*-25-OH-vitamin D_3	9.66	19.5	29.8	< LOQ
25-OH-vitamin D_2	14.3	28.5	57.2	< LOQ
3-*epi*-25-OH-vitamin D_2	9.14	18.7	28.4	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3/D_2 Serum Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
25-OH-vitamin D_3	16.8	40.3
3-*epi*-25-OH-vitamin D_3	16.5	27.5
25-OH-vitamin D_2	16.5	37.2
3-*epi*-25-OH-vitamin D_2	13.2	22.1

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
62029	3PLUS1® Multilevel Serum Calibrator Set 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0310	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0311	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml

Stability of Serum Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 7 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

7.1.3 *MassChrom*® 25-OH-Vitamin D_3/D_2 in Serum/Plasma Standard Method

Parameters:
25-OH-vitamin D_3, 25-OH-vitamin D_2.

Order no.	Product
62000	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma For 200 tests
62000/	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma For 1000 tests, complete with analytical column, trap column, 3PLUS1® calibrators and ***MassCheck***® controls

Components available separately

62001	Mobile Phase A, 1000 ml
62002	Mobile Phase B, 1000 ml
62003	Precipitation Reagent, 5 ml
62004	Internal Standard, 40 ml
62009	Rinsing Solution, 1000 ml
3006	Reaction Vials, 100 pcs.

Startup Accessories

62100	Analytical Column, 1 pc.
62110	Trap Column, 1 pc.
62015	Tuning Mix, Analytes and Internal Standard, 2 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.

Multilevel Calibrators and Controls

62028	3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1 ml
62039	6PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 7 x 1 ml
0221	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0222	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0223	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml
0256	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level III (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 250 µg/l
Limit of quantification:	3.0 µg/l D_3 2.2 µg/l D_2
Intraassay:	CV < 5 %
Interassay:	CV < 6 %
Analysis time:	5 min

Pre-analytic Treatment

Specimen: serum or plasma.
Stability: samples are stable up to 1 week at +2 to +8 °C. For longer storage periods keep samples frozen below -18 °C.

Sample Preparation

→ Place 100 µl sample/calibrator/***MassCheck***® control into a reaction vial.
→ Add 25 µl Precipitation Reagent.
→ Add 200 µl Internal Standard and vortex 20 s.
→ Incubate 10 min at +4 °C.
→ Centrifuge 5 min at 15 000 x g.
→ Transfer 200 µl supernatant into an autosampler vial.
→ Inject 10–50 µl into the LC-MS/MS system.

HPLC Parameters

Injection volume: 10–50 µl

Pump A delivers 100 % Mobile Phase A for loading the trap column.
Flow: 0.02–1.00 ml/min

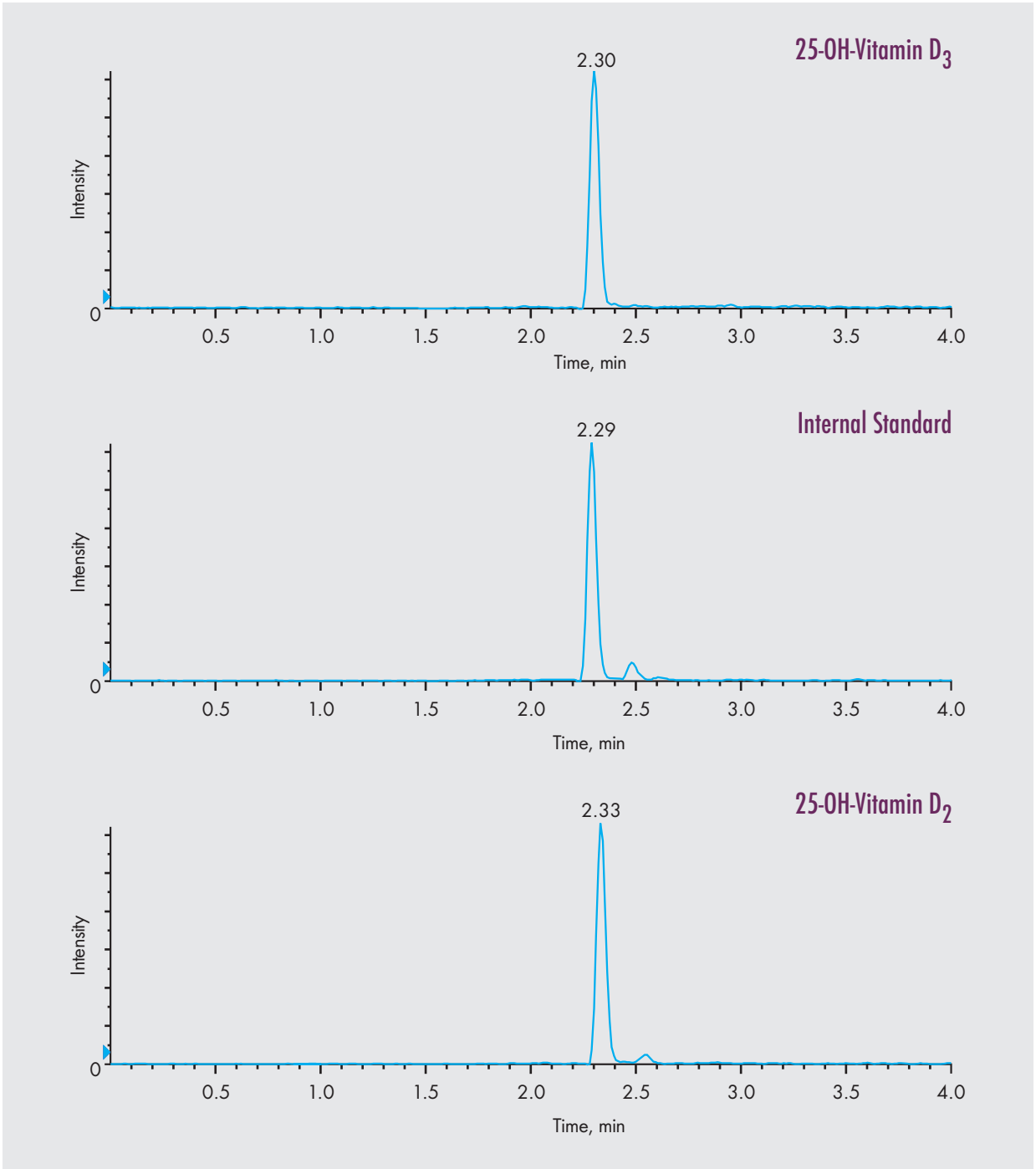
Pump B delivers 100 % Mobile Phase B for separating analytes on the analytical column.
Flow: 0.60–1.00 ml/min

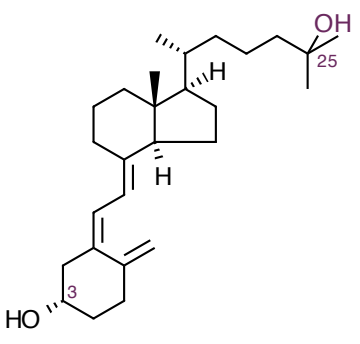
The trap column and the analytical column are linked to the mass spectrometer through a 6-port valve.

MS/MS Parameters

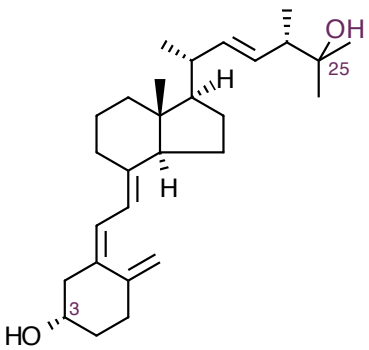
Ionisation:	APCI positive
MS/MS mode:	MRM

MassChrom® 25-OH-Vitamin D_3/D_2 in Serum/Plasma Standard Method





25-OH-Vitamin D_3
$C_{27}H_{44}O_2$
Mw 400.64 g/mol



25-OH-Vitamin D_2
$C_{28}H_{44}O_2$
Mw 412.65 g/mol

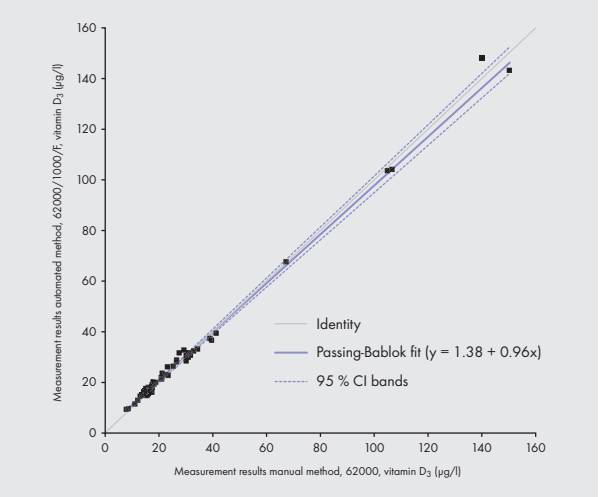
7.1.4 *MassChrom*® 25-OH-Vitamin D_3/D_2 in Serum/Plasma Automated Method

Automated with 96 Well Filter Plates

Order no.	*Product*
62000/ 1000/F	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/ Plasma Automated with 96 Well Filter Plates For 1000 tests, complete with analytical column, trap column, 3PLUS1® calibrators and ***MassCheck***® controls

	Components available separately
62001	Mobile Phase A, 1000 ml
62002	Mobile Phase B, 1000 ml
62003	Precipitation Reagent, 5 ml
62004	Internal Standard, 40 ml
62009	Rinsing Solution, 1000 ml
62057	96 Well Filter Plates, 3 pcs.
62058	Collection Plates, 3 pcs.
62059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
62100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
62110	Trap Column, 1 pc.
62028	3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0222	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0223	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml,

	Multilevel Calibrator and Startup Accessories
62039	6PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 7 x 1 ml
62015	Tuning Mix 25-OH-Vitamin D_3/D_2, Analytes and Internal Standards, 2 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
0221	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0256	***MassCheck***® 25-OH-Vitamin D_3/D_2 Serum Control, Level III (lyoph.), 5 x 1 ml



Automated Workflow

→ Load liquid handling device with samples, reagents, 96 well filter plate and collection plate.
→ Start the **automation routine***.
→ After completion remove collection plate from the liquid handling device, seal with an adhesive seal and transfer to autosampler.
→ Inject 10–50 µl eluate into LC-MS/MS system.

* *Ready to use automation routine provided with the installation by Chromsystems.*

3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
25-OH-vitamin D_3	18.1	32.0	65.0	< LOQ
25-OH-vitamin D_2	14.4	28.4	56.0	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

6PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Calibrator 4* (µg/l)	Calibrator 5* (µg/l)	Calibrator 6* (µg/l)	Blank Calibrator (µg/l)
25-OH-vitamin D_3	9.27	18.5	32.7	66.5	103	140	< LOQ
25-OH-vitamin D_2	5.48	15.6	30.7	61.0	103	105	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® 25-OH-Vitamin D_3/D_2 Serum Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)	Level III Target Value* (µg/l)
25-OH-vitamin D_3	16.1	36.9	104
25-OH-vitamin D_2	16.5	37.1	94.6

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
62028	3PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1ml
62039	6PLUS1® Multilevel Serum Calibrator Set 25-OH-Vitamin D_3/D_2 (lyoph.), 7 x 1ml
0221	*MassCheck*® 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0222	*MassCheck*® 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0223	*MassCheck*® 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml
0256	*MassCheck*® 25-OH-Vitamin D_3/D_2 Serum Control, Level III (lyoph.), 5 x 1 ml

Stability of Serum Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 7 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

7.1.5 Upgrade Set for 3-*epi*-25-OH-Vitamin D_3/D_2

Parameters:
25-OH-vitamin D_3, 3-*epi*-25-OH-vitamin D_3, 25-OH-vitamin D_2, 3-*epi*-25-OH-vitamin D_2.

Order no.	Product
	Upgrade accessories for 62000 and 62000/1000 to analyse the diastereomeric forms of 25-OH-vitamin D_3/D_2
62044	Internal Standard Mix, 40 ml (for 200 tests)
62029	3PLUS1® Multilevel Serum Calibrator Set 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0310	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0311	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml
62120	Analytical Column, 1 pc.
62110/Epi	Trap Column, 1 pc.
62016	Tuning Mix, Analytes and Internal Standards, 1 ml
	Startup Accessories
62001	Mobile Phase A, 1000 ml
62002	Mobile Phase B, 1000 ml
62003	Precipitation Reagent, 5 ml
62009	Rinsing Solution, 1000 ml
3006	Reaction Vials, 100 pcs.
15010	PEEK-Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
15070	Stainless Steel Prefilter Housing, 1 pc.
15071	Stainless Steel Prefilter, 0.5 µm, 5 pcs.
	Controls
0310	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0311	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml

Specifications

Linearity:	up to 250 µg/l
Limit of quantification:	1.0 µg/l (3-*epi*-) 25-OH-vitamin D_2 2.0 µg/l (3-*epi*-) 25-OH-vitamin D_3
Intraassay:	CV < 5 %
Interassay:	CV < 6 %
Analysis time:	8.5–10 min

Pre-analytic Treatment

Specimen: Serum or plasma.
Stability: samples are stable up to 3 days at ambient temperature, or up to one week at +2 to +8 °C. For longer storage periods (up to one month) keep samples frozen below -18 °C.

Sample Preparation

→ Place 100 µl sample/calibrator/***MassCheck***® control into a reaction vial.
→ Add 25 µl Precipitation Reagent.
→ Add 200 µl Internal Standard and vortex 20 s.
→ Incubate 10 min at +4 °C.
→ Centrifuge 5 min at 15 000 x g.
→ Transfer 200 µl supernatant into an autosampler vial.
→ Inject 10–50 µl into the LC-MS/MS system.

HPLC Parameters

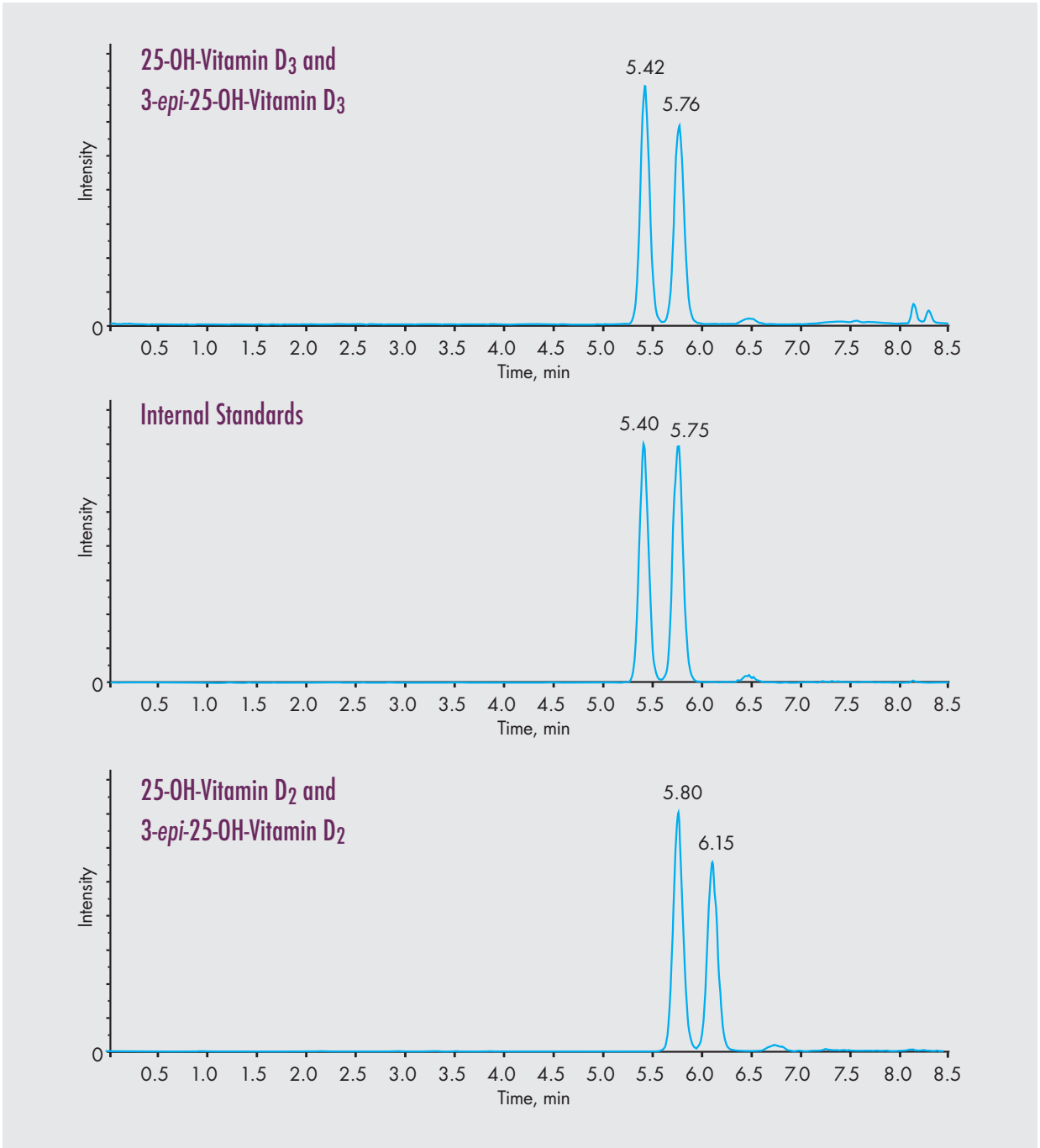
The sample extracts are purified through a trap column and the analytes are subsequently separated on a high-resolution analytical column. A binary gradient pump, a 2-position 6-way switching valve and a column oven are required. Through the use of an additional isocratic pump, the analysis time can be reduced to 8.5 min.

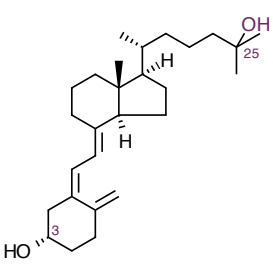
Injection volume:	10–50 µl
Column temperature:	40 °C

MS/MS Parameters

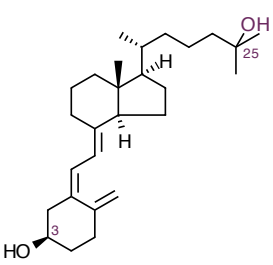
Ionisation: APCI positive
MS/MS mode: MRM

Upgrade Set for 3-*epi*-25-OH-Vitamin D_3/D_2

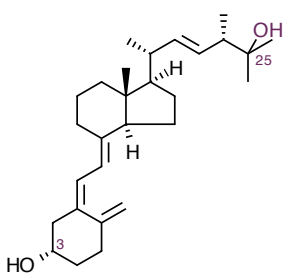




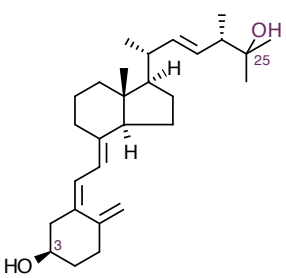
25-OH-Vitamin D_3
$C_{27}H_{44}O_2$
Mw 400.64 g/mol



3-*epi*-25-OH-Vitamin D_3
$C_{27}H_{44}O_2$
Mw 400.64 g/mol



25-OH-Vitamin D_2
$C_{28}H_{44}O_2$
Mw 412.65 g/mol



3-*epi*-25-OH-Vitamin D_2
$C_{28}H_{44}O_2$
Mw 412.65 g/mol

3PLUS1® Multilevel Serum Calibrator Set 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2

Substance	Calibrator 1* (µg/l)	Calibrator 2* (µg/l)	Calibrator 3* (µg/l)	Blank Calibrator (µg/l)
25-OH-vitamin D_3	19.0	33.0	67.2	< LOQ
3-*epi*-25-OH-vitamin D_3	9.66	19.5	29.8	< LOQ
25-OH-vitamin D_2	14.3	28.5	57.2	< LOQ
3-*epi*-25-OH-vitamin D_2	9.14	18.7	28.4	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Controls

Substance	Level I Target Value* (µg/l)	Level II Target Value* (µg/l)
25-OH-vitamin D_3	16.8	40.3
3-*epi*-25-OH-vitamin D_3	16.5	27.5
25-OH-vitamin D_2	16.5	37.2
3-*epi*-25-OH-vitamin D_2	13.2	22.1

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
62029	3PLUS1® Multilevel Serum Calibrator Set 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 (lyoph.), 4 x 1 ml
0310	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0311	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level I (lyoph.), 5 x 1 ml
0312	***MassCheck***® 3-*epi*-25-OH-Vitamin D_3/D_2 and 25-OH-Vitamin D_3/D_2 Serum Control, Level II (lyoph.), 5 x 1 ml

Stability of Serum Calibrators and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 7 days at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

Notes

Vitamin Profiling

Vitamins are essential compounds that cannot be synthesised by the human body in sufficient amounts. Therefore, they are required as vital nutrients that have to be taken up with food. Vitamins play an important role in a variety of biochemical pathways, in the regulation of cell and tissue growth and as antioxidants. Additionally, many of them serve as enzyme cofactors.

With a large array of functions, there is a concomitant range of diseases that are associated with vitamin deficiencies. A lack of vitamins can be identified by the analysis of whole blood or urine from patients, which enables physicians to optimise patients' vitamin intake, for example by changes to the diet or by supplementation, as well as to monitor changes in the vitamin status. Furthermore, increased vitamin levels can also be determined and controlled.

Vitaminstatus

Vitamine sind essentielle Verbindungen, die der menschliche Körper nicht oder in nicht genügendem Umfang selbst bilden kann und deshalb als lebenswichtige Bestandteile mit der Nahrung aufgenommen werden müssen. Sie spielen eine wichtige Rolle bei einer Vielzahl von biochemischen Stoffwechselprozessen, bei der Regulation des Zell- und Gewebewachstums und fungieren als Antioxidantien oder Enzym-Cofaktoren.

Da Vitamine ein so breites Spektrum an Funktionen erfüllen, sind auch eine Vielzahl an Krankheiten mit einer Unterversorgung verbunden. Ein Vitaminmangel kann mittels Blut- oder Urinanalyse bestimmt werden. Dies ermöglicht dem Arzt, beispielsweise durch Änderungen an der Ernährungsweise oder durch Supplementierung die Vitaminaufnahme zu optimieren und den Vitaminstatus kontinuierlich zu beobachten. Erhöhte Vitaminwerte können ebenfalls bestimmt und kontrolliert werden.

8.1 *MassChrom*® Vitamins B_1 and B_6 in Whole Blood

Vitamin B_1 (thiamine) is ingested with food, it is water-soluble and heat sensitive. The active form (thiamine pyrophosphate, TPP) acts as a co-enzyme for a range of enzymatic reactions including the oxidative glucose metabolism – a thiamine deficiency negatively impacts brain and nerve cells, as these cells are highly dependent on the energy generated by glucose. The blood concentration of TPP as the active form is more conclusive than the concentration of total thiamine. Vitamin B_6 is comprised of the pyridoxine-group pyridoxine, pyridoxamine and pyridoxal. It is ingested with food and transferred via several enzymatic conversions into its active form, pyridoxal-5'-phosphate (PLP). PLP acts as a co-factor in amino acid metabolism, in the formation of hemoglobin and other important processes.

This Chromsystems assay allows the determination of the active forms of vitamin B_1 (TPP) and vitamin B_6 (PLP) in whole blood by LC-MS/MS. The sample preparation can be performed very quickly and consists of a simple protein precipitation eliminating the need for derivatisation – ideal for laboratories with higher throughputs. Analytes and interfering substances are effectively separated within 2.5 min, enabling both high selectivity and speed. The two isotopically labelled internal standards for both parameters and our high quality 6PLUS1® calibrators and ***MassCheck***® controls ensure accurate results.

> Fast and easy sample preparation
> No derivatisation necessary
> Robust method with high selectivity
> Short run time of 2.5 minutes

Vitamin B_1 (Thiamin) wird über die Nahrung aufgenommen, ist wasserlöslich und hitzeempfindlich. Die aktive Form (Thiaminpyrophosphat, TPP) ist als Coenzym an einigen enzymatischen Reaktionen beteiligt, wie beispielsweise dem oxidativen Glucoseabbau. Ein Thiaminmangel wirkt sich vor allem auf Gehirn- und Nervenzellen negativ aus, da diese Zellen auf die Energie aus Glucose angewiesen sind. Die Konzentration der aktiven Form TPP im Vollblut ist aussagekräftiger als die des Gesamtthiamins. Vitamin B_6 umfasst die Pyridoxin-Gruppe Pyridoxin, Pyridoxamin und Pyridoxal. Es wird über die Nahrung aufgenommen und über mehrere enzymatische Umwandlungen in die aktive Form Pyridoxal-5'-Phosphat (PLP) überführt. PLP wirkt als Cofaktor beim Aminosäurestoffwechsel, bei der Bildung des Hämoglobins und vielen anderen wichtigen Prozessen.

Dieser Chromsystems Assay ermöglicht die Bestimmung der aktiven Formen von Vitamin B_1 (TPP) und Vitamin B_6 (PLP) im Vollblut mit LC-MS/MS. Die Probenvorbereitung besteht aus einer einfachen Proteinfällung und kann daher sehr schnell durchgeführt werden. Derivatisierung ist nicht notwendig, ideal für Laboratorien mit höherem Probenaufkommen. Die beiden Analyten sowie potentielle Störsubstanzen werden effektiv und schnell innerhalb von 2.5 min getrennt – eine hohe Selektivität ist gleichzeitig gewährleistet. Die isotopenmarkierten internen Standards für beide Parameter sowie unsere 6PLUS1® Kalibratoren und ***MassCheck***® Kontrollen stellen präzise Ergebnisse sicher.

> Schnelle und einfache Probenvorbereitung
> Keine Derivatisierung erforderlich
> Robuste Methode mit hoher Selektivität
> Kurze Laufzeit von 2.5 Minuten

8.1.1 Vitamins B_1 and B_6 in Whole Blood

Parameters:
thiamine pyrophosphate (TPP, vitamin B_1), pyridoxal-5'-phosphate (PLP, vitamin B_6).

Order no.	Product
87000	***MassChrom***® Vitamins B_1 and B_6 in Whole Blood with Reaction Vials For 480 tests
	Components available separately
87001	Mobile Phase A, 700 ml
87002	Mobile Phase B, 350 ml
87046	Internal Standard Set, consisting of: Internal Standard Mix, 5 x 8 ml (lyoph.) Reconstitution Buffer, 5 x 8.5 ml
87005	Precipitation Reagent, 85 ml
87009	Rinsing Solution, 500 ml
33008	Reaction Vials, 2.0 ml, 100 pcs.
	Startup Accessories
87100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
87015	Tuning Mix, Analytes and Internal Standards, 1 ml
87018	Dilution Buffer, 100 ml
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0410	PP Screw-on Caps, pierceable silicone/PTFE septa, 1.0 mm, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
J0505	Micro-inserts for autosampler vials, clear glass, flat bottom, 100 pcs.
	Multilevel Calibrator and Controls
87039	6PLUS1® Multilevel Whole Blood Calibrator Set Vitamins B_1 and B_6 (lyoph.), 7 x 0.5 ml
0273	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level I, 5 x 1 ml
0274	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level II, 5 x 1 ml
0275	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level III, 5 x 1 ml

Specifications

Linearity:	850 µg/l TPP 1000 µg/l PLP
Limit of quantitation:	2.1 µg/l TPP 1.2 µg/l PLP
Intraassay:	< 7 %
Interassay:	< 10 %
Analysis time:	2.5 min

Pre-analytic Treatment

Specimen: whole blood.

Sample Preparation

→ Pipette 40 µl sample/calibrator/***MassCheck***® control into a reaction vial.
→ Add 80 µl Internal Standard, mix briefly (vortex).
→ Add 350 µl Precipitation Reagent, mix 1 min (vortex) and centrifuge.
→ Transfer supernatant into an amber autosampler vial.
→ Dilute supernatant with Dilution Buffer, if necessary.
→ Inject 15 µl into the LC-MS/MS system.

LC-MS/MS Parameters

Injection volume:	15 µl
Flow rate:	0.5 ml/min
Column temperature:	30 °C
Ionisation:	ESI positive
MS/MS mode:	MRM

8.1.2 Vitamins B_1 and B_6 in Whole Blood with 96 Deep Well Plates

Parameters:
thiamine pyrophosphate (TPP, vitamin B_1), pyridoxal-5'-phosphate (PLP, vitamin B_6).

Order no.	Product
87000/ DWP	***MassChrom***® Vitamins B_1 and B_6 in Whole Blood With 96 Deep Well Plates For 480 tests
	Components available separately
87001	Mobile Phase A, 700 ml
87002	Mobile Phase B, 350 ml
87046	Internal Standard Set, consisting of: Internal Standard Mix, 5 x 8 ml (lyoph.) Reconstitution Buffer, 5 x 8.5 ml
87005	Precipitation Reagent, 85 ml
87009	Rinsing Solution, 500 ml
87057	96 Deep Well Plates, 3 pcs.
87058	Collection Plates, 3 pcs.
87059	Pierceable Adhesive Seals for 96 Well Plates, 3 pcs.
	Startup Accessories
87100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
87015	Tuning Mix, Analytes and Internal Standards, 1 ml
87018	Dilution Buffer, 100 ml
	Multilevel Calibrator and Controls
87039	6PLUS1® Multilevel Whole Blood Calibrator Set Vitamins B_1 and B_6 (lyoph.), 7 x 0.5 ml
0273	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level I, 5 x 1 ml
0274	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level II, 5 x 1 ml
0275	***MassCheck***® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level III, 5 x 1 ml

Specifications

Linearity:	850 µg/l TPP 1000 µg/l PLP
Limit of quantitation:	2.1 µg/l TPP 1.2 µg/l PLP
Intraassay:	< 7 %
Interassay:	< 10 %
Analysis time:	2.5 min

Pre-analytic Treatment

Specimen: whole blood.

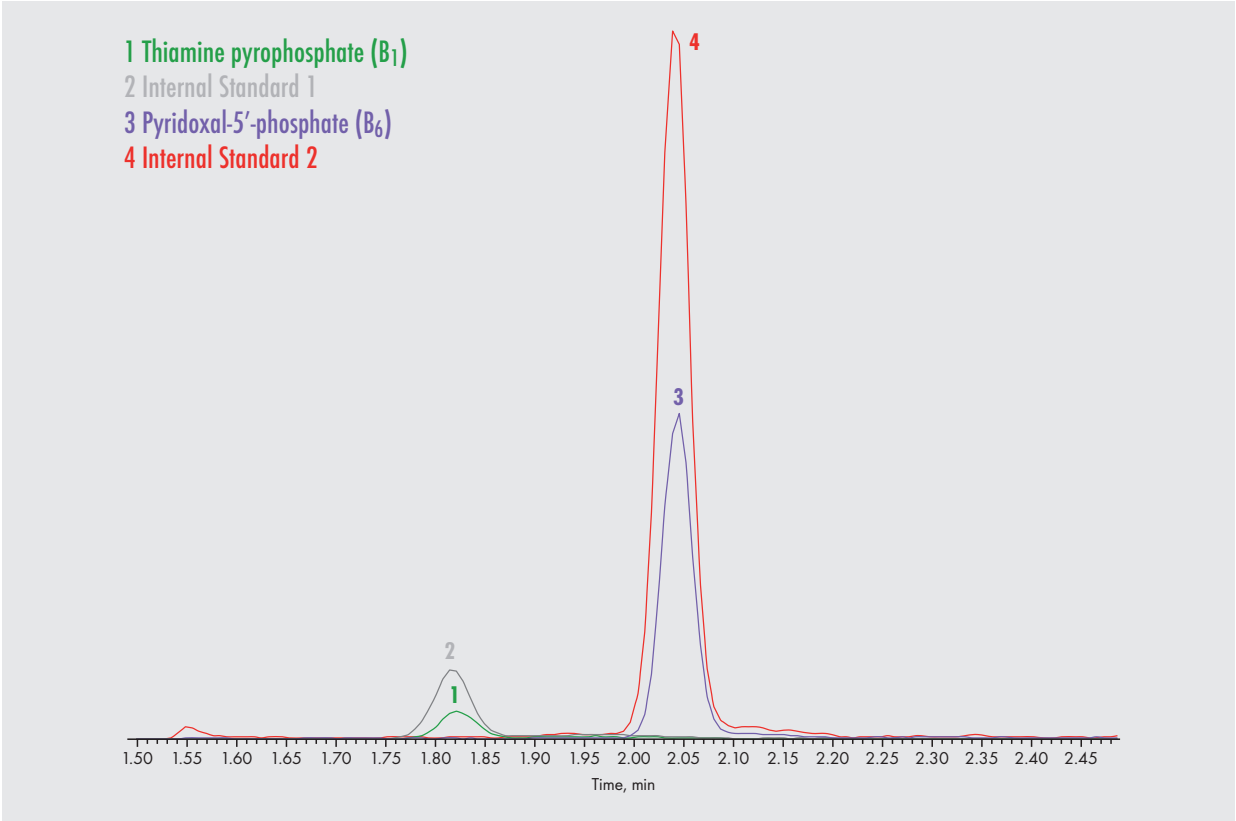
Sample Preparation

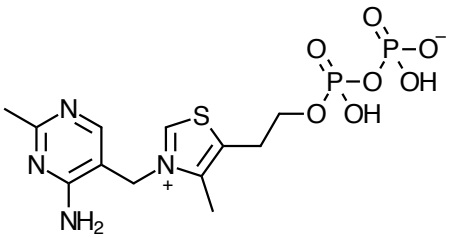
→ Pipette 40 µl sample/calibrator/***MassCheck***® control into a deep well plate.
→ Add 80 µl Internal Standard, shake briefly.
→ Add 350 µl Precipitation Reagent, shake 1 min and centrifuge.
→ Transfer supernatant into a collection plate.
→ Dilute supernatant with Dilution Buffer, if necessary and seal with a pierceable adhesive seal.
→ Inject 15 µl into the LC-MS/MS system.

LC-MS/MS Parameters

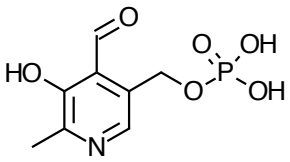
Injection volume:	15 µl
Flow rate:	0.5 ml/min
Column temperature:	30 °C
Ionisation:	ESI positive
MS/MS mode:	MRM

Vitamins B_1 and B_6 in Whole Blood





Thiamine pyrophosphate (TPP)
$C_{12}H_{18}N_4O_7P_2S$
Mw 424.30 g/mol



Pyridoxal-5′-phosphate (PLP)
$C_8H_{10}NO_6P$
Mw 247.14 g/mol

6PLUS1® Multilevel Whole Blood Calibrator Set Vitamins B_1 and B_6

Substance	Calibrator 1* µg/l	Calibrator 2* µg/l	Calibrator 3* µg/l	Calibrator 4* µg/l	Calibrator 5* µg/l	Calibrator 6* µg/l	Low Level Calibrator µg/l
Thiamine pyrophosphate (TPP)	22.6	36.3	52.7	69.8	200	467	9.72
Pyridoxal-5'-phosphate (PLP)	11.9	22.4	31.6	41.6	199	502	5.03

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Vitamins B_1 and B_6 Whole Blood Controls

Substance	Unit	Target Value Level I*	Target Value Level II*	Target Value Level III*
Thiamine pyrophosphate (TPP)	µg/l	26.8	63.0	99.0
Pyridoxal-5'-phosphate (PLP)	µg/l	17.0	36.6	55.2

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
87039	6PLUS1® Multilevel Whole Blood Calibrator Set Vitamins B_1 and B_6 (lyoph.), 7 x 0.5 ml
0273	***Mass****Check*® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level I, 5 x 1 ml
0274	***Mass****Check*® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level II, 5 x 1 ml
0275	***Mass****Check*® Vitamins B_1 and B_6 Whole Blood Control (lyoph.), Level III, 5 x 1 ml

Stability of Whole Blood Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C

8.2 *MassChrom*® Methylmalonic Acid in Plasma/Serum and Urine

CE IVD

Methylmalonic acid (MMA) is an intermediate of amino acid metabolism which results from the conversion of propionyl-coenzyme A to succinyl-coenzyme A in a vitamin B_{12}-dependent reaction, and is regarded as an early, sensitive biomarker of vitamin B_{12}-deficiency. Vitamin B_{12}-insufficiency leads to high concentrations of MMA in plasma, serum and urine.

This assay allows the specific determination of methylmalonic acid in all three matrices. The use of special clean-up tubes enables the removal of interfering compounds quickly and effectively. The isobaric succinic acid is separated chromatographically to prevent false-positive test results. To ensure accurate quantification a stable, isotope-labelled internal standard is used. Matrix effects are minimised and the precision and robustness of the method are optimised. The 3PLUS1® multilevel plasma and urine calibrators ensure precision of the results.

> Fast and easy sample preparation
> Chromatographic separation of succinic acid
> 3PLUS1® Multilevel Calibrator Sets

Methylmalonsäure (MMA) ist ein Intermediat des Aminosäurenstoffwechsels, das bei der Umsetzung von Propionyl-Coenzym A zu Succinyl-Coenzym A in einer Vitamin-B_{12}-abhängigen Reaktion entsteht und als früher sensitiver Biomarker für einen Vitamin-B_{12}-Mangel gilt. Eine Vitamin-B_{12}-Unterversorgung führt zu hohen MMA-Konzentrationen im Plasma, Serum und Urin.

Dieser Test erlaubt die spezifische Bestimmung von Methylmalonsäure im Plasma, Serum und Urin. Durch den Einsatz von speziellen Clean-Up-Tubes werden störende Komponenten schnell und effektiv entfernt. Die isobare Bernsteinsäure wird chromatographisch abgetrennt, um falsch positive Analysenergebnisse zu verhindern. Zur sicheren Quantifizierung wird ein stabiler, isotopenmarkierter interner Standard verwendet. Matrixeffekte sind minimiert, die Präzision und Robustheit der Methode optimiert. Die 3PLUS1® Multilevel Plasma- und Urinkalibratoren gewährleisten eine hohe Genauigkeit der Ergebnisse.

> Schnelle und einfache Probenvorbereitung
> Chromatographische Abtrennung von Bernsteinsäure
> 3PLUS1® Multilevel Calibrator Sets

8.2.1 MMA in Plasma/Serum

Parameter:
methylmalonic acid

Order no.	Product
64000	***MassChrom***® Methylmalonic Acid (MMA) in Plasma/Serum For 400 tests
	Components available separately
64001	Mobile Phase A, 750 ml
64002	Mobile Phase B, 400 ml
64009	Rinsing Solution, 400 ml
64004/P	Internal Standard Methylmalonic Acid in Plasma/Serum, 4 x 5 ml
64008	MMA Clean-Up Tubes, 100 pcs.
	Startup Accessories
64100	***MassChrom***® Analytical Column, equilibrated, with test chromatogram, 1 pc.
64015	Tuning Mix Methylmalonic Acid and Internal Standard, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
	Multilevel Calibrator and Controls
64028	3PLUS1® Multilevel Plasma Calibrator Set Methylmalonic Acid (lyoph.), 4 x 1 ml
0313	***MassCheck***® Methylmalonic Acid Plasma Control (lyoph.), Bi-Level I + II, 2 x 5 x 1 ml
0314	***MassCheck***® Methylmalonic Acid Plasma Control (lyoph.), Level I, 5 x 1 ml
0315	***MassCheck***® Methylmalonic Acid Plasma Control (lyoph.), Level II, 5 x 1 ml

Specifications

Linearity:	3.5–600 µg/l
Limit of quantification:	3.5 µg/l
Intraassay:	CV = 3.1–6.6 %
Interassay:	CV = 3.2–6.7 %
Recovery:	102–114 %
Analysis time:	3.5 min

Pre-analytic Treatment

Specimen: plasma or serum.
Stability: samples are stable for 7 days at ambient temperature. For longer storage they have to be cooled.
At +5 °C the samples are stable for 6 months, at -20 °C for 12 months.

Sample Preparation

→ Pipette 100 µl sample/calibrator/***MassCheck***® control into clean-up tubes.
→ Add 50 µl Internal Standard and mix (vortex) briefly.
→ Centrifuge 10 min at 14 000 x g.
→ Transfer filtrate into an autosampler vial.
→ Inject 10–20 µl into the LC-MS/MS system.

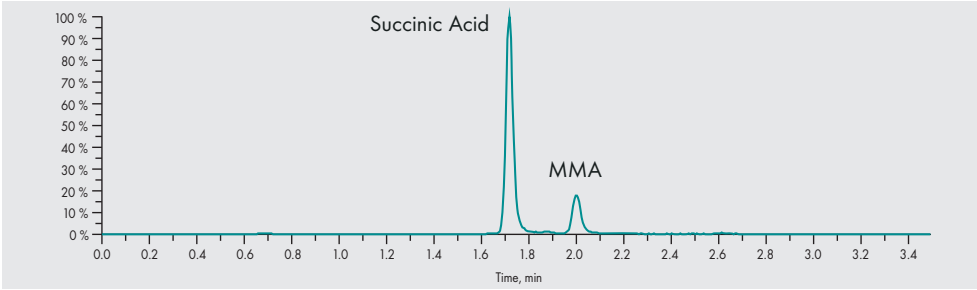
LC-MS/MS Parameters

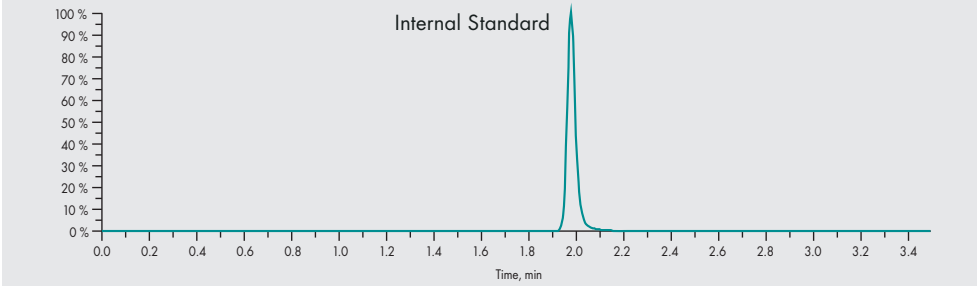
Injection volume:	10–20 µl
Flow rate:	0.7 ml/min
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI negative
MS/MS mode:	MRM

Gradient:
0 min 100 % Mobile Phase A
2.5 min 0 % Mobile Phase A, 100 % Mobile Phase B
2.51–3.5 min 100 % Mobile Phase A

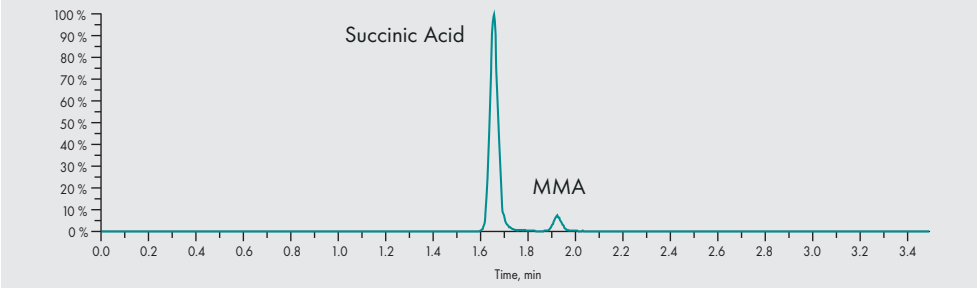
MMA in Plasma/Serum

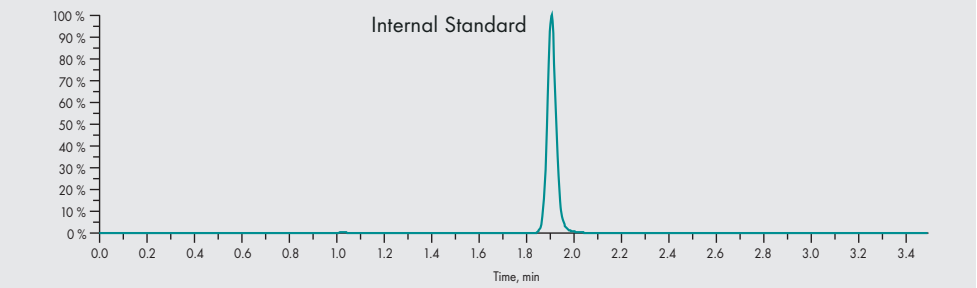
Plasma calibrator, Level II

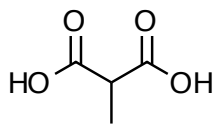
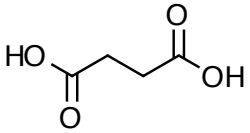




Plasma sample with normal concentration of MMA





Substance	Normal range in serum/plasma (nmol/l) [20]	Mw (g/mol)	Formula	Structure
Methylmalonic acid	50–440	118.09	$C_4H_6O_4$	
Succinic acid	–	118.09	$C_4H_6O_4$	

3PLUS1® Multilevel Plasma Calibrator Set Methylmalonic Acid

Substance	Calibrator 1* µg/l	Calibrator 2* µg/l	Calibrator 3* µg/l	Low Level Calibrator* µg/l
Methylmalonic acid	11.4	81.7	180	3.64

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Methylmalonic Acid Plasma Controls

Substance	Unit	Level I Target Value*	Level II Target Value*
Methylmalonic acid	µg/l nmol/l	23.5 199	39.8 337

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
64028	3PLUS1® Multilevel Plasma Calibrator Set Methylmalonic Acid (lyoph.), 4 x 1 ml
0313	*MassCheck®* Methylmalonic Acid Plasma Control, Bi-Level I + II (lyoph.), 2 x 5 x 1 ml
0314	*MassCheck®* Methylmalonic Acid Plasma Control, Level I (lyoph.), 5 x 1 ml
0315	*MassCheck®* Methylmalonic Acid Plasma Control, Level II (lyoph.), 5 x 1 ml

Stability of Plasma Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date at -18 °C
> Reconstituted up to 2 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 2 months below -18 °C

8.2.2 MMA in Urine

Parameter:
methylmalonic acid

Order no.	Product
	Urine Set for 200 tests
64029	3PLUS1® Multilevel Urine Calibrator Set Methylmalonic Acid (lyoph.), 4 x 2 ml
64007	Dilution Buffer Urine, 75 ml
64044/U	Internal Standard Methylmalonic Acid in Urine, 5 ml
33006	Reaction Vials, 100 pcs.
	Startup Accessories
64100	***MassChrom***® Analytical Column, equilibrated, with test chromatogram, 1 pc.
64001	Mobile Phase A, 750 ml
64002	Mobile Phase B, 400 ml
64009	Rinsing Solution, 400 ml
64015	Tuning Mix Methylmalonic Acid and Internal Standard, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
	Controls
0316	***MassCheck***® Methylmalonic Acid Urine Control, Bi-Level (I + II) (lyoph.), 2 x 5 x 2 ml
0317	***MassCheck***® Methylmalonic Acid Urine Control, Level I (lyoph.), 5 x 2 ml
0318	***MassCheck***® Methylmalonic Acid Urine Control, Level II (lyoph.), 5 x 2 ml

Specifications

Linearity:	86–9500 µg/l
Limit of quantification:	86 µg/l
Intraassay:	CV = 1.3–3.9 %
Interassay:	CV = 2.4–4.2 %
Recovery:	98–102 %
Analysis time:	3.5 min

Pre-analytic Treatment

Specimen: urine.
Stability: samples are stable for 24 hours at ambient temperature. For longer periods (3 months) place the samples in the refrigerator (+2 to +8 °C) or freezer (below -18 °C).

Sample Preparation

→ Pipette 200 µl sample/calibrator/***MassCheck***® control into transparent reaction vials.
→ Add 25 µl Internal Standard and mix 10 s (vortex).
→ Dilute an aliquot of the mixture with Dilution Buffer.
→ Inject 10–20 µl into the LC-MS/MS system.

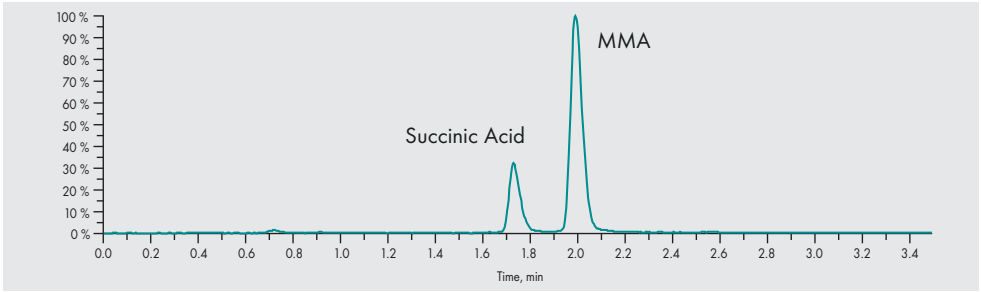
LC-MS/MS Parameters

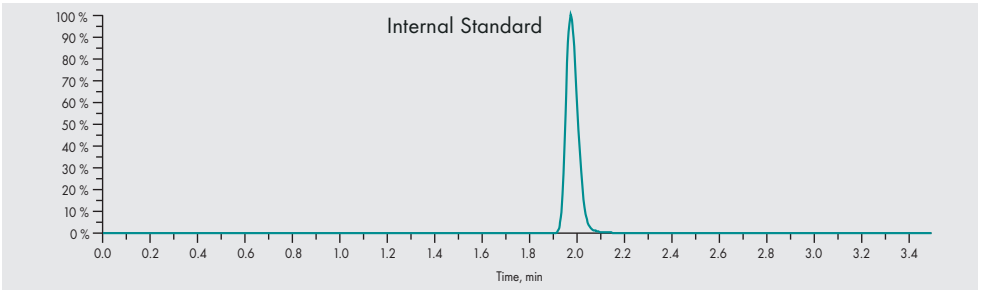
Injection volume:	10–20 µl
Flow rate:	0.7 ml/min
Column temperature:	ambient (~ 25 °C)
Ionisation:	ESI negative
MS/MS mode:	MRM

Gradient:
0 min 100 % Mobile Phase A
2.5 min 0 % Mobile Phase A, 100 % Mobile Phase B
2.51–3.5 min 100 % Mobile Phase A

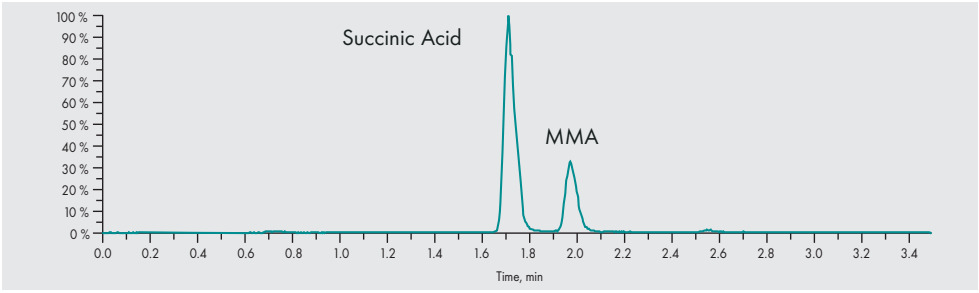
MMA in Urine

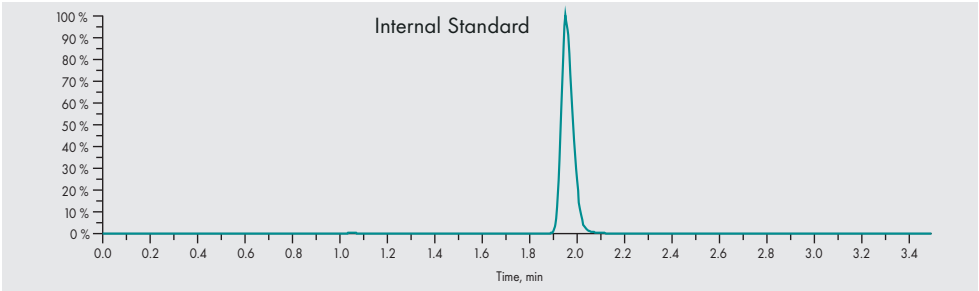
Urine calibrator, Level II

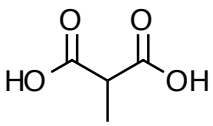
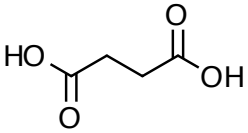




Urine sample with normal concentration of MMA





Substance	Normal range in urine (mmol/mol creatinin) [21]	Mw (g/mol)	Formula	Structure
Methylmalonic acid	0.58–3.56	118.09	$C_4H_6O_4$	
Succinic acid	–	118.09	$C_4H_6O_4$	

3PLUS1® Multilevel Urine Calibrator Set Methylmalonic Acid

Substance	Calibrator 1* mg/l	Calibrator 2* mg/l	Calibrator 3* mg/l	Low Level Calibrator* mg/l
Methylmalonic acid	0.69	2.91	4.98	0.27

** Please check packaging leaflet for specific lot concentrations*

MassCheck® Methylmalonic Acid Urine Controls

Substance	Unit	Level I Target Value*	Level II Target Value*
Methylmalonic acid	mg/l µmol/l	1.10 9.28	3.62 30.6

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
64029	3PLUS1® Multilevel Urine Calibrator Set Methylmalonic Acid (lyoph.), 4 x 2 ml
0316	*MassCheck®* Methylmalonic Acid Urine Control (lyoph.), Bi-Level I + II, 2 x 5 x 2 ml
0317	*MassCheck®* Methylmalonic Acid Urine Control (lyoph.), Level I, 5 x 2 ml
0318	*MassCheck®* Methylmalonic Acid Urine Control (lyoph.), Level II, 5 x 2 ml

Stability of Urine Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date at -18 °C
> Reconstituted up to 2 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 2 months below -18 °C

Biomarker for Alcohol Abuse

Alcohol has been produced and consumed by humans for many centuries and is today one of the most widely used recreational drugs in the world. However, alcohol consumption also contributes to a number of diseases and injury-related health conditions and can lead to alcohol addiction. For 2012, the World Health Organization (WHO) estimates that about 3.3 million deaths or 5.9 % of all global deaths were attributable to alcohol consumption. In the determination of alcohol consumption, the clinical laboratory plays an important role to analyse the level of ethanol and its metabolites in the blood. Legal testing helps to identify alcohol consumption in the context of a variety of different laws, such as underage drinking or traffic accidents.

9

Biomarker für Alkoholmissbrauch

Alkohol gehört heute zu den meistverbreiteten Drogen und wird schon seit jeher produziert und konsumiert. Er begünstigt jedoch auch die Entstehung vieler Krankheiten und Verletzungen und kann zur Abhängigkeit führen. Die WHO (World Health Organization) schätzt, dass allein im Jahr 2012 rund 3,3 Millionen Tote oder 5,9 % aller weltweiten Todesfälle auf Alkoholkonsum zurückzuführen sind. Dem klinischen Labor kommt dabei eine wichtige Rolle bei der Bestimmung des Alkoholkonsums zu und analysiert die Menge des Ethanols und seiner Metaboliten im Blut. Eine Kontrolle des Alkoholkonsums wird oft gerichtlich angeordnet, um die Einhaltung verschiedener Gesetze zu prüfen, wie zum Beispiel beim Alkoholausschank an Minderjährige oder bei Verkehrsunfällen.

9.1 *MassChrom*® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine

CE IVD

EtG/EtS

Alcohol is one of the most frequently consumed drugs that is quickly absorbed in the small intestine of the human body. It is metabolised in the liver to acetaldehyde and then to acetic acid. The elimination is very rapid, subsequently, the detection time is limited to approximately 12 hours. Typically, less than 0.1 % of the consumed ethanol is present as the glucurono- or sulfo-conjugated configuration, which is excreted as ethyl glucuronide (EtG) and ethyl sulfate (EtS), both detectable for a sustained period in comparison to ethanol. Thus, EtG and EtS close the gap between short-term markers (i.e. ethanol itself) and long-term markers such as CDT.

The ***MassChrom***® assay from Chromsystems allows the reliable determination of EtG and EtS from urine with robustness and precision. The assay is validated according to the guidelines of the GTFCh (German Society of Toxicological and Forensic Chemistry) for quality assurance and enables the determination of both parameters with one sample preparation and one single injection with an analysis time of 6 minutes. The straightforward and efficient sample preparation consists of a single pipetting step that includes the instrument-specific dilution. The human-matrix based 6PLUS1® Multilevel Calibrator Set and ***MassCheck***® controls ensure precision and accuracy of results.

> Very high column stability
> Validated according to GTFCh guidelines
> One step sample prep
> Reliable determination also near cut-off values

Alkohol ist eine der am häufigsten konsumierten Drogen und wird im Dünndarm des menschlichen Körpers schnell absorbiert. In der Leber wird der Alkohol zu Acetaldehyd und anschließend in Essigsäure abgebaut. Die Exkretion erfolgt sehr schnell, weshalb die Detektionszeit des Alkohols selbst auf etwa 12 Stunden begrenzt ist. Weniger als 0,1 % des konsumierten Alkohols wird aber glukuroniert bzw. sulfokonjugiert und als Ethylglukuronid (EtG) und Ethylsulfat (EtS) ausgeschieden. Diese sind für längere Zeiträume als der Ethanol detektierbar, was sie zu zuverlässigen und spezifischen Biomarkern für den Alkoholkonsum macht. EtG und EtS schließen damit die Lücke von Kurzzeitmarkern wie dem Ethanol und Langzeitmarkern wie dem CDT.

Der ***MassChrom***® Test von Chromsystems ermöglicht die zuverlässige und präzise Bestimmung von Ethylglucoronid und Ethylsulfat im Urin. Der Assay wurde gemäß den Richtlinien der Gesellschaft für Toxikologische und Forensische Chemie (GTFCH) umfassend validiert und ermöglicht die Bestimmung beider Parameter mit einer Probenvorbereitung und in einem einzigen Lauf von 6 Minuten. Die einfache und effiziente Probenvorbereitung besteht aus einem Pipettierschritt, der die geräteabhängige Verdünnung beinhaltet. Das Humanmatrix-basierte 6PLUS1® Multilevel Calibrator Set und die ***MassCheck***® Kontrollen stellen die Präzision und Exaktheit der Ergebnisse sicher.

> Sehr hohe Säulenstabilität
> Validiert nach den Richtlinien der GTFCh
> Probenvorbereitung mit nur einem Pipettierschritt
> Zuverlässige Bestimmung auch im Cut-off-Bereich

MassChrom® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine

Parameters:
ethyl glucuronide (EtG), ethyl sulfate (EtS).

Order no.	Product
69000	***MassChrom***® Ethyl Glucuronide and Ethyl Sulfate in Urine For 400 tests
	Components available separately
69001	Mobile Phase A, 900 ml
69002	Mobile Phase B, 520 ml
69004	Internal Standard Mix, 2 x 5 ml
69005	Dilution Buffer, 100 ml
69009	Rinsing Solution, 500 ml
J0601	Autosampler Vials, screw neck, amber glass, 1.5 ml, 100 pcs.
J0504	PE Screw-on Caps, rubber/PTFE septa, 9 mm, 100 pcs.
	Startup Accessories
69100	Analytical Column, equilibrated, with test chromatogram, 1 pc.
69015	Tuning Mix ***MassChrom***® Ethyl Glucuronide, Ethyl Sulfate, Analytes and Internal Standards, 1 ml
69012	System Check Solution ***MassChrom***® Ethyl Glucuronide, Ethyl Sulfate, 1 ml
15010	PEEK Prefilter Housing, 1 pc.
15011	PEEK-encased Prefilter, 2 µm, 5 pcs.
	Multilevel Calibrator and Controls
69039	6PLUS1® Multilevel Urine Calibrator Set ***MassChrom***® Ethyl Glucuronide, Ethyl Sulfate (lyoph.), 7 x 1 ml
0367	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level I (lyoph.), 5 x 1 ml
0368	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level II (lyoph.), 5 x 1 ml
0369	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level III (lyoph.), 5 x 1 ml

Specifications

Linearity:	EtG up to 250000 µg/l, EtS up to 15000 µg/l
Limit of quantification:	EtG 35 µg/l EtS 20 µg/l
Intraassay:	CV < 3 %
Interassay:	CV < 4 %
Recovery:	EtG 97–100 % EtS 95–98 %
Analysis time:	6 min

Pre-analytic Treatment

Specimen: urine.
Stability: samples are stable up to 5 days at +2 to +8 °C. For longer storage up to 3 months keep samples frozen below -18 °C.

Sample Preparation

→ Place 50 µl sample/calibrator/***MassCheck***® control in autosampler vial.
→ Dilute as required by the instrument with master mixture* (minimum dilution of 1:5).
→ Vortex briefly.
→ Inject up to 20 µl into the LC-MS/MS system.

***Preparation of master mixture (example):**
for 100 samples and a target dilution of 1:10 add 2.5 ml Internal Standard Mix to 42.5 ml Dilution Buffer.

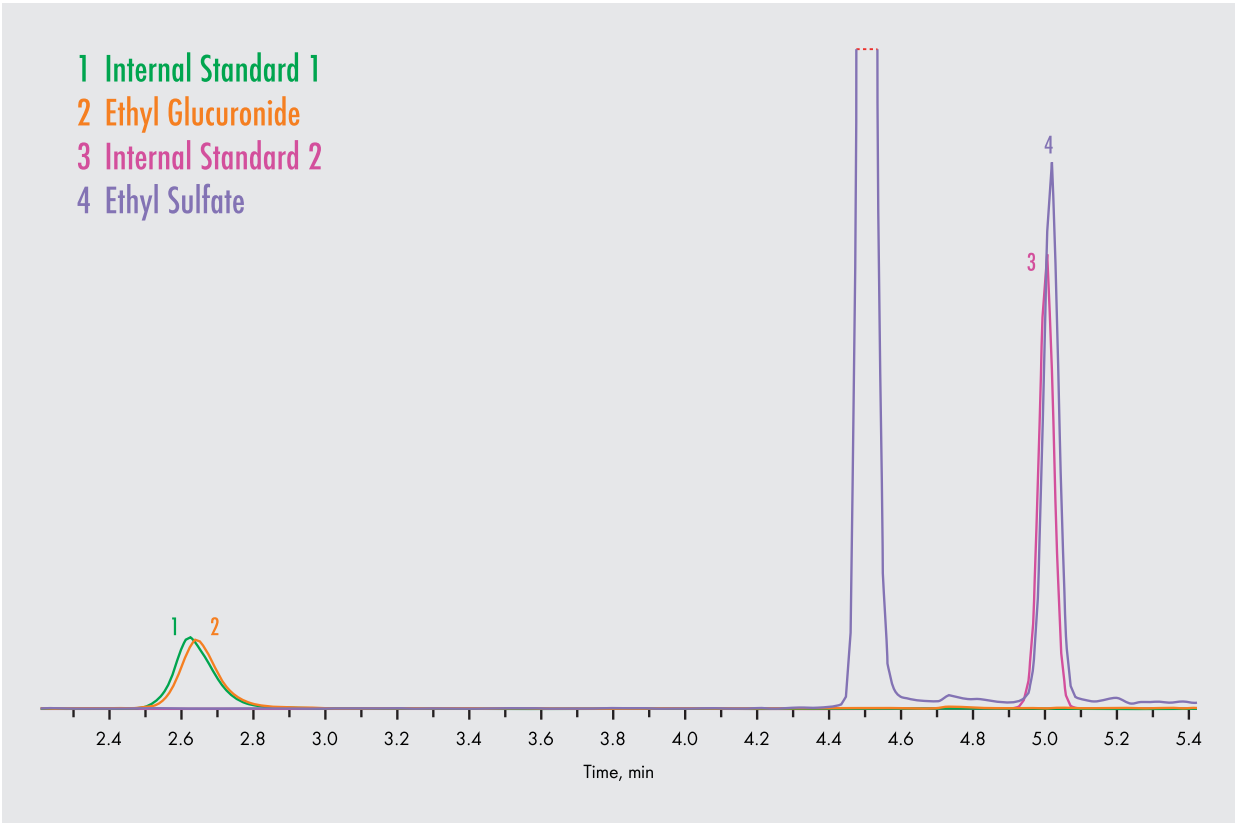
LC-MS/MS Parameters

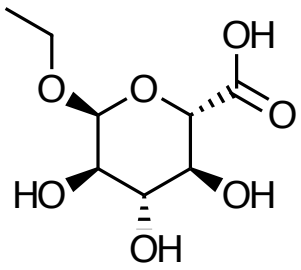
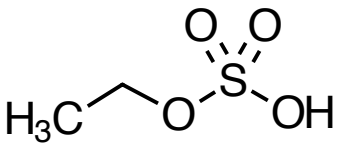
Injection volume:	up to 20 µl
Flow rate:	0.5–1.0 ml/min
Ionisation:	ESI negative
MS/MS mode:	MRM

Gradient:
0.00–3.00 min, 0 % Mobile Phase B
3.01–5.50 min, 100 % Mobile Phase B
5.51–6.00 min, 0 % Mobile Phase B

We recommend setting the scan time to a value that allows a minimum of 10 data points over the whole peak width.

MassChrom® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine



Substance	Mw (g/mol)	Formula	Structure
Ethyl glucuronide	222.19	$C_8H_{14}O_7$	
Ethyl sulfate	126.13	$C_2H_6O_4S$	

6PLUS1® Multilevel Urine Calibrator Set Ethyl Glucuronide, Ethyl Sulfate

Substance	Calibrator 1* µg/l	Calibrator 2* µg/l	Calibrator 3* µg/l	Calibrator 4* µg/l	Calibrator 5* µg/l	Calibrator 6* µg/l	Blank Calibrator µg/l
Ethyl glucuronide	73.5	122	572	1454	6705	11943	< LOQ
Ethyl sulfate	39.2	75.0	313	811	1758	3063	< LOQ

** Please check packaging leaflet for specific lot concentrations*
LOQ = limit of quantification

MassCheck® Ethyl Glucuronide and Ethyl Sulfate Urine Controls

Substance	Unit	Target Value Level I*	Target Value Level II*	Target Value Level III*
Ethyl glucuronide	µg/l	99.7	490	1976
Ethyl sulfate	µg/l	59.3	236	1148

** Please check packaging leaflet for specific lot concentrations*

Order no.	Product
69039	6PLUS1® Multilevel Urine Calibrator Set ***MassChrom***® Ethyl Glucuronide, Ethyl Sulfate (lyoph.), 7 x 1 ml
0367	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level I (lyoph.), 5 x 1 ml
0368	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level II (lyoph.), 5 x 1 ml
0369	***MassCheck***® Ethyl Glucuronide, Ethyl Sulfate Urine Control, Level III (lyoph.), 5 x 1 ml

Stability of Urine Calibrator and Controls

Please check instruction manual for detailed information

> Stable to expiry date below -18 °C
> Reconstituted up to 4 weeks at +2 °C to +8 °C
> Reconstituted aliquots up to 3 months below -18 °C

Parameter Index

Parameter	Assay	Kit page	Calibrator page	Controls page
2C-B	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
2C-I	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Acebutolol	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Acetylcodeine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Acetyltyrosine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Adenosylhomocysteine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Adrenaline (Epinephrine)	***MassChrom***® Catecholamines, Free Metanephrines, Serotonin in Urine	75–78	79	79
Ajmaline	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Alanine	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
β-Alanine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Aldosterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Allobarbital	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Alprazolam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
α-Aminoadipic acid	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
α-Aminobutyric acid	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
β-Aminobutyric acid	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
γ-Aminobutyric acid	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
7-Aminoclonazepam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
7-Aminoflunitrazepam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
7-Aminonitrazepam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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Amisulpride	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Amitriptyline	***MassTox***® TDM Series A Tricyclic Antidepressants TCA 1	174–175	176	176
Amobarbital	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Amphetamine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Amprenavir	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
Androstenedione	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Anserine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Aprindine	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Arginine	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Argininosuccinic acid	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Aripiprazole	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
Asparagine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Aspartic acid	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Atazanavir	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
Atenolol	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Atomoxetine	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Barbital	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
BDB	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Benperidol	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Benzoylecgonine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Bisoprolol	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
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Parameter	Assay	Kit page	Calibrator page	Controls page
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Buprenorphine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Bupropion	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Butalbital	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Butylone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Carbamazepine	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Carbamazepine-10,11-epoxide	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Carbamazepine-diol	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Cariprazine	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Carnitine	MassChrom® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
Carnosin	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Cathinone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Chlordiazepoxide	***MassTox***® TDM Series A Benzodiazepines 1	148–150	151	151
	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Chlorpromazine	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Chlorprothixene	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Citalopram	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
Citrulline	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Clobazam	***MassTox***® TDM Series A Benzodiazepines 1	148–150	151	151
	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Clomethiazole	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
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Clonazepam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Clozapine	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
Cocaethylene	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Cocaine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Codeine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Corticosterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Cortisol	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
	MassChrom® Cortisol, Cortisone in Saliva	66–67	68	68
Cortisone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
	MassChrom® Cortisol, Cortisone in Saliva	66–67	68	68
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Cystathionine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Cysteine-S-sulfate	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Cystine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
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Debutyldronedarone	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
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Dehydroepiandrosterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Dehydroepiandrosterone sulfate	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Delavirdine	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
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11-Deoxycorticosterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
11-Deoxycortisol	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
21-Deoxycortisol	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
Desalkylflurazepam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Desethylamiodarone	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Desipramine	***MassTox***® TDM Series A Tricyclic Antidepressants TCA 1	174–175	176	176
Desmethylcitalopram	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
Desmethylclozapine	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
Desmethyldosulepin	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Desmethylflunitrazepam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Desmethylfluoxetine	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
Desmethylmesuximide	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Desmethylmirtazapine	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
Desmethylolanzapine	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
Desmethylsertraline	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
O-Desmethyltramadol	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
O-Desmethylvenlafaxine	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
DHEA	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
DHEA-S	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
DHT	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
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threo-Dihydrobupropion	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Dihydrocodeine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Dihydrotestosterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
10,11-Dihydroxycarbamazepine	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Diltiazem	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Disopyramide	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Dopamine	***MassChrom***® Catecholamines, Free Metanephrines, Serotonin in Urine	75–78	79	79
Dosulepin	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Doxepin	***MassTox***® TDM Series A Tricyclic Antidepressants TCA 1	174–175	176	176
Dronedarone	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Duloxetine	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
EDDP	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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Elvitegravir	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
3-*epi*-25-OH-vitamin D_2	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
3-*epi*-25-OH-vitamin D_3	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
Epinephrine (Adrenaline)	***MassChrom***® Catecholamines, Free Metanephrines, Serotonin in Urine	75–78	79	79
Estazolam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Estradiol	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64
EtG (Ethyl glucuronide)	***MassChrom***® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine	225–226	227	227
Ethanolamine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Ethosuximide	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Ethyl glucuronide (EtG)	***MassChrom***® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine	225–226	227	227

Parameter	Assay	Kit page	Calibrator page	Controls page
Ethyl sulfate (EtS)	***MassChrom***® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine	225–226	227	227
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EtS (Ethyl sulfate)	***MassChrom***® Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) in Urine	225–226	227	227
Everolimus	***MassTox***® Immunosuppressants in Whole Blood	183–189	190	191
Felbamate	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Fentanyl	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Flecainide	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Fluconazole	***MassTox***® TDM Series A Antimycotic Drugs	143–145	146	146
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Flunarizine	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Flunitrazepam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
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Fluphenazine	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Flurazepam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
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	MassTox® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Gallopamil	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Glutamic acid	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Glutamine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Glycine	***MassChrom***® Amino Acids and Acylcarnitines from Dried Blood	42–49	–	50–51
	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Guanfacine	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Haloperidol	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
Hexobarbital	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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Histidine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Homocitrulline	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Homocystine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Homovanillic acid (HVA)	***MassChrom***® VMA, HVA, 5-HIAA in Urine	86–88	89	89
HVA (Homovanillic acid)	***MassChrom***® VMA, HVA, 5-HIAA in Urine	86–88	89	89
Hydrocodone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Hydromorphone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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3-Hydroxybromazepam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Hydroxybupropion	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
10-Hydroxycarbamazepine	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
5-Hydroxyindoleacetic acid (5-HIAA)	***MassChrom***® VMA, HVA, 5-HIAA in Urine	86–88	89	89
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Hydroxylysine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
1-Hydroxymidazolam (a-OH-midazolam)	***MassTox***® TDM Series A Benzodiazepines 1	148–150	151	151
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17-Hydroxyprogesterone	***MassChrom***® Steroids in Serum/Plasma	56–62	63	64

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9-Hydroxyrisperidone	***MassTox***® TDM Series A Neuroleptics 1/*EXTENDED*	163–165	166	166
a-Hydroxytriazolam	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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25-Hydroxyvitamin D3	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
3-epi-25-Hydroxyvitamin D3	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
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MDEA	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
MDMA	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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Methamphetamine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Methaqualone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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3-Methoxytyramine, free	***MassChrom***® Catecholamines, Free Metanephrines, Serotonin in Urine	75–78	79	79
	MassChrom® Free Metanephrines in Plasma	91–93	94	94
3-Methoxytyramine, total	***MassChrom***® Total Metanephrines (free + conjugated) in Urine	81–83	84	84
1-Methylhistidine	***MassChrom***® Amino Acid Analysis in Plasma/Serum	30–36	37	38
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Naltrexone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
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Nelfinavir-M8	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
Nevirapine	***MassTox***® TDM Series A Anti-HIV Drugs	136–139	140	141
Nitrazepam	***MassTox***® TDM Series A Benzodiazepines 2	152–154	155	155
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11-Nor-9-carboxy-Δ9-THC (THC-COOH)	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Noradrenaline (Norepinephrine)	***MassChrom***® Catecholamines, Free Metanephrines, Serotonin in Urine	75–78	79	79
Norbuprenorphine	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Norclobazam	***MassTox***® TDM Series A Benzodiazepines 1	148–150	151	151
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Norclomipramine	***MassTox***® TDM Series A Tricyclic Antidepressants TCA 2	177–178	179	179
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	MassChrom® Free Metanephrines in Plasma	91–93	94	94
Normetanephrine, total	***MassChrom***® Total Metanephrines (free + conjugated) in Urine	81–83	84	84
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3-*epi*-25-OH-vitamin D2	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
25-OH-vitamin D3	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
3-*epi*-25-OH-vitamin D3	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
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	MassChrom® Amino Acid Analysis in Plasma/Serum	30–36	37	38
Valproic acid	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Vanillylmandelic acid (VMA)	***MassChrom***® VMA, HVA, 5-HIAA in Urine	86–88	89	89

Parameter	Assay	Kit page	Calibrator page	Controls page
Venlafaxine	***MassTox***® TDM Series A Antidepressants 1/*EXTENDED*	113–115	116	116
Verapamil	***MassTox***® TDM Series A Antiarrhythmic Drugs	105–109	110	111
Vigabatrin	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Vilazodone	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Vitamin B_1 (TPP)	***MassChrom***® Vitamins B_1 and B_6 in Whole Blood	211–213	214	214
Vitamin B_6 (PLP)	***MassChrom***® Vitamins B_1 and B_6 in Whole Blood	211–213	214	214
Vitamin D	***MassChrom***® 25-OH-Vitamin D_3/D_2 in Serum/Plasma	196–205	199, 203, 206	199, 203, 206
VMA (Vanillylmandelic acid)	***MassChrom***® VMA, HVA, 5-HIAA in Urine	86–88	89	89
Voriconazole	***MassTox***® TDM Series A Antimycotic Drugs	143–145	146	146
Vortioxetine	***MassTox***® TDM Series A Antidepressants 2/Psychostimulants/*EXTENDED*	117–120	121	122
Zaleplon	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Ziprasidone	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Zolpidem	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Zonisamide	***MassTox***® TDM Series A Antiepileptic Drugs	124–132	133	134
Zopiclone	***MassTox***® Drugs of Abuse Testing in Urine	14–19	20–22	23–25
Zotepine	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172
Zuclopenthixol	***MassTox***® TDM Series A Neuroleptics 2/*EXTENDED 2*	167–170	171	172

Overview of Kit Order Number

Assay	Order number	Automation	Kit page	Calibrator page	Controls page
Chapter 2: Drugs of Abuse (Urine)					
MassTox® Drugs of Abuse Testing – Reaction Vials	96000		14	20–22	23–25
MassTox® Drugs of Abuse Testing – 96 Well Plates	96000/WP		15	20–22	23–25
Chapter 3: Metabolic Diseases and Newborn Screening					
MassChrom® Amino Acids and Acylcarnitines from Dried Blood – 96 Well Plates	55000		42–43	–	50–51
MassChrom® Amino Acids and Acylcarnitines from Dried Blood – 96 Well Filter Plates	55000/F		42–43	–	50–51
MassChrom® Amino Acids and Acylcarnitines from Dried Blood/Non Deriv. – 96 Well Plates	57000		46–47	–	50–51
MassChrom® Amino Acids and Acylcarnitines from Dried Blood/Non Deriv. – 96 Well Filter Plates	57000/F		46–47	–	50–51
MassChrom® Amino Acid Analysis in Plasma/Serum – Reaction Vials	75111		30	37	38
MassChrom® Amino Acid Analysis in Plasma/Serum – 96 Deep Well Plates	75111/DWP		31	37	38
Chapter 4: Steroids					
MassChrom® Steroids in Serum/Plasma – 96 SPE Well Plate (for 96 tests)	72072/96		56–57	63	64
MassChrom® Steroids in Serum/Plasma – 96 SPE Well Plates (for 480 tests)	72072/480		56–57	63	64
MassChrom® Steroids in Serum/Plasma – Sample Clean Up Columns	72072/C		58–59	63	64
MassChrom® Cortisol, Cortisone in Saliva	73000		66	68	68
Chapter 5: Biogenic Amines					
Biogenic Amines/Metabolites Starter Set (Urine)					
MassChrom® Biogenic Amines/Metabolites in Urine, Chromatographic Platform	80000		see Sample Prep Sets below		
Biogenic Amines/Metabolites Sample Prep Sets (Urine)					
MassChrom® Catecholamines, free Metanephrines, Serotonin – 96 SPE Well Plate	80600/96	Tecan, Hamilton, Gilson® Flexus	75–76	79	79
MassChrom® Catecholamines, free Metanephrines, Serotonin – 96 SPE Well Plates	80600/480	Tecan, Hamilton, Gilson® Flexus	75–76	79	79
MassChrom® Catecholamines, free Metanephrines, Serotonin – Sample Clean Up Columns	80600/C		77	79	79
MassChrom® Total Metanephrines (free + conjugated) – 96 SPE Well Plate	80700/96	Tecan, Hamilton, Gilson® Flexus	81	84	84
MassChrom® Total Metanephrines (free + conjugated) – Sample Clean Up Columns	80700/C		82	84	84
MassChrom® VMA, HVA, 5-HIAA – Autosampler Vials	80800		86	89	89
MassChrom® VMA, HVA, 5-HIAA – Collection Plates (for 96 tests)	80800/96	Tecan, Hamilton, Gilson® Flexus	87	89	89
MassChrom® VMA, HVA, 5-HIAA – Collection Plates (for 480 tests)	80800/480	Tecan, Hamilton, Gilson® Flexus	87	89	89
Biogenic Amines (Plasma)					
MassChrom® Free Metanephrines – 96 SPE Well Plates	81000	Tecan, Hamilton, Gilson® Flexus	91	94	94
MassChrom® Free Metanephrines – Sample Clean Up Columns	81000/C		92	94	94
Chapter 6: Therapeutic Drug Monitoring					
Series A - Basic Kits					
MassTox® TDM Basic Kit A (for 200 tests)	92111/200		see Parameter Sets below		
MassTox® TDM Basic Kit A (for 1000 tests)	92111/1000		see Parameter Sets below		
MassTox® TDM Basic Kit A for automated sample preparation (for 1000 tests)	92111/1000/F	Tecan, Hamilton	see Parameter Sets 92916/92921		

Assay	Order number	Automation	Kit page	Calibrator page	Controls page
Series A - Parameter Sets (Serum/Plasma)					
MassTox® TDM Parameter Set Neuroleptics 1/*EXTENDED*	92912/XT		163	166	166
MassTox® TDM Parameter Set Antidepressants 1/*EXTENDED*	92913/XT		113	116	116
MassTox® TDM Parameter Set Neuroleptics 2/*EXTENDED 2*	92914/XT2		167	171	172
MassTox® TDM Parameter Set Antidepressants 2/Psychostimulants/*EXTENDED*	92915/XT		117	121	122
MassTox® TDM Parameter Set Mycophenolic Acid	92916	Tecan, Hamilton	157, 159–160	161	161
MassTox® TDM Parameter Set Benzodiazepines 1	92917		148	151	151
MassTox® TDM Parameter Set Benzodiazepines 2	92918		152	155	155
MassTox® TDM Parameter Set Tricyclic Antidepressants TCA 1	92919		174	176	176
MassTox® TDM Parameter Set Tricyclic Antidepressants TCA 2	92920		177	179	179
MassTox® TDM Parameter Set Antiepileptic Drugs	92921	Tecan, Hamilton	124, 128	133	134
MassTox® TDM Parameter Set Antiepileptic Drugs All-in-One Method	92921/XT		129	133	134
MassTox® TDM Parameter Set Antimycotic Drugs	92922		143	146	146
MassTox® TDM Parameter Set Antiarrhythmic Drugs	92923		105	110	111
MassTox® TDM Parameter Set Anti-HIV Drugs	92924		136	140	141
Immunosuppressants (Whole Blood)					
MassTox® Immunosuppressants (for 400 tests)	93000		183	190	191
MassTox® Immunosuppressants (for 1200 tests)	93000/1200		183	190	191
MassTox® Immunosuppressants, **ONE*MINUTE*** (for 400 tests)	93900/400		186	190	191
MassTox® Immunosuppressants, **ONE*MINUTE*** (for 1200 tests)	93900/1200		186	190	191
MassTox® Immunosuppressants, **ONE*MINUTE*** – Automated Method	93900/1200/F	Tecan, Hamilton	188–189	190	191
Chapter 7: Osteoporosis Diagnosis/Vitamin D Analysis (Serum/Plasma)					
MassChrom® 25-OH-Vitamin D_3 and 25-OH-Vitamin D_2 (for 200 tests)	62000		200	203	203
MassChrom® 25-OH-Vitamin D_3 and 25-OH-Vitamin D_2 (for 1000 tests)	62000/1000		200	203	203
MassChrom® 25-OH-Vitamin D_3 and 25-OH-Vitamin D_2 – Automated Method	62000/1000/F	Tecan, Hamilton	202	203	203
Upgrade Set for 3-epi-25-OH-Vitamin D_3/D_2	Epimer Upgrade		204	206	206
MassChrom® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 – Updated Method	62062		196	199	199
MassChrom® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 – Updated Method	62062/1000		196	199	199
MassChrom® 25-OH-Vitamin D_3/D_2 and 3-*epi*-25-OH-Vitamin D_3 – Automated Method	62062/1000/F	Tecan, Hamilton	198	199	199
Chapter 8: Vitamin Profiling					
MassChrom® Methylmalonic Acid (MMA) in Plasma/Serum	64000		216	218	218
MassChrom® Methylmalonic Acid (MMA) in Urine	Urine Set		219	221	221
MassChrom® Vitamins B_1 and B_6 in Whole Blood – Reaction Vials	87000		211	214	214
MassChrom® Vitamins B_1 and B_6 in Whole Blood – 96 Deep Well Plates	87000/DWP		212	214	214
Chapter 9: Biomarker for Alcohol Abuse					
MassChrom® Ethyl Glucuronide and Ethyl Sulfate in Urine	69000		225	227	227

References

[1] Deutsche Gesellschaft für Verkehrspsychologie (DGVP), Deutsche Gesellschaft für Verkehrsmedizin (DGVM) (Hrsg). Urteilsbildung in der Fahreignungsbegutachtung. Beurteilungskriterien. 3. Aufl, Kirschbaum Verlag Bonn (2013).

[2] European Workplace Drug Testing Society (EWDTS). European Guidelines for Workplace Drug Testing in Urine, 2015-11-01 Version 2.0.: http://www.ewdts.org/ewdts-guidelines.html.

[3] Ludewig, Regenthal (Hrsg). Akute Vergiftungen und Arzneimittelüberdosierungen. 10. Aufl., WVG Stuttgart (2007).

[4] TIAFT reference blood level list of therapeutic and toxic substances, September 2004.

[5] Schulz M, Iwersen-Bergmann S, Adresen H, Schmoldt A. (2012) Therapeutic and toxic blood concentrations of nearly 1000 drugs and other xenobiotics. *Crit Care* **16**(4): R 136.

[6] Hiemke C, Baumann P, Bergemann N, Conca A, Dietmaier O, Egberts K, Fric M, Gerlach M, Greiner C, Grunder G, Haen E, Havemann-Reinecke U, Jaquenoud Sirot E, Kirchherr H, Laux G, Lutz UC, Messer T, Muller MJ, Pfuhlmann B, Rambeck B, Riederer P, Schoppek B, Stingl J, Uhr M, Ulrich S, Waschgler R, Zernig G. (2011) AGNP Consensus guidelines for therapeutic drug monitoring in psychiatry: Update 2011. *Pharmacopsychiatry* **44**(6): 195–235.

[7] Hiemke C, Bergemann, Clement HW, Conca A, Deckert J, Domschke K, Eckermann G, Egberts K, Gerlach M, Greiner C, Gründer G, Haen E, Havemann-Reinecke U, Hefner G, Helmer R, Janssen G, Jaquenoud E, Laux G, Messer T, Mössner R, Müller MJ, Paulzen M, Pfuhlmann B, Riederer P, Saria A, Schoppek B, Schoretsanitis G, Schwarz M, Gracia MS, Stegmann B, Steimer W, Stingl JC, Uhr M, Ulrich S, Unterecker S, Waschgler R, Zernig G, Zurek G, Baumann P. (2018) Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology: Update 2017. *Pharmacopsychiatry* **51**(1-02): 9–62.

[8] Ludewig, Regenthal (Hrsg). Akute Vergiftungen und Arzneimittelüberdosierungen. 11. Aufl., WVG Stuttgart (2015).

[9] Neels HM, Sierens AC, Naelaerts K, Scharpé SL, Hatfield GM, Lambert WE. (2004) Therapeutic drug monitoring of old and newer anti-epileptic drugs. *Clin Chem Lab Med* **42**(11): 1228–55.

[10] Gesellschaft für Epilepsieforschung e. V. Serumkonzentrationen von Antiepileptika (mittlere Wirkungsbereiche), Homepage – Stand August 2011.

[11] Welzen M, Uges DRA. (2004) TIAFT reference blood level list of therapeutic and toxic substances. http://www.gtfch.org/cms/images/stories/Update_TIAFT_list_202005.pdf (accessed July 2013)

[12] Flepp M. Antiretrovirale Therapie (2013). http://www.hiv.ch (accessed July 2013)

[13] Klinker H. (2012) Therapeutisches Drug Monitoring (Medikamentenspiegelmessung). http://www.hivleitfaden.de (accessed July 2013)

[14] Andes D, Pascual A, Marchetti O. (2009) Antifungal therapeutic drug monitoring: established and emerging indications. *Antimicrob Agents Chemother* **53**(1): 24–34.

[15] Schulz M, Schmoldt A. (2003) Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics. Pharmazie 58(7): 447–74.

[16] Thomas L. Labor und Diagnose. 7. Aufl., Verlag TH-Books Frankfurt/Main (2008).

[17] Meiser BM, Pfeiffer M, Schmidt D, Reichenspurner H, Ueberfuhr P, Paulus D, von Scheidt W, Kreuzer E, Seidel D, Reichart B. (1999) Combination therapy with tacrolimus and mycophenolate mofetil following cardiac transplantation: importance of mycophenolic acid therapeutic drug monitoring. *J Heart Lung Transplant* **18**(2): 143–9.

[18] TIAFT reference blood level list of therapeutic and toxic substances, 2008.

[19] Gressner A, Arndt T. Lexikon der Medizinischen Laboratoriumsdiagnostik, 2. Aufl., Springer Medizin Verlag Heidelberg (2013).

[20] Thomas L. Labor und Diagnose. 8. Aufl., Verlag TH-Books Frankfurt/Main (2012).

[21] Rasmussen K, Nathan E. (1990) The clinical evaluation of cobalamin deficiency by determination of methylmalonic acid in serum or urine is not invalidated by the presence of heterozygous methylmalonic-acidaemia. *J Clin Chem Clin Biochem* **28**(6): 419–421.

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