NEOMASS AAAC PLUS

Expanded Newborn Screening

Reagents for Expanded Newborn Screening on Tandem Mass Spectrometry

LABSYSTEMS
DIAGNOSTICS
speaking your language

LABSYSTEMS DIAGNOSTICS OY

Labsystems Diagnostics manufactures and markets high-quality diagnostic products globally for clinical laboratory use, home use and doctors' offices.

Labsystems brings in cutting-edge technologies in the field of laboratory medicine and provide complete solutions in the field of LCMS, HPLC, Fluorescence based Immunoassay, & Real time PCR solutions with own manufacturing in Finland, Turkey & India.

Labsystems is manufacturing products in the segments of - New Born Screening, Infectious diseases, Gastroenterology, biochemistry, Haematology, Point-of-Care, Molecular Diagnostics, Immunology and LC-MS/MS Kits.

BREAKTHROUGHS

- More than 40 Years of Newborn Screening Reagents Manufacturing Experience
- Pioneered Newborn Screening Systems based on a Fluorescence reporter system
- Three dedicated R&D and Manufacturing facilities for Neonatal Screening
- Labsystems Diagnostics has been a pioneer in the field of Newborn Screening bringing unique and relevant products and assays addressing a wide array of medical conditions
- Approximately 3.5 Million Babies per year are screened by Trivitron Labsystems Groups' owned Laboratories or Partners
- Introduced World's first Fluorometric Microplate based assay for screening Phenylalanine in newborns to detect Phenylketonuria (PKU) and now on tandem MS along with more than 50 disorders.
- World first assay to detect Proximal Urea Cycle Disorders on DBS

INBORN ERRORS OF METABOLISM

Inborn errors of metabolism (IEM) are a genetically heterogeneous group of disorders caused by a defect in a metabolic pathway, leading to malfunctioning metabolism and/or the accumulation of toxic intermediate metabolites [1].

To date, more than 1000 different IEM have been identified. While individually rare, the cumulative incidence has been shown to be upwards of 1 in 800 [2].

IEM disorders may manifest to all ethnic groups at any stage of life, from infancy to adulthood.

Few IEM are amenable to treatment. Treatment of IEM correlates with early diagnosis through Newborn screenings (NBS) that provides an opportunity to identify several inherited rare metabolic disorders in pre-symptomatic infants, thereby significantly reducing the morbidity, mortality, and associated disabilities for those affected with many of these conditions [3].

EXPANDED NEWBORN SCREENING

Expanded Newborn Screening is a preventive screening service performed on Tandem mass spectrometer to detect IEMs.

The technology allows inexpensive simultaneous detection of more than 50 different metabolic disorders in one single blood spot specimen with commendable analytical accuracy and precision.

The sensitivity and specificity of this method can be up to 99% and 99.995%, respectively, for most amino acid disorders, organic acidemias, and fatty acid oxidation defects [4].

NEOMASS AAAC PLUS OVERVIEW

NeoMass AAAC Plus kit provides tandem mass spectrometry assay for quantitative measurement of amino acids, free carnitine, acylcamitines, argininosucciric acid and succinylacetone from dried blood spot samples.

Abnormal blood levels of amino acids or acyicarnitines may indicate an inborn error of metabolism (or genetic metabolic deficiency), which may severely affect the health of an infant or even be fatal. Free carnitine and acylcamitines are markers for disorders of fatty acid oxidation disorders and organic aciduria, whereas amino acids, argininosuccinic acid and succinylacetone are markers for aminoacidopathies.

NeoMass AAAC Plus is a kit for analyzing all of these analytes from a single injection.

KEY FEATURES

Kit for 960 tests

Non derivatized extraction procedure for all the analytes

High throughput analysis with shortest extraction time

High specificity and sensitivity by MS/MS detection

ISTD	Amino Acids	ISTD	Acylcarnitines
$^{2}H_{4}$-Alanine	Alanine(Ala)	$^{2}H_{9}$-Carnitine	Carnitine(C0)
$^{2}H_{4}$- ^{13}C Arginine	Arginine(Arg)	$^{2}H_{3}$-Acetylcarnitine	Acetylcarnitine(C2)
$^{2}H_{3}$- Aspartate	Aspartate(Asp)	$^{2}H_{3}$-Propionylcarnitine	Propionylcarnitine(C3)
$^{2}H_{2}$- Citrulline	Citrulline(Cit)	$^{2}H_{3}$-Butyrylcarnitine	Butyrylcarnitine(C4)
$^{2}H_{3}$- Glutamate	Glutamate(Glu)	$^{2}H_{9}$-Isovalerylcarnitine	Isovalerylcarnitine(C5)
^{15}N-^{13}C- Glycine	Glycine(Gly)	$^{2}H_{3}$-Glutarylcarnitine	Glutarylcarnitine(C5DC)
$^{2}H_{3}$- Leucine	Leucine(Leu)	$^{2}H_{3}$-Hexanoylcarnitine	Hexanoylcarnitine(C6)
$^{13}C_{6}$- $^{15}N_{2}$- Lysine	Lysine(Lys)	$^{2}H_{3}$-Octanoylcarnitine	Octanoylcarnitine(C8)
$^{2}H_{3}$- Methionine	Methionine(Met)	$^{2}H_{3}$-Decanoylcarnitine	Decanoylcarnitine(C10)
$^{2}H_{6}$- Ornithine	Ornithine(Orn)	$^{2}H_{3}$-Dodecanoylcarnitine	Dodecanoylcarnitine(C12)
$^{13}C_{6}$ - Phenylalanine	Phenylalanine(Phe)	$^{2}H_{9}$-Myristoylcarnitine	Myristoylcarnitine(C14)
$^{2}H_{5}$- Proline	Proline(Pro)	$^{2}H_{3}$-Palmitoylcarnitine	Palmitoylcarnitine(C16)
$^{13}C_{3}$ - Serine	Serine(Ser)	$^{2}H_{3}$-Stearoylcarnitine	Stearoylcarnitine(C18)
$^{13}C_{6}$ - Tyrosine	Tyrosine(Tyr)	$^{13}C_{5}$ -Succinylacetone	Succinylacetone(SUAC)
$^{2}H_{8}$- Valine	Valine(Val)	$^{15}N_{4}$-$^{13}C_{6}$ Argininosuccinic acid	Argininosuccinic acid (ASA)

Multiple Diagnosis (> 50 Disorders) with single protocol

Amino Acid Disorders

- Argininemia (ARG1 Deficiency)
- Argininosuccinic Aciduria (ASL Deficiency)
- 5-Oxoprolinuria1
- Carbamoylphosphate Synthetase Deficiency 1 (CPS1 Deficiency)
- Citrullinemia I (ASS Deficiency)
- Citrullinemia II
- Homocystinuria
- Hypermethioninemia
- Hyperammonemia, Hyperornithinemia, Homocitrullinemia Syndrome1
- Hyperornithinemia with Gyral Atrophy 1
- Maple Syrup Urine Disease
- N-acetyl Glutamate Synthetase Deficiency (NAGS Deficiency)
- Phenylketonuria
- Classical/Hyperphenylalaninemia
- Defects of Biopterin Cofactor Biosyntheis
- Defects of Biopterin cofactor regeneration
- Tyrosinemia (detected by SUAC)
  - Transient Neonatal Tyrosinemia
  - Tyrosinemia Type I
  - Tyrosinemia Type II
  - Tyrosimenia Type III
- Ornitine transcarbamoylase deficiency (OTC)

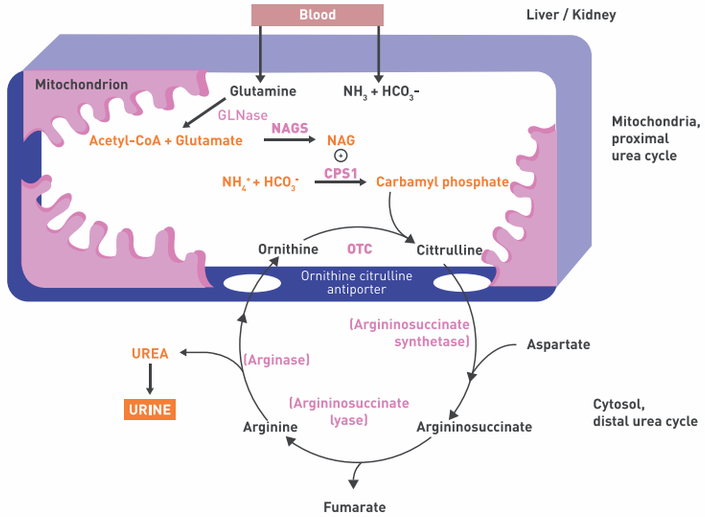
Organic Acid Disorders

- Glutaric Acidemia Type I
- Isobutyryl-CoA Dehydrogenase Deficiency
- Isovaleric Acidemia
- 2-Methylbutryl-CoA Dehydrogenase Deficiency
- 3-Methylcrotonyl-CoA Carboxylase Deficiency
- 3-Methylglutaconyl-CoA Hydratase Deficiency
- Methylmalonic Acidemias
- Methylmalonyl-CoA Mutase Deficiency
- Some Adenosylcobalamin Synthesis Defects
- Maternal Vitamin B12 Deficiency
- Mitochondrial Acetoacetyl-CoA Thiolase Deficiency
- Propionic Acidemia
- Multiple-CoA Carboxylase Deficiency
- Malonic Aciduria

Fatty Acid Oxidation Disorders

- Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
- Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)
- Medium/Short Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency
- 3-Hydroxy Long Chain Acyl-CoA Dehydrogenase Deficiency (LCHAD)
- Short Chain Acyl-CoA Dehydrogenase Deficiency
- Medium Chain Ketoacyl-CoA Thiolase deficiency
- Carnitine uptake deficiency
- Carnitine/Acylcarnitine Translocase Deficiency
- Carnitine Palmitoyl Transferase Deficiency Type II
- Carnitine Palmitoyl Transferase Ia deficiency
- Carnitine Palmitoyl Transferase Ib deficiency
- 2,4-Dienoyl-CoA Reductase Deficiency1
- Glutaric Acidemia type II
- Trifunctional Protein Deficiency

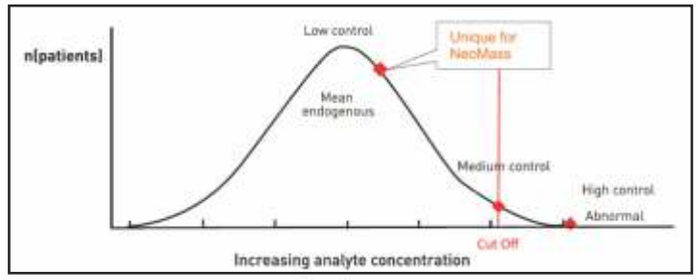
Patented technology for detection of complete Urea cycle disorders (UCDs)



PATENTED INNOVATION

- New Proximal urea cycle deficiencies
  - N-Acetylglutamate Synthase (NAGS) Deficiency
  - Carbamyl Phosphate Synthetase (CPS) Deficiency
  - Ornithine Transcarbamylase (OTC) Deficiency
  - Ornithine Translocase Deficiency (HHH) Syndrome
- Traditional - distal urea cycle deficiences
  - Argininosuccinate Synthetase (ASS) Deficiency [Citrullinemia I)
  - Citrin Deficiency [Citrullinemia II)
  - Argininosuccinate Lyase (ASL) Deficiency[Argininosuccinic Aciduria)
  - Arginase Deficiency (ARG1) [Hyperargininemia)

Three levels of dried blood spot controls covering the clinically valid range



Three dried blood spot controls framing the decisional cut-off area for each of the matching internal standard.

NeoMassAAAC Plus gives excellent Functional Sensitivity and Proficiency.

Analyte	Within-run reproducibility (CV%)			Between-run reproducibility (CV%)			Between-day reproducibility (CV%)			Mean CV%			Total CV%		
	C1	C2	C3	C1	C2	C3	C1	C2	C3	C1	C2	C3	C1	C2	C3
Ala	8%	7%	7%	7%	8%	8%	8%	8%	6%	8%	8%	7%	14%	13%	13%
Arg	5%	4%	4%	5%	6%	5%	6%	4%	4%	5%	5%	4%	9%	8%	7%
Asp	10%	10%	9%	11%	10%	8%	11%	10%	6%	10%	10%	8%	18%	17%	14%
Cit	5%	5%	5%	6%	7%	5%	6%	5%	4%	6%	6%	5%	10%	10%	8%
Glu	10%	9%	10%	14%	14%	13%	14%	11%	13%	13%	11%	12%	22%	20%	20%
Gly	12%	9%	12%	12%	10%	8%	12%	12%	7%	12%	10%	8%	21%	18%	14%
Leu	5%	6%	5%	6%	6%	7%	7%	5%	5%	6%	6%	6%	10%	10%	10%
Lys	5%	5%	4%	5%	6%	5%	5%	5%	4%	5%	5%	4%	8%	9%	8%
Met	9%	7%	7%	8%	8%	6%	8%	7%	5%	8%	7%	6%	15%	12%	10%
Orn	6%	5%	5%	7%	6%	5%	7%	5%	4%	7%	5%	5%	11%	9%	8%
Phe	5%	5%	5%	5%	6%	5%	6%	5%	5%	5%	6%	6%	9%	10%	10%
Pro	6%	5%	5%	6%	6%	5%	6%	5%	4%	6%	5%	5%	11%	9%	8%
Ser	11%	7%	6%	10%	8%	7%	10%	8%	7%	10%	8%	7%	18%	13%	12%
Tyr	7%	6%	6%	6%	7%	7%	6%	6%	7%	6%	6%	7%	11%	11%	12%
Val	6%	6%	6%	8%	7%	7%	7%	6%	5%	7%	6%	6%	12%	11%	10%
C0	6%	6%	5%	8%	7%	7%	7%	6%	5%	7%	6%	6%	12%	11%	10%
C2	5%	5%	5%	7%	7%	7%	5%	6%	4%	6%	6%	5%	10%	11%	9%
C3	6%	6%	5%	7%	7%	7%	7%	7%	5%	6%	7%	6%	11%	12%	10%
C4	9%	6%	6%	10%	7%	8%	9%	7%	6%	9%	7%	6%	16%	12%	11%
C5	9%	6%	5%	11%	8%	7%	11%	8%	7%	10%	7%	6%	17%	13%	11%
C5DC	14%	8%	8%	12%	11%	7%	11%	10%	6%	13%	9%	7%	24%	16%	12%
C6	16%	7%	6%	16%	9%	7%	16%	8%	5%	14%	7%	6%	25%	13%	11%
C8	12%	8%	7%	12%	8%	8%	13%	6%	6%	12%	8%	8%	21%	14%	14%
C10	14%	9%	8%	11%	9%	10%	11%	7%	9%	14%	8%	9%	24%	15%	16%
C12	16%	8%	8%	15%	9%	10%	12%	7%	7%	14%	8%	8%	24%	14%	14%
C14	10%	8%	8%	13%	9%	10%	13%	8%	7%	10%	8%	8%	18%	14%	13%
C16	5%	6%	6%	6%	8%	9%	6%	8%	7%	6%	8%	7%	10%	13%	13%
C18	6%	6%	7%	7%	8%	9%	6%	8%	7%	7%	9%	8%	13%	16%	14%
SUAC	15%	11%	10%	15%	12%	10%	15%	11%	12%	15%	12%	10%	26%	20%	18%
ASA	10%	9%	8%	9%	12%	11%	11%	11%	11%	12%	11%	10%	21%	19%	17%

Within-run reproducibility, between-run reproducibility, between-day reproducibility, mean and total CV% results from validation lots.

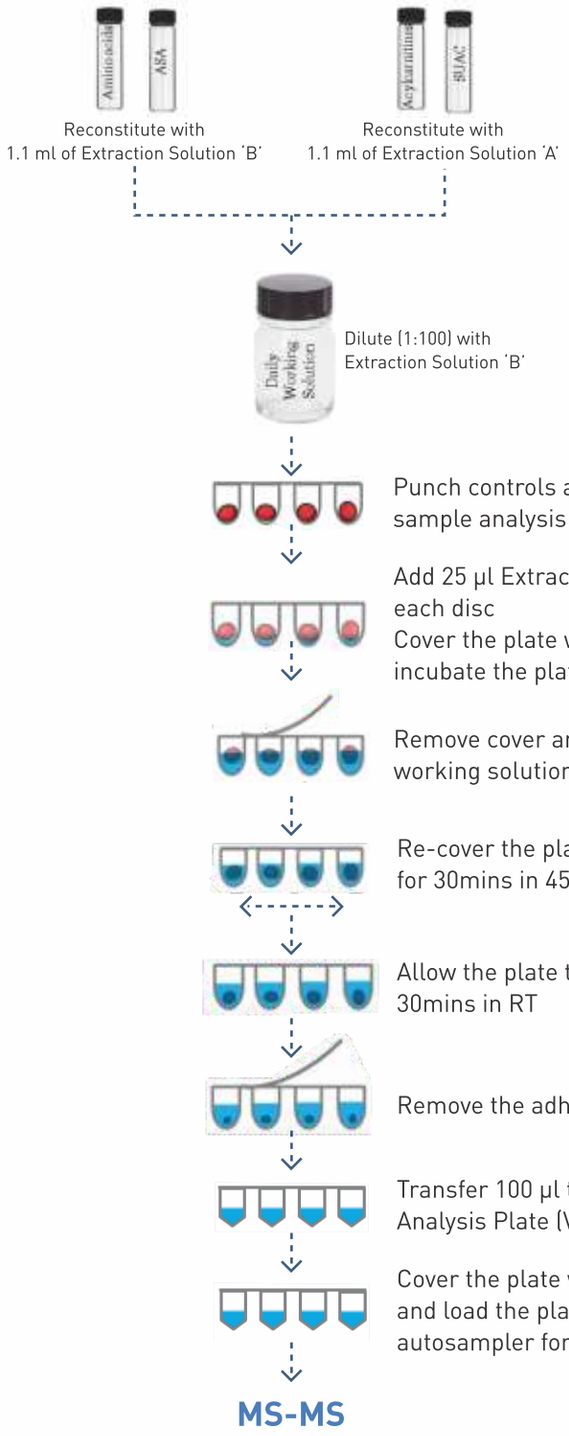
Analyte	Linear Range tested		Slope	Correlation (R^2)	Analyte	Linear Range tested		Slope	Correlation (R^2)
	Lower	Upper				Lower	Upper		
Ala	62.8	3660	1.86	0.9998	C0	8.7	770	1.23	0.9996
Arg	4.5	1737	1.30	0.9999	C2	4.7	549	1.64	0.9953
Asp	113	1728	1.14	0.9982	C3	0.60	139	1.59	0.9997
Cit	9.8	1724	1.59	0.9999	C4	0.34	48.1	1.73	0.9994
Glu	57	4452	0.92	0.9998	C5	0.09	39.3	2.02	0.9998
Gly	186	4224	2.00	0.9986	C5DC	1.1	52.5	1.59	0.9999
Leu	31.9	2068	1.77	0.9995	C6	0.06	43.8	1.71	0.9994
Lys	36.6	2820	1.87	0.9998	C8	0.05	31.1	1.55	0.9998
Met	18.6	1743	1.84	0.9999	C10	0.12	18.8	1.68	0.9990
Orn	21.4	2583	1.67	0.9999	C12	0.22	31.5	1.86	0.9984
Phe	13.3	2014	1.80	0.9998	C14	0.11	39.4	1.39	0.9997
Pro	31.5	2466	1.69	0.9997	C16	1.4	128	1.66	0.9984
Ser	53.9	3435	1.67	0.9998	C18	0.51	27.8	1.46	0.9995
Tyr	21.2	1938	1.83	0.9774	ASA	7.8	563	1.40	0.9997
Val	28.1	3595	1.70	0.9994	SUAC	3.7	102	2.06	0.9999

Testes linear concentration ranges (µM), slope and correlation coefficient R2 of the assay.

Analyte	LOD (µM)	Analyte	LOD (µM)	Analyte	LOD (µM)
Ala	3.2	Phe	0.19	C5DC	0.008
Arg	0.10	Pro	0.39	C6	0.001
Asp	1.5	Ser	0.19	C8	0.002
Cit	0.19	Tyr	0.10	C10	0.002
Glu	0.77	Val	0.39	C12	0.002
Gly	30.9	C0	0.09	C14	0.001
Leu	0.10	C2	0.01	C16	0.001
Lys	0.05	C3	0.01	C18	0.002
Met	0.39	C4	0.002	ASA	0.08
Orn	0.10	C5	0.004	SUAC	0.77

LOD values (µM) for target anlytes.

NeoMassAAAC Plus - Sample Extraction Protocol



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