

Specifications

Version	Change control
02	Update analytical scope
03	Update analytical scope + new chapters „Important information regarding the analytical services“
04	Update analytical scope + update headlines + addition of SOP version
05	Update SOP Versions
06	Update methods

1 Newborn screening

Target disease	Analyte (Measurand)	Analytical technology (SOP / Version)	Sample material (Matrix)	Sample amount	Processing time ¹	Accredited (ISO 15189)
Total amount:				5 Spots		
Congenital Adrenal Hyperplasia	17 α -Hydroxyprogesterone Steroid profile (<i>2nd tier</i>)	Fluorimetry (SOP 2.3.1 / 11) HPLC-MS/MS (SOP 2.3.14 / 1)	DBS	2-3 Spots	24 h	yes -
Maple syrup urine disease (MSUD)	(Iso)leucine	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Biotinidase deficiency	Biotinidase	Fluorimetry (SOP 2.3.1 / 11)	DBS	2-3 Spots	24 h	yes
Carnitine-acylcarnitine translocase deficiency (CACT)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Carnitine-palmitoyltransferase deficiency type 1 (CPT I)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Carnitine-palmitoyltransferase deficiency type 2 (CPT II)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Classical galactosemia	Galactose-1-P-Uridyltransferase Total galactose (<i>2nd tier</i>)	Fluorimetry (SOP 2.3.1 / 11) Photometry (SOP 2.3.5 / 5)	DBS	2-3 Spots	24 h	yes yes
Glutaric aciduria type 1	Glutaryl carnitine	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Hypothyroidism	Thyroid-stimulating hormone (TSH)	Fluorimetry (SOP 2.3.1 / 11)	DBS	2-3 Spots	24 h	yes
Isovaleric acidemia	C5-carnitine, Isovaleryl carnitine, Pivaloyl carnitine (<i>2nd tier</i>)	MS/MS (SOP 2.3.9 / 11) HPLC-MS/MS (SOP 2.3.13 / 2)	DBS	2-3 Spots	24 h	yes yes
LCHAD- deficiency	Long-chain acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
VLCAD- deficiency	(Very) long-chain acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
MCAD-deficiency	Medium chain acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes
Phenylketonuria & hyperphenylalaninemia	Phenylalanine	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes

Methylmalonic acidemia, Propionic acidemia, Homocysteinuria, Vitamin B12 deficiency / isolated and combined remethylation disorder	Propionylcarnitin (C3), Acetylcarnitin (C2), Methionine, Phenylalanine, Homocysteine (<i>2nd tier</i>), Methylmalonic acid (<i>2nd tier</i>), Propionic acid, (<i>2nd tier</i>), Methylcitrate (<i>2nd tier</i>)	MS/MS (SOP 2.3.9 / 11)				yes
		HPLC-MS/MS (SOP 2.3.15 / 1)	T	2-3 Spots	24 h	-
Cystic fibrosis (CF), Mucoviscidosis	Immunoreactive trypsinogen (IRT) Pancreatitis-associated protein (PAP) CF-genetics (31 mutations)	Fluorimetry (SOP 2.3.1 / 11)	DBS (D)	2-3 Spots	24 h	yes
		Fluorimetry (SOP 2.3.7 / 3)		2-3 Spots	2-14 days	yes
		PCR (SOP 2.3.8 / 4)		2-3 Spots	2-14 days	yes
Severe combined immunodeficiency (SCID)	TREC	PCR (SOP 2.3.10 / 2)	DBS (D)	2-3 Spots	24 h	yes
Sickle cell disease (SCD)	Hemoglobin S, C, D, E, O	MS/MS (SOP 2.3.11 / 4)	DBS	2-3 Spots	24 h	yes
Spinal muscular atrophy (SMA)	SMN1	qPCR (SOP 2.3.10 / 2)	DBS (D)	2-3 Spots	24 h	yes
Tyrosinemia Type I	Succinylacetone	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	24 h	yes

¹ The processing time does not include Sundays and public holidays in Germany. The operation time of the laboratory is from Monday – Friday (8 am – 4 pm) and Saturday (8 – 12 am).

Sample types and container:

DBS – Dried blood spot card

D - DNA

1.1 Important information regarding the analytical services

According to the German Genetic Diagnostics Act and the Children's Guidelines, a declaration of consent from at least one legal guardian is required for newborn screening. A corresponding form is available on our website: <https://www.uke.de/kliniken-institute/kliniken/kinder-und-jugendmedizin/für-weisende-ärzte/laborleistungen/>

For all diseases included in the newborn screening, variants are known that are not detected by the offered tests. Further diagnostics must be carried out, regardless of the newborn screening result, if a disease is persistently suspected.

The newborn screening results are only valid if no blood product transfusion and no corticosteroids or catecholamine administration have been applied prior to the blood sampling.

The TREC-based newborn screening for severe combined immunodeficiencies (SCID) does not detect certain mild (e.g. ADA gene) or rare forms of SCID (e.g. ORAI1, CARD11, IKBKB, MHC-II deficiency).

The IRT-based newborn screening for cystic fibrosis can produce false negative results in case of meconium ileus. Therefore, further diagnostics for cystic fibrosis (e.g. sweat test) must be carried out in the case of meconium ileus.

The screening for 5q-associated SMA only detects 5q-associated spinal muscular atrophy caused by homozygous deletions of the SMN1 gene, which causes around 95% of severe infantile SMA forms. Compound heterozygous carriers of point mutations of the SMN1 gene are not detected.

2 Selective metabolic diagnostics

Target disease	Analyte (Measurand)	Analytical technology (SOP / Version)	Sample material (Matrix)	Sample amount	Sampling instructions	Processing time ²	Accredited (ISO 15189)
Lysosomal enzymes		Total amount:		3-5 Spots			
Pompe disease	α-Glucosidase	Fluorimetry (SOP 2.4.1 / 3)	DBS	2-3 Spots		1-2 weeks	yes
Gaucher disease	β-Glucosidase	MS/MS (SOP 2.4.3 / 5)	DBS	2-3 Spots		1-2 weeks	yes
Acid sphingomyelinase deficiency (formerly: Niemann-Pick A/B disease)	Acid sphingomyelinase	MS/MS (SOP 2.4.3 / 5)	DBS	2-3 Spots		1-2 weeks	yes
Fabry disease	α-Galactosidase	MS/MS (SOP 2.4.2 / 4)	DBS	2-3 Spots		1-2 weeks	yes
Mucopolysaccharidosis		Total amount:		3-5 Spots			
Multiplex (MPS II, IIIB, IVA, IVB, VI, VII) - MPS II - MPS IIIB - MPS IVA - MPS IVB - MPS VI - MPS VII - Mukopolipidose II/III	Iduronat-2-sulfatase N-Acetylglucosaminidase N-Acetylgalactosamin-6-sulfatase β-Galactosidase Arylsulfatase B β-Glucuronidase N-Acetylglucosamin-1-Phosphotransferase	MS/MS (SOP 2.4.8 / 2)	DBS	2-3 Spots		2 weeks	yes
MPS I	α-Iduronidase	MS/MS (SOP 2.4.5 / 5)	T	2-3 Spots		2 weeks	yes
MPS IIIA (Sanfilippo A)	Heparan-N-sulfatase	Fluorimetry (SOP 2.4.18)	E	5-10 ml	**	2 weeks	-
MPS IIIC (Sanfilippo C)	Acetyl CoA: α-Glucosaminid-N-acetyltransferase	Fluorimetry (SOP 2.4.18)	E	5-10 ml	**	2 weeks	-
Neuronal ceroid lipofuscinosis		Total amount:		3-5 Spots			
Neuronal Ceroid Lipofuscinnoses Type 1 (CLN1)	Palmitoyl protein thioesterase 1	Fluorimetry (SOP 2.4.6 / 3)	DBS	2-3 Spots		1-2 weeks	yes
Neuronal Ceroid Lipofuscinnoses Type 2 (CLN2)	Tripeptidyl peptidase 1	Fluorimetry (SOP 2.4.7 / 3)	DBS	2-3 Spots		1-2 weeks	yes
Oligosaccharidosis		Total amount:		3-5 Spots			
α-Mannosidosis	α-Mannosidase	Fluorimetry (SOP 2.4.12)	DBS	2-3 Spots		1-2 weeks	-
β-Mannosidosis	β-Mannosidase	Fluorimetry (SOP 2.4.13)	DBS	2-3 Spots		1-2 weeks	-
α-Fucosidosis	α-Fucosidase	Fluorimetry (SOP 2.4.14)	DBS	2-3 Spots		1-2 weeks	-

Gangliosidosis				Total amount:	3-5 Spots		
GM1-Gangliosidosis	β-Galactosidase	Fluorimetry (SOP 2.4.15)	DBS	2-3 Spots		1-2 weeks	-
GM2-Gangliosidosis	Total hexosaminidase	Fluorimetry (SOP 2.4.9)	DBS	2-3 Spots		1-2 weeks	-
GM2-Gangliosidosis	Hexosaminidase A	Fluorimetry (SOP 2.4.9)	DBS	2-3 Spots		1-2 weeks	-
Leukodystrophies				Total amount:	3-5 Spots		
Metachromatic leukodystrophy	Arylsulfatase A	Fluorimetry (SOP 2.4.17)	E	5-10 ml	**	1-2 weeks	-
Krabbe disease	β-Galactocerebrosidase	MS/MS (SOP 2.4.4 / 3)	DBS	2-3 Spots		1-2 weeks	yes
Other							
Wolman disease, CESD	Lysosomal acid lipase	Fluorimetry (SOP 2.4.10 / 5)	DBS	2-3 Spots		1-2 weeks	yes
Other enzymes							
Biotinidase deficiency	Biotinidase	Fluorimetry (SOP 2.3.1 / 11)	DBS	2-3 Spots	*	2-4 weeks	yes
		Photometry (SOP 2.4.28)	P	1 ml			-
		Photometry (SOP 2.4.28)	S	1-2 ml			-
Galactosemia	Galactose-1-P-Uridyltransferase	Fluorimetry (SOP 2.3.1 / 11)	DBS	2-3 Spots		24 h	yes
Fatty acid oxidation disorders, organic acids							
Several diseases	Acylcarnitines	MS/MS (SOP 2.3.9 / 11)	DBS P	1 Spot 1 ml		24-48 h	yes -
Several diseases	Organic acids	GC/MS (SOP 2.4.29)	U	5-10 ml		1-2 weeks	-
Amino acids							
Several diseases	Amino acids	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots	*	24 h	yes
		HPLC-MS/MS (SOP 2.4.36 / 1)	P	1 ml		24-72 h	yes
		HPLC-MS/MS (SOP 2.4.36 / 1)	S	1-2 ml		24-72 h	yes
		HPLC-MS/MS (SOP 2.4.36 / 1)	CSF	1 ml		24-72 h	-
		HPLC-MS/MS (SOP 2.4.37)	U	5-10 ml		24-72 h	-
Diagnosis: Argininosuccinic aciduria	Argininosuccinic acid	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots		24 h	yes
Diagnosis / Follow-up: Tyrosinemia Type I	Succinylacetone	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots		24 h	yes
Follow-up: Phenylketonuria (PKU)	Phenylalanine, Tyrosine	MS/MS (SOP 2.3.9 / 11)	DBS	2-3 Spots		24 h	yes
Follow up: MSUD	Leucine, Isoleucine, Valine	MS/MS (SOP 2.3.9 / 11) HPLC-MS/MS (SOP 2.4.36 / 1)	DBS P	2-3 Spots 1 ml	*	24 h 24-72 h	yes yes

Fatty acids							
Follow-up of known patients e.g. under dietary treatment	Essential fatty acids	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Peroxisomal disorders	Very long-chain fatty acids	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Peroxisomal disorders	Phytanic acid	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Special diagnostics in urine							
Lysosomal storage diseases (MPS / multiple sulfatase deficiency)	Glycosaminoglycans (GAG)	Photometry (SOP 2.4.30)	U	1-2 ml		2-3 weeks	-
Other special diagnostics							
Sweat test for cystic fibrosis (<i>internal samples only!</i>)	Chloride	Titrimetry (SOP 2.4.35)	SW	50 – 100 µl		24 h	-
Several liver diseases	Total bile acids	Photometry (SOP 2.4.24)	S	1 ml		48-72 h	-
Other diagnostics in blood							
Galactokinase deficiency (and other galactosemias)	Total galactose	Photometry (SOP 2.3.5 / 5)	DBS	2-3 Spots		24 h	yes
Congenital disorders of glycosylation	CDG-diagnostics, Transferrin	Gel electrophoresis, IEF (SOP 2.4.27)	S	1-2 ml		2-3 weeks	-

² The processing time does not include weekends and public holidays in Germany. Express analysis can be offered for most diseases. Please contact us in advance for further details. Express samples must arrive before 11 am.

The operation time of the laboratory for selective metabolic diagnostics is from Monday – Friday (8 am – 4 pm)

* cooled shipping required. Please send the centrifugation supernatant only!

** Amongst others, EDTA-blood is required for leukocyte isolation. Please send the EDTA-blood samples uncooled by express mail at the beginning of the week (samples must arrive before Friday, 12 am, not on Saturday).

Sample types and container:

E - Blood collection tube (with EDTA as anticoagulant)

P – Plasma or blood collection tube (with anticoagulants like EDTA or heparin)

S - Serum tube (without anticoagulants)

DBS –Dried blood spot card

U – Urine tubes / screw cap container

CSF – Cerebrospinal fluid

SW – Sweat

2.1 Important information regarding the analytical services

For all offered enzyme activity tests, rare atypical disease variants are known that are not detected by these tests. Further diagnostics (e.g. other biochemical or genetic tests) must be carried out, regardless of the enzyme activity test result, if a disease is persistently suspected.