National

Screening Report

Germany 2010

Deutsche Gesellschaft für Neugeborenenscreening e.V.

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Abbreviations

CAH	Congenital adrenal hyperplasia
CACT - Deficiency	Carnitin-Acylcarnitin-Translocase-Deficiency
CPTI - Deficiency	Carnitin- Palmitoyl-CoA-Transferase I-Deficiency
CPTII - Deficiency	Carnitin- Palmitoyl-CoA-Transferase II-Deficiency
GA I	Glutaric acidaemia Type I
BW	Birth weight
HPA	Hyperphenylalaninaemia
IVA	Isovaleric anacidaemia
LCHAD Deficiency	Long-Chain-3-Hydroxy-Acyl-CoA-Dehydrogenase-Deficiency
DoL	Day of life
GV 1 - 3	Guide value 1 - 3
MCAD - Deficiency	Medium-Chain-Acyl-CoA-Dehydrogenase-Deficiency
MSUD	Maple syrup urine disease
NBS	Newborn screening
PKU	Phenylketonuria
PPV	Positive predictive value
Second-tier Process	In suspicious results secondary analysis of additional parameter or alternative analytical methods from the same test cards
WoG	Week of gestation
VLCAD Deficiency	Very-Long-Chain-Acyl-CoA-Dehydrogenase-Deficiency

Screening Laboratories and Screening Centres

Screening Centres (laboratories) with different localities or laboratories which are connected to a screening centre are analysised stratified.

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1 Introduction

The newborn screening is a medical population based preventative measure with the aim of early and sufficient detection and high quality therapy of all newborns with treatable endocrine metabolic diseases.

The guidelines of prevention of disease for children up to 6 years of age („Kinder-Richtlinien“) outline the details of newborn screening (NBS) in the appendices 2-4 [1].

The National Screening Report 2010 was composed by the “Deutschen Gesellschaft für Neugeborenenscreening (DGNS e.V.)” as well as the German screening laboratories. The statistical analysis of the screening data was according to the guidelines and their quality criteria of the NBS implementation. This report targets only the metabolic and endocrine diseases which are defined in these guidelines. It provides a wide statistical summary of disease related screening numbers and recall numbers at diagnoses for the year 2010. Additionally, data for process quality are presented.

Process quality describes the process flow and its evaluation through specialists according to defined indicators. These are the following for the newborn screening:

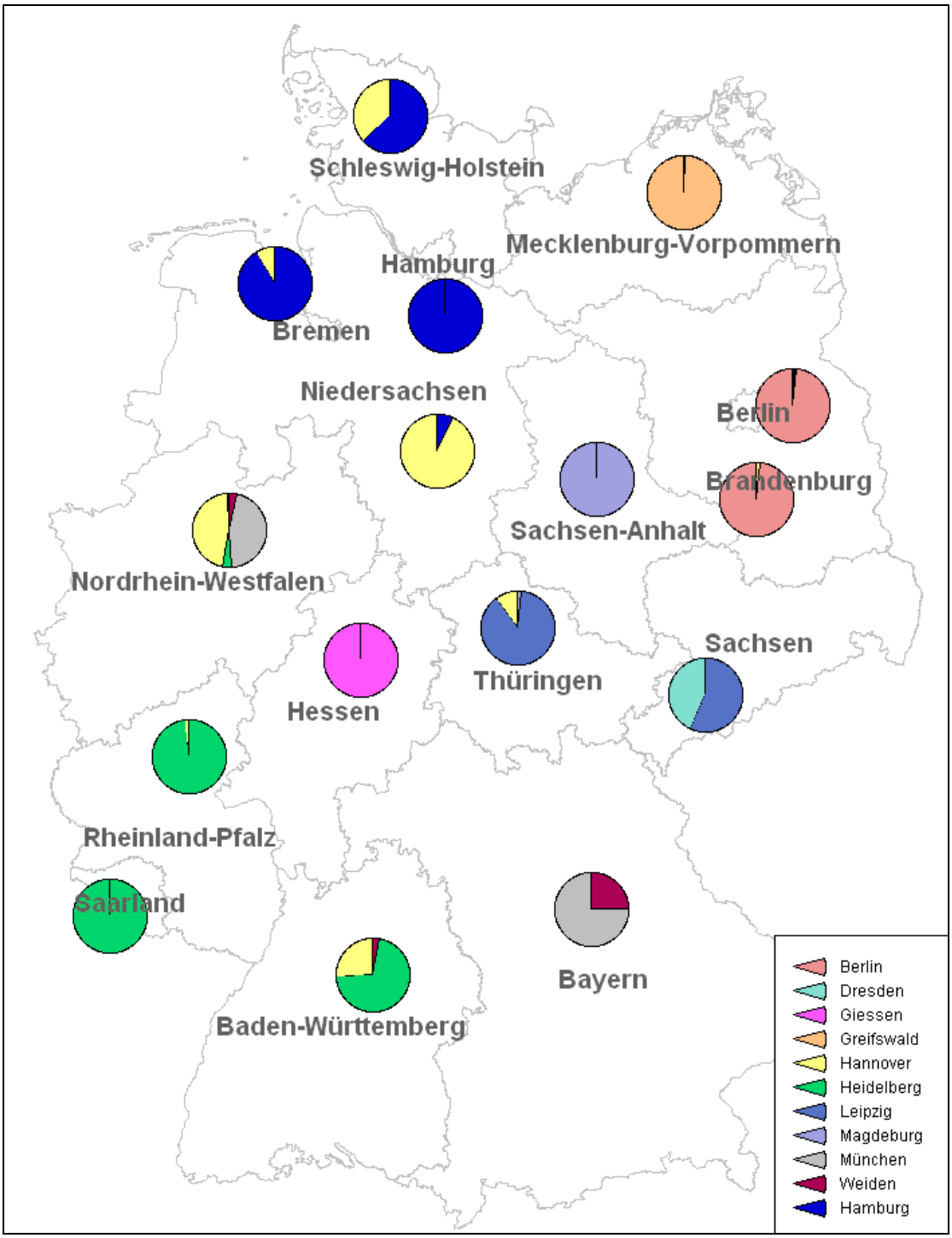
- Total survey of the targeted population
    - Collection method and rate
    - Blank card system
- Completeness of the control and the follow-up studies
- Collection of test parameters and cut offs
- Stratified rates of recall, positive predictive values and prevalence according to laboratory, age as well as gestational age,
- Specificity and sensitivity of diagnostic tests
- Process times (pre analytic and laboratory), age at blood collection, time within blood collections, time of arrival in the laboratory and time of result communication
- Screening values of newborns for which further testing is emphasized
- Diagnostics for confirmation
    - Type of diagnostics
    - Time of diagnostics
- Final diagnosis
- Start of therapy

Previously, laboratories are listed which have undertaken the screening in 2010 for Germany. (12 and 13 relate to the same laboratory, one with and without the co-operation of the Screening Centre, same for 14 and 15). In the tables the laboratories are encrypted. Paragraphs in the text relate to the guidelines for children from 21/12/04 [1]. Tables are numbered according to the chapters.

We would like to thank all the laboratories for provision of their data. The data was checked for plausibility. Remaining inconsistencies of data was analysed according to the reported data. (Inconsistencies can sometimes be due to the system).

The screening samples of the federal states are spread to the laboratories according to Figure1

Figure 1: Distribution of analysis according to county and laboratory



2 Results

In the year 2010 677.947 children were born in Germany [2].The total recorded screening exceeds this number slightly at 678.362. A cause for the additional screening cards could be wrongly labelled cards or test cards of newborns not registered in Germany.

A secure statement about the rate of participation in NGS can only be made by comparison of person related data or the population. By law this is only legal in the county of Bavaria.

Births [2]:	677.947
First screening:	678.362
Final diagnosis (seeTable 3):	518

In the German guidelines the targeted diseases are defined for the nationwide screening. Some laboratories screen for additional diseases embedded in scientific studies. These results are not presented in this report. Out of 1 in 1.309 newborns, one targeted disease according to the guidelines is found. Table 2 shows the prevalence of targeted diseases in the year 2010 in Germany.

Table: 2 Absolute number of detected diseases found by screening 2010

Disease	Confirmed cases	Prevalence
Hypothyroidism	207	1: 3275
Congenital adrenal hyperplasia (CAH)	39	1: 17.383
Biotinidase deficiency (incl. partial defect)	28	1: 24.212
Galactosaemia (classic)	6	1: 112.991
Phenylketonuria (PKU) n=73 / Hyperphenylalaninaemia (HPA) n=61 /Cofactor deficiency n=1	135	1: 5.022
Maple syryp urine disease (MSUD)	6	1: 112.991
Medium-Chain-Acyl-CoA-Dehydrogenase (MCAD)-Disease	63	1: 10.761
Long-Chain-3-OH-Acyl-CoA-Dehydrogenase (LCHAD)-Disease	5	1: 135.589
(Very-)Long-Chain-Acyl-CoA-Dehydrogenase (VLCAD)-Disease	12	1: 56.496
Carnitin-Palmitoyl-CoA-Transferase I (CPTI)-Disease	2	1: 338.974
Carnitin-Palmitoyl-CoA-Transferase II (CPTII)-Disease		
Carnitin-Acylcarnitin-Translocase (CACT)-Disease		
Glutarac aciduria Type (GA I)	3	1: 225.982
Isovaleric acidaemia (IVA)	12	1: 56.496
Total	**518**	1: 1.309

2.1 Data of primary screening

According to the guidelines of children, every newborn should be screened before leaving the birth facility. A reliable screening can only be undertaken with blood sampling beyond the completed 32nd gestational week and 36th hour of life. A primary screening before the 36th hour of life or before the completed 32nd week of gestation should be followed by a repeat screening. The following table shows the stratified results of the primary screening according to age and gestational age.

Table 2.1: Age at primary screening

Lab	Total	≥36h and ≥32WoG		<36h and ≥32WoG		<32WoG	
		n	%	n	%	n	%
1	51377	49536	96.42	1164	2.27	677	1.32
3	15483	15104	97.55	185	1.19	194	1.25
5	53203	51489	96.78	1150	2.16	564	1.06
6	13182	12621	95.74	399	3.03	162	1.23
7	44646	43099	96.53	944	2.11	603	1.35
8	159950	156099	97.59	1891	1.18	1960	1.23
9	108779	105840	97.30	1498	1.38	1441	1.32
10	35288	34528	97.85	401	1.14	359	1.02
11	17084	16498	96.57	379	2.22	207	1.21
12	78385	76697	97.85	819	1.04	869	1.11
13	68484	66709	97.41	951	1.39	824	1.20
14	24791	24288	97.97	276	1.11	227	0.92
15	7710	7505	97.34	78	1.01	127	1.65
Total	**678362**	**660013**	**97.30**	**10135**	**1.49**	**8214**	**1.21**

2.2 Relation of requested to received repeat screenings

In Table 2.2.1 the repeat screenings are listed stratified according to their base of request defined as:

- **„<32WoG“:** all sample of newborns before 32 WoG, independent of age and result of primary screening
- **„<36h“:** all sample of newborns beyond 32 WoG, but age less than 36h, independent of the result of primary screening
- **Recall:** essential repeat testing due to suspicious primary screening at a gestational age > 32 WoG and age > 36h

Repeat screenings from other laboratories and samples of deceased newborns (especially < 32 WoG) have often not been integrated in the statistics, since in-between laboratories no data transfer is implemented (data protection), resulting in implausible ranges.

Table 2.2: Requested and received repeat screenings

Lab	Total[a] requested	Total[a] received	%	Recall requested	Recall received	%
1	2458	2197	89.38	676	659	97.49
3[b,c]	468	467				
5	2181	2003	91.84	467	462	98.93
6	656	652	99.39	95	95	100
7[b]	2178	n/a		631	n/a	
8	5233	4486	85.73	976	929	95.18
9	3696	2495	67.51	433	370	85.45
10	1200	1187	98.92	413	413	100
11	659	640	97.12	71	70	98.59
12	2453	2437	99.35	821	818	99.63
13	2379	2367	99.50	604	600	99.34
14	598	595	99.50	105	105	100
15	261	182	69.73	50	48	96.00
Total	**24420**	**19708**	**88.37**[b]	**5342**	**4569**	**96.99**[b]

Lab	<36h requested	<36h received	%	<32WoG requested	<32WoG received	%
1	1105	948	85.79	561	476	84.85
3[b]	206	206	100	205	205	100
5	1150	1118	97.22	564	423	75.00
6	399	396	99.25	162	161	99.38
7[b]	944	n/a		603	n/a	
8	1891	1672	88.42	1960	1631	83.21
9	1498	813	54.27	1441	1091	75.71
10	401	397	99.00	358	350	97.77
11	379	370	97.63	207	198	95.65
12	811	798	98.40	821	821	100
13	951	945	99.37	824	822	99.76
14	275	272	98.91	218	218	100
15	78	22	28.21	127	106	83.46
Total	**10088**	**7957**	**87.02**[b]	**8051**	**6502**	**87.30**[b]

[a] Inclusive secondary screening due to blood transfusion, parenteral nutrition or medication
[b] Implausible data was not included in the table and the calculations
[c] total numbers without recall due to implausibility

2.3 Tracking of completeness of screening

The newborn screening is a measure of public health and should be given to all German born children. To guarantee that the screening is offered to all newborns the tracking of completeness is necessary. For children born in obstetric units, control can be undertaken through hospital records or if permitted by state law through the birth registry.

Currently both measures are not undertaken nationwide. To target the tracking of completeness the following rule was included into the "guidelines". The obstetric unit should document on a blank test card refusal of screening or death of a neonate. This test card should then be sent to the screening centre. The laboratory received blank test cards in various numbers. The number of blank screening cards due to refusal was low in 2010, but about 90% higher than in previous years.

Table 2.3: Laboratory received blank cards

Lab	Deceased	Screening declined	Transfer of newborn	Earling screening declined	Total
	n	n	n	n	n
1	44	0	0	3221	3265
3	32	24	1276	952	2284
5	33	103	0	2812	2948
6	1	4	0	69	74
7	0	7	0	251	258
8	n/a	n/a	n/a	n/a	1312
9	14	119	63	541	737
10	76	16	0	1485	1577
11	54	8	40	217	319
12	13	3	79	1068	1163
13	n/a	n/a	n/a	n/a	n/a
14	0	0	10	45	55
15	n/a	n/a	n/a	n/a	n/a
Total	**267**	**284**	**1468**	**10661**	**13992**

Table 2.4: Secondary screening due to poor quality of primary screening

Lab	Primary screening	Control requested	Control received	received/ requested (%)	Percentage of non processable screening cards/ Primary screening (%)
1	51377	251	235	93.63	0.49
3	15483	57	56	98.25	0.37
5	53203	377	370	98.14	0.71
6	13182	36	36	100	0.27
7	44646	80	66	82.50	0.18
8	159950	198	179	90.40	0.12
9	108779	604	578	95.70	0.56
10	35288	112	111	99.11	0.32
11	17084	1	1	100	0.01
12	78385	264	261	98.86	0.34
13	68484	234	229	97.86	0.34
14	24791	14	13	92.86	0.06
15	7710	7	7	100	0.09
Total	**678362**	**2235**	**2142**	**95.84**	**0.33**

3 Recall Rate, prevalence, positive predictive value and specificity

The excellence of a test is measured by the sensitivity, the specificity as well as the positive predictive value. In screening, the sensitivity (true-test positives) but more so the specificity (true-test negatives), should be high to find all diseases and to avoid unnecessary worries and costs. The lower the rate of necessary control screening due to positive first screening (recall rate) the higher the specificity. In 2010 the recall rate accounted for 0.81%. If we consider only screening cards of term newborns sampled beyond the 36th hour of life, the recall rate is 0.61%, meaning of 1000 tests only 6 are recalled. With sampling before the 36th hour of life or the 32nd WoG a secondary screening has to be done irrespective of the results.

The positive predictive value estimates the risk of disease with a positive test result. It depends on the sensitivity, the specificity and also the prevalence of the targeted disease, meaning the rarer a disease the lower the PPV, even with a high sensitivity and specificity. The total specificity was 99.47%. The sensitivity cannot be quoted, because systematic registration of unscreened neonates is not done. For the calculation of the PPV the sensitivity is estimated 99.5%.

Only screening sampled beyond the 32nd WoG and beyond the 36th hour of life the PPV is considered for analysis. Overall the PPV is 11.80% meaning that about 12% of suspicious screening results indicate the targeted disease. For several diseases the PPV is high, e.g. for HPA / PKU 56.47% for MCAD-Deficiency 34.52% and for hypothyroidism 35.23%. The range of PPV between the single laboratories is high.

Table 3: Recall rate, Specificity, Prevalence and PPV for Germany 2010 N= 678.362*

Disease	Recall >=36h	Recall rate (%) ≥36h	Confirmed cases	PPV ≥36h (%)	Prevalence (based on primary screening)	Not found in the screening
Hypothyroidism	528	0.08	207	35.23	1: 3277	9
CAH	2164	0.33	39	1.34	1: 17394	2
Biotinidase-Disease	169	0.03	28	16.57	1: 24227	
Classic Galactosaemia	388	0.06	6	1.55	1: 113060	
PKU/HPA	232	0.04	135	56.47	1: 5025	
MSUD	36	0.01	6	11.11	1: 113060	
MCAD	168	0.03	63	34.52	1: 10768	
LCHAD	18		5	16.67	1: 135672	
VLCAD	110	0.02	12	10	1: 56530	
CPT I-Disease	6		2	33.33	1: 339181	
CPT II-Disease	6				.	
CAT-Disease	0				.	
GA I	116	0.02	3	1.72	1: 226121	
IVA	60	0.01	12	20	1: 56530	
Total	**4001**	**0.61**	**518**	**11.80**	**1: 1310**	**11**

* Primary screening Total: n= 678.362; Primary screening ≥ 36h und ≥ 32WoG n= 660.013

3.1 Recall rate, prevalence stratified

The following tables show recall rates and prevalence of newborns > 36 hours of age and > 32 weeks gestational age stratified according to laboratories. The reference of > 36 hours automatically includes > 32 weeks gestational age. The confirmed diagnosis, confirmed cases and their prevalence relate to the total screening tests, irrespective of age and gestational age. The validation of confirmed cases was performed for metabolic diseases by Professor Andreas Schulze and Dr. Regina Ensenauer, for endocrine diseases by Dr. Oliver Blankenstein and PD Dr. Heiko Krude. Excluded and therefore not reported are cases with missing data of confirmation diagnostics (n=17) (Table 3.1.a) and cases where the confirmation diagnostics were negative (n=2). For that reason, for some diseases the true prevalence may be higher as reported. Double reported cases were included only once.

Table 3.1: Cases with missing data of confirmation diagnostics

Disease	Data missing
Hypothyroidism	14
CAH	2
Biotinidase Deficiency	
Galactosaemia (classic)	
PKU/HPA	
MSUD	
MCAD	1
LCHAD	
VLCAD	
CPT II-Disease	
GA I	
IVA	
Total	**17**

The next tables do not show recall rates <0.01% since small n cause a big variability.

3.1.1 Hypothyroidism*

Lab	Primary screening total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)	Confirmed cases*	Not found in the screening
1	51377	49536	47	0.09	22	1
3	15483	15104	2	0.01	2	0
5	53203	51489	72	0.14	11	0
6	13182	12621	8	0.06	2	0
7	44646	43099	31	0.07	10	0
8	159950	156099	137	0.09	47	2
9	108779	105840	84	0.08	42	0
10	35288	34528	16	0.05	8	1
11	17084	16498	14	0.08	8	0
12	78385	76697	43	0.06	23	2
13	68484	66709	47	0.07	15	2
14	24791	24288	20	0.08	13	1
15	7710	7505	7	0.09	4	0
Total	**678362**	**660013**	**528**	**0.08**	**207**	**9[a]**

* incl transient hypothyroidsm n=3

[a] Not found in the screening: 5 premature babies <31WoG see Tab. 5.3; 1 newborn with sampling at 15h of life, catecholamine infusion? ; 3 Children with Trisomy 21;see also following table 3.1.1a

Additionally n=8 persistent TSH-elevations were reported and validated. These are not included in the calculation of prevalence.

Table 3.1.1a: Congenital hypothyroidism not found in screening at preterm delivery (<32 WoG)

Patient	WoG	Day of primary screening	TSH value primary screening (mU/l)	Day of secondary screening	TSH value secondary screening (mU/l)	Age of control screening (WoG)*	Day of confirmation diagnostics	Age of confirmation (weeks)
1**	24	6	1.5	14	6.33	32	184	27
2	25	2	<2	101	82.1	39	98	14
3	27	2	3.6	89	76.3	40	91	13
4	27	2	<10	87	324	39	90	13
5	26	2	3.09	56	18.2	34	67	19

* Last reported control card
** Diagnosis of congenital hypothyroidism was confirmed

3.1.2 Congenital adrenal hyperplasia (CAH)

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)	Confirmed cases	Not found in the screening
1	51377	49536	185	0.37	5	1
3	15483	15104	2		1	0
5	53203	51489	250	0.49	3	0
6	13182	12621	44	0.35	0	0
7	44646	43099	254	0.59	0	0
8*	159950	156099	56	0.04	13	0
9	108779	105840	224	0.21	7	0
10	35288	34528	140	0.41	1	1
11	17084	16498	37	0.22	2	0
12	78385	76697	558	0.73	3	0
13	68484	66709	339	0.51	4	0
14	24791	24288	51	0.21	0	0
15	7710	7505	24	0.32	0	0
Total	**678362**	**660013**	**2164**	**0.33**	**39**	**2** [a]

* Laboratory used second-tier process
[a] Term babies, timely screened

3.1.3 Biotinidase deficiency

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	8	0.02	0
3	15483	15104	1		0
5	53203	51489	2		0
6	13182	12621	15	0.12	1
7	44646	43099	10	0.02	0
8	159950	156099	85	0.05	17
9	108779	105840	6	0.01	2
10	35288	34528	3		2
11	17084	16498	1		0
12	78385	76697	15	0.02	4
13	68484	66709	17	0.03	1
14	24791	24288	2		1
15	7710	7505	4		0
Total	**678362**	**660013**	**169**	**0.03**	**28**
thereof complete defect					**8**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.4 Galactosaemia

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	21	0.04	6
3	15483	15104	3		0
5	53203	51489	35	0.07	10
6	13182	12621	2		0
7	44646	43099	20	0.05	7
8	159950	156099	50	0.03	12
9	108779	105840	13	0.01	1
10	35288	34528	21	0.06	9
11	17084	16498	6	0.04	0
12	78385	76697	110	0.14	6
13	68484	66709	79	0.12	0
14	24791	24288	20	0.08	2
15	7710	7505	8	0.11	1
Total	**678362**	**660013**	**388**	**0.06**	**54**
thereof classic					**6**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.5 PKU / HPA

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	50	0.10	17
3	15483	15104	14	0.09	3
5	53203	51489	11	0.02	3
6	13182	12621	4		0
7	44646	43099	23	0.05	4
8	159950	156099	16	0.01	17 [b]
9	108779	105840	28	0.03	25
10	35288	34528	8	0.02	5
11	17084	16498	7	0.04	7
12	78385	76697	36	0.05	26
13	68484	66709	19	0.03	19
14	24791	24288	14	0.06	9
15	7710	7505	2		0
Total	678362	660013	232	0.04	135
thereof PKU					**73**

* Recall rate recorded only if ≥ 0.01% and n > 5.

[b] Recall in n=1 case <36h

3.1.6 MSUD

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	9		1
3	15483	15104	0		0
5	53203	51489	4		1
6	13182	12621	4		0
7	44646	43099	4		1
8	159950	156099	2		1
9	108779	105840	4		2
10	35288	34528	0		0
11	17084	16498	2		0
12	78385	76697	1		0
13	68484	66709	4		0
14	24791	24288	1		0
15	7710	7505	1		0
Total	**678362**	**660013**	**36**	**0.01**	**6**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.7 MCAD-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	36	0.07	6
3	15483	15104	4		1
5	53203	51489	59	0.11	4
6	13182	12621	7	0.06	2
7	44646	43099	12	0.03	4
8	159950	156099	12	0.01	11
9	108779	105840	14	0.01	11
10	35288	34528	2		2
11	17084	16498	2		1
12	78385	76697	12	0.02	14 [b]
13	68484	66709	2		2
14	24791	24288	5	0.02	4
15	7710	7505	1		1
Total	**678362**	**660013**	**168**	**0.03**	**63**

[*] Recall rate recorded only if ≥ 0.01% and n > 5.

[b] Recall in n=1 case <36h, in n=1 no information of age at primary screening. These cases do not account for recall rate

3.1.8 LCHAD-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	6		0
3	15483	15104	0		0
5	53203	51489	0		0
6	13182	12621	0		0
7	44646	43099	3		1
8	159950	156099	3		1
9	108779	105840	4		2
10	35288	34528	1		0
11	17084	16498	0		0
12	78385	76697	0		1
13	68484	66709	1		0
14	24791	24288	0		0
15	7710	7505	0		0
Total	**678362**	**660013**	**18**	**0.003**	**5**

[*] Recall rate due to small numbers only in absolute

3.1.9 VLCAD-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	26	0.05	2
3	15483	15104	3	0.02	1
5	53203	51489	15	0.03	0
6	13182	12621	2		0
7	44646	43099	37	0.09	0
8	159950	156099	3		3
9	108779	105840	17	0.02	2
10	35288	34528	1		0
11	17084	16498	0		0
12	78385	76697	4		3
13	68484	66709	1		1
14	24791	24288	1		0
15	7710	7505	0		0
Total	**678362**	**660013**	**110**	**0.02**	**12**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.10 CPT I-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	4		1
3	15483	15104	0		0
5	53203	51489	0		0
6	13182	12621	0		0
7	44646	43099	0		0
8	159950	156099	0		0
9	108779	105840	1		0
10	35288	34528	0		0
11	17084	16498	0		0
12	78385	76697	1		1
13	68484	66709	0		0
14	24791	24288	0		0
15	7710	7505	0		0
Total	**678362**	**660013**	**6**		**2**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.11 No confirmed cases of CPTII-Deficiency and for CACT-Deficiency

3.1.12 Glutaric acidaemia Type I

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	58	0.12	1
3	15483	15104	0		0
5	53203	51489	15	0.03	0
6	13182	12621	6	0.05	0
7	44646	43099	24	0.06	0
8	159950	156099	0		0
9	108779	105840	10	0.01	0
10	35288	34528	0		0
11	17084	16498	0		0
12	78385	76697	2		1
13	68484	66709	1		1
14	24791	24288	0		0
15	7710	7505	0		0
Total	**678362**	**660013**	**116**	**0.02**	**3**

* Recall rate recorded only if ≥ 0.01% and n > 5.

3.1.13 Isovaleric acidaemia

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall rate(%)*	Confirmed cases
1	51377	49536	27	0.05	0
3	15483	15104	0		0
5	53203	51489	4		2
6	13182	12621	1		0
7	44646	43099	2		2
8	159950	156099	1		1
9	108779	105840	3		3
10	35288	34528	3		0
11	17084	16498	2		0
12	78385	76697	8	0.01	1
13	68484	66709	8	0.01	2
14	24791	24288	1		1
15	7710	7505	0		0
Total	**678362**	**660013**	**60**	**0.01**	**12**

* Recall rate recorded only if ≥ 0.01% and n > 5

3.2 Recall rate stratified according to time of primary screening

The number of positives, especially false positive screening results and therefore the recall rate depends on age and gestational age. Earlier testing than the 36th hour of life and a gestational age of <32 weeks increases the risk of false negative and false positive results. This differs for the targeted diseases. In the following tables we stratify the recall rates by gestational age and timing of the sampling. Recall rate is recorded only if it exceeds 0.01% and n > 5 since small numbers cause a high variability.

3.2.1 Hypothyroidism

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate
1	49536	47	0.09	1164	6	0.52	677	1	0.15
3	15104	2		185	0		194	0	
5	51489	72	0.14	1150	8	0.70	564	5	0.89
6	12621	8	0.06	399	0		162	0	
7	43099	31	0.07	944	48	5.08	603	0	
8	156099	137	0.09	1891	160	8.46	1960	13	0.66
9	105840	84	0.08	1498	2		1441	4	
10	34528	16	0.05	401	43	10.72	359	0	
11	16498	14	0.08	379	66	17.41	207	0	
12	76697	43	0.06	819	31	3.79	869	0	
13	66709	47	0.07	951	4		824	19	2.31
14	24288	20	0.08	276	10	3.62	227	0	
15	7505	7	0.09	78	1		127	0	
Total	**660013**	**528**	**0.08**	**10135**	**379**	**3.74**	**8214**	**42**	**0.51**

3.2.2 Congenital adrenal hyperplasia (CAH)

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate
1	49536	185	0.37	1164	37	3.18	677	55	8.12
3	15104	2		185	1		194	3	
5	51489	250	0.49	1150	9	0.78	564	28	4.96
6	12621	44	0.35	399	0		162	0	
7	43099	254	0.59	944	38	4.03	603	156	25.87
8	156099	56	0.04*	1891	163	8.62	1960	32	1.63*
9	105840	224	0.21	1498	5		1441	13	0.90
10	34528	140	0.41	401	76	18.95	359	23	6.41
11	16498	37	0.22	379	17	4.49	207	6	2.90
12	76697	558	0.73	819	53	6.47	869	100	11.51
13	66709	339	0.51	951	23	2.42	824	34	4.13
14	24288	51	0.21	276	5		227	12	5.29
15	7505	24	0.32	78	2		127	13	10.24
Total	**660013**	**2164**	**0.33**	**10135**	**429**	**4.23**	**8214**	**475**	**5.78**

* Laboratoryoratory used second-tier process at screening >36h und <32 WoG

3.2.3 Biotinidase Deficiency

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	8	0.02	1164	3		677	3	
3	15104	1		185	0		194	0	
5	51489	2		1150	0		564	0	
6	12621	15	0.12	399	0		162	0	
7	43099	10	0.02	944	0		603	0	
8	156099	85	0.05	1891	6		1960	6	
9	105840	6	0.01	1498	0		1441	0	
10	34528	3		401	0		359	0	
11	16498	1		379	0		207	1	
12	76697	15	0.02	819	0		869	0	
13	66709	17	0.03	951	0		824	0	
14	24288	2		276	1		227	0	
15	7505	4		78	0		127	0	
Total	**660013**	**169**	**0.03**	**10135**	**10**	**0.10**	**8214**	**10**	**0.12**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.4 Galactosaemia

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	21	0.04	1164	0		677	1	
3	15104	3		185	0		194	0	
5	51489	35	0.07	1150	2		564	2	
6	12621	2		399	0		162	0	
7	43099	20	0.05	944	0		603	0	
8	156099	50	0.03	1891	0		1960	0	
9	105840	13	0.01	1498	0		1441	0	
10	34528	21	0.06	401	1		359	0	
11	16498	6	0.04	379	0		207	0	
12	76697	110	0.14	819	1		869	1	
13	66709	79	0.12	951	0		824	1	
14	24288	20	0.08	276	0		227	0	
15	7505	8	0.11	78	0		127	0	
Total	**660013**	**388**	**0.06**	**10135**	**4**	**0.04**	**8214**	**5**	**0.06**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.5 PKU/HPA

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate
1	49536	50	0.10	1164	9		677	8	1.18
3	15104	14	0.09	185	1		194	0	
5	51489	11	0.02	1150	0		564	6	1.06
6	12621	4		399	0		162	0	
7	43099	23	0.05	944	0		603	2	
8	156099	16	0.01	1891	2		1960	0	
9	105840	28	0.03	1498	1		1441	1	
10	34528	8	0.02	401	0		359	7	1.95
11	16498	7	0.04	379	0		207	0	
12	76697	36	0.05	819	1		869	2	
13	66709	19	0.03	951	1		824	4	
14	24288	14	0.06	276	2		227	2	
15	7505	2		78	0		127	1	
Total	**660013**	**232**	**0.04**	**10135**	**17**	**0.17**	**8214**	**33**	**0.40**

**Recall rate for screening < 36h only in total.

3.2.6 MSUD

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	9	0.02	1164	0		677	3	
3	15104	0		185	0		194	1	
5	51489	4		1150	0		564	0	
6	12621	4		399	0		162	0	
7	43099	4		944	0		603	2	
8	156099	2		1891	0		1960	0	
9	105840	4		1498	0		1441	0	
10	34528	0		401	0		359	0	
11	16498	2		379	0		207	0	
12	76697	1		819	1		869	0	
13	66709	4		951	0		824	1	
14	24288	1		276	0		227	0	
15	7505	1		78	0		127	2	
Total	**660013**	**36**	**0.01**	**10135**	**1**	**0.01**	**8214**	**9**	**0.11**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.7 MCAD-Disease

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	36	0.07	1164	1		677	1	
3	15104	4		185	0		194	0	
5	51489	59	0.11	1150	3		564	1	
6	12621	7	0.06	399	0		162	0	
7	43099	12	0.03	944	0		603	0	
8	156099	12	0.01	1891	1		1960	0	
9	105840	14	0.01	1498	0		1441	0	
10	34528	2		401	0		359	0	
11	16498	2		379	0		207	0	
12	76697	12	0.02	819	0		869	0	
13	66709	2		951	0		824	0	
14	24288	5		276	0		227	0	
15	7505	1		78	0		127	0	
Total	**660013**	**168**	**0.03**	**10135**	**5**	**0.05**	**8214**	**2**	**0.02**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.8 LCHAD-Disease

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate
1	49536	6		1164	0		677	0	
3	15104	0		185	0		194	0	
5	51489	0		1150	0		564	0	
6	12621	0		399	0		162	0	
7	43099	3		944	0		603	0	
8	156099	3		1891	0		1960	1	
9	105840	4		1498	1		1441	1	
10	34528	1		401	0		359	0	
11	16498	0		379	0		207	0	
12	76697	0		819	1		869	0	
13	66709	1		951	0		824	0	
14	24288	0		276	0		227	0	
15	7505	0		78	0		127	0	
Total	**660013**	**18**	**0.003**	**10135**	**2**	**0.02**	**8214**	**2**	**0.02**

*Recall rate for screening only in total due to small numbers

3.2.9 VLCAD-Disease

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	26	0.05	1164	1		677	1	
3	15104	3		185	0		194	0	
5	51489	15	0.03	1150	0		564	12	2.13
6	12621	2		399	0		162	0	
7	43099	37	0.09	944	1		603	1	
8	156099	3		1891	0		1960	1	
9	105840	17	0.02	1498	0		1441	1	
10	34528	1		401	0		359	0	
11	16498	0		379	0		207	0	
12	76697	4		819	0		869	0	
13*	66709	1		951	0		824	0	
14	24288	1		276	0		227	0	
15	7505	0		78	0		127	0	
Total	**660013**	**110**	**0.02**	**10135**	**2**	**0.02**	**8214**	**16**	**0.19**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.10 CPTI-Disease

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate
1	49536	4		1164	0		677	0	
3	15104	0		185	0		194	0	
5	51489	0		1150	0		564	0	
6	12621	0		399	0		162	0	
7	43099	0		944	0		603	0	
8	156099	0		1891	0		1960	0	
9	105840	1		1498	0		1441	0	
10	34528	0		401	0		359	0	
11	16498	0		379	0		207	0	
12	76697	1		819	0		869	0	
13	66709	0		951	0		824	0	
14	24288	0		276	0		227	0	
15	7505	0		78	0		127	0	
Total	**660013**	**6**		**10135**	**0**		**8214**	**0**	

*Recall rate for screening only in total due to small numbers

3.2.11 CPTII-Disease/CACT-Disease

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate
1	49536	1		1164	0		677	0	
3	15104	0		185	0		194	0	
5	51489	0		1150	0		564	0	
6	12621	1		399	0		162	0	
7	43099	0		944	0		603	0	
8	156099	0		1891	0		1960	0	
9	105840	1		1498	0		1441	0	
10	34528	0		401	0		359	0	
11	16498	0		379	0		207	0	
12	76697	0		819	0		869	0	
13	66709	3		951	0		824	0	
14	24288	0		276	0		227	0	
15	7505	0		78	0		127	0	
Total	**660013**	**6**		**10135**	**0**		**8214**	**0**	

*Recall rate for screening only in total due to small numbers

3.2.12 Glutaric aciduria type I

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	58	0.12	1164	0		677	1	
3	15104	0		185	0		194	0	
5	51489	15	0.03	1150	0		564	2	
6	12621	6	0.05	399	1		162	0	
7	43099	24	0.06	944	1		603	1	
8	156099	0		1891	0		1960	0	
9	105840	10	0.01	1498	0		1441	1	
10	34528	0		401	0		359	0	
11	16498	0		379	0		207	0	
12	76697	2		819	2		869	1	
13	66709	1		951	0		824	0	
14	24288	0		276	0		227	0	
15	7505	0		78	0		127	0	
Total	**660013**	**116**	**0.02**	**10135**	**4**	**0.04**	**8214**	**6**	**0.07**

*Recall rate for screening < 36h und < 32 WoG only in total.

3.2.13 Isovaleric acidaemia

Lab	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Primary screening	Recall	Recall rate	Primary screening	Recall	Recall rate*	Primary screening	Recall	Recall rate*
1	49536	27	0.05	1164	0		677	14	
3	15104	0		185	0		194	1	
5	51489	4		1150	0		564	0	
6	12621	1		399	0		162	0	
7	43099	2		944	0		603	0	
8	156099	1		1891	0		1960	0	
9	105840	3		1498	0		1441	0	
10	34528	3		401	0		359	0	
11	16498	2		379	0		207	0	
12	76697	8	0.01	819	0		869	0	
13	66709	8	0.01	951	1		824	1	
14	24288	1		276	0		227	0	
15	7505	0		78	0		127	1	
Total	**660013**	**60**	**0.01**	**10135**	**1**	**0.01**	**8214**	**17**	**0.21**

*Recall rate for screening < 36h und < 32 WoG only in total.

4 Process Periods

4.1 Age at blood collection

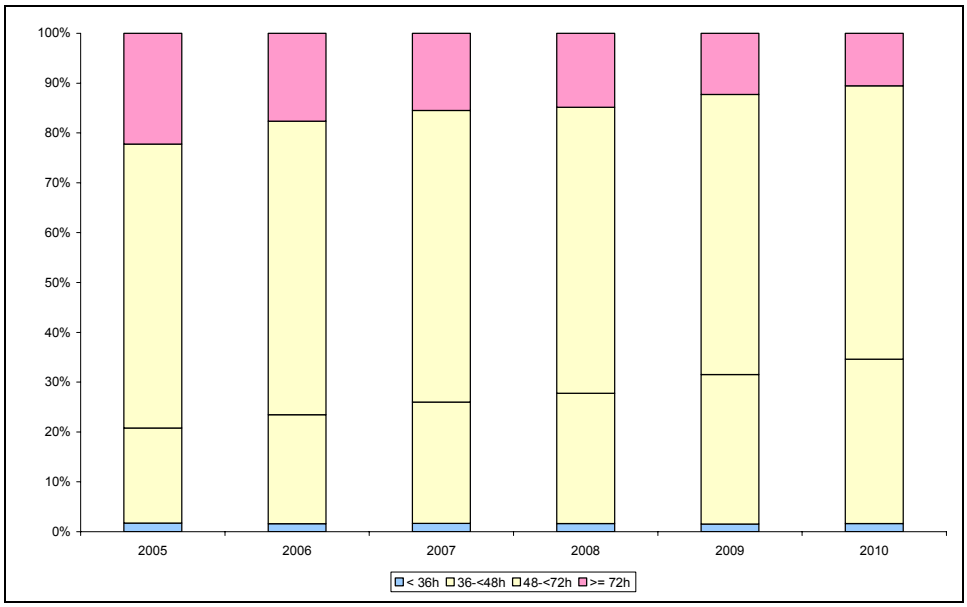
According to the guidelines (§8.1) of children, every newborn should be screened beyond the completed 32nd gestational week and 36th hour of life. In 88% of cases, with specification of collection time, the collection was according to the guidelines, in 10.5% (5.29-16.07%) beyond the 72nd hour of life, in 1.6% (1.09-3.03%) before the 36th hour of life (see Table 4.1). The proportion of samples which were sampled after 72 hours could be lowered from 22.25% in 2005 to 10.54 % in 2010 (see figure 2). These numbers clearly imply an improvement of the process quality, since the adherence to the optimal timeframe is of great importance to the efficiency of the screening. Life threatening metabolic or electrolyte crisis can be prevented by early diagnosis and therapy.

Table 4.1: Age at blood collection, primary screening

Lab	Total	<36h		36h-<48h		48h-<72h		≥72h	
	n	n	%	n	%	n	%	n	%
1[a]	51289	1275	2.49	9291	18.11	33008	64.36	7715	15.04
3[a]	15475	226	1.46	2082	13.45	12348	79.79	819	5.29
5[a]	53141	1203	2.26	31753	59.75	17959	33.79	2226	4.19
6	13182	399	3.03	3445	26.13	8445	64.06	893	6.77
7	44646	938	2.10	12327	27.61	24205	54.22	7176	16.07
8[a]	147878	1891	1.28	55731	37.69	75931	51.35	14325	9.69
9[a]	108766	1639	1.51	27502	25.29	64230	59.05	15395	14.15
10	35288	414	1.17	7965	22.57	22700	64.33	4209	11.93
11	17084	406	2.38	3900	22.83	11570	67.72	1208	7.07
12[a]	75408	838	1.11	27691	36.72	39821	52.81	7058	9.36
13	68484	1256	1.83	24932	36.41	36589	53.43	5707	8.33
14[a]	24124	292	1.21	8792	36.45	12695	52.62	2345	9.72
15	7710	84	1.09	3072	39.84	3827	49.64	727	9.43
Total	**662475**	**10861**	**1.64**	**218483**	**32.98**	**363328**	**54.84**	**69803**	**10.54**

The number of samples with unrecorded sampling time is smaller than the totally primary screening (marked with [a]).

Figure 2: Comparison: Age at blood collection 2005 and 2010



Predicted time of screening

4.2 Period from sampling to laboratory receipt

The time span between sampling and report of suspect results should not exceed 72 hours (section 6. paragraph 3). In 20.5% of cases with statement of the delivery time the probe was received 72 hours after sampling, in 23.6% of the cases between 48 and 72 hours. Shorter periods of delivery times are desirable, especially at the weekend. (Table 4.2, Figure 3)

Figure 3: Period between sampling and laboratory receipt: Comparison 2005 to 2010

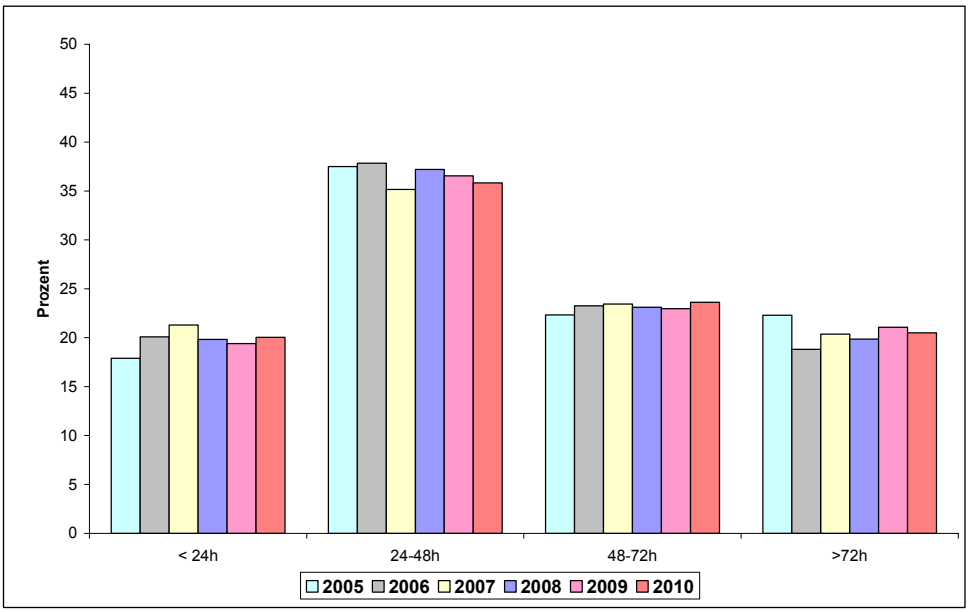


Table 4.2: Period between sampling and laboratory receipt

Lab	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1[a]	51212	12379	24.17	20220	39.48	10781	21.05	7832	15.29
3[a]	15405	5182	33.64	6145	39.89	2739	17.78	1339	8.69
5[a]	53141	6671	12.55	24694	46.47	14061	26.46	7715	14.52
6[a]	12317	1975	16.03	5988	48.62	2945	23.91	1409	11.44
7	44646	10228	22.91	13942	31.23	9005	20.17	11471	25.69
8[a]	151256	17803	11.77	51304	33.92	40122	26.53	42027	27.79
9[a]	108774	10048	9.24	34592	31.80	27672	25.44	36462	33.52
10	35288	5013	14.21	13021	36.90	9468	26.83	7786	22.06
11[a]	17080	2717	15.91	8064	47.21	4287	25.10	2012	11.78
12[a]	75408	26571	35.24	27535	36.51	13564	17.99	7738	10.26
13	68484	20085	29.33	23555	34.39	17624	25.73	7220	10.54
14[a]	24130	14052	58.23	6373	26.41	2661	11.03	1044	4.33
15	7710	544	7.06	2771	35.94	2115	27.43	2280	29.57
Total	**664851**	**133268**	**20.04**	**238204**	**35.83**	**157044**	**23.62**	**136335**	**20.51**

The number of samples with unrecorded sampling time is smaller than the total number of primary screening in previous tables (marked with [a]).

4.3 Period between laboratory receipt and result reporting

In more than three quarters of probes the results get reported within 24 hours. The process time in borderline elevated results can be prolonged due to repeat testing (quality control) (Table 4.3, Figure 4).

Figure 4: Time between receipt and report, comparison of the years 2005 to 2010

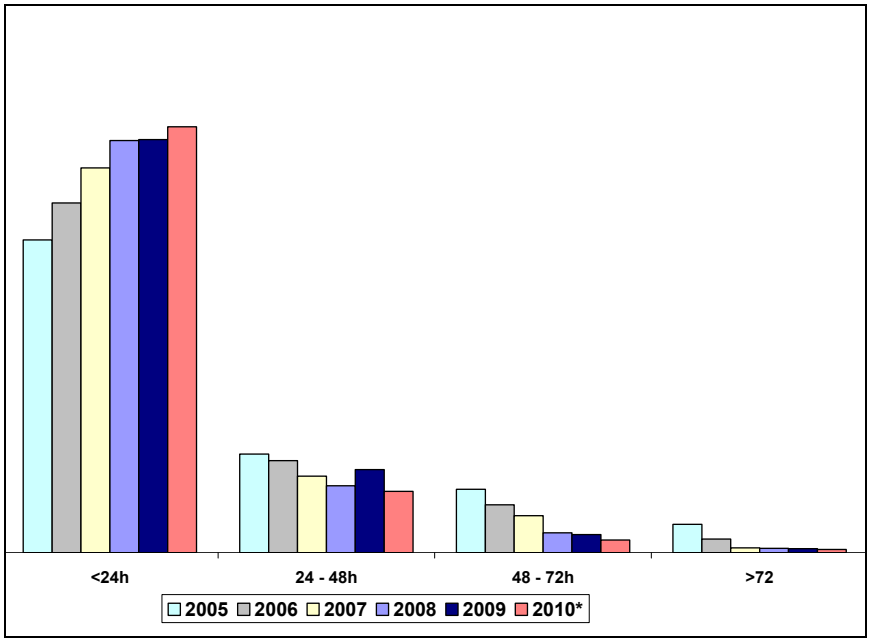


Table 4.3 Period between laboratory receipt and report

Lab	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1[a]	51374	27614	53.75	19143	37.26	3545	6.90	1072	2.09
3[a]	15451	11784	76.27	2820	18.25	230	1.49	617	3.99
5[a]	53122	397	0.75	35833	67.45	10720	20.18	6172	11.62
8	159950	153554	96.00	5869	3.67	111	0.07	416	0.26
9[a]	108702	106574	98.04	1849	1.70	140	0.13	139	0.13
10	35288	29785	84.41	5223	14.80	247	0.70	33	0.09
11[a]	17083	11307	66.19	5439	31.84	317	1.86	20	0.12
12[a]	76731	59858	78.01	12132	15.81	4468	5.82	273	0.36
13	68484	52974	77.35	10464	15.28	4108	6.00	938	1.37
14[a]	24298	17150	70.58	5807	23.90	1116	4.59	225	0.93
15[a]	7700	7541	97.94	155	2.01	4	0.05	0	
Total*	**618183**	**478538**	**84.62***	**104734**	**12.19***	**25006**	**2.53***	**9905**	**0.66***

The number of samples with unrecorded sampling time is smaller than the total number of primary screening in previous tables (marked with [a]).
Listed are only laboratories which provide data.
*Percentages without Lab 5

5 Time of screening in the confirmed cases

5.1 Primary Screening

Crucial for a successful screening is the reliability of results and the promptness of further diagnostic evaluation and therapy in suspect cases. The optimal sampling time is the 48th to the 72nd hour of life. The probe should not be sampled before the 36th and not after the 72nd hour of life. Any delay means a potential risk for affected children.

The time of primary screening is shown for the targeted disease in Table 5.1. For clarity reasons the description >72 hours of age is reported in days. About 7% of diseased children were at the time of sampling older than 72 hours.

Table 5.1 Time of primary screening in confirmed cases

Disease	36-72h	4-7d	>7d	<36h	<32WoG	≥36h, n.s. time *	No information**	Total
Hypothyroidism	172	15	2	4	14			**207**
CAH	32	2		3	1			**39**
Biotinidase	24	2				2		**28**
Classic Galactosaemia	5	1						**6**
PKU/HPA	120	10		3	1	1		**135**
MSUD	4						2	**6**
MCAD	52	3	1	2	1	2	2	**63**
LCHAD	3			1	1			**5**
VLCAD	10	1					1	**12**
CPT I	1	1						**2**
GA I	2			1				**3**
IVA	12							**12**
Total	**437**	**35**	**3**	**14**	**19**	**5**	**5**	**518**

*≥ 36h n.s. does not include repeat testing with early sampling or preterm birth, exact age of sampling time not stated.
** No information, neither WoG nor age at sampling.

5.2 Indication for request of repeat testing in the confirmed cases.

An indication for a secondary screening could be early sampling before the 32nd week of pregnancy or before the 36th hour of life, even in children with confirmed diagnosis. In Table 5.2 the indications for repeat testing are shown.

Table 5.2: Indication for request of repeat testing in the confirmed cases

Disease	Indication for repeat screening				Total
	Suspicious Primary screening	< 36h*	<32WoG*	n/a*	
Hypothyroidism	186	4	14	3	**207**
CAH	32	3	2	2	**39**
Biotinidase	28				**28**
classic Galactosaemia	6				**6**
PKU/HPA	131	3	1		**135**
MSUD	4			2	**6**
MCAD	58	2	1	2	**63**
LCHAD	3	1	1		**5**
VLCAD	11			1	**12**
CPT I	2				**2**
GA I	2	1			**3**
IVA	12				**12**
Total	**475**	**14**	**19**	**10**	**518**

* incl. cases not found in screening

6 Confirmation of pathological results

The following chapter outlines the diagnostic measures for confirmation of the suspected diagnosis as known to the laboratories. This information is used for quality control by the individual laboratories but does not always get reported by the physicians, taking care of the patient. For the year 2010 in 22 out of 516 confirmed cases no detailed information about the confirmation diagnostics is available, the available data though allows a plausible analysis. In a further 18 cases only limited information is given, that confirmation can not be accepted and we therefore do not list it in our analysis.

6.1 Hypothyroidism

Lab	Confirmed cases*	TSH (Serum)	T3	fT3	T4	fT4	Ultrasound	Thyroid antibodies
1	22	22	4	1	6	22	22	3
3	2	2	2	1	2	2	1	2
5	11	11	n/a	10	n/a	8	9	9
6	2	2	1	2	1	2	2	2
7	10	8	n/a	7	n/a	7	6	4
8	47	45	0	32	0	41	35	24
9	42	41	14	22	13	40	5	1
10	8	7	2	4	2	7	6	4
11	8	7	n/a	5	1	8	5	5
12	23	23	2	17	n/a	22	18	14
13	15	15	n/a	n/a	n/a	15	n/a	n/a
14	13	13	n/a	10	n/a	13	5	2
15	4	4	n/a	4	n/a	4	2	2
Total	**207**	**200**	**25**	**115**	**25**	**191**	**116**	**72**

* incl n=3 cases without detailed information of confirmation diagnostics

6.2 Congenital adrenal hyperplasia (CAH)

Lab	Confirmed cases*	17-OHP (Serum)	Steroid (Serum/TB)	Urinary steroids	Molecular genetic testing
1	5	4	4	n/a	4
3	1	1	1	n/a	1
5	3	2	2	2	n/a
8	13	12	12	2	11
9	7	7	4	1	n/a
10	1	n/a	n/a	n/a	n/a
11	2	2	1	n/a	1
12	3	2	2	n/a	n/a
13	4	1	1	n/a	2
Total	**39**	**31**	**27**	**5**	**19**

* incl n=5 cases without detailed information of confirmation diagnostics

6.3 Biotinidase Deficiency

Lab	Confirmed cases*	Biotinidase (Serum/TB)	Molecular genetic testing
6	1	1	n/a
8	17	15	0
9	2	2	n/a
10	2	2	n/a
12	4	4	3
13	1	1	n/a
14	1	n/a	n/a
Total	**28**	**25**	**3**

* incl n=3 cases without detailed information of confirmation diagnostics

6.4 Classic Galactosaemia

Lab	Confirmed cases	Enzyme assay	Galactose, Gal1P	Molecular genetic testing
5	1	1	0	1
7	2	n/a	0	2
8	2	2	2	0
9	1	0.	1	n/a
Total	**6**	**3**	**3**	**3**

6.5 PKU / HPA

Lab	Confirmed cases*	Phe (Serum/TB)	Phe/Tyr	BH4-Test	Molecular genetic testing	Pterine in urine	DHPR in dried blood
1	17	17	16	5	11	17	17
3	3	3	3	3	n/a	3	1
5	3	3	3	3	n/a	2	2
7	4	3	3	2	2	3	3
8	17	17	7	10	2	11	10
9	25	19	18	4	0	15	15
10	5	5	4	1	4	5	5
11	7	7	6	6	1	6	6
12	26	24	13	13	7	20	18
13	19	18	16	10	n/a	18	18
14	9	7	5	9	1	3	3
Total	**135**	**123**	**94**	**66**	**28**	**103**	**98**

* incl n=6 cases without detailed information of confirmation diagnostics

6.6 MSUD

Lab	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	1	1	1	n/a	n/a
5	1	1	n/a	n/a	n/a
7	1	1	1	n/a	n/a
8	1	1	0	0	0
9	2	2	2	n/a	n/a
Total	**6**	**6**	**4**		

6.7 MCAD-Disease

Lab	Confirmed cases*	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	6	6	6	4	5
3	1	n/a	n/a	n/a	n/a
5	4	n/a	3	n/a	4
6	2	n/a	1	n/a	2
7	4	3	3	n/a	3
8	11	4	2	3	9
9	11	10	8	n/a	1
10	2	2	2	n/a	2
11	1	1	1	n/a	n/a
12	14	7	7	n/a	13
13	2	n/a	1	n/a	2
14	4	3	n/a	n/a	4
15	1	1	1	n/a	n/a
Total	**63**	**37**	**35**	**7**	**45**

* incl n=5 cases without detailed information of confirmation diagnostics

6.8 LCHAD-Disease

Lab	Confirmed cases	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
7	1	1	1	n/a	1
8	1	0	1	0	1
9	2	2	1	n/a	1
12	1	n/a	1	1	1
Total	**5**	**3**	**4**	**1**	**4**

6.9 VLCAD-Disease

Lab	Confirmed cases	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	2	1	2	2	2
3	1	1	n/a	1	1
8	3	2	2	3	1
9	2	1	n/a	1	2
12	3	2	3	2	3
13	1	n/a	n/a	n/a	1
Total	**12**	**7**	**7**	**9**	**10**

6.10 CPT I-Disease

Lab	Confirmed cases	Confirmation Serum/TB	Enzyme activity	Molecular genetic testing
1	1	1	n/a	1
12	1	n/a	n/a	1
Total	**2**	**1**	**n/a**	**2**

6.11 No confirmed cases of CPT II-Disease, CACT-Disease

6.12 Glutaric aciduria Type I

Lab	Confirmed cases	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	1	1	1	n/a	1
12	1	1	1	n/a	1
13	1	1	1	n/a	n/a
Total	**3**	**3**	**3**	**n/a**	**2**

6.13 Isovaleric acidaemia

Lab	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
5	2	n/a	2	n/a	2
7	2	2	2	n/a	2
8	1	1	1	0	0.
9	3	3	3	n/a	n/a
12	1	1	1	n/a	1
13	2	n/a	2	n/a	2
14	1	1	1	n/a	n/a
Total	**12**	**8**	**12**	**n/a**	**7**

7 Methods and cut offs in screening

7.1 Filter paper for sampling

Lab	Filterpaper
1	ID Biological (Ahlstrom 226)
3	ID Biological (Ahlstrom 226)
5	TFN (Munktell)
6	ID Biological (Ahlstrom 226)
7	WS 903
8	TFN (Munktell)
9	WS 903
10	WS 903
11	ID Biological (Ahlstrom 226)
12	Munktell
13	Munktell
14	WS 903
15	WS 903

7.2 Hypothyroidism

Lab	Parameter	Cut off	Method
1	TSH	15 mU/l	AutoDELFIA
3	TSH	15 mU/l	AutoDELFIA
5	TSH	13 mU/l	AutoDELFIA
6	TSH	15 mU/l	DELFIA
7	TSH	15 mU/l	AutoDELFIA
8	TSH	> 15 mU/l	DELFIA
9	TSH	15 mU/l	AutoDELFIA
10	TSH	15 mU/l	AutoDELFIA
11	TSH	15 mU/l	DELFIA
12	TSH	>20 mU/l	AutoDELFIA
13	TSH	>20 mU/l	AutoDELFIA
14	TSH	> 20 mU/l	AutoDELFIA
15	TSH	> 20 mU/l	AutoDELFIA

7.3 Biotinidase Deficiency

Lab	Parameter	Cut off	Method
1	Biotinidase	30% board mean	Colorimetry qualitative
3	Biotinidase	30% day mean	Colorimetry qualitative
5	Biotinidase	n/a	n/a
6	Biotinidase	70 U	Flurometrie (PE)
7	Biotinidase	2.7 U/g Hb	Colorimetry quantitative
8	Biotinidase	< 30% day mean	Colorimetry quantitative
9	Biotinidase	< 30%	Colorimetry qualitative
10	Biotinidase	< 30%	Colorimetry qualitative
11	Biotinidase	n/a	Colorimetry qualitative
12	Biotinidase	< 30%	Fluorometry quantitative
13	Biotinidase	< 30%	Fluorometry quantitative
14	Biotinidase	< 30%	Colorimetry quantitative
15	Biotinidase	< 30%	Colorimetry quantitative

7.4 Galactosaemia

Lab	Parameter	Cut off	Method
1	GALT Galactose	3.5 U/gHb 20 mg/dl	Fluorometry(PE) BIORAD Quantase
3	GALT Galactose	2.3 Ug/Hb 15 mg/dl	BIORAD Quantase
5	GALT Galactose	n/a	n/a
6	GALT	3.5 U/g Hb	Fluorometry (PE)
7	GALT	3.5 U/g Hb	Fluorometry quantitative
8	GALT Galactose	<20 % day mean >30mg/dl	Fluorometry quantitative Colorimetry quantitative
9	GALT Galactose*	<2.3 U/gHb 20 mg/dl	BIORAD Quantase BIORAD Quantase
10	GALT Galactose	2.3 U/gHb 1111 µmol/l	BIORAD Quantase BIORAD Quantase
11	GALT	3.5 U/gHb	Fluorometry quantitative
12	GALT Galactose	<30% 15 mg/dl	Fluoro. quant.(non-kit) Colorimetry non Kit
13	GALT Galactose	<30% 15 mg/dl	Fluoro. quant.(non-kit) Colorimetry non Kit
14	GALT Galactose	<2.3 U/g Hb >15 mg/dl	BIORAD Quantase BIORAD Quantase
15	GALT Galactose	<2.3 U/g Hb >15 mg/dl	BIORAD Quantase BIORAD Quantase

* galactose as second-tier process

7.5 MS/MS

Lab	Method
1	derivative Chromsystems
3	non-derivat. non Kit
5	non-derivat. non Kit
6	non-derivat.PE Kit
7	derivative PE Kit
8	derivative non Kit
9	derivative non Kit
10	derivative non Kit
11	non-derivat.non Kit
12	derivative non Kit
13	derivative non Kit
14	derivatisiert non Kit
15	derivatisiert non Kit

7.6 Congenital adrenal hyperplasia (CAH)

Term babies

Lab	Parameter	Method	Dependant on age	Dependant on WoG	Dependant on BW	Formula	Constant value
1	17 OHP	AutoDELFIA	yes			ln(OHP)=2.90798-0.40653ln(LT)	
3	17 OHP	AutoDELFIA	yes			ln (OHP) = 1.868 - 0.374(ln LT)	
5	17 OHP	AutoDELFIA		yes			
6	17 OHP	DELFIA	yes				
7	17 OHP	AutoDELFIA					30
8*	17 OHP	DELFIA	yes				
9	17 OHP	AutoDELFIA		yes			
10	17 OHP	AutoDELFIA	yes				
11	17 OHP	DELFIA	yes				
12	17 OHP	AutoDELFIA	yes		yes		
13	17 OHP	AutoDELFIA	yes		yes		
14	17 OHP	AutoDELFIA	yes		yes		
15	17 OHP	AutoDELFIA	yes		yes		

*Laboratory 8: with raised Delfia 17OHP TMS Steroidprofile with 17OHP, 21-Desoxycortisol, 11-Desoxycortisol, Cortisol and Androstendion.

Preterm babies

Lab	Parameter	Method	Dependant on age	Dependant on WoG	Dependant on BW	Formula	Constant value
1	17 OHP	AutoDELFIA	yes	yes		ln(OHP)=3.470-0.121ln(days)	
3	17 OHP	AutoDELFIA	yes	yes		ln (OHP) = -118.7 + 75.164(ln (korr GA)) -11.564(ln(korr GA)²)	
5	17 OHP	AutoDELFIA		yes			
6	17 OHP	DELFIA	yes	yes			
7	17 OHP	AutoDELFIA			yes		
8*	17 OHP	DELFIA	yes	yes	yes		
9	17 OHP	AutoDELFIA		yes			
10	17 OHP	AutoDELFIA	yes	yes			
11	17 OHP	DELFIA	yes	yes			
12	17 OHP	AutoDELFIA	yes		yes		
13	17 OHP	AutoDELFIA	yes		yes		
14	17 OHP	AutoDELFIA		yes			
15	17 OHP	AutoDELFIA		yes			

*Laboratory 8: with raised Delfia 17OHP TMS Steroidprofile with 17OHP, 21-Desoxycortisol, 11-Desoxycortisol, Cortisol and Androstendion.

7.7 Parameter of MS/MS

Key values (KV) and secondary values (SV) are listed. When a cut off is given for the key value by the individual laboratories, it is listed. Lab 12 means Lab 12 und 13 (one laboratory) and lab 14 means lab 14 and 15 (one laboratory).

Notes for the listed laboratories

Lab	note
3	Half yearly actualisation of cut off values dependent on kit charge and machine status on the base of all results > 32. WoG and > 36 hours of life
6	All cut offs calculated from percentiles and are therefore dynamic

7.7.1 PKU

Parameter /Cut off	1	3	5	6	7	8	9	10	11	12	14
Phe	**112**	**120**	**150**	**144**	**139**	**150**	**123**	**150**	**123**	**120**	**129**
Tyr								**SV**		**SV**	**SV**
Phe/Tyr	**SV**	**SV**	**SV**	**SV**	**2.5**	**2.5**	**SV**	**SV**	**2.0**	**2.0**	**SV**

7.7.2 MSUD

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[b]	14
Ala				**SV**				**SV**		**KV**	
Val	**SV**	**SV**	**SV**	**291**	**280**	**SV**	**SV**	**SV**	**185**	**KV**	**SV**
Leu/Ile	**294**	**310**	**z ≥ 3.5[a]**	**340**	**300**	**400**	**299**	**314**	**289**	**KV**	**350**
Fischer-Q	**SV**	**4.0**		**SV**					**3.3**	**KV**	**3**
Leu/Ile:Phe	**SV**		**z ≥ 3.5[a]**			**10**		**SV**		**KV**	**SV**
Val/Phe			**SV**					**SV**		**KV**	**SV**
Leulle/Ala	**SV**	**SV**	**z ≥ 3.5[a]**	**SV**			**SV**	**SV**	**SV**	**KV**	

[a] z ≥ 3.5 means: measured value ≥ mean + z* sd

[b] Multi analyte pattern recognition

7.7.3 MCAD-Disease

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[b]	14
C0								SV			
C6	SV	SV	SV	SV	0.18	SV	SV	SV	SV	KV	SV
C8	0.24	0.32	z ≥ 3.5[a]	0.388	0.4	0.2	0.28	0.3	0.24	KV	0.34
C8/C10	SV	4.0	SV	SV		2.5	SV	SV	2.0	KV	SV
C8/C12	SV		SV	SV		5	SV		SV	KV	
C8/C16					SV			SV		KV	
C10	SV	SV	SV	SV		SV	SV	SV	SV	KV	SV
C10:1	SV	SV	SV	SV	0.15	SV	SV	SV	0.11	KV	SV
C8/C2	SV			SV		0.02	SV				SV
C8/C6			SV							KV	

[a] z ≥ 3.5 means: measured value ≥ mean + z* sd

[b] Multi analyte pattern recognition

7.7.4 LCHAD-Disease

Parameter / Cut off	1	3[a]	5	6	7	8	9	10	11	12[b]	14
C0								SV			
C14:1			SV	SV		SV		SV		SV	
C14OH			SV	0.052			SV	SV	SV	KV	
C16OH	0.091	0.07	z ≥ 3.5	0.082	0.11	0.1	0.1	0.15	0.048	KV	0.60
C16:1OH			SV	SV			SV	SV		KV	SV
C18OH	0.042	SV		0.06	0.1	SV	0.07	SV	0.031	KV	SV
C18:1OH	0.052	SV	z ≥ 3.5	0.077	0.1	0.1	0.11	SV	0.042	KV	SV
C18:2OH						SV		SV			SV
C16OH/C16	SV	0.02	SV						0.018		

[a] Ratio C16OH/C16 at sampling > 7 d;

[b] Multi analyte pattern recognition

7.7.5 VLCAD-Disease

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
C0								SV			
C12			SV							KV	
C14	SV	SV	SV	SV	0.65	SV	SV	SV	0.459	KV	SV
C14:1	0.49	0.35	z ≥ 3.5	0.294	0.40	0.40	0.43	0.36	0.32	KV	0.25
C16:1		SV		SV			SV	SV			
C14:2	SV	SV	SV	SV	SV	SV			0.048	KV	SV
C14:1/C16	SV	0.10	SV	SV					0.125		0.1
C14/C4								SV			SV
C14:1/C4			SV				SV	SV		KV	SV
C14:1/C12			SV								
C14:1/C12:1			SV			3.0					

[a] Multi analyte pattern recognition

7.7.6 CPT I-Disease

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
C0	SV	5.7	SV	57.39	70	80	65.49	50	SV	SV	>70
C8											
C16	1.2	SV	SV	0.333	<0.6		KV	0.56	0.69	KV	<1
C18	0.36	SV	SV	0.137	<0.3		KV	0.21	0.2	KV	SV
C18:1	0.64			0.298				SV	0.315	KV	
C16/C2											
(C16+C18:1)/C2											
C0/(C16+C18)	SV	1.3	≥ 70	SV		40	KV		19.3	KV	KV

[a] Multi analyte pattern recognition

7.7.7 CPT II-Disease

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
AC ges								SV			
C0	SV	SV		4.6	<10			SV	5.1	SV	SV
C16	8.00	8.73	SV	8.819	8.0	8	7.65	8.83	7.5	KV	>6
C16:1					0.6		0.67	SV		KV	SV
C18	2.24			2.139	2.6		2.34	3.65	1.94	KV	>2.5
C18:1	3.45	2.76	SV	3.604	3.5	3.0	1.92	SV	3.27	KV	SV
(C16+C18:1)/C2	SV	SV	z ≥ 3.5	SV		0.3	SV	20.3	SV		
C18:2						SV		SV		KV	
C16/C2			SV								
C0/(C16+C18)			SV	SV			SV	SV			

[a] Multi analyte pattern recognition

7.7.8 CACT-Disease

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
AC ges								SV			
C0	SV	SV		SV	<10	<25		SV	5.1	KV	SV
C16	5.55	8.73	SV	8.819	8.0	8.0	6.85	8.83	7.5	KV	
C16:1							SV	SV		KV	>6
C18	1.45			2.139	2.6	2.5	2.34	2.65	1.94	KV	SV
C18:1	2.22	2.76	SV	3.604	3.5			3.9	3.27	KV	SV
(C16+C18:1)/C2	SV	SV	z ≥ 3.5	SV		0.3		SV	SV		
C18:2										KV	
C0/AC ges								SV			
C16/C2			z ≥ 3.5								
C0/(C16+C18)			SV	SV			SV	SV			
C0/(C16+C18:1)							SV	SV			

[a] Multi analyte pattern recognition

7.7.9 Glutaric aciduria type I

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
C5DC (Glut)	0.18	0.5	z ≥ 0.13	0.778	0.33	0.20	0.17	0.25	0.45	KV	<0.15
C5DC/C0			SV	SV		0.005					
C5DC/C2										KV	
C5DC/C4				SV				SV		KV	
C5DC/C8		SV		SV	5.9		SV	SV			SV
C5DC/C12	SV	SV							SV	KV	
C5DC/C16	SV		SV	SV			SV	SV	SV	KV	SV
C5DC/(C8+C10)			SV								

[a] Multi analyte pattern recognition

7.7.10 Isovaleric acidaemia

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12[a]	14
C0		SV						SV			
C5	0.36	0.5	z ≥ 3.5	0.6	1	0.5	0.63	0.6	0.57	KV	0.6
C5/C2			SV	SV		0.02	SV				
C5/C3								SV			SV
C5/C8	SV	SV	SV	SV	SV			SV	SV	KV	SV
C5/C4	SV	SV	SV	SV				SV	SV	KV	SV

[a] Multi analyte pattern recognition

Literature

1 Beschluss über eine Änderung der Richtlinien des Bundesausschusses der Ärzte und Krankenkassen über die Früherkennung von Krankheiten bei Kindern bis zur Vollendung des 6. Lebensjahres (Kinder-Richtlinien) zur Einführung des erweiterten Neugeborenen-Screenings vom 21. Dezember 2004; Dt. Ärzteblatt 2005, 102: A1158-63

2 Statistisches Jahrbuch 2011 Herausgeber: Statistisches Bundesamt, Wiesbaden www.destatis.de