National

Screening Report

Germany 2011

Deutsche Gesellschaft für Neugeborenenscreening e.V.

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Contents

Figures:

Abbreviations:

n.a.	not reported
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 acidaemia
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 - Disease	Very-Long-Chain-Acyl-CoA-Dehydrogenase-Deficiency

Screening Laboratories and Screening Centres

Screening Centres (laboratories) with different localities or laboratories which are linked 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.

The National Screening Report 2011 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 2011. 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:

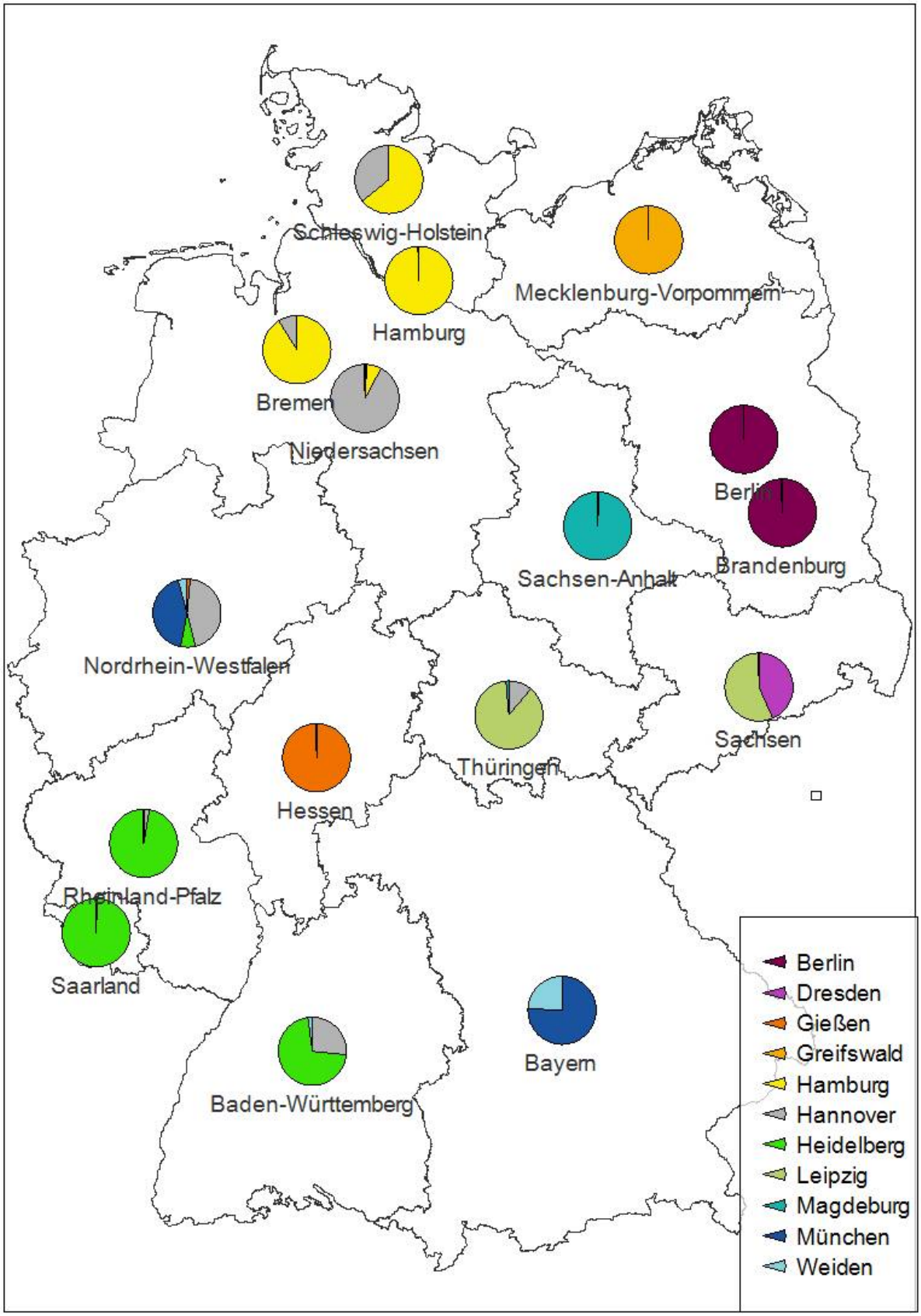
- Total survey of the targeted population
    - Collection method and rate
    - Blank card system
- Completeness of the control and the follow-up studies
- Collection of test parameters and cut offs
- Stratified rates of recall, positive predictive values and prevalence according to laboratory, age 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 were listed which have undertaken the screening in 2011 for Germany. (12 and 13 relate to the same laboratory, one with and without the cooperation 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 2011 662.685 children were born in Germany [2]. The total recorded screening exceeds this number at 666.145. A cause for the additional screening cards could be wrongly labelled cards or test cards of newborns not registered in Germany. Further investigations cannot be undertaken as data exchange is not legalised.

Births [**Fehler! Textmarke nicht definiert.**]:
662.685

First screening: 666.145

Final diagnosis (see Table 3): 511

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

In the German guidelines, the targeted diseases are defined for the nationwide screening. Some laboratories will also screen for scientific purposes. These results will not be addressed in this report. Out of 1 in 1.297 newborns, one targeted disease according to the guidelines is found. Table 2 shows the prevalence of targeted diseases in the year 2011 in Germany.

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Table: 2 Absolute numbers of detected diseases found by screening 2011

Disease	Confirmed cases	Prevalence
Hypothyroidism	207	1: 3.201
Congenital adrenal hyperplasia (CAH)	44	1: 15.061
Biotinidase deficiency (incl. partial defect)	22	1: 30.122
Galactosaemia (classic)	14	1: 47.335
Phenylketonuria (PKU) n=58 / Hyperphenylalaninaemia (HPA) n=56 /Cofactor disease n=1	115	1: 5.762
Maple syrup urine disease (MSUD)	4	1: 165.671
Medium-Chain-Acyl-CoA-Dehydrogenase (MCAD)-Disease	76	1: 8.720
Long-Chain-3-OH-Acyl-CoA-Dehydrogenase (LCHAD)-Disease	4	1: 165.671
(Very-)Long-Chain-Acyl-CoA-Dehydrogenase (VLCAD)-Disease	11	1: 60.244
Carnitin-Palmitoyl-CoA-Transferase I (CPTI)-Disease	0	
Carnitin-Palmitoyl-CoA-Transferase II (CPTII)-Disease	0	
Carnitin-Acylcarnitin-Translocase (CACT)-Disease	1	1: 662.685
Glutaric aciduria Type I (GA I)	7	1: 94.669
Isovaleric acidaemia (IVA)	6	1: 110.448
Total	**511**	1: 1.297

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

		≥36h and ≥32WoG		<36h and ≥32WoG		<32WoG	
Lab	Total	n	%	n	%	n	%
1	50697	48889	96,43	1202	2,37	606	1,20
3	15299	14955	97,75	160	1,05	184	1,20
5	52569	51187	97,37	876	1,67	506	0,96
6	12655	12152	96,03	365	2,88	138	1,09
7	43238	41990	97,11	739	1,71	509	1,18
8	154425	151052	97,82	1616	1,05	1757	1,14
9	110779	107829	97,34	1377	1,24	1573	1,42
10	34325	33585	97,84	387	1,13	353	1,03
11	16668	16132	96,78	331	1,99	205	1,23
12	78965	77334	97,93	787	1,00	844	1,07
13	63163	61619	97,56	787	1,25	757	1,20
14	25240	24759	98,09	272	1,08	209	0,83
15	8122	7898	97,24	89	1,10	135	1,66
Total	**666145**	**649381**	**97,48**	**8988**	**1,35**	**7776**	**1,17**

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 (Datenschutz, GenDG), resulting in implausible ranges.

Table 2.2: Requested and received repeat screenings

Lab	Total[a] [c] requested	Total[a] received	%	Recall requested [c]	Recall received	%
1	2560	2339	91,37	712	695	97,61
3	470	459	97,66	131	131	100,00
5	1774	1603	90,36	398	395	99,25
6	584	583	99,83	84	84	100,00
7[b]	1918	n.a.		673	n.a.	
8	4675	4256	91,04	1027	964	93,87
9	3705	2664	71,90	490	356	72,65
10	983	980	99,69	226	226	100,00
11	573	570	99,48	51	51	100,00
12	2221	2213	99,64	661	659	99,70
13	2036	1955	96,02	492	477	96,95
14	561	558	99,47	125	124	99,20
15	328	255	77,74	78	78	100,00
Total	**22388**	**18435**	**90,06**	**5148**	**4240**	**94,75**

Lab	<36h requested [c]	<36h received	%	<32WoG requested [c]	<32WoG received	%
1	1202	1061	88,27	583	523	89,71
3	160	150	93,75	179	178	99,44
5	876	749	85,50	500	459	91,80
6	365	364	99,73	135	135	100,00
7[b]	739	n.a.		506	n.a.	
8	1608	1474	91,67	1690	1615	95,56
9	1371	817	59,59	1569	1309	83,43
10	381	378	99,21	347	347	100,00
11	331	328	99,09	191	191	100,00
12	772	766	99,22	788	788	100,00
13	787	771	97,97	757	707	93,39
14	236	234	99,15	200	200	100,00
15	97	57	58,76	135	120	88,89
Total	**8925**	**7149**	**87,33**	**7580**	**6572**	**92,90**

[a] Inclusive secondary screening due to blood transfusion, parenteral nutrition or medication
[b] Calculation without labs giving not differentiated numbers
[c] Deaths are not included in the number of requested samples

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 laboratories receive blank test cards in various numbers. The number of blank screening cards due to refusal is still low but higher than the previous years and in 2011 partly doubled compared to 2010. To what extent this is due to, a better reply or raised true refusals, is not clear.

This system seems to work mainly with the refusals respectively the declined screening before 36 hours of life. Both, before screening deceased and the transferred neonates, would give expectations to higher numbers.

Table 2.3: Laboratory received blank cards

	Deceased	Screening declined	Transfer of newborn	Early screening declined	Total
Lab	n	n	n	n	n
1	48	9	n.a.	3310*	3367
3	49	19	14	588	670
5	67	359	0	2540	2966
6	1	3	0	212	216
7	0	0	0	196	196
8	n.a.	n.a.	n.a.	n.a.	1507
9	7	105	76	498	686
10	169	26	0	1662	1857
11	65	4	36	214	319
12	6	26	116	1055	1203
13	n.a.	n.a.	n.a.	n.a.	n.a.
14	2	9	7	12	30
15	n.a.	n.a.	n.a.	n.a.	n.a.
Total	**414**	**560**	**249**	**10.287**	**13.017**

* including early screening/transfer/reason for blank cards not reported

Table 2.4: Secondary screening due to poor quality of primary

Lab	Primary screening	Control requested	Control received	received/ requested (%)	Percentage of unprocessed screening cards/ Primary screening (%)
1	50697	313	307	98,08	0,62
3	15299	58	58	100,00	0,38
5	52569	866	866	100,00	1,65
6	12655	22	22	100,00	0,17
7	43238	136	n.a.		0,31
8	154425	235	222	94,47	0,15
9	110779	568	517	91,02	0,51
10	34325	110	108	98,18	0,32
11	16668	1	1	100,00	0,01
12	78965	271	264	97,42	0,34
13	63163	199	195	97,99	0,32
14	25240	29	28	96,55	0,11
15	8122	17	17	100,00	0,21
Total	**666145**	**2825**	**2605**	**96,88***	**0,42**

***** Calculation without the information from laboratory 7

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 2011 the recall rate accounted for 0.83%. 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 irrespectively 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 99.25%. 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 11.83% meaning that about 12% of suspicious screening results indicate the targeted disease. For several diseases the PPV is high, e.g. for HPA / PKU 49.77% for MCAD-Deficiency 33.79% and for hypothyroidism 35.11%. The range of PPV between the single laboratories is high.

Table 3: Recall rate, Specificity, Prevalence and PPV for Germany 2011 N= 666.145*

Disease	Recall >=36h	Recall rate (%) ≥36h	Confirmed cases	PPV ≥36h (%)	Prevalence (based on primary screening)	Not found in the screening
Hypothyroidism	524	0,08	207	35,11	1: 3218	6
CAH	1949	0,30	44	1,90	1: 15140	0
Biotinidase-Disease classic	159	0,02	22	13,84	1: 30279	0
Galactosaemia	310	0,05	14	4,52	1: 47582	0
PKU/HPA	219	0,03	115	49,77	1: 5793	0
MSUD	64	0,01	4	6,25	1: 166536	0
MCAD	219	0,03	76	33,79	1: 8765	0
LCHAD	105	0,02	4	2,86	1: 166536	0
VLCAD	169	0,03	11	6,51	1: 60559	0
CPT I-Disease	14		0			0
CPT II-Disease	18		0			0
CAT-Disease	1		1		1: 666145	0
GA I	164	0,03	7	4,27	1: 95164	0
IVA	74	0,01	6	8,11	1: 111024	0
Total	**3989**	**0,61**	**511**	**11,83**	**1: 1304**	**6**

* Primary screening Total: n= 666.145; Primary screening ≥ 36h and ≥ 32WoG n= 649.381

3.1 Recall rate and confirmed cases stratified

The following tables show recall rates ≥36h and confirmed cases stratified for the laboratory. 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, irrespectively of age and gestational age. The validation of confirmed cases was tested for plausibility of 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=16) (Tab.3.1.a) and cases where the confirmation diagnostics were negative (n=8). For some diseases the true prevalence could be higher. Double reported cases were included only once**.**

For the next tables recall rates <0.01% and for low n were not calculated, since random fluctuations would have great influence on small numbers.

Table 3.1: Cases with missing data of confirmation diagnostics

Disease	Data missing
Hypothyroidism	9
CAH	5
Biotinidase deficiency	
Galactosaemia (classic)	
PKU/HPA	1
MSUD	
MCAD	
LCHAD	
VLCAD	
CACT-Disease	
GA I	1
IVA	
Total	**16**

3.1.1 Hypothyroidism*

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)	Confirmed cases*	Not found in the screening
1	50697	48889	42	0,09	20	0
3	15299	14955	14	0,09	5	0
5	52569	51187	78	0,15	11	1
6	12655	12152	8	0,07	4	0
7	43238	41990	8	0,02	3	0
8	154425	151052	170	0,11	64	2
9	110779	107829	75	0,07	34	1
10	34325	33585	17	0,05	11	1
11	16668	16132	8	0,05	4	0
12	78965	77334	41	0,05	33	1
13	63163	61619	30	0,05	9	0
14	25240	24759	24	0,10	5	0
15	8122	7898	9	0,11	4	0
Total	**666145**	**649381**	**524**	**0,08**	**207[a]**	**6[a]**

* including transient hypothyroidism n =7

[a] Not found in the screening: n= 2 Premature babies blood collection <32WoG, n=4 Premature babies blood collection 32-34 WoG. (See Table 5.2)

Additionally n=2 latent Hypothyroidism and n=9 Hyperthyrotropinaemia were reported and validated. These are not included in the calculation of the prevalence.

3.1.2 Congenital adrenal hyperplasia (CAH)

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases
1	50697	48889	147	0,30	5
3	15299	14955	6	0,04	2
5	52569	51187	278	0,54	1
6	12655	12152	37	0,30	0
7	43238	41990	270	0,64	3
8*	154425	151052	76	0,05	11
9	110779	107829	249	0,23	10
10	34325	33585	111	0,33	3
11	16668	16132	33	0,20	0
12	78965	77334	411	0,53	4
13	63163	61619	245	0,40	2
14	25240	24759	60	0,24	2
15	8122	7898	26	0,33	1
Total	**666145**	**649381**	**1949**	**0,30**	**44**

* Laboratory used second-tier process

3.1.3 Biotinidase deficiency

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases	Including complete defect
1	50697	48889	9	0,02	2	1
3	15299	14955	0		0	
5	52569	51187	2		0	
6	12655	12152	12	0,10	1	0
7	43238	41990	20	0,05	2	0
8	154425	151052	73	0,05	13	3
9	110779	107829	3		0	
10	34325	33585	5		2	0
11	16668	16132	1		1	1
12	78965	77334	18	0,02	0	
13	63163	61619	10	0,02	0	
14	25240	24759	1		0	
15	8122	7898	5		1	1
Total	**666145**	**649381**	**159**	**0,02**	**22**	**6**

* 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	Including classic
1	50697	48889	14	0,03	7	0
3	15299	14955	5		0	
5	52569	51187	19	0,04	4	1
6	12655	12152	2		0	
7	43238	41990	14	0,03	1	1
8	154425	151052	84	0,06	21	6
9	110779	107829	2		0	
10	34325	33585	18	0,05	9	3
11	16668	16132	2		0	
12	78965	77334	58	0,07	8	3
13	63163	61619	75	0,12	0	
14	25240	24759	8	0,03	1	0
15	8122	7898	9	0,11	0	
Total	**666145**	**649381**	**310**	**0,05**	**51**	**14**

* 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	Including PKU
1	50697	48889	31	0,06	8	5
3	15299	14955	7	0,05	2	1
5	52569	51187	20	0,04	9	2
6	12655	12152	1		0	
7	43238	41990	20	0,05	10	5
8	154425	151052	19	0,01	17	10
9	110779	107829	23	0,02	19	10
10	34325	33585	11	0,03	7	5
11	16668	16132	4		4	3
12	78965	77334	35	0,05	17	8
13	63163	61619	29	0,05	15	8
14	25240	24759	14	0,06	7	1
15	8122	7898	5		0	
Total	**666145**	**649381**	**219**	**0,03**	**115**	**58**

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

3.1.6 MSUD

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases
1	50697	48889	24	0,05	1
3	15299	14955	4		0
5	52569	51187	2		0
6	12655	12152	0		0
7	43238	41990	6	0,01	0
8	154425	151052	0		0
9	110779	107829	9	0,01	2
10	34325	33585	4		0
11	16668	16132	0		0
12	78965	77334	2		0
13	63163	61619	9	0,01	1
14	25240	24759	2		0
15	8122	7898	2		0
Total	**666145**	**649381**	**64**	**0,01**	**4**

* 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	50697	48889	109	0,22	6
3	15299	14955	1		1
5	52569	51187	14	0,03	5
6	12655	12152	5		1
7	43238	41990	8	0,02	3
8	154425	151052	27	0,02	24
9	110779	107829	19	0,02	14
10	34325	33585	12	0,04	3
11	16668	16132	0		0
12	78965	77334	8	0,01	7
13	63163	61619	11	0,02	8
14	25240	24759	4		3
15	8122	7898	1		1
Total	**666145**	**649381**	**219**	**0,03**	**76**

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

3.1.8 LCHAD-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)	Confirmed cases
1	50697	48889	84	0,17	1
3	15299	14955	0		0
5	52569	51187	0		0
6	12655	12152	4		0
7	43238	41990	6		0
8	154425	151052	1		1
9	110779	107829	4		0
10	34325	33585	0		1
11	16668	16132	1		1
12	78965	77334	0		0
13	63163	61619	5		0
14	25240	24759	0		0
15	8122	7898	0		0
Total	**666145**	**649381**	**105**	**0,02**	**4**

3.1.9 VLCAD-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases
1	50697	48889	60	0,12	1
3	15299	14955	5		0
5	52569	51187	11	0,02	3
6	12655	12152	7	0,06	0
7	43238	41990	29	0,07	0
8	154425	151052	3		1
9	110779	107829	37	0,03	3
10	34325	33585	8	0,02	1
11	16668	16132	3		0
12	78965	77334	1		0
13	63163	61619	2		1
14	25240	24759	2		1
15	8122	7898	1		0
Total	**666145**	**649381**	**169**	**0,03**	**11**

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

3.1.10 No confirmed cases of CPTI-Deficiency and for CPT II-Deficiency

3.1.11 CACT-Disease

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases
1	50697	48889	0		0
3	15299	14955	0		0
5	52569	51187	0		0
6	12655	12152	0		0
7	43238	41990	0		0
8	154425	151052	1		1
9	110779	107829	0		0
10	34325	33585	0		0
11	16668	16132	0		0
12	78965	77334	0		0
13	63163	61619	0		0
14	25240	24759	0		0
15	8122	7898	0		0
Total	**666145**	**649381**	**1**		**1**

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

3.1.12 Glutaric aciduria Type I

Lab	Primary screening Total	Primary screening ≥36h	Recall ≥36h	Recall-rate(%)*	Confirmed cases
1	50697	48889	61	0,12	0
3	15299	14955	1		1
5	52569	51187	2		0
6	12655	12152	2		0
7	43238	41990	38	0,09	1
8	154425	151052	2		2
9	110779	107829	52	0,05	2
10	34325	33585	0		0
11	16668	16132	0		0
12	78965	77334	1		0
13	63163	61619	2		0
14	25240	24759	1		1
15	8122	7898	2		0
Total	**666145**	**649381**	**164**	**0,03**	**7**

* 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	50697	48889	50	0,10	0
3	15299	14955	0		0
5	52569	51187	2		0
6	12655	12152	5		0
7	43238	41990	0		0
8	154425	151052	1		0
9	110779	107829	2		2
10	34325	33585	1		1
11	16668	16132	0		0
12	78965	77334	3		2
13	63163	61619	8	0,01	0
14	25240	24759	2		1
15	8122	7898	0		0
Total	**666145**	**649381**	**74**	**0,01**	**6**

* 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

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate
1	48889	42	0,09	1202	8	0,67	606	0	
3	14955	14	0,09	160	0		184	1	
5	51187	78	0,15	876	2	0,23	506	2	
6	12152	8	0,07	365	0	0,00	138	0	
7	41990	8	0,02	739	40	5,41	509	1	
8	151052	170	0,11	1616	182	11,26	1757	11	0,63
9	107829	75	0,07	1377	1	0,07	1573	1	
10	33585	17	0,05	387	46	11,89	353	0	
11	16132	8	0,05	331	57	17,22	205	1	
12	77334	41	0,05	787	35	4,45	844	5	
13	61619	30	0,05	787	20	2,54	757	0	
14	24759	24	0,10	272	10	3,68	209	0	
15	7898	9	0,11	89	0		135	0	
Total	**649381**	**524**	**0,08**	**8988**	**401**	**4,46**	**7776**	**22**	**0,28**

3.2.2 Congenital adrenal hyperplasia (CAH)

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate
1	48889	147	0,30	1202	31	2,58	606	56	9,24
3	14955	6	0,04	160	0		184	0	
5	51187	278	0,54	876	4		506	32	6,32
6	12152	37	0,30	365	0		138	0	
7	41990	270	0,64	739	20	2,71	509	192	37,72
8	151052	76	0,05*	1616	142	8,79	1757	34	1,94*
9	107829	249	0,23	1377	6	0,44	1573	2	
10	33585	111	0,33	387	23	5,94	353	34	9,63
11	16132	33	0,20	331	21	6,34	205	8	3,90
12	77334	411	0,53	787	92	11,69	844	116	13,74
13	61619	245	0,40	787	79	10,04	757	35	4,62
14	24759	60	0,24	272	5	1,84	209	14	6,70
15	7898	26	0,33	89	1	1,12	135	17	12,59
Total	**649381**	**1949**	**0,30**	**8988**	**424**	**4,72**	**7776**	**540**	**6,94**

*Laboratory used second-tier process at screening >36h and <32 WoG

3.2.3 Biotinidase deficiency[a]

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate
1	48889	9	0,02	1202	1		606	4	
3	14955	0		160	0		184	0	
5	51187	2		876	0		506	1	
6	12152	12	0,10	365	0		138	0	
7	41990	20	0,05	739	0		509	0	
8	151052	73	0,05	1616	3		1757	6	0,34
9	107829	3		1377	0		1573	0	
10	33585	5		387	1		353	0	
11	16132	1		331	0		205	0	
12	77334	18	0,02	787	1		844	2	
13	61619	10	0,02	787	1		757	1	
14	24759	1		272	0		209	0	
15	7898	5		89	0		135	0	
Total	**649381**	**159**	**0,02**	**8988**	**7**	**0,08**	**7776**	**14**	**0,18**

* Recall rate for screening < 36h and < 32 WoG only in total.
[a] The guidelines do not suggest an approach on suspicion of partial biotinidase deficiency (targeted disease biotinidase deficiency)

3.2.4 Galactosaemia[a]

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	14	0,03	1202	0		606	1	
3	14955	5	0,03	160	0		184	0	
5	51187	19	0,04	876	0		506	1	
6	12152	2		365	0		138	0	
7	41990	14	0,03	739	0		509	0	
8	151052	84	0,06	1616	2		1757	2	
9	107829	2		1377	0		1573	0	
10	33585	18	0,05	387	1		353	1	
11	16132	2		331	0		205	0	
12	77334	58	0,07	787	2		844	3	
13	61619	75	0,12	787	2		757	0	
14	24759	8	0,03	272	0		209	0	
15	7898	9	0,11	89	0		135	0	
Total	**649381**	**310**	**0,05**	**8988**	**7**	**0,08**	**7776**	**8**	**0,10**

* Recall rate for screening < 36h and < 32 WoG only in total.
[a] The guidelines do not suggest an approach on suspicion of variant Galactosaemia deficiency (targeted disease Galactosaemia)

3.2.5 PKU/HPA

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate
1	48889	31	0,06	1202	6	0,50	606	4	
3	14955	7	0,05	160	0		184	0	
5	51187	20	0,04	876	2		506	0	
6	12152	1	0,01	365	0		138	0	
7	41990	20	0,05	739	1		509	1	
8	151052	19	0,01	1616	1		1757	0	
9	107829	23	0,02	1377	1		1573	1	
10	33585	11	0,03	387	1		353	5	
11	16132	4	0,02	331	0		205	0	
12	77334	35	0,05	787	0		844	0	
13	61619	29	0,05	787	1		757	0	
14	24759	14	0,06	272	1		209	6	2,87
15	7898	5	0,06	89	0		135	1	
Total	**649381**	**219**	**0,03**	**8988**	**14**	**0,16**	**7776**	**18**	**0,23**

3.2.6 MSUD

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	24	0,05	1202	0		606	1	
3	14955	4		160	0		184	0	
5	51187	2		876	0		506	0	
6	12152	0		365	0		138	0	
7	41990	6	0,01	739	0		509	0	
8	151052	0		1616	0		1757	0	
9	107829	9	0,01	1377	0		1573	0	
10	33585	4		387	0		353	1	
11	16132	0		331	0		205	0	
12	77334	2		787	0		844	0	
13	61619	9	0,01	787	0		757	0	
14	24759	2		272	1		209	0	
15	7898	2		89	0		135	0	
Total	**649381**	**64**	**0,01**	**8988**	**1**	**0,01**	**7776**	**2**	**0,03**

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

3.2.7 MCAD-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	109	0,22	1202	2		606	0	
3	14955	1		160	0		184	0	
5	51187	14	0,03	876	1		506	0	
6	12152	5		365	0		138	1	
7	41990	8	0,02	739	0		509	0	
8	151052	27	0,02	1616	0		1757	0	
9	107829	19	0,02	1377	0		1573	0	
10	33585	12	0,04	387	0		353	0	
11	16132	0		331	0		205	0	
12	77334	8	0,01	787	0		844	0	
13	61619	11	0,02	787	0		757	0	
14	24759	4		272	0		209	0	
15	7898	1		89	0		135	1	
Total	**649381**	**219**	**0,03**	**8988**	**3**	**0,03**	**7776**	**2**	**0,03**

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

3.2.8 LCHAD-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	84	0,17	1202	0		606	0	
3	14955	0		160	0		184	0	
5	51187	0		876	0		506	0	
6	12152	4		365	0		138	0	
7	41990	6	0,01	739	0		509	1	
8	151052	1		1616	0		1757	0	
9	107829	4		1377	0		1573	0	
10	33585	0		387	0		353	1	
11	16132	1		331	0		205	0	
12	77334	0		787	0		844	0	
13	61619	5		787	0		757	0	
14	24759	0		272	0		209	0	
15	7898	0		89	0		135	0	
Total	**649381**	**105**	**0,02**	**8988**	**0**		**7776**	**2**	**0,03**

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

3.2.9 VLCAD-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	60	0,12	1202	0		606	3	
3	14955	5		160	0		184	0	
5	51187	11	0,02	876	0		506	2	
6	12152	7	0,06	365	0		138	0	
7	41990	29	0,07	739	0		509	0	
8	151052	3		1616	0		1757	0	
9	107829	37	0,03	1377	1		1573	1	
10	33585	8	0,02	387	0		353	0	
11	16132	3		331	0		205	0	
12	77334	1		787	0		844	0	
13*	61619	2		787	0		757	0	
14	24759	2		272	0		209	0	
15	7898	1		89	0		135	0	
Total	**649381**	**169**	**0,03**	**8988**	**1**	**0,01**	**7776**	**6**	**0,08**

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

3.2.10 CPTI-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	9	0,02	1202	0		606	3	
3	14955	0		160	0		184	0	
5	51187	1		876	0		506	0	
6	12152	1		365	0		138	0	
7	41990	0		739	0		509	0	
8	151052	0		1616	0		1757	0	
9	107829	0		1377	0		1573	0	
10	33585	0		387	0		353	0	
11	16132	0		331	0		205	0	
12	77334	0		787	0		844	0	
13	61619	3		787	0		757	0	
14	24759	0		272	0		209	0	
15	7898	0		89	0		135	0	
Total	**649381**	**14**	**0,002**	**8988**	**0**		**7776**	**3**	**0,04**

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

3.2.11 CPTII-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate
1	48889	6	0,01	1202	0		606	0	
3	14955	0		160	0		184	0	
5	51187	2		876	0		506	0	
6	12152	0		365	0		138	0	
7	41990	0		739	0		509	0	
8	151052	0		1616	0		1757	0	
9	107829	2		1377	0		1573	0	
10	33585	4		387	0		353	0	
11	16132	0		331	0		205	0	
12	77334	0		787	0		844	0	
13	61619	3		787	0		757	0	
14	24759	1		272	0		209	0	
15	7898	0		89	0		135	0	
Total	**649381**	**18**	**0,003**	**8988**	**0**		**7776**	**0**	

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

3.2.12 CACT-Disease

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate
1	48889	0		1202	0		606	0	
3	14955	0		160	0		184	0	
5	51187	0		876	0		506	0	
6	12152	0		365	0		138	0	
7	41990	0		739	0		509	0	
8	151052	1		1616	0		1757	0	
9	107829	0		1377	0		1573	0	
10	33585	0		387	0		353	0	
11	16132	0		331	0		205	0	
12	77334	0		787	0		844	0	
13	61619	0		787	0		757	0	
14	24759	0		272	0		209	0	
15	7898	0		89	0		135	0	
Total	**649381**	**1**		**8988**	**0**		**7776**	**0**	

3.2.13 Glutaric aciduria Type I

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate*	Primary screening	Recall	Recall-rate*
1	48889	61	0,12	1202	2		606	6	0,99
3	14955	1		160	0		184	0	
5	51187	2		876	0		506	0	
6	12152	2		365	0		138	0	
7	41990	38	0,09	739	0		509	0	
8	151052	2		1616	0		1757	0	
9	107829	52	0,05	1377	2		1573	0	
10	33585	0		387	0		353	0	
11	16132	0		331	0		205	0	
12	77334	1		787	0		844	0	
13	61619	2		787	0		757	0	
14	24759	1		272	0		209	0	
15	7898	2		89	0		135	0	
Total	**649381**	**164**	**0,03**	**8988**	**4**	**0,04**	**7776**	**6**	**0,08**

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

3.2.14 Isovaleric acidaemia

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Lab	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall-rate	Primary screening	Recall	Recall rate
1	48889	50	0,10	1202	6	0,50	606	21	3,47
3	14955	0		160	0		184	0	
5	51187	2		876	0		506	2	
6	12152	5		365	0		138	0	
7	41990	0		739	0		509	0	
8	151052	1		1616	0		1757	0	
9	107829	2		1377	0		1573	0	
10	33585	1		387	0		353	2	
11	16132	0		331	0		205	0	
12	77334	3		787	0		844	1	
13	61619	8	0,01	787	0		757	0	
14	24759	2		272	0		209	1	
15	7898	0		89	0		135	0	
Total	**649381**	**74**	**0,01**	**8988**	**6**	**0,07**	**7776**	**27**	**0,35**

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 88.1% of cases, with specification of collection time, the collection was according to the guidelines, in 9.67% (3.3-14.11%) beyond the 72nd hour of life, in 1.52% (1.15-2.99%) 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 9.67 % in 2011 (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

	Total	<36h		36h-<48h		48h-<72h		≥72h	
Lab	n	n	%	n	%	n	%	n	%
1[a]	50586	1319	2,61	10834	21,42	32494	64,24	5939	11,74
3[a]	15245	196	1,29	2422	15,89	11884	77,95	743	4,87
5	52569	917	1,74	34293	65,23	15624	29,72	1735	3,30
6	12655	378	2,99	3994	31,56	7655	60,49	628	4,96
7	43238	859	1,99	12835	29,68	23621	54,63	5923	13,70
8[a]	143510	1802	1,26	55572	38,72	73301	51,08	12835	8,94
9[a]	110749	1507	1,36	33060	29,85	64073	57,85	12109	10,93
10	34325	404	1,18	8415	24,52	21618	62,98	3888	11,33
11[a]	16666	358	2,15	4311	25,87	10803	64,82	1194	7,16
12[a]	76406	882	1,15	30704	40,19	38435	50,30	6385	8,36
13[a]	62376	923	1,48	23366	37,46	29284	46,95	8803	14,11
14[a]	24409	281	1,15	9464	38,77	12533	51,35	2131	8,73
15	8122	97	1,19	3640	44,82	3781	46,55	604	7,44
Total	**650856**	**9923**	**1,52**	**232910**	**35,79**	**345106**	**53,02**	**62917**	**9,67**

[a] due to missing data n is smaller than the number of totally primary samples

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 20.7% of cases with statement of the delivery time the probe was received 72 hours after sampling, in 23.11% of the cases between 48 and 72 hours. Shorter periods of delivery times are desirable, especially at the weekend. (Table 4.2, Figure 3).

Table 4.2: Period between sampling and laboratory receipt

	Total	≤24h		>24h-48h		>48h-72h		>72h	
Lab	n	n	%	n	%	n	%	n	%
1[a]	50541	13901	27,50	19770	39,12	10062	19,91	6808	13,47
3[a]	15212	5848	38,44	5605	36,85	2358	15,50	1401	9,21
5	52559	6284	11,96	23600	44,90	14690	27,95	7985	15,19
6	12655	1819	14,37	5379	42,50	3059	24,17	2398	18,95
7	43238	10295	23,81	13308	30,78	8462	19,57	11173	25,84
8[a]	146592	17097	11,66	49235	33,59	40422	27,57	39838	27,18
9[a]	110756	11305	10,21	35242	31,82	28183	25,45	36026	32,53
10	34325	4555	13,27	12882	37,53	9248	26,94	7640	22,26
11[a]	16664	2781	16,69	7695	46,18	4070	24,42	2118	12,71
12[a]	77167	27760	35,97	27163	35,20	14128	18,31	8116	10,52
13[a]	62376	19618	31,45	21617	34,66	11725	18,80	9416	15,10
14[a]	24697	14303	57,91	6774	27,43	2655	10,75	965	3,91
15	8122	1130	13,91	3032	37,33	2289	28,18	1671	20,57
Total	**654904**	**136696**	**20,87**	**231302**	**35,32**	**151351**	**23,11**	**135555**	**20,70**

[a] due to missing data n is smaller than the number of totally primary samples

4.3 Period between laboratory receipt and result reporting

In more than 84.6% 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).

Table 4.3 Period between laboratory receipt and report

	Total	≤24h		>24h-48h		>48h-72h		>72h	
Lab	n	n	%	n	%	n	%	n	%
1[a]	50685	31922	62,98	14840	29,28	2799	5,52	1124	2,22
3[a]	15237	13264	87,05	1287	8,45	287	1,88	399[b]	2,62[b]
5	52569	39822	75,75	9693	18,44	2793	5,31	261	0,50
7	n.a.	n.a.		n.a.		n.a.		n.a.	
8	154425	148586	96,22	5597	3,62	96	0,06	146	0,09
9[a]	110573	107202	96,95	2648	2,39	547	0,49	176	0,16
10	34325	29347	85,50	4589	13,37	335	0,98	54	0,16
11[a]	16666	11508	69,05	4847	29,08	292	1,75	19	0,11
12[a]	77376	58974	76,22	13181	17,03	5063	6,54	158	0,20
13	62376	46262	74,17	10964	17,58	4247	6,81	903	1,45
14[a]	24699	18740	75,87	4774	19,33	1018	4,12	167	0,68
15	8122	7965	98,07	157	1,93				
Total	**607053**	**513592**	**84,60**	**72577**	**11,96**	**17477**	**2,88**	**3407**	**0,56**

[a] due to missing data n is smaller than the number of totally primary samples
[b] CF-recalls account for the high percentage on samples with report >72h

Figure 2: Age at blood collection 2005 and 2011

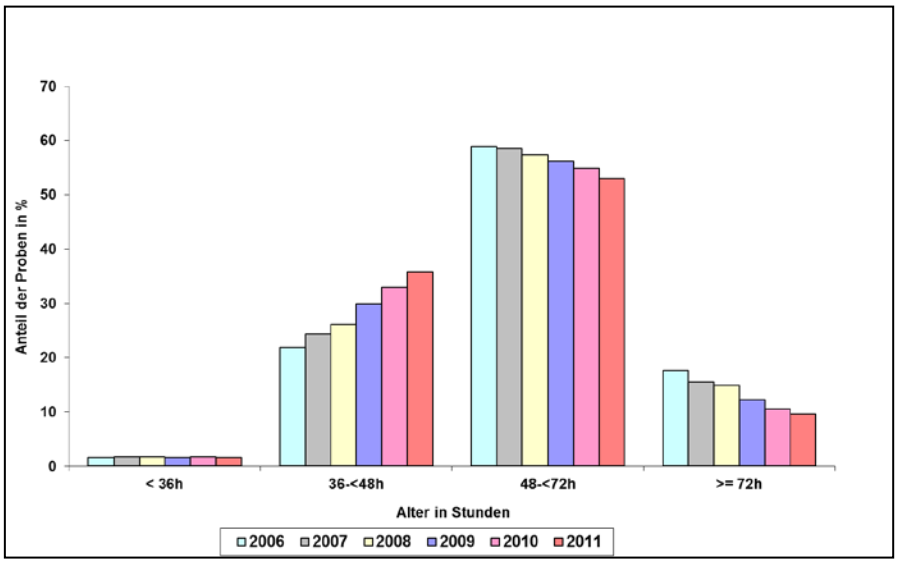


Figure 3: Period between sampling and laboratory receipt

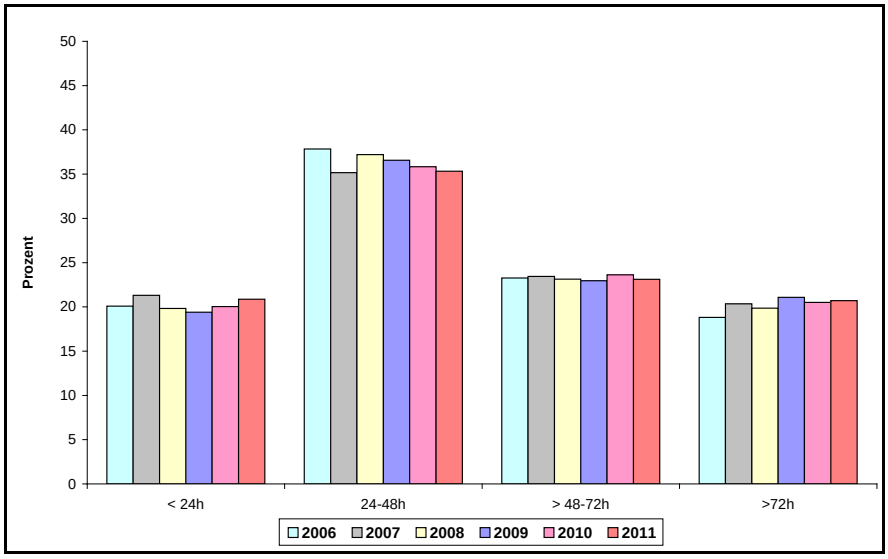
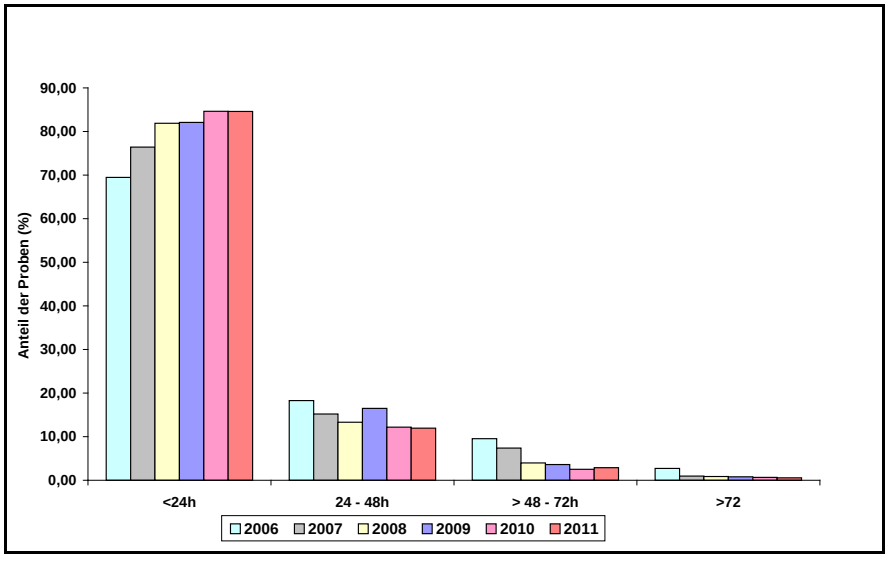


Figure 4: Period from laboratory receipt to report



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, Time not specified[a]	Not specified[b]	Total
Hypothyroidism	177	11	1	6	12			207
CAH	35	2		6	1			44
Biotinidase	20	2						22
Classic Galactosaemia	8	5				1		14
PKU/HPA	97	11	1	5			1	115
MSUD	4							4
MCAD	69	3	2	2				76
LCHAD	3				1			4
VLCAD	10	1						11
CACT							1[c]	1
GA I	7							7
IVA	5	1						6
Total	**435**	**36**	**4**	**19**	**14**	**1**	**2**	**511**

[a] ≥36h n.s. does not include repeat testing with early sampling or preterm birth, exact age of sampling time not stated.
[b] No information, neither WoG nor age at sampling.
[c] Full-term baby

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

	Indication for repeat screening				
Disease	Suspicious Primary screening	< 36h	<32WoG	unknown	Total
Hypothyroidism	185	6	12 [a]	4 [b]	**207**
CAH	37	6	1		**42**
Biotinidase	22				**22**
Classic Galactosaemia	14				**14**
PKU/HPA	109	5		1	**115**
MSUD	4				**4**
MCAD	74	2			**76**
LCHAD	3		1		**4**
VLCAD	11				**11**
CACT-Disease	1				**1**
GA I	7				**7**
IVA	6				**6**
Total	**473**	**19**	**14**	**5**	**511**

* incl. cases not found in screening: [a] n=1 Blood collection 30. WoG, [a] n=1 Blood collection 29. WoG; [b] n=4 Preterm blood collection 32.-34. WoG

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 2011 in 20 out of confirmed cases no detailed information about the confirmation diagnostics is available, the available data though allows a plausible analysis. In a further 16 cases (see Table 3.1) 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	20	20	2	2	1	20	20	12
3	5	5	4	3	2	5	5	5
5	11	11	n.a.	11	n.a.	11	11	10
6	4	4	1	3	n.a.	4	4	4
7	3	2	n.a.	2	n.a.	2	n.a.	n.a.
8	64	62	3	47	1	62	53	43
9	34	33	5	24	5	33	8	1
10	11	11	4	6	1	11	8	7
11	4	4	n.a.	2	n.a.	4	3	2
12	33	32	1	23	2	31	27	17
13	9	9	n.a.	n.a.	n.a.	9	n.a.	n.a.
14	5	5	n.a.	5	n.a.	5	5	3
15	4	4	n.a.	3	n.a.	3	2	2
Total	**207**	**202**	**20**	**131**	**12**	**200**	**146**	**106**

* incl n=2 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	5	4	n.a.	5
3	2	2	1	1	1
5	1	n.a.	n.a.	1	n.a.
7	3	n.a.	2	n.a.	1
8	11	7	10	3	10
9	10	10	8	1	3
10	3	3	2	n.a.	3
12	4	1	2	n.a.	4
13	2	2	2	n.a.	n.a.
14	2	n.a.	1	n.a.	1
15	1	1	1	n.a.	1
Total	**44**	**31**	**33**	**6**	**29**

* incl n=2 cases without detailed information of confirmation diagnostics

6.3 Biotinidase deficiency

Lab	Confirmed cases*	Biotinidase (Serum/TB)	Molecular genetic testing
1	2	2	n.a.
6	1	n.a.	n.a.
7	2	2	n.a.
8	13	12	n.a.
10	2	2	n.a.
11	1	1	n.a.
15	1	1	n.a.
Total	**22**	**20**	**n.a.**

* incl n=2 cases without detailed information of confirmation diagnostics

6.4 Classic Galactosaemia

Lab	Confirmed cases	Enzyme assay	Galactose, Gal1P	Molecular genetic testing
5	1	1	1	n.a.
7	1	n.a.	n.a.	1
8	6	5	6	1
10	3	2	3	1
12	3	2	3	2
Total	**14**	**10**	**13**	**5**

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	8	8	n.a.	6	8	8	8
3	2	2	2	n.a.	n.a.	2	2
5	9	9	9	6	n.a.	9	9
7	10	8	n.a.	n.a.	n.a.	7	7
8	17	16	8	8	3	11	11
9	19	16	13	3	2	10	10
10	7	7	4	3	4	7	7
11	4	4	4	3	n.a.	3	3
12	17	14	11	10	6	12	11
13	15	10	1	6	1	9	8
14	7	7	6	4	2	6	6
Total	**115**	**101**	**58**	**49**	**26**	**84**	**82**

* 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.
9	2	2	n.a.	n.a.	n.a.
13	1	1	n.a.	n.a.	n.a.
Total	**4**	**4**	**1**	**n.a.**	**n.a.**

6.7 MCAD-Disease

Lab	Confirmed cases*	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	6	6	6	6	6
3	1	1	n.a.	n.a.	n.a.
5	5	1	4	n.a.	4
6	1	1	1	n.a.	1
7	3	n.a.	3	1	2
8	24	15	7	3	18
9	14	13	11	4	8
10	3	3	3	2	3
12	7	4	4	n.a.	3
13	8	1	1	n.a.	3
14	3	1	1	n.a.	1
15	1	n.a.	n.a.	1	1
Total	**76**	**46**	**41**	**17**	**50**

incl n=7 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
1	1	n.a.	1	n.a.	1
8	1	1	1	n.a.	1
10	1	1	1	n.a.	1
11	1	1	1	n.a.	1
Total	**4**	**3**	**4**	**n.a.**	**4**

6.9 VLCAD-Disease

Lab	Confirmed cases	Confirmation Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	1	1	1	1	n.a.
5	3	1	2	2	2
8	1	1	n.a.	1	1
9	3	2	n.a.	3	2
10	1	1	1	1	1
13	1	n.a.	n.a.	n.a.	1
14	1	1	n.a.	1	n.a.
Total	**11**	**7**	**4**	**9**	**7**

6.10 No confirmed cases of CPT I-Disease, CPT II-Disease

6.11 CACT-Disease

Lab	Confirmed cases	Confirmation Serum/TB	Enzyme activity	Molecular genetic testing
8	1	n.a.	n.a.	1
Total	**1**	**n.a.**	**n.a.**	**1**

6.12 Glutaric aciduria Type I

Lab	Confirmed cases	Confirmed Serum/TB	Urinary organic acids	Enzyme activity	Molecular genetic testing
3	1	1	1	n.a.	n.a.
7	1	1	1	n.a.	n.a.
8	2	2	1	n.a.	1
9	2	2	2	n.a.	2
14	1	n.a.	1	n.a.	1
Total	**7**	**6**	**6**	**n.a.**	**4**

6.13 Isovaleric acidaemia

Lab	Confirmed cases	Confirmed Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
9	2	1	n.a.	n.a.	n.a.
10	1	1	1	n.a.	n.a.
12	2	2	2	n.a.	n.a.
14	1	1	1	n.a.	n.a.
Total	**6**	**5**	**4**	**n.a.**	**n.a.**

incl n=7 cases without detailed information of confirmation diagnostics

7 Methods and cut offs in screening

7.1 Filter paper for sampling

Lab	Filter paper
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	Method
1	TSH	AutoDELFIA
3	TSH	AutoDELFIA
5	TSH	AutoDELFIA
6	TSH	DELFIA
7	TSH	AutoDELFIA
8	TSH	DELFIA
9	TSH	AutoDELFIA
10	TSH	AutoDELFIA
11	TSH	DELFIA
12	TSH	AutoDELFIA
13	TSH	AutoDELFIA
14	TSH	AutoDELFIA
15	TSH	AutoDELFIA

7.3 Biotinidase deficiency

Lab	Parameter	Method
1	Biotinidase	Colorimetry qualitative
3	Biotinidase	Colorimetry qualitative
5	Biotinidase	n.a.
6	Biotinidase	Flurometry (PE)
7	Biotinidase	Colorimetry quantitative
8	Biotinidase	n.a.:iv
9	Biotinidase	Colorimetry qualitative
10	Biotinidase	Colorimetry qualitative
11	Biotinidase	Colorimetry qualitative
12	Biotinidase	Fluorometry quantitative
13	Biotinidase	Fluorometry quantitative
14	Biotinidase	Colorimetry quantitative
15	Biotinidase	Colorimetry quantitative

7.4 Galactosaemia

Lab	Parameter	Method
1	GALT Galactose	Fluorometry(PE) BIORAD Quantase
3	GALT Galactose	BIORAD Quantase
5	GALT Galactose	n.a.
6	GALT	Fluorometry (PE)
7	GALT	Fluorometry quantitative
8	GALT Galactose	n.a.
9	GALT Galactose*	BIORAD Quantase BIORAD Quantase
10	GALT Galactose	BIORAD Quantase BIORAD Quantase
11	GALT	Fluorometry quantitativ
12	GALT Galactose	Fluoro. quant.(non-kit) Colorimetry non Kit
13	GALT Galactose	Fluoro. quant.(non-kit) Colorimetry non Kit
14	GALT Galactose	BIORAD Quantase BIORAD Quantase
15	GALT Galactose	BIORAD Quantase BIORAD Quantase

* Galactose as a second-tier method

7.5 MS/MS

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

8 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 16. Dezember 2010; Bundesanzeiger 2011 Nr.40: S.1013 in Kraft getreten 12. März 2011

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