National

Screening Report 2008

DGNS

Deutsche Gesellschaft für Neugeborenenscreening e.V.

**Dr. med. Uta Nennstiel-Ratzel MPH, Dr. med. Anja Lüders MPH,
Dr. med. Oliver Blankenstein, Dr. rer. nat. Uta Ceglarek, Dr. med. Regina Ensenauer,
Dr. rer. nat. Ralph Fingerhut, Dr. rer. nat. Jeannette Klein, Dr. med. Martin Lindner,
Dr. rer. nat. Cornelia Müller, PD Dr. med. Michael Peter, Prof. Dr. med. Ernst Rauterberg,
Inge Schneider, Dr. med. Dr. rer. nat. Wolfgang Schultis, Prof. Dr. med. Andreas Schulze,
Dipl.-Biochem. Irmgard Starke, Dipl. Ing. Maren Stehn, Dr. rer. nat. Marina Stopsack,
Prof. Dr. med. Christoph Fusch**

Stand 01.08.2010

Correspondence author:
Dr. med Uta Nennstiel-Ratzel MPH
Screening Centre
Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit
Veterinärstr. 2
D-85764 Oberschleißheim
Germany
Email: uta.nennstiel-ratzel@lgl.bayern.de

Contents

Figures

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 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
SP	secondary parameter
PKU	Phenylketonuria
PPV	positive predictive value
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.

1) Neugeborenen Screeninglabor Berlin
Dr. med. Oliver Blankenstein
Augustenburger Platz 1
13353 **Berlin**
030/450 566678
Oliver.Blankenstein@charite.de

Screeningzentrum Sachsen
Prof. Dr. med. Joachim Thiery,
Universitätsklinikum Leipzig
3) Standort **Dresden**
PF 160252
01288 Dresden
0351/458 5230 / 5229
marina.stopsack@uniklinikum-dresden.de
10) Standort **Leipzig**
Paul-Listr-Str. 13-15
04103 Leipzig
0341/9722222 (Leitstelle ILM)
uta.ceglarek@medizin.uni-leipzig.de
http://www.screeningzentrum-sachsen.de/

5) Screening-Zentrum Hessen
Prof. Dr. med. Ernst W. Rauterberg
Feulgenstr. 12
35392 **Giessen**
0641/9943681
ernst.w.rauterberg@paediat.med.uni-giessen.de

6) Neugeborenenscreeninglabor M-V
Prof. Dr. med. Christoph Fusch,
Prof. Dr. med. Matthias Nauck
Soldmannstr. 15
17489 **Greifswald**
03834/866409
fusch@uni-greifswald.de; nauck@uni-greifswald.de; http://www.medizin.uni-greifswald.de/kind_med/neugeborenscreening-Dateien/slide0001.htm

7) Screening-Labor Universitätskinderklinik Hamburg
Prof. Dr. med. René Santer
Martinistr. 52
20246 **Hamburg**
040/42803 0
r.santer@uke.uni-hamburg.de

8) Screening-Labor Hannover
Prof. Dr. med. J. Sander, PD Dr. med. M. Peter
Postfach 911009
D 30430 **Hannover**
05108/92163 0
j.sander@metabscreen.de
m.peter@metabscreen.de
www.metabscreen.de

9) Neugeborenenscreening Heidelberg
Prof. Dr. med. G.F. Hoffmann
Im Neuenheimer Feld 153
69120 **Heidelberg**
06221/56 2311
martin.lindner@med.uni-heidelberg.de
www.Neugeborenenscreening.uni-hd.de

11) Screeninglabor, Universitäts-Kinderklinik
PD Dr. med Klaus Mohnike
PSF 140274
39043 **Magdeburg**
0391/6713986
irmgard.starke@med.ovgu.de
http://www.stoffwechselzentrum-magdeburg.de

13) Labor Becker, Olgemöller & Kollegen
Prof. Dr. med. Dr. rer. nat. Bernhard Olgemöller
Ottobrunner Str. 6
81737 **München**
089/544 654 0
Olgemoeller@labor-bo.de
www.labor-bo.de

15) Medizinisches Versorgungszentrum für Laboratoriumsmedizin u. Mikrobiologie
Dr. med. Dr. rer. nat. Hans-Wolfgang Schultis
Zur Kesselschmiede 4
92637 **Weiden**
0961/309 0
schultis@synlab.de
www.mfl-weiden.synlab.de

Screeningzentrum Bayern (12/14)
Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit
Dr. med. Uta Nennstiel-Ratzel MPH
Veterinärstr.2
85764 **Oberschleißheim**
089/31560204
screening@lgl.bayern.de
http://www.lgl.bayern.de/gesundheit/neugeborenenscreening.htm

12) Labor Becker, Olgemöller & Kollegen
See 13
14) Medizinisches Versorgungszentrum für Laboratoriumsmedizin u. Mikrobiologie
See 15

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) since 1.7.2005.

The National Screening Report 2008 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 2008. 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:

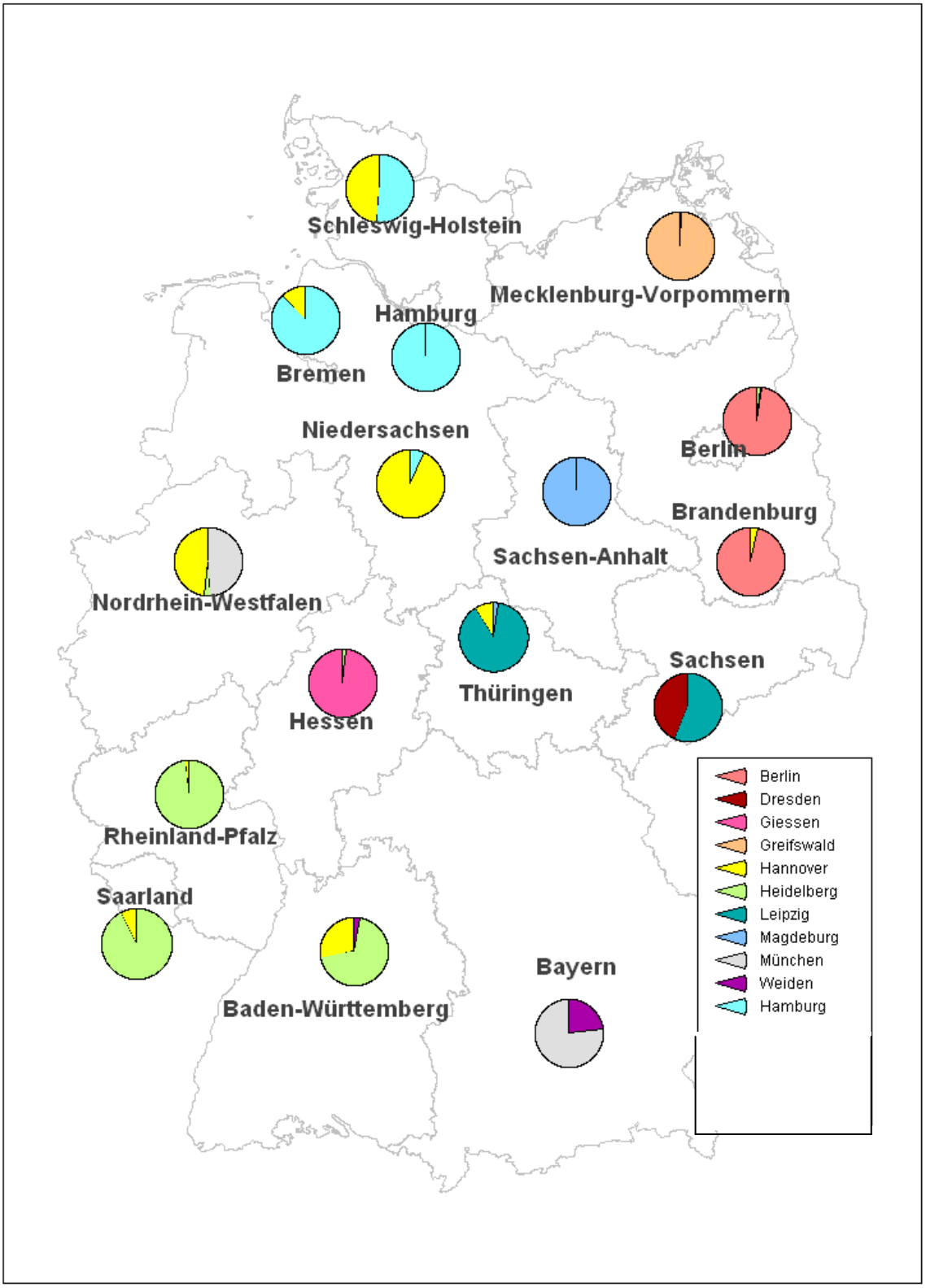
- Total Survey of the population
    - Collection method and rate
    - Blank card system
- Completeness of the control and the secondary testing
- Collection of test parameters and cut offs
- According to laboratory, age as well as gestational age, stratified rates of recall, positive predictive values and prevalence
- 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
- Diagnostic for confirmation
    - Type of diagnostic
    - Time of diagnostic
- Final diagnosis
- Start of therapy

On the previous page laboratories are listed which have undertaken the screening in 2008 for Germany. (12 and 13 relate to the same laboratory, ones with and without the co-operation of the Screening Centre, same for 14 and 15). Laboratories are encoded in the listed tables. Paragraphs in the text relate to the altered guidelines for children from 21/12/04 (1). Tables are numbered according to the chapters.

We thank all the laboratories for provision of their data. The data was checked for plausibility. Finally, the provided, and if necessary corrected, data was analysed. Remaining inconsistencies of data was analysed according to the reported data. (Inconsistency is partly 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 2008, 682.514 children were born in Germany. The total recorded screening exceeds this number slightly at 689.262. The reason is because a second screening card is sometimes recorded at a different laboratory, as some cards are sent to a different laboratory than the original.

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. The screening rate for Germany is 101%.

Births [2]:	682.514
First screening:	689.262
Final diagnosis (see Table 3):	495

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. Of 1.379 newborns one targeted disease according to the guidelines is found. Table 2 shows the prevalence of targeted diseases in the year 2008 in Germany.

Table: 2 Absolute number of detected diseases found by screening

Disease	Confirmed cases	Prevalence
Hypothyroidism	184	1: 3.709
Congenital adrenal hyperplasia (CAH)	43	1: 15.872
Biotinidase Deficiency	31	1: 22.017
Galactosaemia (Classic)	7	1: 97.502
Phenylketonuria (PKU) n=65 /Hyperphenylalaninaemia (HPA) n=75	140	1: 4.875
Maple syrup urine disease (MSUD)	5	1: 136.503
Medium-Chain-Acyl-CoA-Dehydrogenase (MCAD)-Deficiency	61	1: 11.189
Long-Chain-3-OH-Acyl-CoA-Dehydrogenase (LCHAD)-Deficiency	2	1: 341.257
(Very-)Long-Chain-Acyl-CoA-Dehydrogenase (VLCAD)-Deficiency	9	1: 75.835
Carnitin-Palmitoyl-CoA-Transferase I (CPTI)-Deficiency	1	1: 682.514
Carnitin-Palmitoyl-CoA-Transferase II (CPTII)-Deficiency	0	
Carnitin-Acylcarnitin-Translocase (CACT)-Deficiency	0	
Glutaric acidaemia Typ I (GA I)	9	1: 75.835
Isovaleric acidaemia (IVA)	3	1: 227.505
Total	**495**	1: 1.379

2.1 Data of primary screening

According to the guidelines for 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

Laboratory	Total	≥36h and ≥32WOG		<36h and ≥32WOG		<32WOG	
		n	%	n	%	n	%
1	49201	47214	95.96	1411	2.87	576	1.17
3	15218	14804	97.28	273	1.79	141	.93
5*	51129	50300	98.38	351	0.69*	478	.93
6	13004	12497	96.10	346	2.66	161	1.24
7	42439	40654	95.79	1143	2.69	642	1.51
8	169536	165714	97.75	1854	1.09	1968	1.16
9	109172	106525	97.58	1300	1.19	1347	1.23
10	35240	34394	97.60	506	1.44	340	.96
11	17542	16803	95.79	523	2.98	216	1.23
12	80229	78642	98.02	838	1.04	749	.93
13	76038	74417	97.87	1130	1.49	491	.65
14	24512	23896	97.49	349	1.42	267	1.09
15	6002	5790	96.47	172	2.87	40	.67
Total	689262	671650	97.44	10196	1.48	7416	1.08

***** Laboratory declined in 8% early screening

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

For some laboratories the repeat testing did not match the clarified results, because some analysis was repeated in other laboratories and deceased neonates (mainly < 32 WoG) were not fully accounted. This partly explains the range of results.

Table 2.2.1 Requested and received repeat screenings

Laboratory	Total[a] requested	Total[a] received	%[a]	Recall requested	Recall received	%
1	2630	2575	97.91	667	655	98.20
3	457	496	[d]	46	50	[d]
5	1516	1251	82.52	687	558	81.22
6	695	647	93.61	188	186	98.94
7[c]	2273			675	656	97.19
8	5483	4347	79.28	1290	1139	88.29
9	3595	2659	73.96	694	642	92.51
10	989	949	95.96	162	156	96.30
11	785	698	88.92	46	46	100.00
12	2186	2115	96.75	642	638	99.38
13	2065			444		
14	786	769	97.84	176	174	98.86
15	284	72	25.35	71	39	54.93
Total	**23744**	**16578**	**85.42[b]**	**5788**	**4939**	**92.42[c]**

Laboratory	<36h requested	<36h received	%	<32WOG requested	<32WOG received	%[f]
1	1387	1361	98.13	576	559	97.05
3	268	296	[d]	141	141	100.00
5	351	282	80.34	478	411	85.98
6	346	321	92.77	161	140	86.96
7[c]	1143			455		
8	1854	1385	74.70	1968	1607	81.66
9	1300	846	65.08	1347	993	73.72
10	494	468	94.74	333	320	96.10
11	523	464	88.72	216	188	87.04
12	796	779	97.86	748	698	93.32
13	1130			491		
14	349	343	98.28	261	252	96.55
15	172	3	1.7	40	29	72.50
Total	**10113**	**6548**	**83.52[b]**	**7215**	**5338**	**85.12[b]**

Laboratory	Other requested[e]	Other received[e]	%
Total	**628**	**409**	**65.13**

[a] Inclusive secondary screening due to blood transfusion, parenteral nutrition or medication
[b] calculation excluding laboratory 7 and 13, because secondary screening could not be fully differentiated
[c] calculation excluding laboratory 13, because secondary screening could not be fully differentiated
[d] n received > n requested, therefore no percentage calculation

[e] secondary screening due to blood transfusion, parenteral nutrition or medication [f] low rate due to deceased neonates

2.3 Tracking of completeness of screening

The newborn screening is a measure of public health and should be given to all in Germany born children. To guarantee that the screen is offered to all newborns the tracking of completeness is necessary. For children born in obstetric units, an alignment of the recorded birth number on the screening card along with the recorded birth number of the sending unit would be possible, or if legally allowed, by comparing with data from the birth register.

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.

Overall the number of received blank cards did not match the expected amount. Of the neonates deceased within the first 3 days about 1250 [2] cards were expected, but only 274 were received. Decline of screening occurs in around 1‰ [3]. This would match to 680 blank screening cards, but only 104 were received. (Table 2.3). In 2008 the amount of received blank screening cards with declined early screening has risen clearly compared to previous years.

Table 2.3: Laboratory received blank cards

	Deceased	Screening declined	Transfer	Early screening declined	Total	Relation to screened children
Laboratory	n	n	n	n	n	%
1	27	0	0	3.365	3.392	6.89
3	40	23	1069	518	1.650	10.84
5	36	5	0	4.187	4.228	8.27
6	50	3	3	254	310	2.38
7	0	0	0	184	184	0.43
8	0	0	0	1.114	1.114	0.66
9	10	26	40	1.324	1.400	1.28
10	33	13	0	1.147	1.193	3.39
11	72	4	58	300	434	2.47
12	6	30	70	952	1.058	1.32
13	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
14	0	0	0	35	35	0.14
15	0	0	0	0		
Total	**274**	**104**	**1240**	**13.380**	**14.998**	**2.18**

2.4 Requirements to a repeat screening card due to bad sample quality

Lab.	Primary Screening	Control requested	Control received	received/ requested (%)	Percentage of unprocessed screening cards/ Primary Screening (%)
1	49201	422	422	100.00	0.86
3	15218	n.s.	n.s.		
5	51129	n.s.	n.s.		
6	13004	36	36	100.00	0.28
7	42439	79	69	87.34	0.19
8	169536	384	363	94.53	0.23
9	109172	468	417	89.10	0.43
10	35240	131	129	98.47	0.37
11	17542	3	3	100.00	0.02
12	80229	471	465	98.73	0.59
13	76038	419	367	87.59	0.55
14	24512	9	8	88.89	0.04
15	6002	n.s..	n.s..		
Total	**689262**	**2422**	**2279**	**94,10**	**0,35**

3 Recall Rate, Prevalence, Positive predictive value 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 2008 the recall rate accounted for 0.7 %, meaning 7 control screenings per 1000. The positive predictive value determines the probability that a person with a positive test result is really diseased. 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 sensitivity cannot be quoted, because systematic registration of diseased children missed by neonate screening is not done. For the calculation of the PPV the sensitivity is estimated 99,5%. False negative cases, if reported to the DGNS, are listed in the tables.

Only for neonates born after the 32nd WoG and screening sampled beyond the 36th the PPV is considered for analysis. Overall the PPV is 9,8%, meaning that about 10% of suspicious screening results indicate the targeted disease. For several diseases the PPV is high, e.g. for HPA / PKU 56,3%, for MCAD-Deficiency 28,7% and for Hypothyroidism 28,6%. The range of PPV between the single laboratories differs.

Table 3: Recall, PPV with a Screening ≥36h und ≥32 WOG

Disease	Primary Screening	Recall	Recall-rate(%)	Confirmed cases**	PPV(%)	Specificity ≥ 36h(%)
Hypothyroidism	671650	587	0.09	168	28.62	99.94
AGS	671650	2577	0.38	38	1.47	99.62
Biotinidase	671650	174	0.03	30	17.24	99.98
Classic Galactosaemia	671650	373	0.06	6	1.88	99.95
MS/MS*	671650	922	0.14	213	23.10	99.89
Total	**671650**	**4633**	**0.69**	**453**	**9.78**	**99.38**

*Only targeted diseases
** considered are only neonates with screening ≥36h und ≥32 WOG, hence results differ

3.1 Recall rate, prevalence stratified

Recall rates of the following tables as well as PPV are of newborns that were screened > 32 weeks gestational age and 36 hours age. 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 to 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=15), cases with implausible data (n=17) and cases where the confirmation diagnostics was negative (n=4) (Tab.3.1.a). As a result the true prevalence could be higher. Double reported cases were included only once.

Table 3.1.a :Cases with missing/implausible data of confirmation diagnostics

Disease	Data missing	Data implausible
Hypothyroidism	**4**	**6**
AGS		
Biotinidase Deficiency		
Galactosaemia	**1**	**6**
PKU/HPA	**4**	**2**
MSUD		**1**
MCAD	**3**	**2**
LCHAD	**1**	
VLCAD		
CPT I-Deficiency		
CPT II-Deficiency		
CAT-Deficiency		
GA I		
IVA	**2**	
Total	**15**	**17**

The following tables did not report recall rates which are < 0.01% and have a very small n

Table 3.1: All targeted diseases

Disease	Primary Screening Total	Primary Screening ≥36h	Recall ≥36h	Recall-rate % ≥36h	Confirmed cases Total	PPV % ≥36h	Prevalence Total	False negative
Hypothyroidism	689262	671650	587	0.09	184	28.62	1: 3746	1
AGS	689262	671650	2577	0.38	43	1.47	1: 16029	
Biotinidase-Deficiency	689262	671650	174	0.03	31	17.24	1: 22234	
Galactosaemia	689262	671650	373	0.06	7	1.88	1: 98466	
PKU/HPA	689262	671650	231	0.03	140	56.28	1: 4923	
MSUD	689262	671650	75	0.01	5	6.67	1: 137852	
MCAD	689262	671650	192	0.03	61	28.65	1: 11299	
LCHAD	689262	671650	16		2	6.25	1: 344631	
VLCAD	689262	671650	171	0.03	9	5.26	1: 76585	
CPT I-Deficiency	689262	671650	4		1		1: 689262	
CPT II-Deficiency	689262	671650	13		0			
CAT-Deficiency	689262	671650	0		0			
GA I	689262	671650	162	0.02	9	5.56	1: 76585	
IVA	689262	671650	58	0.01	3	5.17	1: 229754	
Total	**689262**	**671650**	**4633**	**0.69**	**495**	**9.78**	**1: 1392**	**1**

3.1.1 Hypothyroidism[a]

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)	Confirmed cases	False negative.
1	49201	47214	23	0.05	14	1
3	15218	14804	4	0.03	2	
5	51129	50300	111	0.22	11	
6	13004	12497	7	0.06	5	
7	42439	40654	26	0.06	3	
8	169536	165714	230	0.14	43	
9	109172	106525	66	0.06	37	
10	35240	34394	15	0.04	6	
11	17542	16803	7	0.04	5	
12	80229	78642	35	0.04	29	
13	76038	74417	50	0.07	21	
14	24512	23896	9	0.04	6	
15	6002	5790	4	0.07	2	
Total	**689262**	**671650**	**587**	**0.09**	**184**	**1**

[a] including temporary hypothyroidismn n=7

Additionally n=7 hyperthyreothropinaemias were diagnosed but not counted in the prevalence

3.1.2 Congenital adrenal hyperplasia (CAH) [a]

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)	Confirmed cases
1	49201	47214	145	0.31	2
3	15218	14804	3	0.02	1
5	51129	50300	320	0.64	4
6	13004	12497	143	1.14	0
7	42439	40654	217	0.53	0
8	169536	165714	565	0.34	13
9	109172	106525	242	0.23	7
10	35240	34394	51	0.15	3
11	17542	16803	25	0.15	2
12	80229	78642	469	0.60	8
13	76038	74417	267	0.36	2
14	24512	23896	101	0.42	1
15	6002	5790	29	0.50	0
Total	**689262**	**671650**	**2577**	**0.38**	**43**

[a] Confirmed cases inclusive n=1: 11ß-hydroxylase deficiency

3.1.3 Biotinidase Deficiency

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	9	0.02	1
3	15218	14804	4	0.03	0
5	51129	50300	5	0.01	1
6	13004	12497	0		0
7	42439	40654	11	0.03	1
8	169536	165714	103	0.06	23
9	109172	106525	4		1
10	35240	34394	5	0.01	2
11	17542	16803	1		0
12	80229	78642	18	0.02	2
13	76038	74417	14	0.02	0
14	24512	23896	0		0
15	6002	5790	0		0
Total	**689262**	**671650**	**174**	**0.03**	**31**

* Recall rate recorded only if ≥ 0.01% and n > 1.

3.1.4 Galactosaemia incl. variants / classic

Laboratory [a]	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)	Confirmed cases
1	49201	47214	65	0.14	14
3	15218	14804	4	0.03	2
5	51129	50300	61	0.12	1
6	13004	12497	2	0.02	0
7 [b]	42439	40654	28	0.07	6
8	169536	165714	32	0.02	10
9	109172	106525	7	0.01	0
10	35240	34394	12	0.03	7
11	17542	16803	5	0.03	0
12	80229	78642	35	0.04	3
13	76038	74417	47	0.06	2
14	24512	23896	51	0.21	8
15	6002	5790	24	0.41	0
Total	**689262**	**671650**	**373**	**0.06**	**53**
Classic					**7**

3.1.5 MS/MS

MS/MS only targeted diseases

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)	Confirmed cases
1	49201	47214	192	0.41	15
3	15218	14804	31	0.21	10
5	51129	50300	190	0.38	19
6	13004	12497	30	0.24	6
7	42439	40654	98	0.24	11
8	169536	165714	70	0.04	62
9	109172	106525	147	0.14	33
10	35240	34394	19	0.06	6
11	17542	16803	7	0.04	9
12	80229	78642	55	0.07	26
13	76038	74417	58	0.08	26
14	24512	23896	16	0.07	6
15	6002	5790	9	0.16	1
Total	**689262**	**671650**	**922**	**0.14**	**230**

3.1.5.1 PKU / HPA

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	41	0.09	8
3	15218	14804	13	0.09	9
5	51129	50300	22	0.04	11
6	13004	12497	10	0.08	5
7	42439	40654	21	0.05	7
8	169536	165714	38	0.02	36
9	109172	106525	25	0.02	22
10	35240	34394	5	0.01	3
11	17542	16803	4	0.02	6
12	80229	78642	23	0.03	16
13	76038	74417	24	0.03	13
14	24512	23896	4	0.02	3
15	6002	5790	1		1
Total	**689262**	**671650**	**231**	**0.03**	**140**
Only PKU					**65**

* Recall rate recorded only if ≥ 0.01% und n > 1.

3.1.5.2 MSUD

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	33	0.070	2
3	15218	14804	1		0
5	51129	50300	16	0.032	0
6	13004	12497	1		0
7	42439	40654	3	0.007	0
8	169536	165714	2		0
9	109172	106525	16	0.015	1
10	35240	34394	0		0
11	17542	16803	0		0
12	80229	78642	2		1
13	76038	74417	1		1
14	24512	23896	0		0
15	6002	5790	0		0
Total	689262	671650	75	0.011	5

* Recall rate recorded only if ≥ 0.01% und n > 2.

3.1.5.3 MCAD-Deficiency

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)	Confirmed cases
1	49201	47214	50	0.11	3
3	15218	14804	5	0.03	1
5	51129	50300	51	0.10	8
6	13004	12497	5	0.04	1
7	42439	40654	10	0.02	2
8	169536	165714	15	0.01	14
9	109172	106525	15	0.01	7
10	35240	34394	8	0.02	2
11	17542	16803	3	0.02	3
12	80229	78642	12	0.02	8
13	76038	74417	11	0.01	10
14	24512	23896	5	0.02	2
15	6002	5790	2	0.03	0
Total	**689262**	**671650**	**192**	**0.03**	**61**

3.1.5.4 LCHAD-Deficiency

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	5		0
3	15218	14804	0		0
5	51129	50300	0		0
6	13004	12497	1		0
7	42439	40654	1		1
8	169536	165714	0		0
9	109172	106525	4		1
10	35240	34394	0		0
11	17542	16803	0		0
12	80229	78642	4		0
13	76038	74417	1		0
14	24512	23896	0		0
15	6002	5790	0		0
Total	**689262**	**671650**	**16**	**0.002**	**2**

* due to the small numbers, recall rates are quoted in absolute numbers

3.1.5.5 VLCAD-Deficiency

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	27	0.06	2
3	15218	14804	5	0.03	0
5	51129	50300	5	0.01	0
6	13004	12497	3	0.02	0
7	42439	40654	40	0.10	0
8	169536	165714	4		3
9	109172	106525	56	0.05	1
10	35240	34394	3	0.01	1
11	17542	16803	0		0
12	80229	78642	7	0.01	1
13	76038	74417	11	0.01	0
14	24512	23896	6	0.03	1
15	6002	5790	4	0.07	0
Total	**689262**	**671650**	**171**	**0.03**	**9**

* Recall rate recorded only if ≥ 0.01%.

.

3.1.5.6 CPT I-Deficiency

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	1		0
3	15218	14804	0		0
5	51129	50300	0		0
6	13004	12497	0		0
7	42439	40654	0		0
8	169536	165714	1		1
9	109172	106525	1		0
10	35240	34394	1		0
11	17542	16803	0		0
12	80229	78642	0		0
13	76038	74417	0		0
14	24512	23896	0		0
15	6002	5790	0		0
Total	**689262**	**671650**	**4**	**0.006**	**1**

* due to the small numbers, recall rates are quoted in absolute numbers

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

3.1.5.8 Glutaric acidaemia Type I

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	13	0.03	0
3	15218	14804	6	0.04	0
5	51129	50300	77	0.15	0
6	13004	12497	4	0.03	0
7	42439	40654	23	0.06	1
8	169536	165714	9	0.01	8
9	109172	106525	23	0.02	0
10	35240	34394	0		0
11	17542	16803	0		0
12	80229	78642	5	0.01	0
13	76038	74417	2		0
14	24512	23896	0		0
15	6002	5790	0		0
Total	**689262**	**671650**	**162**	**0.02**	**9**

* Recall rate recorded only if ≥ 0.01%.

.

3.1.5.9 Isovaleric acidaemia

Laboratory	Primary Screening Total	Primary Screening >=36h	Recall >=36h	Recall-rate(%)*	Confirmed cases
1	49201	47214	20	0.04	0
3	15218	14804	1		0
5	51129	50300	18	0.04	0
6	13004	12497	3	0.02	0
7	42439	40654	0		0
8	169536	165714	1		0
9	109172	106525	2		1
10	35240	34394	2		0
11	17542	16803	0		0
12	80229	78642	1		0
13	76038	74417	7	0.01	2
14	24512	23896	1		0
15	6002	5790	2	0.03	0
Total	**689262**	**671650**	**58**	**0.01**	**3**

Recall rate recorded only if ≥ 0.01% und n > 2.

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. Since this is different for the individual diseases we show the recall rate stratified to targeted diseases and age / gestational age. Recall rate is recorded only if it exceeds 0.01% and n > 2.

3.2.1 Hypothyroidism

	Primary Screening ≥ 36h			Primary Screening < 36h			Primary Screening < 32WOG		
Laboratory	Primary Screening	Recall	Recall-rate	Primary Screening	Recall	Recall-rate	Primary Screening	Recall	Recall-rate
1	47214	23	0.05	1411	12	0.85	576	1	
3	14804	4	0.03	273	51	18.68	141	0	
5	50300	111	0.22	351	7	1.99	478	2	
6	12497	7	0.06	346	0		161	0	
7	40654	26	0.06	1143	51	4.46	642	1	
8	165714	230	0.14	1854	205	11.06	1968	8	0.41
9	106525	66	0.06	1300	3	0.23	1347	0	
10	34394	15	0.04	506	21	4.15	340	0	
11	16803	7	0.04	523	59	11.28	216	1	
12	78642	35	0.04	838	35	4.18	749	4	0.53
13	74417	50	0.07	1130	31	2.74	491	3	0.61
14	23896	9	0.04	349	4	1.15	267	1	
15	5790	4	0.07	172	0		40	0	
Total	**671650**	**587**	**0.09**	**10196**	**479**	**4.70**	**7416**	**21**	**0.28**

3.2.2 Congenital adrenal hyperplasia (CAH)

	Primary Screening ≥ 36h			Primary Screening < 36h			Primary Screening < 32WOG		
Laboratory	Primary Screening	Recall	Recall-rate	Primary Screening	Recall	Recall-rate	Primary Screening	Recall	Recall-rate
1	47214	145	0.31	1411	41	2.91	576	17	2.95
3	14804	3	0.02	273	57	20.88	141	0	
5	50300	320	0.64	351	12	3.42	478	24	5.02
6	12497	143	1.14	346	0		161	2	
7	40654	217	0.53	1143	50	4.37	642	184	28.66
8	165714	565	0.34	1854	216	11.65	1968	257	13.06
9	106525	242	0.23	1300	13	1.00	1347	9	0.67
10	34394	51	0.15	506	19	3.75	340	6	1.76
11	16803	25	0.15	523	12	2.29	216	6	2.78
12	78642	469	0.60	838	24	2.86	749	158	21.09
13	74417	267	0.36	1130	27	2.39	491	54	11.00
14	23896	101	0.42	349	5	1.43	267	30	11.24
15	5790	29	0.50	172	1		40	3	7.50
Total	**671650**	**2577**	**0.38**	**10196**	**477**	**4.68**	**7416**	**750**	**10.11**

3.2.3 Biotinidase Deficiency

Laboratory	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	47214	9	0.02	1411	3		576	1	
3	14804	4	0.03	273	2		141	0	
5	50300	5	0.01	351	0		478	0	
6	12497	0		346	1		161	1	
7	40654	11	0.03	1143	1		642	0	
8	165714	103	0.06	1854	0		1968	4	
9	106525	4		1300	0		1347	0	
10	34394	5	0.01	506	0		340	0	
11	16803	1		523	1		216	0	
12	78642	18	0.02	838	0		749	2	
13	74417	14	0.02	1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**174**	**0.03**	**10196**	**8**	**0.08**	**7416**	**8**	**0.11**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.4 Galactosaemia

Laboratory	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	47214	65	0.14	1411	0		576	0	
3	14804	4	0.03	273	10	3.66	141	0	
5	50300	61	0.12	351	1		478	2	
6	12497	2	0.02	346	0		161	0	
7	40654	28	0.07	1143	1		642	0	
8	165714	32	0.02	1854	1		1968	1	
9	106525	7	0.01	1300	0		1347	0	
10	34394	12	0.03	506	0		340	0	
11	16803	5	0.03	523	0		216	0	
12	78642	35	0.04	838	2		749	4	
13	74417	47	0.06	1130	3	0.27	491	3	
14	23896	51	0.21	349	1		267	1	
15	5790	24	0.41	172	0		40	0	
Total	**671650**	**373**	**0.06**	**10196**	**19**	**0.19**	**7416**	**11**	**0.15**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5 MS/MS Total (only targeted disease)

Laboratory	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	47214	192	0.41	1411	12	0.85	576	26	4.51
3	14804	31	0.21	273	20	7.33	141	4	2.84
5	50300	190	0.38	351	1		478	19	3.97
6	12497	30	0.24	346	1		161	1	
7	40654	98	0.24	1143	3	0.26	642	2	
8	165714	70	0.04	1854	0		1968	0	
9	106525	147	0.14	1300	2		1347	6	0.45
10	34394	19	0.06	506	3	0.59	340	0	
11	16803	7	0.04	523	1		216	0	
12	78642	55	0.07	838	1		749	3	0.40
13	74417	58	0.08	1130	1		491	3	0.61
14	23896	16	0.07	349	3	0.86	267	0	
15	5790	9	0.16	172	0		40	1	
Total	**671650**	**922**	**0.14**	**10196**	**48**	**0.47**	**7416**	**65**	**0.88**

3.2.5.1 PKU/HPA

Laboratory	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	47214	41	0.09	1411	7	0.50	576	8	1.39
3	14804	13	0.09	273	20	7.33	141	3	2.13
5	50300	22	0.04	351	0		478	2	
6	12497	10	0.08	346	0		161	0	
7	40654	21	0.05	1143	3	0.26	642	0	
8	165714	38	0.02	1854	0		1968	0	
9	106525	25	0.02	1300	1		1347	2	
10	34394	5	0.01	506	1		340	0	
11	16803	4	0.02	523	1		216	0	
12	78642	23	0.03	838	0		749	2	
13	74417	24	0.03	1130	0		491	1	
14	23896	4	0.02	349	3	0.86	267	0	
15	5790	1	0.02	172	0		40	1	
Total	**671650**	**231**	**0.03**	**10196**	**36**	**0.35**	**7416**	**19**	**0.26**

3.2.5.2 MSUD

Laboratory	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	47214	33	0.07	1411	1		576	1	
3	14804	1		273	0		141	0	
5	50300	16	0.03	351	0		478	0	
6	12497	1		346	0		161	0	
7	40654	3	0.01	1143	0		642	0	
8	165714	2		1854	0		1968	0	
9	106525	16	0.02	1300	0		1347	1	
10	34394	0		506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	2		838	0		749	0	
13	74417	1		1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**75**	**0.01**	**10196**	**1**	**0.01**	**7416**	**2**	**0.03**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.3 MCAD-Deficiency

Laboratory	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	47214	50	0.11	1411	1		576	2	
3	14804	5	0.03	273	0		141	0	
5	50300	51	0.10	351	0		478	2	
6	12497	5	0.04	346	1		161	0	
7	40654	10	0.02	1143	0		642	0	
8	165714	15	0.01	1854	0		1968	0	
9	106525	15	0.01	1300	1		1347	0	
10	34394	8	0.02	506	0		340	0	
11	16803	3	0.02	523	0		216	0	
12	78642	12	0.02	838	1		749	0	
13	74417	11	0.01	1130	0		491	2	
14	23896	5	0.02	349	0		267	0	
15	5790	2		172	0		40	0	
Total	**671650**	**192**	**0.03**	**10196**	**4**	**0.04**	**7416**	**6**	**0.08**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.4 LCHAD-Deficiency

Laboratory	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	47214	5		1411	0		576	0	
3	14804	0		273	0		141	0	
5	50300	0		351	0		478	0	
6	12497	1		346	0		161	0	
7	40654	1		1143	0		642	1	
8	165714	0		1854	0		1968	0	
9	106525	4		1300	0		1347	0	
10	34394	0		506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	4		838	0		749	0	
13	74417	1		1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**16**	**0.002**	**10196**	**0**		**7416**	**1**	**0.01**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.5 VLCAD-Deficiency

Laboratory	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	47214	27	0,06	1411	0		576	1	
3	14804	5	0,03	273	0		141	1	
5	50300	5	0,01	351	0		478	4	
6	12497	3	0,02	346	0		161	0	
7	40654	40	0,10	1143	0		642	0	
8	165714	4		1854	0		1968	0	
9	106525	56	0,05	1300	0		1347	0	
10	34394	3	0,01	506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	7	0,01	838	0		749	0	
13*	74417	11	0,01	1130	0		491	0	
14	23896	6	0,03	349	0		267	0	
15	5790	4	0,07	172	0		40	0	
Total	**671650**	**171**	**0.03**	**10196**	**0**		**7416**	**6**	**0.08**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.6 CPTI-Deficiency

Laboratory	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	47214	1		1411	0		576	0	
3	14804	0		273	0		141	0	
5	50300	0		351	0		478	1	
6	12497	0		346	0		161	0	
7	40654	0		1143	0		642	0	
8	165714	1		1854	0		1968	0	
9	106525	1		1300	0		1347	0	
10	34394	1		506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	0		838	0		749	0	
13	74417	0		1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**4**	**0.0006**	**10196**	**0**		**7416**	**1**	**0.01**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.7 CPTII-Deficiency

Laboratory	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	47214	2		1411	0		576	0	
3	14804	0		273	0		141	0	
5	50300	1		351	0		478	0	
6	12497	3		346	0		161	0	
7	40654	0		1143	0		642	0	
8	165714	0		1854	0		1968	0	
9	106525	5		1300	0		1347	0	
10	34394	0		506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	1		838	0		749	0	
13*	74417	1		1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**13**	**0.002**	**10196**	**0**		**7416**	**0**	

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.8 For CACT- deficiency no recall is reported

3.2.5.9 Glutaric acidaemia Type I

Laboratory	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	47214	13	0.03	1411	2		576	1	
3	14804	6	0.04	273	0		141	0	
5	50300	77	0.15	351	1		478	6	
6	12497	4	0.03	346	0		161	0	
7	40654	23	0.06	1143	0		642	1	
8	165714	9	0.01	1854	0		1968	0	
9	106525	23	0.02	1300	0		1347	3	
10	34394	0		506	0		340	0	
11	16803	0		523	0		216	0	
12	78642	5	0.01	838	0		749	0	
13	74417	2		1130	0		491	0	
14	23896	0		349	0		267	0	
15	5790	0		172	0		40	0	
Total	**671650**	**162**	**0.02**	**10196**	**3**	**0.03**	**7416**	**11**	**0.15**

* due to the small numbers, recall rates are quoted in absolute numbers

3.2.5.10 Isovaleric acidaemia

Laboratory	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	47214	20	0.04	1411	1		576	13	
3	14804	1		273	0		141	0	
5	50300	18	0.04	351	0		478	4	
6	12497	3	0.02	346	0		161	1	
7	40654	0		1143	0		642	0	
8	165714	1		1854	0		1968	0	
9	106525	2		1300	0		1347	0	
10	34394	2		506	2		340	0	
11	16803	0		523	0		216	0	
12	78642	1		838	0		749	1	
13	74417	7	0.01	1130	1		491	0	
14	23896	1		349	0		267	0	
15	5790	2		172	0		40	0	
Total	**671650**	**58**	**0.01**	**10196**	**4**	**0.04**	**7416**	**19**	**0.26**

* due to the small numbers, recall rates are quoted in absolute numbers

4 Process Periods

4.1 Age at blood collection

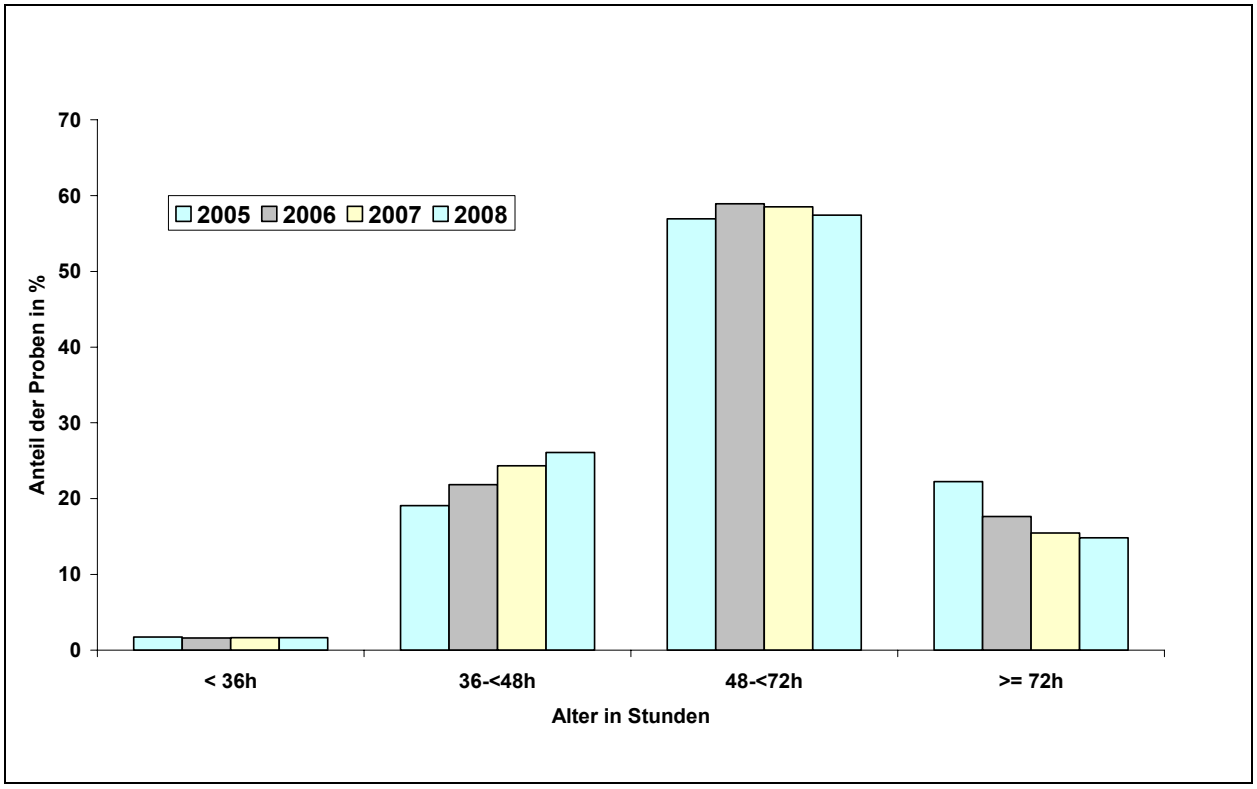
According to the guidelines (Kinderrichtlinien, section 8, paragraph 1) the sampling should be performed between the 36th and 72nd hour of life. In 83,52% of cases, with specification of collection time, the collection was according to the guidelines, in 14,84% (6,34-32,02%) beyond the 72nd hour of life, in 1,65% (1,15-3,18%) before the 36th hour of life (see Tab.4.1). Due to missing data the number of samples with recorded sampling times is sometimes lower than the total number of primary screening samples (marked as [a] in table 4.1 ff). Due to consideration of secondary samples, the reported number of screening cards exceeds the total number of primary screening samples at times (in table 4.1 ff marked with [b]). The proportion of samples which were sampled after 72 hours could be lowered from 22,25% in 2005 to 14,84% in 2008 (see figure 2), meaning a significant improvement in process quality. The adherence to the optimal sampling time improves the efficacy of screening. By early diagnosis and therapy, life threatening metabolic or electrolyte crisis can be prevented.

Table 4.1: Age at blood collection, primary screening

Lab.	Total	<36h		36h-<48h		48h-<72h		≥72h	
	n	n	%	n	%	n	%	n	%
1[a]	49119	1474	3.00	7929	16.14	30233	61.55	9483	19.31
3[b]	15220	322	2.12	1831	12.03	12102	79.51	965	6.34
5[a]	51034	903	1.77	27474	53.83	19361	37.94	3296	6.46
6	13004	359	2.76	2706	20.81	8135	62.56	1804	13.87
7	42439	695	1.64	6960	16.40	21194	49.94	13590	32.02
8[a]	154146	2197	1.43	54147	35.13	79423	51.52	18379	11.92
9[a]	109069	1429	1.31	16063	14.73	68176	62.51	23401	21.46
10	35240	524	1.49	7674	21.78	22581	64.08	4461	12.66
11[a]	17540	557	3.18	3507	19.99	11805	67.30	1671	9.53
12[a]	78493	900	1.15	26277	33.48	42247	53.82	9069	11.55
13[a]	74410	1130	1.52	10659	14.32	53131	71.40	9490	12.75
14[a]	24250	369	1.52	8348	34.42	13057	53.84	2476	10.21
15[a]	6000	175	2.92	1324	22.07	3167	52.78	1334	22.23
Total	**669964**	**11034**	**1.65**	**174899**	**26.11**	**384612**	**57.41**	**99419**	**14.84**

[a] and [b] see text

Figure 2: Comparison: Age at blood collection 2005 and 2008



4.2 Period from sampling to laboratory receipt

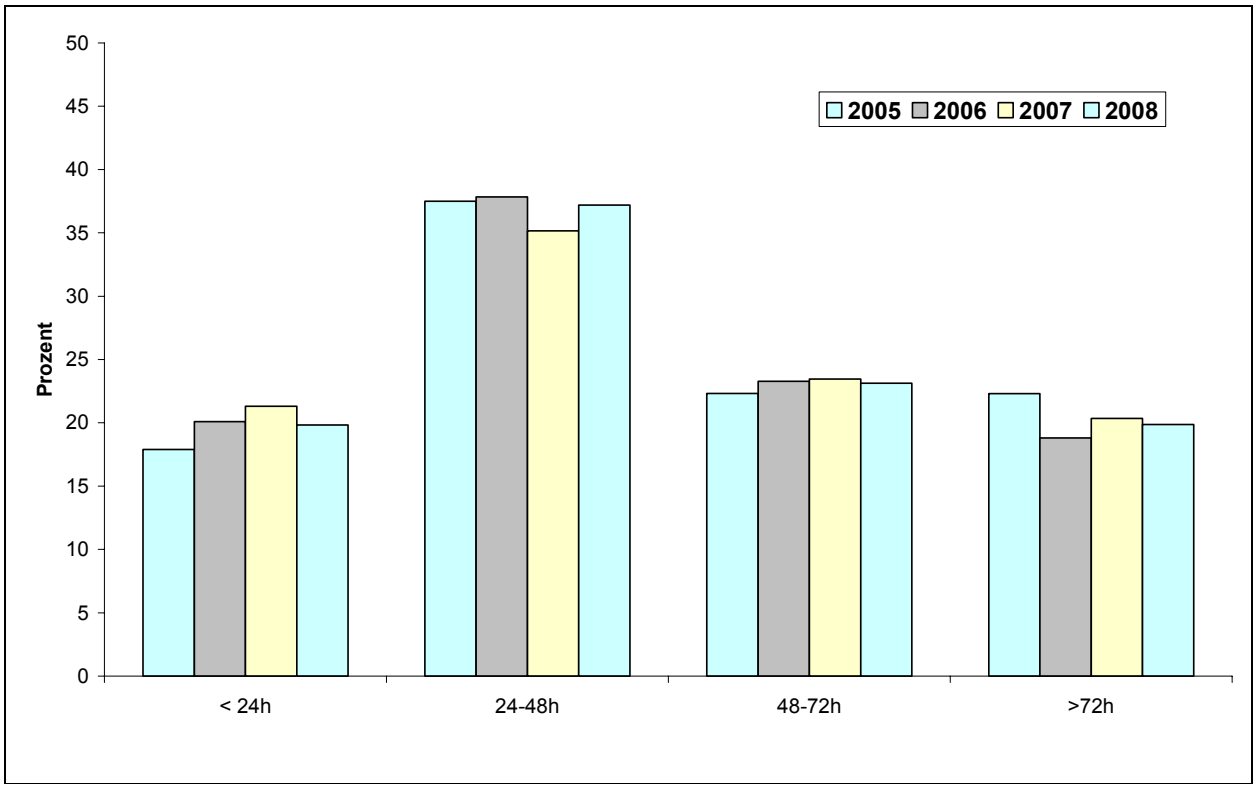
The time span between sampling and conveyance of suspect results should not exceed 72 hours (section 6, paragraph 3). In 19.86% (3.06-35.18%) of cases with statement of the delivery time the probe was received after 72 hours of sampling. In further 23.13% (9.28-29.27%) of the cases in a period between 48 and 72 hours. Shorter periods of delivery times are desirable, especially on the weekends. (Tab. 4.2, [a] and [b] see text 4.1)

Table 4.2: Period between sampling and laboratory receipt

Lab.	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1[a]	49083	13027	26.54	19286	39.29	9707	19.78	7063	14.39
3[b]	15220	2679	17.60	6994	45.95	3515	23.09	2032	13.35
5[a]	51025	3921	7.68	24180	47.39	14935	29.27	7989	15.66
6	13004	1887	14.51	5562	42.77	3132	24.08	2423	18.63
7	42439	9245	21.78	13631	32.12	8697	20.49	10866	25.60
8[a]	157813	20792	13.18	58316	36.95	41405	26.24	37300	23.64
9[a]	109130	8903	8.16	36166	33.14	28948	26.53	35113	32.18
10	35240	4362	12.38	13194	37.44	9734	27.62	7950	22.56
11[a]	17540	2878	16.41	8102	46.19	4370	24.91	2190	12.49
12[a]	79439	28785	36.24	28238	35.55	14255	17.94	8161	10.27
13[a]	74410	21465	28.85	29200	39.24	13683	18.39	10062	13.52
14[a]	24504	15433	62.98	6047	24.68	2274	9.28	750	3.06
15[a]	6000	350	5.83	2115	35.25	1424	23.73	2111	35.18
Total	**674847**	**133727**	**19.82**	**251031**	**37.20**	**156079**	**23.13**	**134010**	**19.86**

[a] and [b] see text 4.1

Figure 3: Period between sampling and laboratory receipt: Comparison 2005 to 2008



4.3 Period between laboratory receipt and conveyance

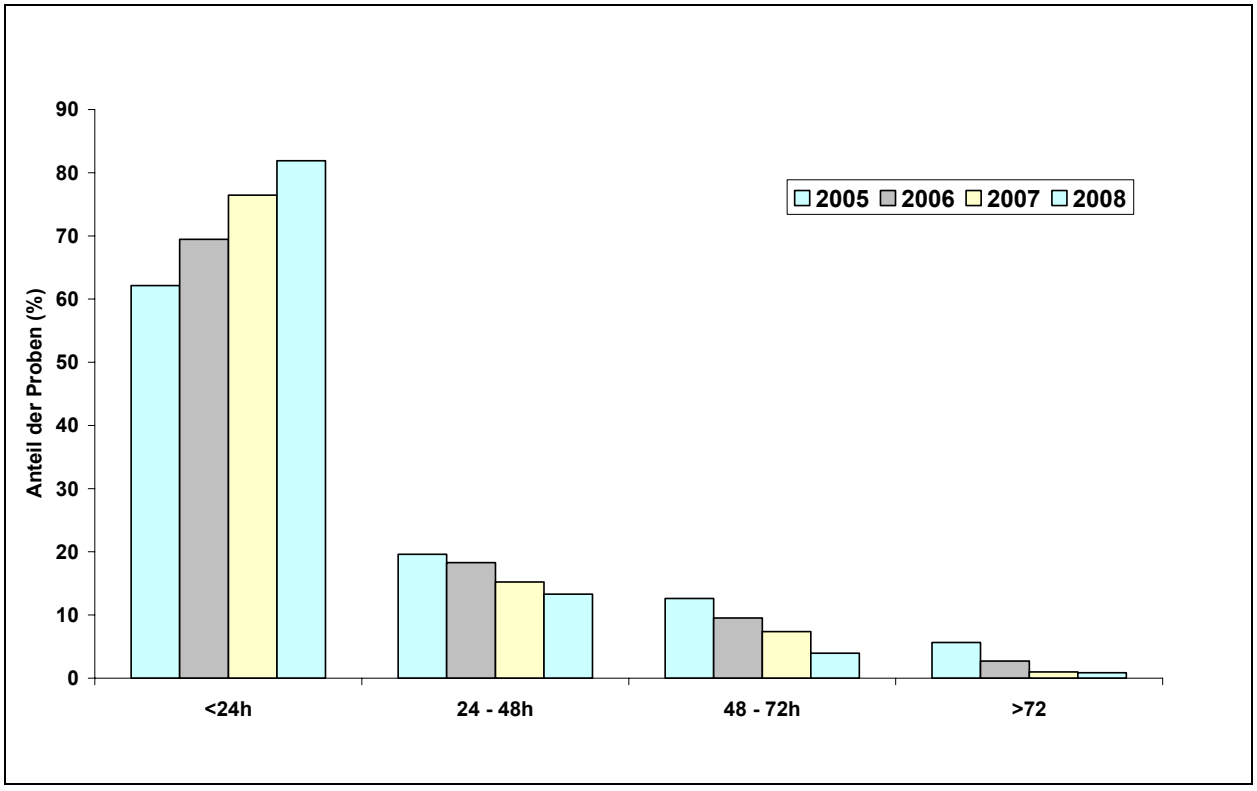
According to §14 paragraph 3 analysis, as well as reporting suspicious results of the screening card have to be conducted on the same day as receipt. Generally suspicious results are firstly notified by telephone or fax. (Table 4.3). This standard is met in more than three quarters of screening. Since 2005 the process quality could be improved significantly in this field (Figure 4).

Table 4.3 Period between laboratory receipt and conveyance

Lab.[c]	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1	49201	25072	50.96	16182	32.89	5330	10.83	2617	5.32
3[b]	15220	12592	82.73	2157	14.17	324	2.13	147	0.97
5[b]	51155	32143	62.83	14241	27.84	4660	9.11	111	0.22
8	169535	163130	96.22	5273	3.11	397	0.57	11	0.03
9	109172	104291	95.53	3852	3.53	732	0.67	297	0.27
10	35240	30835	87.50	4193	11.90	201	0.57	11	0.03
11[a]	17539	11849	67.56	5373	30.63	312	1.78	5	0.03
12	80229	61050	76.09	12769	15.92	6160	7.68	250	0.31
13[a]	74410	55513	74.60	12800	17.20	5386	7.24	711	0.96
14	24512	15696	64.03	6903	28.16	1498	6.11	415	1.69
15[a]	5959	5459	91.61	364	6.11	55	0.92	81	1.36
Total	**632172**	**517630**	**81.88**	**84107**	**13.3**	**25055**	**3.96**	**5380**	**0.85**

[a] and [b] see 4.1
[c] only laboratories who provided data are listed

Figure 4: Period from laboratory receipt to conveyance, comparison of 2005 to 2008



5 Time of screening in the confirmed cases.

5.1 Primary Screening

Crucial for successful screening are 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.

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 10% of diseased children were at the time of sampling older than 72 h.

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	148	18	1	6	10	1		**184**
CAH	36	1		4			2	**43**
Biotinidase	25	2				3	1	**31**
Classic Galactosaemia	5			1		1		**7**
PKU/HPA	120	9	1	4	2		4	**140**
MSUD	4			1				**5**
MCAD	47	7		3	1	1	2	**61**
LCHAD	1				1			**2**
VLCAD	5	2				2		**9**
CPT I		1						**1**
GA I	5	3	1					**9**
IVA	3							**3**
Total	**399**	**43**	**3**	**19**	**14**	**8**	**9**	**495**

*≥ 36h n.s. does not include repeat testing with early sampling or preterm birth, but 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.

Even in children with confirmed diagnosis early sampling before the 32nd week of gestation or before the 36th hour of life can be the primary reason for a secondary screening. 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	Recall	< 36.h	<32WOG	No information	Total
Hypothyroidism	168	6[a]	10[b]		**184**
CAH	37	4[c]		2	**43**
Biotinidase	30			1	**31**
Classic Galactosaemia	6	1			**7**
PKU/HPA	130	4	2	4	**140**
MSUD	4	1			**5**
MCAD	55	3	1	2	**61**
LCHAD	1		1		**2**
VLCAD	9				**9**
CPTI	1				**1**
GA I	9				**9**
IVA	3				**3**
Total	**453**	**19**	**13**	**9**	**495**

[a] in one case TSH primary screening <20 mU/l, sampling under contrast agent.
[b] in 6 cases TSH primary screening <20 mU/l, where n=2 infusion of catecholamins.
[C] in one case 17-OHP primary screening <6 µmol/l, prenatal therapy

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; unfortunately feedback by the clinicians is not always warranted. For the year 2008 in 43 out of 495 confirmed cases no detailed information about the confirmation diagnostics is available, in a further 15 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

Laboratory	Confirmed cases*	TSH	T3	fT3	T4	fT4	ultrasound	Thyroid antibodies
1	14	14	1	5	5	13	12	9
3	2	2	1	1	1	2	2	2
5	11	11	n.s..	11	n.s..	11	11	8
6	5	5	n.s..	5	n.s..	5	4	4
7	3	1	n.s..	1	n.s.	1	1	1
8	43	41	0	32	1	38	35	28
9	37	36	21	15	22	34	8	3
10	6	6	n.s..	3	1	6	3	2
11	5	5	2	4	3	5	3	3
12	29	28	3	24	3	25	21	10
13	21	12	1	9	1	8	n.s..	1
14	6	5	1	3	n.s..	6	4	1
15	2	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Total	**184**	**166**	**30**	**113**	**37**	**154**	**104**	**72**

*including n=15 cases without proper confirmation

6.2 Congenital adrenal hyperplasia (CAH)

Laboratory	Confirmed cases*	17-OHP (Serum)	Serum-steroids	Urinary steroids	Molecular genetic testing
1	2	2	2	n.s..	2
3	1	1	1	n.s..	1
5	4	2	2	4	1
8	13	10	13	2	9
9	7	7	4	n.s..	n.s..
10	3	3	1	1	2
11	2	2	2	n.s..	2
12	8	5	2	1	8
13	2	n.s.	n.s.	n.s.	n.s.
14	1	1	1	n.s..	1
Total	**43**	**33**	**28**	**8**	**26**

*including n=2 cases without proper confirmation

6.3 Biotinidase Deficiency

Laboratory	Confirmed cases*	Serum Biotinidase	Molecular genetic testing
1	1	1	n.s..
5	1	n.s..	n.s..
7	1	1	1
8	23	22	0
9	1	1	n.s.
10	2	2	n.s.
12	2	2	n.s.
Total	**31**	**29**	**1**

*including n=2 cases without proper confirmation

6.4 Galactosaemia

Classic

Laboratory	Confirmed cases	Red cell GALT	Molecular genetic testing
5	1	1	1
7	2	n.s..	2
8	2	2	2
10	1	n.s.	1
14	1	1	1
Total	**7**	**4**	**7**

Galactosaemia inc. variants

Laboratory	Confirmed cases*	Red cell GALT	Molecular genetic testing
1	14	13	10
3	2	n.s..	2
5	1	1	1
7	6	3	5
8	10	9	3
10	7	6	5
12	3	3	1
13	2	n.s.	2
14	8	8	1
Total	**53**	**43**	**30**

*including n=1 case without proper confirmation

6.5 PKU / HPA

Lab.	Confirmed cases*	Phe (Serum)	Phe/Tyr	BH4-Test	BH4 sensitive	Molecular genetic testing	Pterine in Urine	DHPR in dried blood
1	8	8	2	5	1	8	8	8
3	9	8	8	7	2	1	4	4
5	11	5	5	6	n.s..	n.s..	5	n.s..
6	5	3	n.s..	5	4	n.s..	3	3
7	7	5	6	5	3	n.s..	7	7
8	36	29	18	26	6	9	21	21
9	22	9	18	6	n.s..	1	13	14
10	3	2	2	2	n.s..	2	3	3
11	6	3	6	3	1	n.s..	3	3
12	16	15	6	15	4	5	15	15
13	13	1	1	1	n.s..	n.s.	n.s.	n.s.
14	3	3	1	3	1	1	3	3
15	1	n.s.	1	n.s.	n.s.	n.s.	n.s.	n.s.
Total	**140**	**91**	**74**	**84**	**22**	**27**	**85**	**81**

*including n=17 cases without proper confirmation

6.6 MSUD

Laboratory	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	2	2	2	n.s.	n.s.
9	1	1	n.s..	n.s.	n.s.
12	1	1	1	n.s.	n.s.
13	1	1	n.s.	n.s.	n.s.
Total	**5**	**5**	**3**	**n.s..**	**n.s..**

6.7 MCAD-Deficiency

Laboratory	Confirmed cases*	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	3	n.s..	3	n.s..	3
3	1	1	n.s..	n.s..	n.s..
5	8	n.s..	2	n.s..	8
6	1	1	1	n.s..	1
7	2	1	2	n.s..	2
8	14	6	5	1	8
9	7	7	6	n.s..	4
10	2	n.s.	1	n.s..	2
11	3	3	3	n.s..	3
12	8	7	3	2	8
13	10	2	n.s.	3	5
14	2	2	n.s.	n.s.	2
Total	**61**	**30**	**26**	**6**	**46**

*including n=7 cases without proper confirmation

6.8 LCHAD-Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
7	1	n.s.	n.s.	n.s.	1
9	1	1	1	n.s..	n.s.
Total	**2**	**1**	**1**	**n.s..**	**1**

6.9 VLCAD-Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
1	2	n.s..	2	2	2
8	3	0	2	3	1
9	1	1	1	1	1
10	1	1	1	1	1
12	1	n.s.	n.s.	1	1
14	1	n.s.	n.s.	1	1
Total	**9**	**2**	**6**	**9**	**7**

6.10 CPT I-Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Enzyme activity	Molecular genetic testing
8	1	1	0	1

6.11 Glutaric acidaemia Type I

Laboratory	Confirmed cases	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
7	1	1	1	n.s.	1
8	8	8	8	2	7
Total	**9**	**9**	**9**	**2**	**8**

6.11.1

6.12 Isovaleric acidaemia

Laboratory	Confirmed cases*	Confirmation Serum	Urinary organic acids	Enzyme activity	Molecular genetic testing
9	1	1	1	n.s.	n.s.
13	2	1	n.s.	n.s.	n.s.
Total	**3**	**2**	**1**	**n.s.**	**n.s.**

*including n=1 cases without proper confirmation

7 Laboratory Organisation

7.1 Acquisition of completeness

Laboratory	Comparison with birth records	Name based comparison with birth registry
1	Yes	
3	Yes	
5	Yes	
6	Yes	
7		
8	Yes	
9	Yes	
10	Yes	
11	Yes	
12		Yes
13		
14		Yes
15	Yes	
Total	**6**	**2**

7.2 Tracking

Tracking means active demand of the laboratory or the regional screening centre until final clarification. In the listed setting the laboratories conduct tracking.

Laboratory	Suspicious Primary Screening	Primary Screening < 36 Hr.	Primary Screening < 32 WOG	Empty cards	Bad sample quality	Confirmation	Therapy
1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9	Yes	Yes			Yes	Yes	
10	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13	Yes	Yes	Yes		Yes	Yes	Yes
14	Yes	Yes	Yes	Yes	Yes	Yes	Yes
15	Yes	Yes	Yes		Yes	Yes	Yes

8 Methods and cut offs in screening

8.1 Filter paper for sampling

Laboratory	Filter paper
1	WS 903
3	WS 903
5	S&S 920
6	WS 903
7	WS 2992
8	WS 903
9	WS 903
10	WS 903
11	WS 903
12	Macherey and Nagel
13	Macherey and Nagel
14	WS 903
15	WS 903

8.2 Hypothyroidism

Laboratory	Parameter	Cut-off [mU/l]	Method
1	TSH	15	AutoDELFIA
3	TSH	15	AutoDELFIA
5	TSH	n.s.	AutoDELFIA
6	TSH	15	DELFIA
7	TSH	15 nmol/l	AutoDELFIA
8	TSH	>15	DELFIA
9	TSH	15	AutoDELFIA
10	TSH	15	AutoDELFIA
11	TSH	15	DELFIA
12	TSH	>20	AutoDELFIA
13	TSH	>20	AutoDELFIA
14	TSH	> 20	AutoDELFIA
15	TSH	> 20	AutoDELFIA

8.3 Biotinidase Deficiency

Laboratory	Parameter	Cut-off	Method
1	Biotinidase	30% plate mean	Colorimetrie qualitative
3	Biotinidase	30 % day mean	Colorimetrie qualitative
5	Biotinidase	n.s.	n.s.
6	Biotinidase	70 U	Flurometrie (PE)
7	Biotinidase	2,7 U/g Hb	Colorimetrie quantitative
8	Biotinidase	< 30% day mean	Colorimetrie quantitative
9	Biotinidase	0.2	Colorimetrie qualitative
10	Biotinidase	< 30%	Colorimetrie qualitative
11	Biotinidase	n.s.	Colorimetrie qualitative
12	Biotinidase	< 30%	Fluorometrie quantitative
13	Biotinidase	< 30%	Fluorometrie quantitative
14	Biotinidase	< 30 %	Colorimetrie quantitative
15	Biotinidase	< 30 %	Colorimetrie quantitative

8.4 Galactosaemia

Laboratory	Parameter	Cut-off	Method
1	GALT Galactose	3.5 U/gHb 15 mg/dl	Fluorometrie(PE) BIORAD Quantase
3	GALT Galactose	2.3 Ug/Hb 15 mg/dl	BIORAD Quantase
5	GALT Galactose	n.s.	n.s.
6	GALT	3.5 U/g Hb	Fluorometrie (PE)
7	GALT	3.5 U/g Hb	Fluorometrie quantitative
8	GALT Galactose	<20 % day mean >30mg/dl	Fluorometrie quantitative Colorimetrie 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	Fluorometrie quantitative
12	GALT Galactose	< 30% 15 mg/dl	Fluoro. quant.(non-kit) Colorimetrie non Kit
13	GALT Galactose	< 30% 15 mg/dl	Fluoro. quant.(non-kit) Colorimetrie 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

8.5 MS/MS

Laboratory	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	derivative non Kit
15	derivative non Kit

8.6 Congenital adrenal hyperplasia (CAH)

Term babies

Laboratory	Parameter	Method	Dependent on age	Dependent on WOG	Dependent on BW	Formula	Constant value
1	17 OHP	AutoDELFIA	Yes			ln(OHP)=2.90798-0.40653ln(age)	
3	17 OHP	AutoDELFIA	Yes			ln (OHP) = 1.868 - 0.374ln(age)	
5	17 OHP	AutoDELFIA		Yes		Value from B015112	
6	17 OHP	DELFIA		Yes			40
7	17 OHP	AutoDELFIA					30
8*	17 OHP	DELFIA	Yes				
9	17 OHP	AutoDELFIA		Yes			30
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 steroid profile with 17OHP, 21-Desoxycortisol, 11-Desoxycortisol, cortisol and androstendion.

Preterm babies

Laboratory	Parameter	Method	Dependent on age	Dependent on WOG	Dependent on BW	Formula	Constant value
1	17 OHP	AutoDELFIA	Yes	Yes		ln(OHP)=3.470-0.121ln(age)	
3	17 OHP	AutoDELFIA	Yes	Yes		ln (OHP) = -118.7 + 75.164 (ln (corrected GA)) -11.564 (ln(corr GA)^2)	
5	17 OHP	AutoDELFIA		Yes		Before discharge, analogue 36-38 WOG	
6	17 OHP	DELFIA		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		Yes		
15	17 OHP	AutoDELFIA	Yes		Yes		

*Laboratory 8: with raised Delfia 17OHP TMS steroid profile with 17-OHP, 21-Desoxycortisol, 11-Desoxycortisol, cortisol and androstendion.

8.7 MS/MS Parameter

Guide (GV) and secondary (SP) parameters are listed. If the laboratory has given the cut off value for their guide value, it is taken as a guide value. Laboratory 12 accounts for laboratory 12 and 13 (one lab) and laboratory 14 accounts for laboratory 14 and 15 (one lab)

Remarks to testing for parameters in MS/MS

Laboratory	Comment
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

8.7.1 PKU

Parameter /Cut off	1	3	5	6	7	8	9	10	11	12	14
Phe	**112**	**120**	**120**	**148**	**139**	**150**	**123**	**150**	**126**	**120**	**129**
Tyr								**NW**		**NW**	
Phe/Tyr	**NW**	**NW**	**NW**	**NW**	**2.5**	**2.5**	**1.88**	**NW**	**2.0**	**2.0**	**NW**

8.7.2 MSUD

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
Ala								**NW**		**LW**	
Val	**NW**	**NW**	**NW**	**NW**	**280**	**NW**	**NW**	**NW**	**185**	**LW**	**NW**
Leu/Ile	**294**	**320**	**z ≥ 3.5***	**397**	**300**	**400**	**299**	**314**	**289**	**LW**	**350**
Fischer-Q	**NW**	**2.75**		**NW**					**3.3**	**LW**	**LW**
Leu/Ile:Phe	**NW**		**z ≥ 3.5***			**10**		**NW**		**LW**	**NW**
Val/Phe			**NW**					**NW**		**LW**	**NW**
Leulle/Ala	**NW**	**NW**	**z ≥ 3.5***	**NW**			**NW**	**NW**	**NW**	**LW**	

***z ≥ 3.5 means: measured value ≥ mean + z-* sd

8.7.3 MCAD-Deficiency

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
C0								NW			
C6	NW	NW	NW	NW	0.18	NW	NW	NW	NW	LW	NW
C8	0.18	0.25	z ≥ 3.5*	0.28	0.4	0.3	0.28	0.3	0.24	LW	0.34
C8/C10	NW	3.9	NW	NW		5.0	NW	NW	2.0	LW	NW
C8/C12	NW		NW	NW			NW		NW	LW	
C8/C16					NW			NW		LW	
C10	NW	NW	NW	NW		NW	NW	NW	NW	LW	NW
C10:1	NW	NW	NW	NW	0.15	NW	NW	NW	0.11	LW	NW
C8/C2	NW			NW		0.02	NW				NW
C8/C6			NW				NW			LW	

z ≥ 3.5 means: measured value ≥ mean + z- sd

8.7.4 LCHAD-Deficiency

Parameter / Cut off	1	3[a]	5[b]	6	7	8	9	10	11	12	14
C0								NW			
C14:1			NW	NW		NW		NW	NW	NW	
C14OH			NW	0.043			NW	NW	NW	LW	
C16OH	0.069	0.07	z ≥ 3.5	0.069	0.11	0.1	0.1	0.15	0.048	LW	0.60
C16:1OH			NW	NW			NW	NW		LW	NW
C18OH	0.027	NW		0.044	0.1	NW	0.07	NW	0.031	LW	NW
C18:1OH	0.033	NW	z ≥ 3.5	0.06	0.1	0.1	0.11	NW	0.042	LW	NW
C18:2OH						NW		NW			NW
C16OH/C16	NW	0.02	NW					NW	0.018		

a ratio C16OH/C16 at sampling > 7 d; b recall, even if C16:1OH/C16OH <1

8.7.5 VLCAD-Deficiency

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
C0								NW			
C12			NW							LW	
C14	NW	NW	NW	NW	0.65	NW	NW	NW	0.459	LW	NW
C14:1	0.34	0.35	z ≥ 3.5	0.272	0.4	0.3	0.43	0.36	0.32	LW	0.25
C16:1							NW	NW			
C14:2	NW	NW		NW	NW	NW			0.048	LW	NW
C14:1/C16	NW	0.10	NW	NW					0.125		LW
C14/C4								NW			NW
C14:1/C4			NW				NW	NW		LW	NW
C14:1/C12			NW								
C14:1/C12:1			NW			NW					

8.7.6 CPT I-Deficiency

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
C0	NW	5.5	NW	58.1	70	80	65.49	50	NW	NW	NW
C8											
C16	0.87	NW	NW	8.56	<0.6		LW	0.56	0.69	LW	<1
C18	0.23	NW	NW	2.09	<0.3		LW	0.21	0.2	LW	NW
C18:1	0.30			3.53				NW	0.315	LW	
C16/C2											
(C16+C18:1)/C2				NW							
C0/(C16+C18)	NW	1.3	≥ 70	NW		40	LW		19.3	LW	NW

8.7.7 CPT II-Deficiency

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
AC ges								NW			
C0	NW	NW		5.0	<10			NW	5.1	NW	NW
C16	5.55	9.43	NW	8.56	8.0	8	7.65	8.83	7.5	LW	>6
C16:1					0.6		0.67	NW		LW	NW
C18	1.45			2.09	2.6		2.34	3.65	1.94	LW	>2.5
C18:1	2.22	3.52	NW	3.53	3.5	3.4	1.92	NW	3.27	LW	NW
(C16+C18:1)/C2	NW	NW	z ≥ 3.5			0.3	NW	20.3	NW		
C18:2								NW		LW	
C16/C2			NW								
C0/(C16+C18)			NW	NW			NW	NW			

8.7.8 CACT-Deficiency

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
AC ges								NW			
C0	NW	NW		NW	<10			NW	5.1	LW	NW
C0/AC ges								0.46			
C16	5.55	9.43	NW	5.6	8.0	8.0	6.85	8.83	7.5	LW	
C16:1								NW		LW	NW
C18	1.45			2.09	2.6	3.4	2.34	2.65	1.94	LW	NW
C18:1	2.22	3.52	NW	3.53	3.5	0.3		3.9	3.27	LW	NW
(C16+C18:1)/C2	NW	NW	z ≥ 3.5					NW	NW		
C18:2										LW	
C0/AC ges								NW			
C16/C2			z ≥ 3.5								
C0/(C16+C18)			NW	NW			NW	NW			
C0/(C16+C18:1)							NW	NW			

8.7.9 Glutaric acidaemia Type I

Parameter / Cut off	1	3	5	6	7	8	9	10	11	12	14
C5DC (Glut)	0.26	0.5	z ≥ 0.13	0.644	0.33	0.20	0.17	0.25	0.45	LW	<0.15
C5DC/C0	NW		NW	NW		NW					
C5DC/C2										LW	
C5DC/C4				NW				NW		LW	
C5DC/C8		NW		NW	5.9		NW	NW			NW
C5DC/C12	NW	NW							NW	LW	
C5DC/C16	NW		NW	NW			NW	NW	NW	LW	NW
C5DC/(C8+C10)			NW								

8.7.10 Isovaleric acidaemia

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C0								NW			
C5	0.36	0.5	z ≥ 3.5	0.6	1	0.5	0.63	0.6	0.57	LW	0.6
C5/C2			NW	NW		0.02	NW				
C5/C3								NW			NW
C5/C8	NW	NW	NW	NW	NW			NW	NW	LW	
C5/C4	NW	NW	NW	NW				NW	NW	LW	

* consideration of C0

9 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

1) Statistisches Jahrbuch 2008 Herausgeber: Statistisches Bundesamt, Wiesbaden www.destatis.de

1) Nennstiel-Ratzel U, Liebl B, Zapf A. Modellprojekt zur Neuordnung des Neugeborenen-Screening in Bayern. Gesundheitswesen 2003 Mar;65 Suppl 1:S31-5.