National

Screening Report 2006

DGNS

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Abbreviations:

CAH	Congenital adrenal hyperplasia
CACT- Deficiency	Carnitin-Acylcarnitin-Translocase-Deficiency
CPTI- Deficiency	Carnitin- Palmitoyl-CoA-Transferase I-Deficiency
CPTII- Deficiency	Carnitin- Palmitoyl-CoA-Transferase II-Deficiency
GA I	Glutaric acidaemia type I
BW	Birth weight
HPA	Hyperphenylalaninaemia
IVA	Isovaleric acidaemia
LCHAD-Deficiency	Long-Chain-3-hydroxy-Acyl-CoA-Dehydrogenase-Deficiency
DoL	Day of life
GV 1 bis 3	guide value 1 - 3
MCAD-Deficiency	Medium-Chain-Acyl-CoA-Dehydrogenase-Deficiency
MSUD	Maple syrup urine disease
NBS	New born screening
SP	secondary parameter
PKU	Phenylketonuria
PPV	positive predictive value
Recall	Recall due to abnormality
WoG	Week of gestation
VLCAD-Deficiency	Very-Long-Chain-Acyl-CoA-Dehydrogenase-Deficiency

1. Introduction

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

The details of newborn screening (NBS) are outlined in the current guidelines (1) from 1/7/2005. The national screening report 2006 was composed by the "Deutschen Gesellschaft für Neugeborenenscreening (DGNS)" 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, recall numbers at diagnoses for the year 2006. Additionally, data for process quality are presented. The analysis data was done with SPSS for Windows (Version 13.0) and Excel (Microsoft Office XP).

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 between blood collections and arrival in the laboratory and until communication of results
- Screening values of newborns for which further testing is emphasized
- Diagnostic for confirmation
    - Type of diagnostic
    - Time of diagnostic
- Final diagnosis
- Start of therapy

In chapter 2, laboratories are listed which have undertaken the screening in 2006 for Germany. From chapter 3 the laboratories are listed scrambled. (see chapter 2 - laboratory number, numbers 12 and 13 relate to the same laboratory, ones with and without the co-operation of the Screening Centre, same for 14 and 15). 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 partly due to the system).

2 Screening Laboratories and Screening Centres

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

1) Neugeborenen Screeninglabor Berlin
Dr. med. Oliver Blankenstein
Augustenburger Platz 1
13353 **Berlin**
030/450 50
Oliver.Blankenstein@charite.de

Screeningzentrum Sachsen
3) Standort **Dresden**
Prof. Dr. med. Joachim Thiery,
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Standort **Dresden**
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01288 Dresden
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10) Standort **Leipzig**
Postfach 500356
04303 Leipzig
0341/9722222 (Leitstelle ILM)
screening@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
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Soldmannstr. 15
17489 **Greifswald**
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fusch@uni-greifswald.de
http://www.medizin.uni-greifswald.de/kind_med/neugeborenscreening-Dateien/slide0001.htm

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

8) Screening-Labor Hannover
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D 30430 **Hannover**
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j.sander@metabscreen.de,
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www.metabscreen.de

9) Neugeborenenscreening Heidelberg
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www.Neugeborenenscreening.uni-hd.de

11) Screeninglabor, Universitäts-Kinderklinik
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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
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Zur Kesselschmiede 4
92637 **Weiden**
0961/309 0
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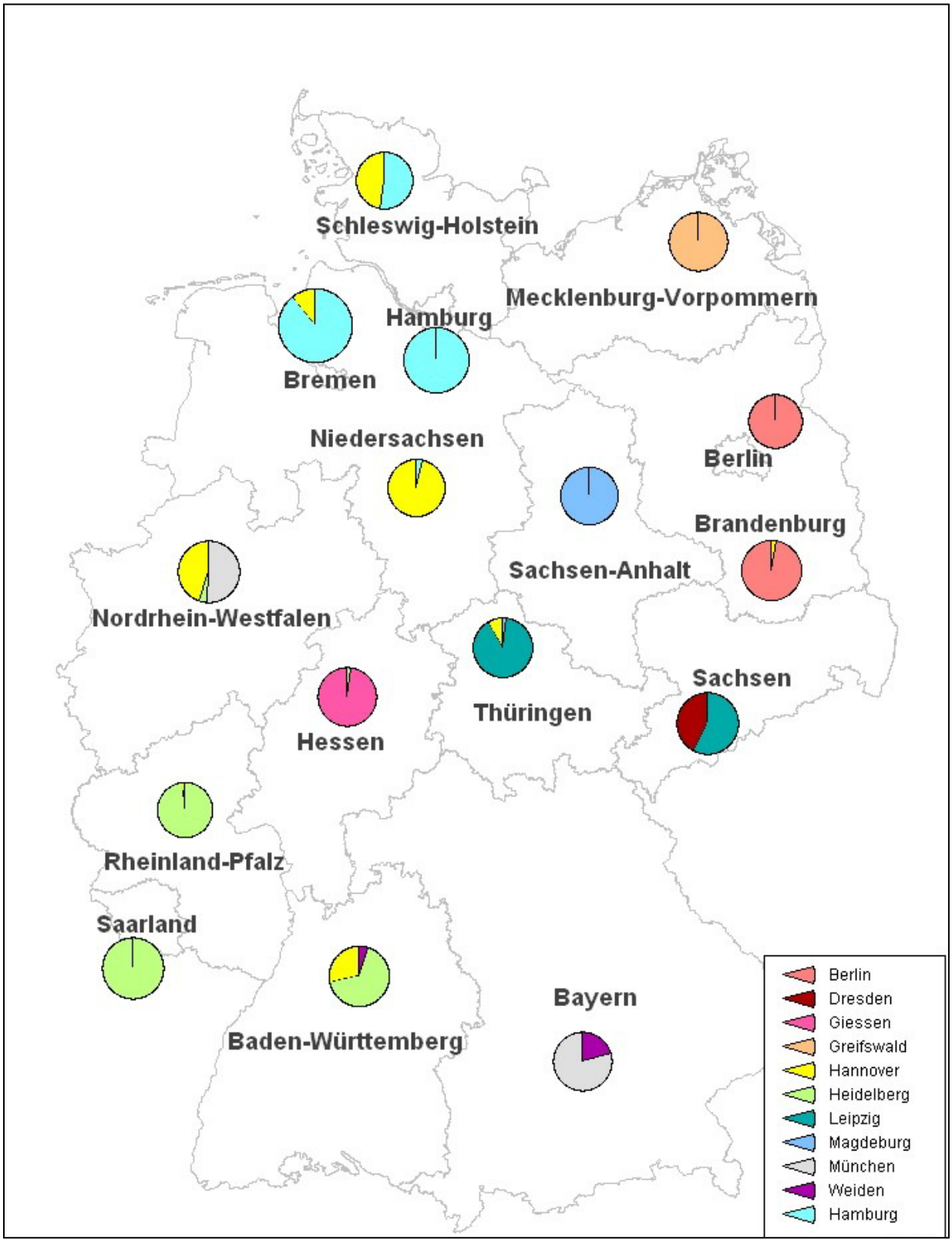
Screeningzentrum Bayern (12/14)
Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit
Dr.med Uta Nennstiel-Ratzel MPH
Veterinärstr.2
85764 **Oberschleißheim**
089/31560204
screening@lgl.bayern.de
http://www.lgl.bayern.de/gesundheit/neugeborenenscreening.htm

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

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

Figure 1: sample distribution according to state and laboratory



3 Results 2006

In the year 2006, 672.724 children were born in Germany. In several federal states the number of screened children out raised the number of newborns, because:

- If a repeat screening is sent to a different laboratory than the primary screening, the receiving laboratory will record the test as a primary screening.
- In some laboratories primary and repeat screening are not recorded separately.

A secure statement about the rate of participation in NBS can only be made by comparison of person related data of the population. By law this is only legal in the state of Bavaria. The screening rate for Germany is 102,7%. Analysis which are not recorded as secondary testing are responsible for 0,6%, therefore it can be concluded that at least 2% of newborns are screened twice without indication.

Births (2)	672.724
Primary screening	690.143
Confirmed diagnosis (see Table 3)	482

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. One of 1423 newborns one targeted disease according to the guidelines is found. Table 3 shows the prevalence of targeted diseases in the year 2006 in Germany.

Table 3. Absolute number of detected diseases found by screening

Disease	Confirmed cases	Prevalence *
Hypothyroidism	165	1: 4.156
Congenital adrenal hyperplasia (CAH)	57	1: 12.032
Biotinidase Deficiency	27	1: 25.400
Classic galactosaemia	14	1: 48.986
Phenylketonuria (PKU)/ Hyperphenylalaninaemia (HPA)	116	1: 5.912
Maple syrup urine disease (MSUD)	5	1: 137.161
Medium-Chain-Acyl-CoA-Dehydrogenase-Deficiency (MCAD)	67	1: 10.236
Long-Chain-3-hydroxy-Acyl-CoA-Dehydrogenase-Deficiency (LCHAD)	5	1: 137.161
Very-Long-Chain-Acyl-CoA-Dehydrogenase-Deficiency (VLCAD)	9	1: 76.200
Carnitin- Palmitoyl-CoA-Transferase I-Deficiency (CPT I)	3	1: 228.601
Carnitin- Palmitoyl-CoA-Transferase II-Deficiency (CPT II)	0	
Carnitin-Acylcarnitin-Translocase-Deficiency (CACT)	0	
Glutaric acidaemia type I (GA I)	4	1: 171.451
Isovaleric acidaemia (IVA)	10	1: 68.580
Total	**482**	**1: 1.423**

* calculated with N=685.804 screened newborns, laboratory 15 could not give any results for 4.339 newborns

3.1 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 (Section 8 - paragraph 2,4). The following table shows the stratified results of the primary screening according to age and gestational age. Laboratory 15 cannot differentiate the screening probes according to their time of collection, the necessity of repeat screening nor a secure final result.

Table 3.1 Age at primary screening

Laboratory	Total	>=36h and >32WoG		<36h and >32WoG		<32WoG	
		n	%	n	%	n	%
1	45963	43897	95,51	1506	3,28	560	1,22
3	14175	13532	95,46	352	2,48	291	2,05
5	50667	49141	96,99	985	1,94	541	1,07
6	12578	12055	95,84	370	2,94	153	1,22
7*	42688						
8	174015	170118	97,76	1996	1,15	1901	1,09
9	107433	104997	97,73	1125	1,05	1311	1,22
10	33320	32396	97,23	611	1,83	313	0,94
11	16833	16174	96,09	495	2,94	164	0,97
12	82561	81313	98,49	963	1,17	285	0,35
13	84588	83302	98,48	1035	1,22	251	0,30
14	20983	20491	97,66	307	1,46	185	0,88
15*	4339						
Total	**690143**	**627416**	**97,56**	**9745**	**1,52**	**5955**	**0,93**

***Laboratory cannot completely differentiate the timing of blood collection according to age and gestational age and therefore data is not considered for percentage calculation but included in the total

3.2 Relation of requested to received repeat screenings

In table 3.2 the repeat screenings are listed stratified according to their base of request. Repeat screening due to parental nutrition, blood transfusion or medication are not recorded.

Table 3.2 Requested and received repeat screenings

Laboratory	Total requested	Total received	%	Recall requested	Recall received	%
1	2771	2576	92,96	386	380	98,45
3	609	622	102,13	71	75	105,63
6	400	400	100,00	272	272	100,00
7*	824					
8	5735	4353	75,90	1838	1631	88,74
9	3934	2748	69,85	528	501	94,89
10	1232	1105	89,69	151	151	100,00
11	739	720	97,43	55	55	100,00
12	2408	2342	97,26	1160	1142	98,45
13	2007	1580	78,72	1034	856	82,79
14	699	674	96,42	207	201	97,10
Total	**21358**	**17120**	**83,37***	**5702**	**5264**	**92,32**

Laboratory**	< 36h requested	< 36h received	%	< 32 WoG requested	< 32 WoG received	%
1	1469	1412	96,12	557	434	77,92
3	414	420	101,45	124	127	102,42
6	104	104	100,00	24	24	100,00
7*						
8	1996	1338	67,03	1901	1384	72,80
9	1244	764	61,41	1854	1190	64,19
10	599	529	88,31	296	261	88,18
11	515	507	98,45	164	153	93,29
12	963	936	97,20	285	264	92,63
13*	973	724	74,41	n.s.	n.s.	
14	307	295	96,09	185	178	96,22
Total	**8584**	**7029**	**81,88**	**5390**	**4015**	**74,49**

*Laboratory cannot completely differentiate repeat screening and therefore data is not considered for percentage calculation but included in the total
** Laboratory 15 and Laboratory 5 cannot specify

- **„<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

3.3 Received and registered blank cards by the laboratory

As stated in section 9 paragraph 6 the Obstetric Units should document on a blank test card if a screening was denied or the newborn was deceased. This test card should be sent to the laboratory. The number of received cards in 2006 has drastically increased compared to 2005 but does not reflect the expected numbers. 1250 cards should have been received from children deceased within the first 3 days of life (2). Only 236 were received (Table 3.3). Refusal of screening could be expected in about 1‰ (3) roughly corresponding to 690 blank cards, only 91 were received (Table 3.3).

Table 3.3 Laboratory received blank cards

Laboratory*	deceased	Refusal of screening	Transfer to a different Unit	Early testing refused
	n	n	n	n
1	38	7		3096[a]
3	37	5	8	0
5	70	7	0	0
6	0	3	0	226
8[b]				896
9	22	57	54	203
10	26	4	0	938
11	41	3	45	278
12	2	5	16	445
14	0	0	0	4
Total	**236**	**91**	**123**	**6086**

* Laboratories who cannot provide data are not listed
[a] Laboratory 1 cannot differentiate between primary testing and transferal, so these numbers were counted as primary testing
[b] Laboratory 8 - a reason for sending blank cards is not recorded. A refusal of early testing in context with early discharge after delivery is presumed, all numbers were counted to this point.

3.4 Tracking of Completeness

The newborn screening is a measure of public health and should be received by all 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 with the recorded birth number of the sending unit would be possible, or if legally allowed, by comparing with data from the birth register.

Table 3.4.1 screened newborns due to tracking of completeness

Laboratory*	alignment Birth Register	alignment Blank Cards	alignment Recorded birth number
	n	n	n
1	0	185	85
3	0	0	95
5	0	169	4
6	0	0	2
11	0	0	34
12	50	0	0
14	10	0	0
Total	**60**	**354**	**220**

*Laboratories who cannot provide data are not listed

4 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 a screening, the sensitivity (true-test positives) but more the specificity (true-test negatives) should be high to avoid unnecessary worries and costs. A measure for the specificity in newborn screening is the recall rate. The smaller the recall rate the higher the specificity. The positive predictive value estimates the risk of disease with a positive test result. It depends on the prevalence of the targeted disease. In Table 4 listed epidemiologic numbers concern all screened children independently of age and gestational age. The sensitivity cannot be calculated since the number of unscreened children is not recorded systematically. Recall is a necessary follow-up testing due a positive primary screening.

Table 4 Specificity, PPV related to the total number of primary screening tests independent of age and gestational age.

Disease	Primary screening	Total Recall	Recall-rate (%)	Confirmed diagnosis	PPV (%)	Specificity (%)	False negative
Hypothyroidism	685804	1139	0,17	165	14,49	99,86	0
CAH	685804	5154	0,75	57	1,11	99,26	1
Biotinidase-def.	685804	163	0,02	27	16,56	99,98	0
Classic Galactosaemia	685804	627	0,09	14	2,23	99,91	0
MS/MS	685804	871	0,13	219	25,14	99,90	0
Total*	**685804**	**7954**	**1,16**	**482**	**6,06**	**98,91**	**1**

***For Laboratory 15 no numbers for recall or confirmed diagnosis can be established therefore the numbers for primary screening (n=4339) are not added to the total.

For hyperphenylalaninaemia including the PKU the PPV of newborns who are screened after the 36th hour of life and beyond the 32nd gestational week is 51,69% and for MCAD deficiency 38,04% meaning that half to a third of recalled children are diseased. For hypothyroidism, less than a quarter (PPV = 23,5%) of suspected newborns are diseased. Further, positive predictive values of children who were screened after the 36th hour of life and the 32nd week of gestation are listed in Table 4a. These numbers are different from Table 4.

Table 4a: Recall PPV with a screening > 36 hours of life and >32 WoG

Disease	Primary Screening	Recall	Recall-rate(%)	Confirmed cases	PPV(%)	Specificity ≥ 36h(%)
Hypothyroidism	670084	651	0,10	153	23,50	99,93
CAH	670084	3966	0,59	50	1,26	99,42
Biotinidase def.	670084	146	0,02	27	18,49	99,98
Classic Galactosaemia	670084	611	0,09	13	2,13	99,91
MS/MS*	670084	808	0,12	204	25,25	99,91
Total	**670084**	**6182**	**0,92**	**447**	**7,23**	**99,14**

***Only targeted diseases

Recall rates of the following tables as well as PPV are of newborns who were screened > 32 weeks gestational age and 36 hours age. The reference of > 36 hours is 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. Cases with implausible (n= 17) or missing data (n=24) as well as cases which did not have the necessary data for validation (n=41) were excluded from analysis. All double cases were included only once.

4.1 All targeted diseases

Table 4.1 All targeted diseases

Disease	Total primary screening	Primary screening ≥36h	Recall ≥36h	Recall rate % [a]	Confirmed cases	PPV ≥36h (%)[b]	Prevalence total	False negative
Hypothyroidism	685804	670084	651	0,10	165	23,50	1: 4156	0
CAH	685804	670084	3966	0,59	57	1,26	1: 12032	1
Biotinidase-deficiency	685804	670084	146	0,02	27	18,49	1: 25400	0
Classic Galactosaemia	685804	670084	611	0,09	14	2,13	1: 48986	0
Disease	685804	670084	207	0,03	116	51,69	1: 5.912	0
MSUD	685804	670084	82	0,01	5	6,10	1: 137161	0
MCAD	685804	670084	163	0,02	67	38,04	1: 10236	0
LCHAD	685804	670084	19	0,003	5	21,05	1: 137161	0
VLCAD	685804	670084	143	0,02	9	6,29	1: 76200	0
CPT I Def.	685804	670084	5		3	60,00	1: 228601	0
CPT II Def.	685804	670084	2		0			0
CACT Def.	685804	670084	0		0			0
GA I	685804	670084	96	0,01	4	4,17	1: 171451	0
IVA	685804	670084	91	0,01	10	10,99	1: 68.580	0
Total	**685804**	**670084**	**6182**	**0,92**	**482**	**7,23**	**1: 1.423**	**1**

[a] Recall rate calculated only for n ≥ 10.
[b] PPV ≥36h (%) = (confirmed cases ≥36h / Recall ≥36h) x 100.

In the following tables the recall rate, confirmed diagnosis and prevalence are listed stratified according to the laboratories. As no data for recall or confirmed diagnoses are available for Laboratory 15, their data for primary screening (n=4339) is not included in the total: For plausible analysis of laboratory's 7 data primary screening total and primary screening > 36 hours were equalized since no differentiation was possible.

4.1.1 Hypothyroidism

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	34	0,08	9	1: 5107	0
3	14175	13532	2		2	1: 7088	0
5	50667	49141	85	0,17	11	1: 4606	0
6	12578	12055	11	0,09	4	1: 3145	0
7[b]	42688	42668	26	0,06	2	1: 21344	0
8	174015	170118	310	0,18	53	1: 3283	0
9	107433	104997	56	0,05	27	1: 3979	0
10	33320	32396	13	0,04	6	1: 5553	0
11	16833	16174	6		1	1: 16833	0
12	82561	81313	56	0,07	32	1: 2580	0
13	84588	83302	47	0,06	16	1: 5287	0
14	20983	20491	5		2	1: 10492	0
Total	**685804**	**670084**	**651**	**0,10**	**165**	**1: 4156**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.2 Congenital adrenal hyperplasia (CAH)

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	123	0,28	5	1: 9193	0
3	14175	13532	17	0,13	1	1: 14175	0
5	50667	49141	282	0,57	4	1: 12667	0
6	12578	12055	182	1,51	1	1: 12578	0
7[b]	42688	42668	662	1,55	4	1: 10672	0
8	174015	170118	644	0,38	21	1: 8286	1
9	107433	104997	238	0,23	7	1: 15348	0
10	33320	32396	36	0,11	1	1: 33320	0
11	16833	16174	26	0,16	1	1: 16833	0
12	82561	81313	986	1,21	5	1: 16512	0
13	84588	83302	636	0,76	6	1: 14098	0
14	20983	20491	134	0,65	1	1: 20983	0
Total	**685804**	**670084**	**3966**	**0,59**	**57**	**1: 12032**	**1**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.3 Biotinidase deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	1		1	1: 45963	0
3	14175	13532	0		0		0
5	50667	49141	1		0		0
6	12578	12055	2		0		0
7 [b]	42688	42668	12	0,03	2	1: 21344	0
8	174015	170118	90	0,05	18	1: 9668	0
9	107433	104997	2		2	1: 53717	0
10	33320	32396	2		0		0
11	16833	16174	1		0		0
12	82561	81313	19	0,02	2	1: 41281	0
13	84588	83302	14	0,02	1	1: 84588	0
14	20983	20491	2		1	1: 20983	0
Total	**685804**	**670084**	**146**	**0,02**	**27**	**1: 25400**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.4 Galactosaemia including variants / classic

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	29	0,07	12	1: 3830	0
3	14175	13532	9		2	1: 7088	0
5	50667	49141	75	0,15	3	1: 16889	0
6	12578	12055	17	0,14	5	1: 2516	0
7 [b]	42688	42668	34	0,08	0		0
8	174015	170118	290	0,17	45	1: 3867	0
9	107433	104997	7		1	1: 107433	0
10	33320	32396	33	0,10	2	1: 16660	0
11	16833	16174	5		2	1: 8417	0
12	82561	81313	36	0,04	6	1: 13760	0
13	84588	83302	38	0,05	1	1: 84588	0
14	20983	20491	38	0,19	1	1: 20983	0
Total	**685804**	**670084**	**611**	**0,09**	**80**	**1: 8573**	**0**
Classic					**14**	**1: 48986**	

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5 MS/MS

MS/MS only targeted diseases

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	False negative
1	45963	43897	160	0,36	17	0
3	14175	13532	32	0,24	4	0
5	50667	49141	73	0,15	27	0
6	12578	12055	59	0,49	6	0
7 [c]	42688	42668	90	0,21	12	0
8	174015	170118	57	0,03	54	0
9	107433	104997	140	0,13	34	0
10	33320	32396	42	0,13	10	0
11	16833	16174	13	0,08	5	0
12	82561	81313	48	0,06	24	0
13	84588	83302	73	0,09	17	0
14	20983	20491	21	0,10	9	0
Total	**685804**	**670084**	**808**	**0,12**	**219**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.1 PKU / HPA

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	21	,05	9	1: 5107	0
3	14175	13532	7	.	3	1: 4725	0
5	50667	49141	11	,02	9	1: 5630	0
6	12578	12055	10	,08	3	1: 4193	0
7	42688	42668	29	,07	10	1: 4269	0
8	174015	170118	21	,01	22	1: 7910	0
9	107433	104997	32	,03	21	1: 5116	0
10	33320	32396	23	,07	5	1: 6664	0
11	16833	16174	4	.	3	1: 5611	0
12	82561	81313	22	,03	16	1: 5160	0
13	84588	83302	15	,02	9	1: 9399	0
14	20983	20491	12	,06	6	1: 3497	0
Total	**685804**	**670084**	**207**	**,03**	**116**	**1: 5912**	**0**
PKU					**59**	**1: 11624**	

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.2 MSUD

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	4		1	1: 45963	0
3	14175	13532	1		0		0
5	50667	49141	19	0,04	0		0
6	12578	12055	6		0		0
7 [b]	42688	42668	22	0,05	0		0
8	174015	170118	3		3	1: 58005	0
9	107433	104997	20	0,02	0		0
10	33320	32396	2		0		0
11	16833	16174	1		0		0
12	82561	81313	1		0		0
13	84588	83302	2		1	1: 84588	0
14	20983	20491	1		0		0
Total	**685804**	**670084**	**82**	**0,01**	**5**	**1: 137161**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.3 MCAD-Deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	32	0,07	5	1: 9193	0
3	14175	13532	10	0,07	1	1: 14175	0
5	50667	49141	24	0,05	14	1: 3619	0
6	12578	12055	19	0,16	2	1: 6289	0
7 [b]	42688	42668	9		2	1: 21344	0
8	174015	170118	20	0,01	18	1: 9668	0
9	107433	104997	13	0,01	11	1: 9767	0
10	33320	32396	10	0,03	3	1: 13760	0
11	16833	16174	3		0		0
12	82561	81313	10	0,01	6	1: 13760	0
13	84588	83302	11	0,01	3	1: 28196	0
14	20983	20491	2		2	1: 10492	0
Total	**685804**	**670084**	**163**	**0,02**	**67**	**1: 10236**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.4 LCHAD-Deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	4		0		0
3	14175	13532	0		0		0
5	50667	49141	0		0		0
6	12578	12055	3		0		0
7 [b]	42688	42668	0		0		0
8	174015	170118	3		2	1: 87008	0
9	107433	104997	4		2	1: 53717	0
10	33320	32396	0		0		0
11	16833	16174	0		0		0
12	82561	81313	2		0		0
13	84588	83302	2		0		0
14	20983	20491	1		1	1: 20983	0
Total	**685804**	**670084**	**19**	**0,003**	**5**	**1: 137161**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.5. VLCAD-Deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	25	0,06	2	1: 22982	0
3	14175	13532	4		0		0
5	50667	49141	4		1	1: 50667	0
6	12578	12055	7		0		0
7 [b]	42688	42668	13	0,03	0		0
8	174015	170118	2		2	1: 87008	0
9	107433	104997	52	0,05	0		0
10	33320	32396	3		1	1: 33320	0
11	16833	16174	1		1	1: 16833	0
12	82561	81313	8		0		0
13	84588	83302	20	0,02	2	1: 42294	0
14	20983	20491	4		0		0
Total	**685804**	**670084**	**143**	**0,02**	**9**	**1: 76200**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.6 CPT I-Deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	0		0		0
3	14175	13532	0		0		0
5	50667	49141	0		0		0
6	12578	12055	0		0		0
7 [b]	42688	42668	1		0		0
8	174015	170118	2		2	1: 87008	0
9	107433	104997	0		0		0
10	33320	32396	0		0		0
11	16833	16174	0		0		0
12	82561	81313	1		1	1: 82561	0
13	84588	83302	1		0		0
14	20983	20491	0		0		0
Total	**685804**	**670084**	**5**	**0,0007**	**3**	**1: 228601**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.7. CPT II Deficiency

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	0		0		0
3	14175	13532	0		0		0
5	50667	49141	1		0		0
6	12578	12055	0		0		0
7 [b]	42688	42668	0		0		0
8	174015	170118	0		0		0
9	107433	104997	1		0		0
10	33320	32396	0		0		0
11	16833	16174	0		0		0
12	82561	81313	0		0		0
13	84588	83302	0		0		0
14	20983	20491	0		0		0
Total	**685804**	**670084**	**2**	**0,00003**	**0**		**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.8. Glutaric acidaemia type I

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	42	0,10	0		0
3	14175	13532	3		0		0
5	50667	49141	5		0		0
6	12578	12055	9		0		0
7 [b]	42688	42668	3		0		0
8	174015	170118	3		2	1: 87008	0
9	107433	104997	18	0,02	0		0
10	33320	32396	0		0		0
11	16833	16174	2		1	1: 16833	0
12	82561	81313	0		0		0
13	84588	83302	10	0,01	1	1: 84588	0
14	20983	20491	1		0		0
Total	**685804**	**670084**	**96**	**0,01**	**4**	**1: 171451**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.1.5.9. Isovaleric acidaemia

Laboratory [a]	Total primary screening	Primary screening >=36h	Recall >=36h	Recall-rate(%)[c]	Confirmed cases	Prevalence	False negative
1	45963	43897	32	0,07	0		0
3	14175	13532	7		0		0
5	50667	49141	9		3	1: 16889	0
6	12578	12055	5		1	1: 12578	0
7 [b]	42688	42668	13	0,03	0		0
8	174015	170118	3		3	1: 58005	0
9	107433	104997	0		0		0
10	33320	32396	4		1	1: 33320	0
11	16833	16174	2		0		0
12	82561	81313	4		1	1: 82561	0
13	84588	83302	12	0,01	1	1: 84588	0
14	20983	20491	0		0		0
Total	**685804**	**670084**	**91**	**0,01**	**10**	**1: 68580**	**0**

[a] Laboratory 15 cannot give information for recall or confirmed cases therefore the data for complete primary screening (n=4339) is not considered for the total.
[b] The complete primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.
[c] Recall rate calculated only for n ≥ 10.

4.2 Recall rate stratified according to age 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 increase 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 disease and age / gestational age. For statistical reasons recall rates n<10 were not calculated. Laboratory 15 cannot give information for recall or confirmed cases therefore the data for total primary screening (n=4339) is not considered for the total.

The total primary screening of Laboratory 7 was equalised with primary screening > 36 hours to allow plausible calculations in the following tables since differentiation could not be made.

4.2.1 Hypothyroidism

	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
Laboratory	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	34	43897	0,08	13	1506	0,86	3	560	
3	2	13532		0	352		0	291	
5	85	49141	0,17	9	985		3	541	
6	11	12055	0,09	44	370	11,89	0	153	
7	26	42668	0,06						
8	310	170118	0,18	219	1996	10,97	10	1901	0,53
9	56	104997	0,05	8	1125		1	1311	
10	13	32396	0,04	1	611		0	313	
11	6	16174		76	495	15,35	0	164	
12	56	81313	0,07	52	963	5,40	2	285	
13	47	83302	0,06	42	1035	4,06	0	251	
14	5	20491		4	307		1	185	
Total	**651**	**670084**	**0,10**	**468**	**9745**	**4,80**	**20**	**5955**	**0,34**

4.2.2 Congenital adrenal hyperplasia (CAH)

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	123	43897	0,28	36	1506	2,39	68	560	12,14
3	17	13532	0,13	1	352		0	291	
5	282	49141	0,57	8	985		19	541	3,51
6	182	12055	1,51	60	370	16,22	17	153	11,11
7	662	42668	1,55						
8	644	170118	0,38	152	1996	7,62	273	1901	14,36
9	238	104997	0,23	17	1125	1,51	10	1311	0,76
10	36	32396	0,11	2	611		2	313	
11	26	16174	0,16	12	495	2,42	4	164	
12	986	81313	1,21	56	963	5,82	200	285	70,18
13	636	83302	0,76	55	1035	5,31	155	251	61,75
14	134	20491	0,65	15	307	4,89	26	185	14,05
Total	**3966**	**670084**	**0,59**	**414**	**9745**	**4,25**	**774**	**5955**	**13,00**

4.2.3 Biotinidase Defiency

Laboratory	Primary screening ≥ 36h			Primary screening< 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	1	43897		0	1506		1	560	
3	0	13532		0	352		0	291	
5	1	49141		0	985		0	541	
6	2	12055		0	370		0	153	
7	12	42668	0,03						
8	90	170118	0,05	4	1996		3	1901	
9	2	104997		5	1125		1	1311	
10	2	32396		0	611		0	313	
11	1	16174		0	495		0	164	
12	19	81313	0,02	2	963		1	285	
13	14	83302	0,02	0	1035		0	251	
14	2	20491		0	307		0	185	
Total	**146**	**670084**	**0,02**	**11**	**9745**	**0,11**	**6**	**5955**	**0,1**

4.2.4 Galactosaemia including variants/classic

Laboratory	Primary screening≥ 36h			Primary screening< 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall rate
1	29	43897	0,07	1	1506		0	560	
3	9	13532		0	352		0	291	
5	75	49141	0,15	1	985		2	541	
6	17	12055	0,14	0	370		0	153	
7	34	42668	0,08						
8	290	170118	0,17	2	1996		2	1901	
9	7	104997		3	1125		0	1311	
10	33	32396	0,10	0	611		1	313	
11	5	16174		0	495		0	164	
12	36	81313	0,04	0	963		1	285	
13	38	83302	0,05	0	1035		0	251	
14	38	20491	0,19	1	307		2	185	
Total	**611**	**670084**	**0,09**	**8**	**9745**	**0,08**	**8**	**5955**	**0,13**

4.2.5 MS/MS total

Laboratory	Primary screening≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	160	43897	0,36	9	1506		8	560	
3	32	13532	0,24	0	352		0	291	
5	73	49141	0,15	2	985		6	541	
6	59	12055	0,49	0	370		7	153	
7	90	42668	0,21						
8	57	170118	0,03	1	1996		0	1901	
9	140	104997	0,13	3	1125		7	1311	
10	42	32396	0,13	1	611		1	313	
11	13	16174	0,08	2	495		0	164	
12	48	81313	0,06	6	963		7	285	
13	73	83302	0,09	1	1035		0	251	
14	21	20491	0,10	0	307		2	185	
Total	**808**	**670084**	**0,12**	**25**	**9745**	**0,26**	**38**	**5955**	**0,64**

4.2.5.1 PKU/HPA

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	21	43897	0,05	5	1506		0	560	
3	7	13532		0	352		0	291	
5	11	49141	0,02	0	985		0	541	
6	10	12055	0,08	0	370		6	153	
7	29	42668	0,07						
8	21	170118	0,01	1	1996		0	1901	
9	32	104997	0,03	3	1125		3	1311	
10	23	32396	0,07	1	611		0	313	
11	4	16174		2	495		0	164	
12	22	81313	0,03	2	963		3	285	
13	15	83302	0,02	0	1035		0	251	
14	12	20491	0,06	0	307		2	185	
Total	**207**	**670084**	**0,03**	**14**	**9745**	**0,14**	**14**	**5955**	**0,24**

4.2.5.2 MSUD

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	4	43897		0	1506		0	560	
3	1	13532		0	352		0	291	
5	19	49141	0,04	1	985		3	541	
6	6	12055		0	370		1	153	
7	22	42668	0,05						
8	3	170118		0	1996		0	1901	
9	20	104997	0,02	0	1125		0	1311	
10	2	32396		0	611		0	313	
11	1	16174		0	495		0	164	
12	1	81313		1	963		0	285	
13	2	83302		0	1035		0	251	
14	1	20491		0	307		0	185	
Total	**82**	**670084**	**0,01**	**2**	**9745**	**0,02**	**4**	**5955**	**0,07**

4.2.5.3 MCAD-Deficiency

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	32	43897	0,07	1	1506		1	560	
3	10	13532	0,07	0	352		0	291	
5	24	49141	0,05	1	985		2	541	
6	19	12055	0,16	0	370		0	153	
7	9	42668							
8	20	170118	0,01	0	1996		0	1901	
9	13	104997	0,01	0	1125		0	1311	
10	10	32396	0,03	0	611		0	313	
11	3	16174		0	495		0	164	
12	10	81313	0,01	1	963		0	285	
13	11	83302	0,01	0	1035		0	251	
14	2	20491		0	307		0	185	
Total	**163**	**670084**	**0,02**	**3**	**9745**	**0,03**	**3**	**5955**	**0,05**

4.2.5.4 LCHAD-Deficiency

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	4	43897		0	1506		0	560	
3	0	13532		0	352		0	291	
5	0	49141		0	985		0	541	
6	3	12055		0	370		0	153	
7	0	42668							
8	3	170118		0	1996		0	1901	
9	4	104997		0	1125		1	1311	
10	0	32396		0	611		0	313	
11	0	16174		0	495		0	164	
12	2	81313		0	963		0	285	
13	2	83302		0	1035		0	251	
14	1	20491		0	307		0	185	
Total	**19**	**670084**	**0,003**	**0**	**9745**		**1**	**5955**	**0,02**

4.2.5.5 VLCAD-Deficiency

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	25	43897	0,06	1	1506		3	560	
3	4	13532		0	352		0	291	
5	4	49141		0	985		1	541	
6	7	12055		0	370		0	153	
7	13	42668	0,03						
8	2	170118		0	1996		0	1901	
9	52	104997	0,05	0	1125		0	1311	
10	3	32396		0	611		0	313	
11	1	16174		0	495		0	164	
12	8	81313		1	963		0	285	
13	20	83302	0,02	1	1035		0	251	
14	4	20491		0	307		0	185	
Total	**143**	**670084**	**0,02**	**3**	**9745**	**0.03**	**4**	**5955**	**0,07**

4.2.5.6 CPT I-Deficiency

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	0	43897		0	1506		1	560	
3	0	13532		0	352		0	291	
5	0	49141		0	985		0	541	
6	0	12055		0	370		0	153	
7	1	42668							
8	2	170118		0	1996		0	1901	
9	0	104997		0	1125		0	1311	
10	0	32396		0	611		0	313	
11	0	16174		0	495		0	164	
12	1	81313		0	963		0	285	
13	1	83302		0	1035		0	251	
14	0	20491		0	307		0	185	
Total	**5**	**670084**	**0,0007**	**0**	**9745**		**1**	**5955**	**0,02**

4.2.5.7 CPT II-Deficiency

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	0	43897		0	1506		0	560	
3	0	13532		0	352		0	291	
5	1	49141		0	985		0	541	
6	0	12055		0	370		0	153	
7	0	42668							
8	0	170118		0	1996		0	1901	
9	1	104997		0	1125		0	1311	
10	0	32396		0	611		0	313	
11	0	16174		0	495		0	164	
12	0	81313		0	963		0	285	
13	0	83302		0	1035		0	251	
14	0	20491		0	307		0	185	
Total	**2**	**670084**	**0,00003**	**0**	**9745**		**0**	**5955**	

4.2.5.8 Glutaric acidaemia type I

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	42	43897	0,10	1	1506		1	560	
3	3	13532		0	352		0	291	
5	5	49141		0	985		0	541	
6	9	12055		0	370		0	153	
7	3	42668							
8	3	170118		0	1996		0	1901	
9	18	104997	0,02	0	1125		3	1311	
10	0	32396		0	611		0	313	
11	2	16174		0	495		0	164	
12	0	81313		0	963		2	285	
13	10	83302	0,01	0	1035		0	251	
14	1	20491		0	307		0	185	
Total	**96**	**670084**	**0,01**	**1**	**9745**	**0,01**	**6**	**5955**	**0,1**

4.2.5.9 Isovaleric acidaemia

Laboratory	Primary screening ≥ 36h			Primary screening < 36h			Primary screening < 32WoG		
	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate	Recall	Primary screening	Recall-rate
1	32	43897	0,07	1	1506		2	560	
3	7	13532		0	352		0	291	
5	9	49141		0	985		0	541	
6	5	12055		0	370		0	153	
7	13	42668	0,03						
8	3	170118		0	1996		0	1901	
9	0	104997		0	1125		0	1311	
10	4	32396		0	611		1	313	
11	2	16174		0	495		0	164	
12	4	81313		1	963		2	285	
13	12	83302	0,01	0	1035		0	251	
14	0	20491		0	307		0	185	
Total	**91**	**670084**	**0,01**	**2**	**9745**	**0,02**	**5**	**5955**	**0,08**

5 Process Periods

5.1 Time from birth to blood sampling

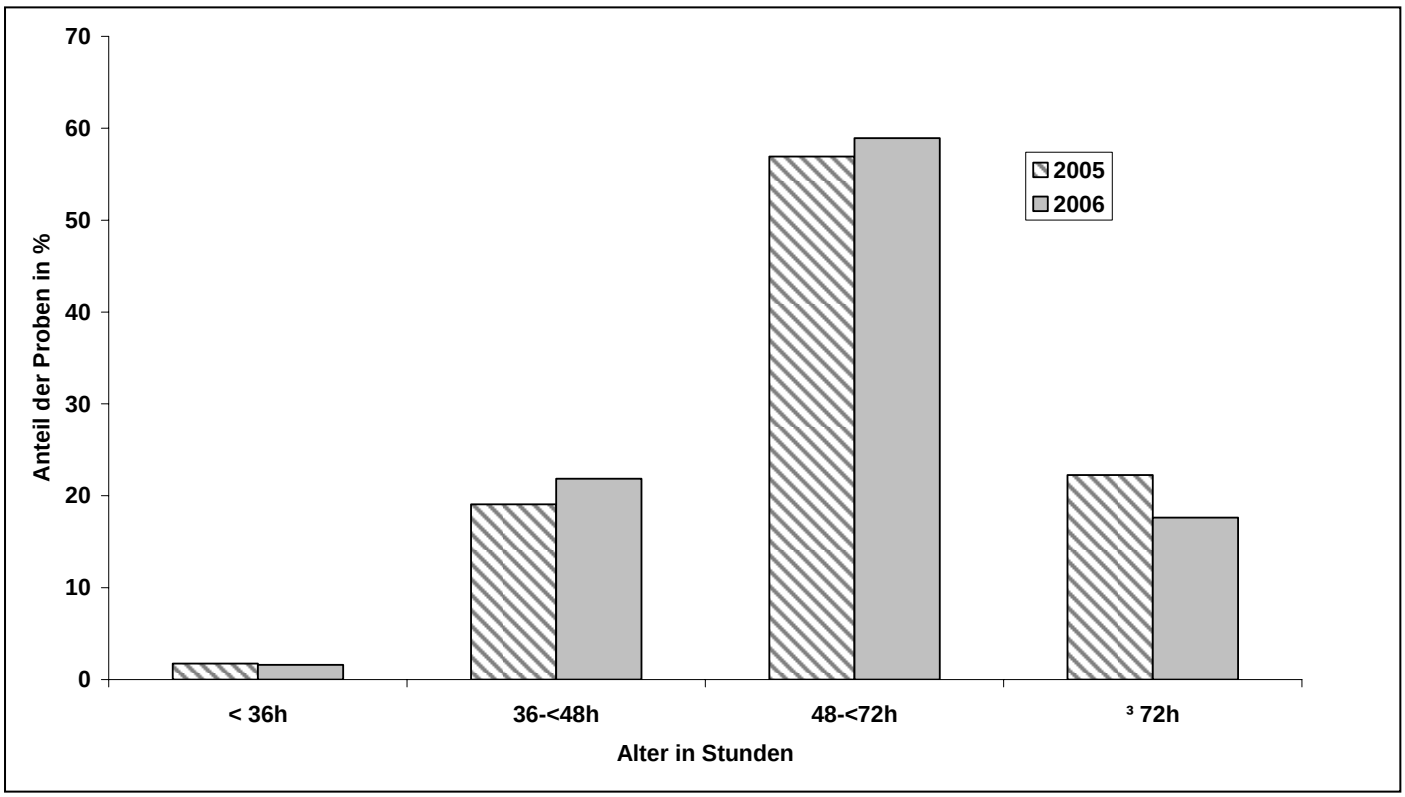
According to the guidelines (Kinderrichtlinien, section 8, paragraph 1) the sampling should be performed between the 36th and 72nd hour of life. In 82,3% of cases, with specification of collection time, the collection was according to the guidelines. In 17,63% (6,55-27,06%) beyond the 72nd hour of life, in 1,6% (0,82-3,47%) before the 36th hour of life (see Table 5.1, figure 2)

Table 5.1 Age at blood collection, primary screening

Laboratory [a]	total	<36h		36h-<48h		48h-<72h		≥72h	
	n	n	%	n	%	n	%	n	%
1	45904	1594	3,47	5272	11,48	27219	59,30	11819	25,75
3	14175	427	3,01	1162	8,20	11658	82,24	928	6,55
5	49549	405	0,82	19976	40,32	23129	46,68	6039	12,19
6	12524	384	3,07	1752	13,99	6985	55,77	3403	27,17
8	153641	2361	1,54	47227	30,74	79949	52,04	24104	15,69
9	107433	1272	1,18	11962	11,13	65125	60,62	29074	27,06
10	33007	611	1,85	5870	17,78	21778	65,98	4748	14,38
11	16833	516	3,07	2399	14,25	11913	70,77	2005	11,91
12	80716	963	1,19	17438	21,60	48916	60,60	13399	16,60
13	83225	1035	1,24	17246	20,72	54977	66,06	9967	11,98
14	20829	316	1,52	4757	22,84	12320	59,15	3436	16,50
Total	**617836**	**9884**	**1,60**	**135061**	**21,86**	**363969**	**58,91**	**108922**	**17,63**

[a] Laboratory 7 and 15 did not differentiate the times and therefore are not listed. For all laboratories the number of probes with a time stamp is less than the total number of probes

Figure 2: Comparison: Age at blood collection 2005 and 2006



5.2 Period from sampling to laboratory receipt

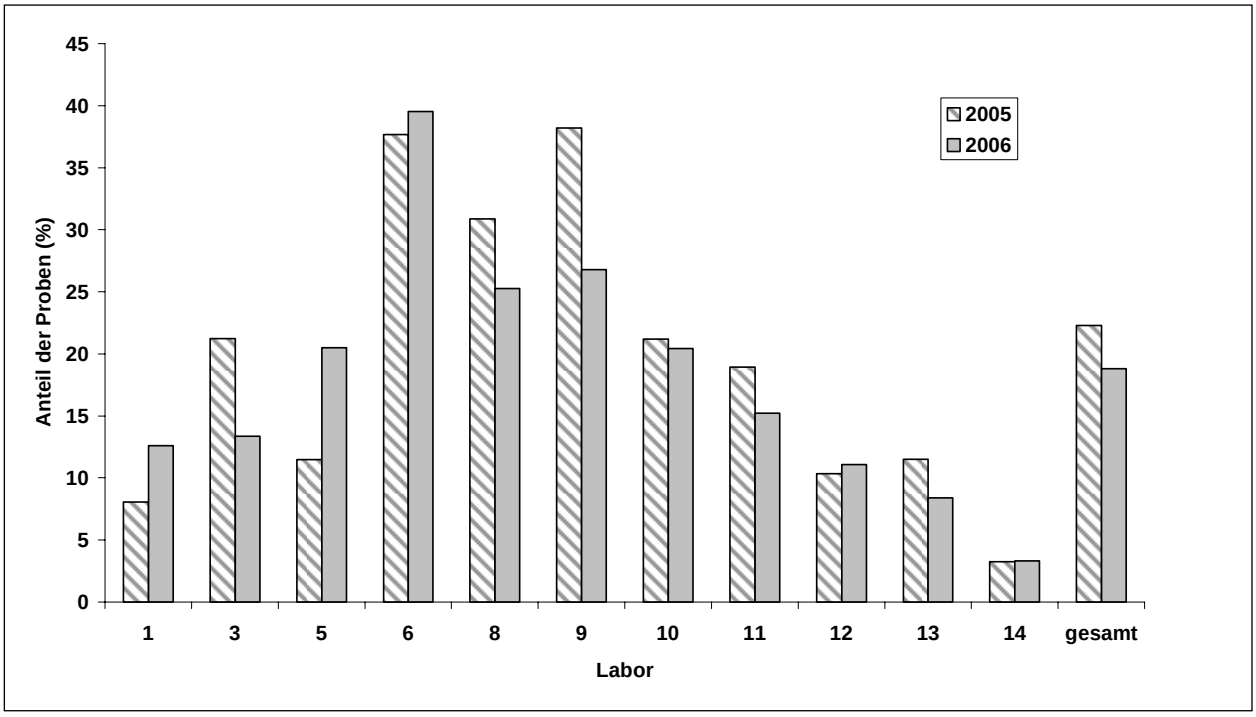
The time span between sampling and conveyance of suspect results should not exceed 72 hours (section 6, paragraph 3). In 18,8% (3,3-39,5%) of cases with statement of the delivery time the probe was received after 72 hours of sampling. In further 23,3% (8,4-29,7%) of the cases in a period between 48 and 72 hours. Shorter periods of delivery times are desirable, especially on the weekends. (Table 5.2, figure 3)

Table 5.2: Period between sampling and laboratory receipt

Laboratory [a]	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1	45963	14731	32,05	17054	37,10	8383	18,24	5795	12,61
3	14175	3361	23,71	6292	44,39	2627	18,53	1895	13,37
5	49856	3878	7,78	20933	41,99	14832	29,75	10213	20,48
6	11925	1422	11,92	3158	26,48	2631	22,06	4714	39,53
8	154957	12321	7,95	63288	40,84	40193	25,94	39155	25,27
9	107433	11740	10,93	39121	36,41	27771	25,85	28801	26,81
10	33007	3366	10,20	13766	41,71	9127	27,65	6748	20,44
11	16833	1989	11,82	7740	45,98	4544	26,99	2560	15,21
12	81828	29045	35,50	28344	34,64	15367	18,78	9072	11,09
13	83225	28737	34,53	30401	36,53	17102	20,55	6985	8,39
14	20980	13926	66,38	4603	21,94	1754	8,36	697	3,32
Total	**620182**	**124516**	**20,08**	**234700**	**37,84**	**144331**	**23,27**	**116635**	**18,81**

[a] Laboratories which cannot differentiate the progress are not listed.
The amount of probes with known time stamps is less than the total number of probes.

Figure 3: Proportion of probes with an delivery time of > 72h: Comparison 2005 and 2006



5.3 Period between laboratory receipt and conveyance

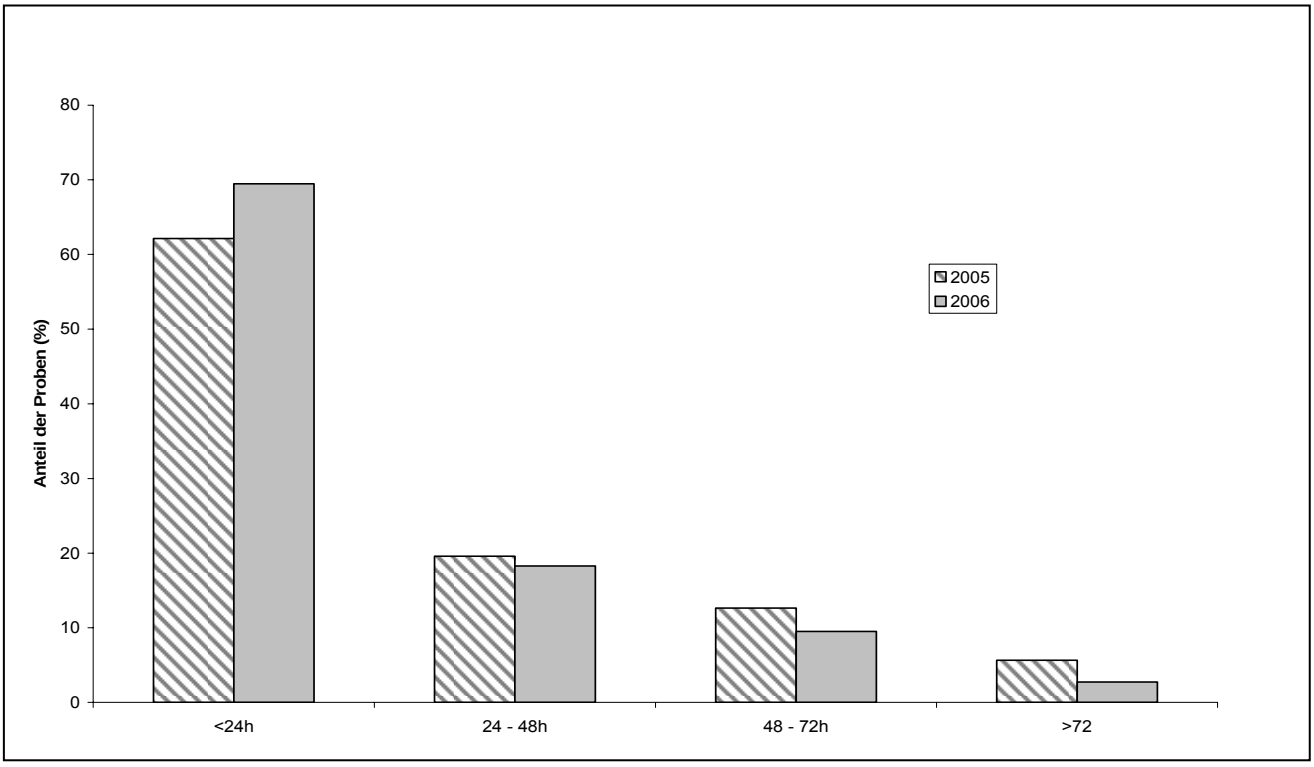
With pathological results it has to be assured that testing and reporting of probes is done on the day of laboratory receipt. (§14.3). Usually, this reporting is done via Telephone or Fax (§14.3).

Table 5.3 Period between laboratory receipt and conveyance

Laboratory[a]	Total	≤24h		>24h-48h		>48h-72h		>72h	
	n	n	%	n	%	n	%	n	%
1	45963	25051	54,50	16495	35,89	3397	7,39	1020	2,22
3	14175	11563	81,57	2008	14,17	305	2,15	299	2,11
5	48066	26663	55,47	10007	20,82	9877	20,55	1519	3,16
8	174342	142344	81,65	6132	3,52	23890	13,70	1976	1,13
9	107433	87257	81,22	12204	11,36	6199	5,77	1773	1,65
10	33047	21966	66,47	8788	26,59	1916	5,80	377	1,14
11	16833	10586	62,89	5926	35,20	316	1,88	5	,03
12	82560	61025	73,92	13528	16,39	7236	8,76	771	,93
13	83812	61146	72,96	14589	17,41	7050	8,41	1027	1,23
14	20983	16200	77,21	3757	17,90	669	3,19	357	1,70
Total	**627214**	**463801**	**73,95**	**93434**	**14,90**	**60855**	**9,70**	**9124**	**1,45**

[a] Laboratories which cannot differentiate the progress are not listed..
The amount of probes with known time stamps is less than the total number of probes.

Figure 4: Period from laboratory receipt to conveyance, comparison of 2005, 2006



6 Time of screening in the confirmed cases.

6.1 Primary screening

Crucial for 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 (§6.1). The probe should not be sampled before the 36th and not after the 72nd hour of life.

The age of primary screening is shown for the targeted disease in Table 6.1. For clarity reasons the description >72 hours of age is reported in days.

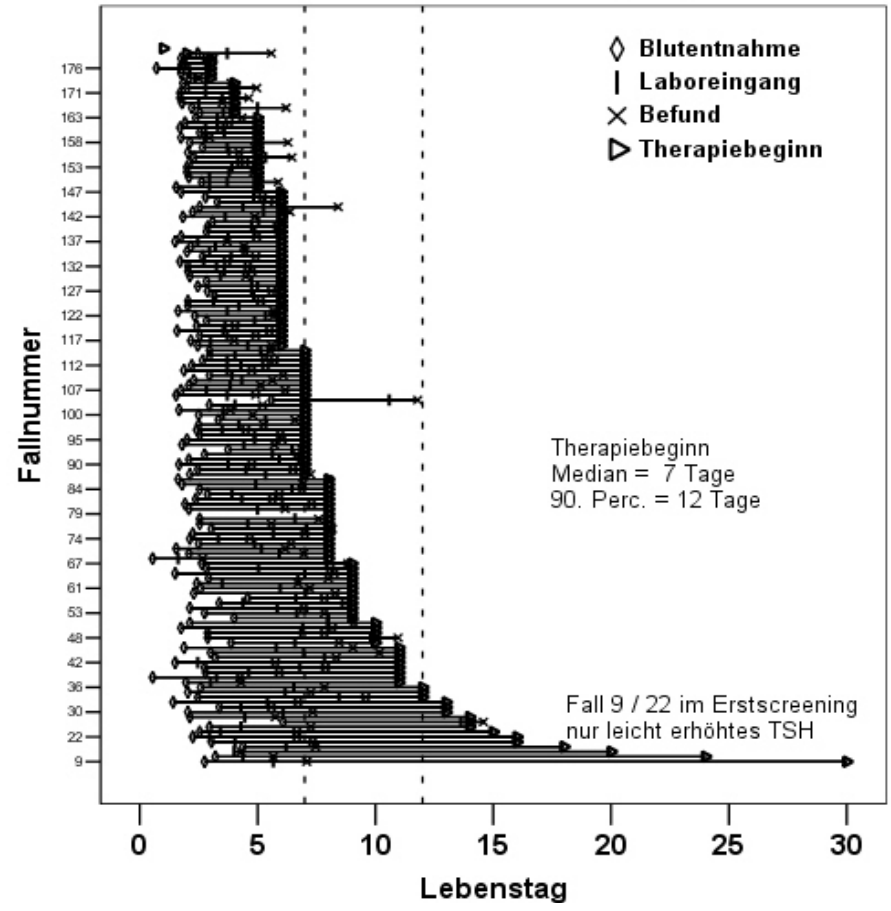
Exemplary the age of the children and the time of sampling, laboratory receipt, reporting and start of therapy is shown for children with hypothyroidism, CAH and PKU in figure 5, 6 and 7.

Table 6.1 Time of primary screening in confirmed cases

Disease	36-72h	4-7d	>7d	<36h	<32WoG	≥36h*	No information	Total
Hypothyroidism	130	20	0	4	8	3	0	**165**
CAH	38	10	0	5	2	2	0	**57**
Biotinidase defiency	21	3	0	0	0	3	0	**27**
Classic Galactosaemia	13	0	0	1	0	0	0	**14**
PKU/HPA	88	16	2	3	3	1	3	**116**
MSUD	4	1	0	0	0	0	0	**5**
MCAD	49	11	1	3	0	1	2	**67**
LCHAD	3	0	0	0	0	1	1	**5**
VLCAD	7	2	0	0	0	0	0	**9**
CPT I	2	0	0	0	0	1	0	**3**
GA I	4	0	0	0	0	0	0	**4**
IVA	6	3	0	0	0	1	0	**10**
Total	**365**	**66**	**3**	**16**	**13**	**13**	**6**	**482**

*≥ 36h does not include repeat testing with early sampling or preterm birth, but exact age of sampling time not stated.

Figure 5: Time elapsed from initiation of therapy in children with hypothyroidism. Illustration of single cases as boxplot



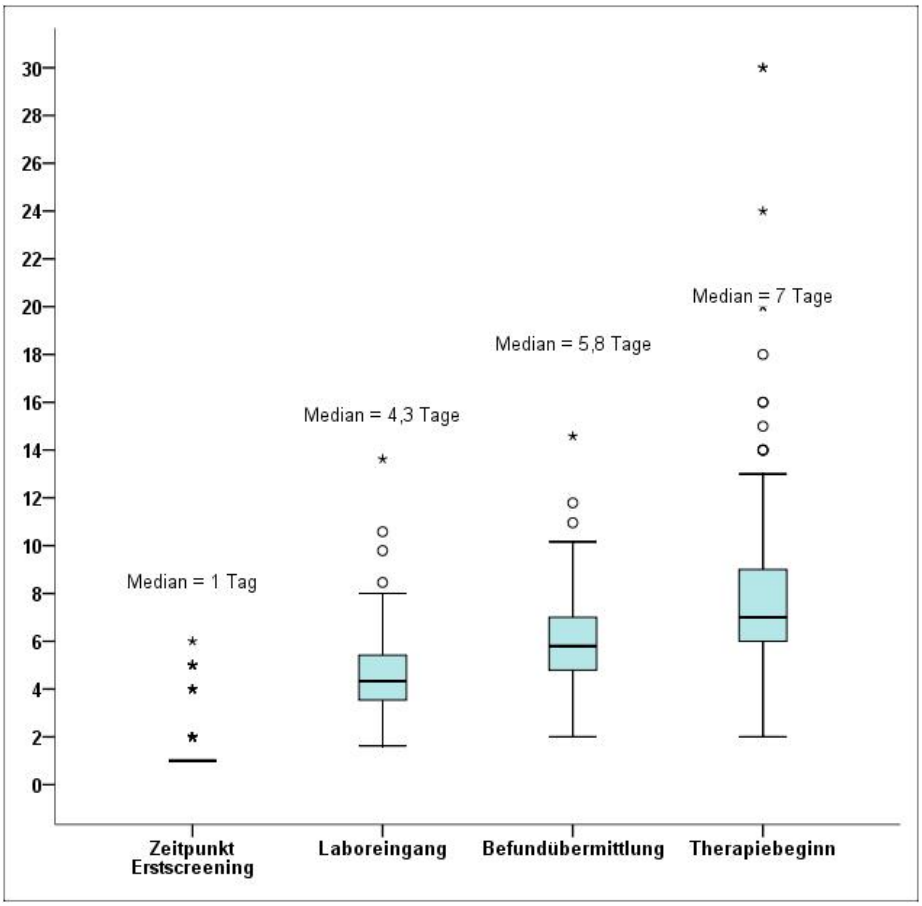
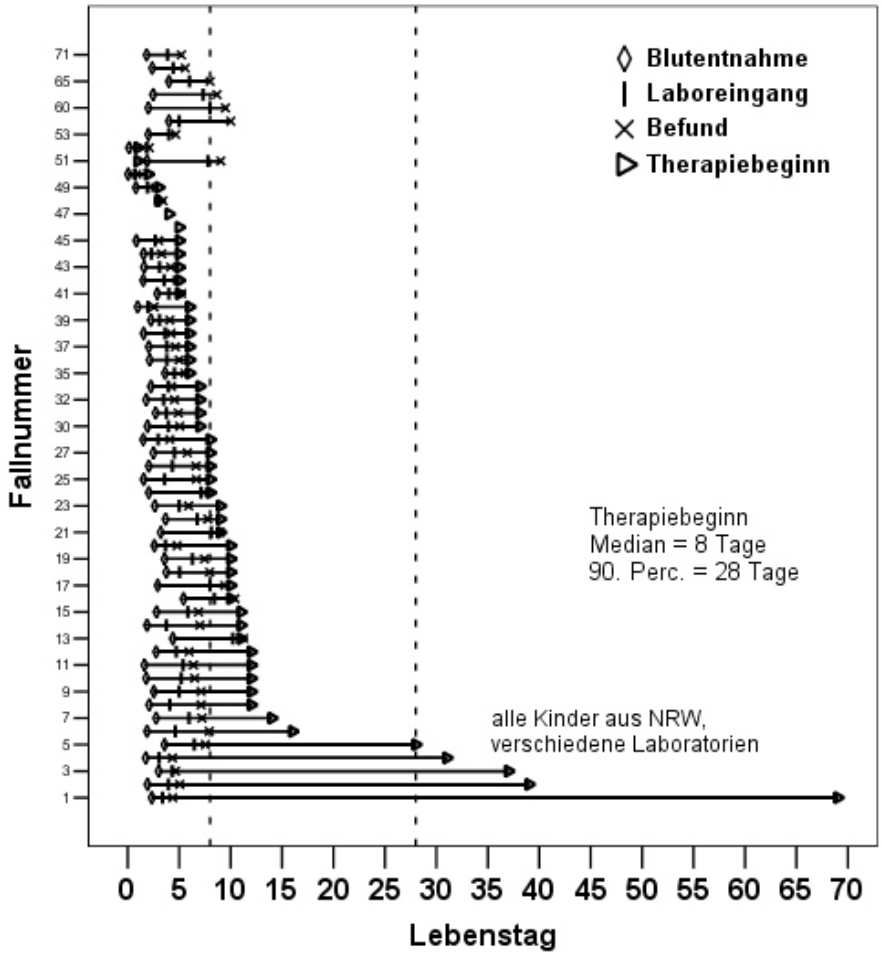


Figure 6: Time elapsed from initiation of therapy in children with CAH. Illustration of single cases as boxplot



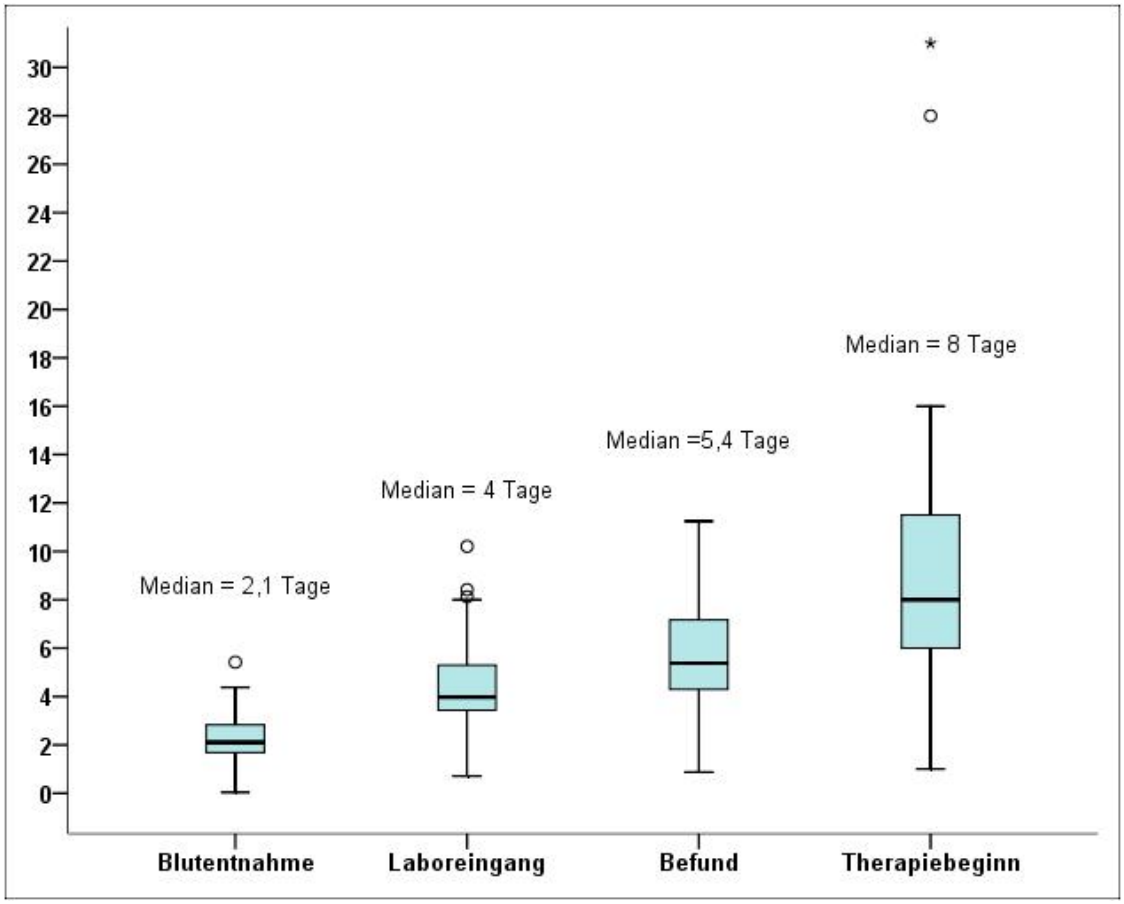
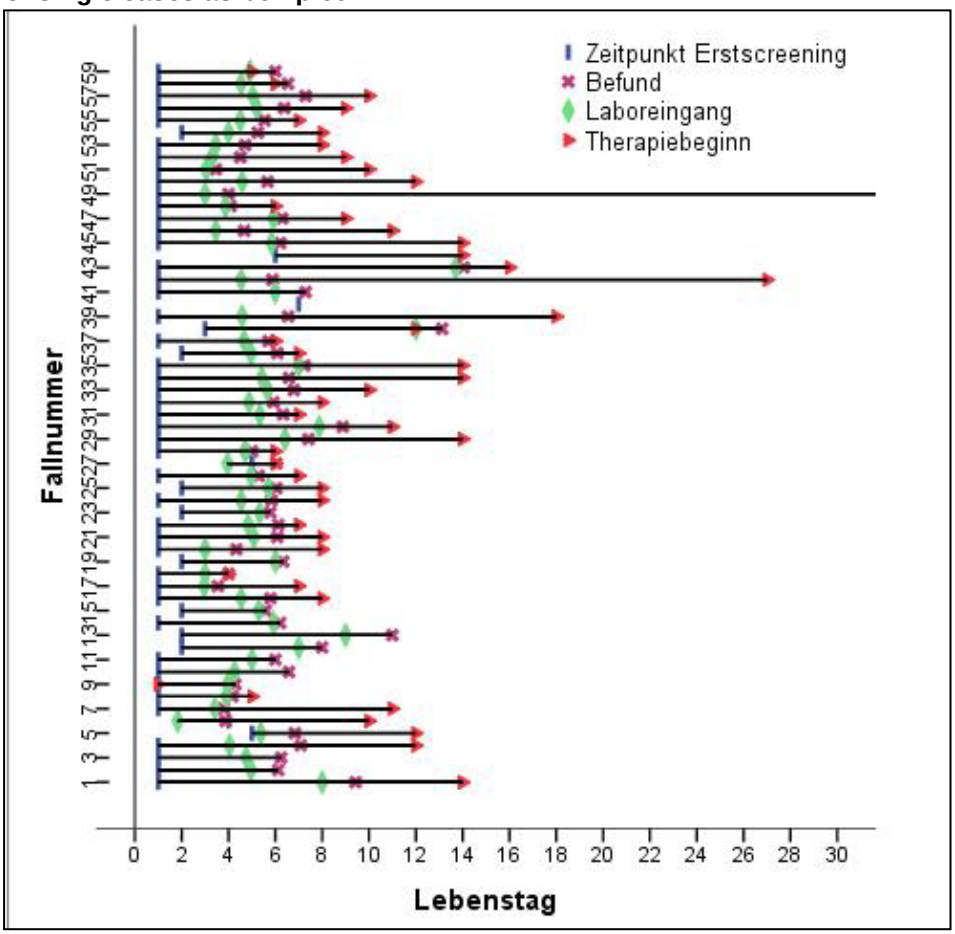
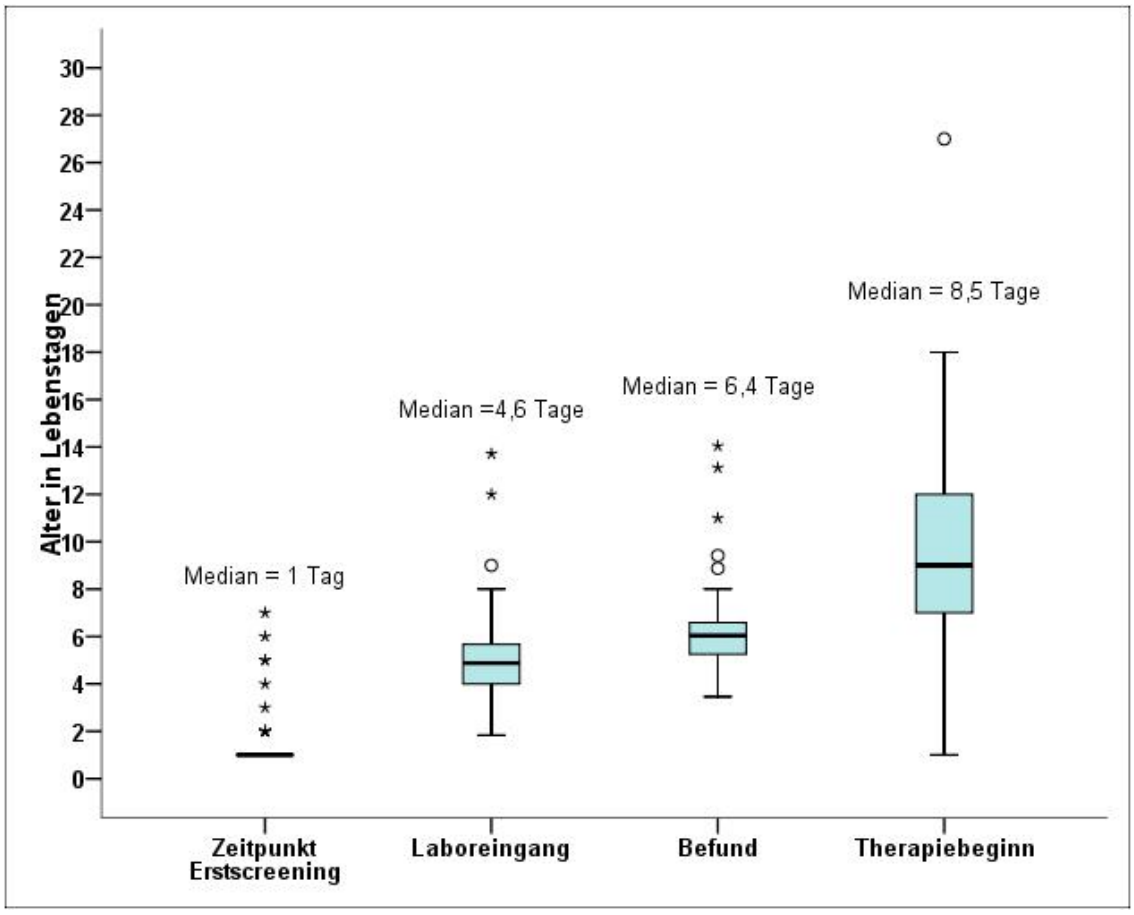


Figure 7: Time elapsed from initiation of therapy in children with PKU (only PKU no HPA). Illustration of single cases as box plot





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

An indication for a second 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 6.2 the indications for repeat testing are shown. Occasionally, the confirmation diagnostics are undertaken without sending the repeat screening to the laboratory as stated in the guidelines (§6 paragraph 2).

Table 6.2 : Indication for request of repeat testing in the confirmed cases

	Indication for repeat screening				
Disease	Recall	< 36h	<32 weeks gestation	No information	Total
Hypothyroidism	153	4	8*	0	165
CAH	50	5	2	0	57
Biotinidase deficiency	27	0	0	0	27
Classic Galactosaemia	13	1	0	0	14
PKU/HPA	107	3	3	3	116
MSUD	5	0	0	0	5
MCAD	62	3	0	2	67
LCHAD	4	0	0	1	5
VLCAD	9	0	0	0	9
CPT I	3	0	0	0	3
GA I	4	0	0	0	4
IVA	10	0	0	0	10
Total	**447**	**16**	**13**	**6**	**482**

*4 out of 8 cases: TSH primary screening <20 mU/l

7 Confirmation of pathological results

The plausibility of the laboratory reported results were checked by a Pediatric Endocrinologist or by experts in metabolic disease (see above). 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. In 2006 50 of 482 cases lacked detailed information regarding the confirmation diagnostics.

7.1.1 Hypothyroidism

Laboratory	Confirmed cases	TSH	T3	fT3	T4	fT4	ultrasound	Thyroid antibodies
1	9	8	4	1	6	5	7	6
3	2	2	2	2	1	2	2	2
5	11	11	3	7	3	8	9	7
6	4	4	1	4	1	4	4	4
7	2	2	1	n.s.	n.s.	n.s.	n.s.	n.s.
8	53	48	15	22	9	37	27	17
9	27	26	19	8	18	25	3	n.s.
10	6	5	1	2	3	4	1	1
11	1	1	1	1	1	1	1	n.s.
12	32	31	9	19	6	24	23	2
13	16	13	1	7	1	7	7	n.s.
14	2	2	n.s	2	n.s.	2	1	n.s.
Total	**165***	**153**	**57**	**75**	**49**	**121**	**85**	**39**

*including n=4 cases without proper confirmation

7.1.2 Congenital adrenal hyperplasia (CAH)

Laboratory	Confirmed cases	17-OHP (Serum)	Serum-steroids	Urinary steroids	Molecular genetic testing
1	5	5	5	1	5
3	1	1	1	n.s.	1
5	4	2	n.s.	3	1
6	1	1	n.s.	n.s.	1
7	4	n.s.	n.s.	n.s.	n.s.
8	21	13	20	3	17
9	7	6	4	n.s.	4
10	1	1	n.s.	n.s.	n.s.
11	1	1	n.s.	1	n.s.
12	5	2	1	n.s.	5
13	6	2	2	1	3
14	1	1	1	n.s.	1
Total	**57***	**35**	**34**	**9**	**38**

*including n=6 cases without proper confirmation

7.1.3 Biotinidase deficiency

Laboratory	Confirmed cases	Serum Biotinidase	Molecular genetic testing
1	1	1	n.s.
7	2	2	n.s.
8	18	18	1
9	2	2	n.s.
12	2	1	n.s.
13	1	1	n.s.
14	1	1	n.s.
Total	**27***	**25**	**1**

*including n=1 Case without proper confirmation

7.1.4 Galactosaemia classic form

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

*including n=2 cases without proper confirmation

Including variants

Laboratory	Confirmed cases	Red cell GALT	Molecular genetic testing
1	12	8	6
3	2	n.s.	1
5	3	3	3
6	5	2	3
8	45	35	10
9	1	1	n.s.
10	2	1	n.s.
11	2	2	2
12	6	5	1
13	1	n.s.	n.s.
14	1	1	n.s.
Total	**80***	**57**	**26**

*including n=10 cases without proper confirmation

7.1.5 PKU / HPA

Laboratory	Confirmed cases	Phe (Serum)	Phe/ Tyr	BH4-Test	BH4 sensitive	Molecular genetic testing	Pterine in Urine	DHPR in dried blood
1	9	9	5	7	1	9	9	9
3	3	2	2	2	n.s.	n.s.	1	1
5	9	9	2	8	5	n.s.	8	8
6	3	3	1	2	1	n.s.	n.s.	1
7	10	2	1	5	1	n.s.	1	1
8	22	17	6	11	4	4	9	9
9	21	21	21	n.s.	n.s.	n.s.	21	n.s.
10	5	2	3	n.s.	n.s.	n.s.	2	2
11	3	3	3	2	n.s.	n.s.	2	2
12	16	15	9	9	3	2	10	10
13	9	3	n.s.	2	n.s.	n.s.	1	1
14	6	5	4	4	1	n.s.	1	1
Total	**116**	**91**	**57**	**52**	**16**	**15**	**65**	**45**

*including n=17 cases without proper confirmation

7.1.6 MSUD

Laboratory	Confirmed cases	Serum leucine	Serum isoleucine	Serum valine	Serum alloisoleucine	Urinary organic acids
1	1	1	1	1	1	1
8	3	3	3	3	2	n.s.
13	1	n.s.	n.s.	n.s.	n.s.	n.s.
Total	**5***	**4**	**4**	**4**	**3**	**1**

*including n=1 cases without proper confirmation

7.1.7 MCAD-Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Molecular genetic testing	Urinary organic acids
1	5	n.s.	5	5
3	1	n.s.	1	n.s.
5	14	12	11	11
6	2	1	2	1
7	2	n.s.	n.s.	n.s.
8	18	9	9	11
9	11	9	1	8
10	3	2	3	2
12	6	1	5	1
13	3	n.s.	n.s.	n.s.
14	2	1	2	2
Total	**67**	**39**	**39**	**41**

*including n=10 cases without proper confirmation

7.1.8 LCHAD - Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Molecular genetic testing	Urinary organic acids	Enzyme activity (Fibroblast)
8	2	n.s.	1	2	1
9	2	n.s.	1	2	n.s.
14	1	n.s.	n.s.	n.s.	n.s.
Total	**5**	**n.s.**	**2**	**4**	**1**

*including n=1 case without proper confirmation

7.1.9 VLCAD- Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Molecular genetic testing	Urinary organic acids	Enzyme activity (Fibroblast)
1	2	n.s.	1	n.s.	1
5	1	n.s.	n.s.	n.s.	1
8	2	1	2	n.s.	2
10	1	1	1	1	1
11	1	n.s.	1	1	1
13	2	n.s.	n.s.	n.s.	n.s.
Total	**9**	**2**	**5**	**2**	**6**

*including n=3 cases without proper confirmation

7.1.10CPT I - Deficiency

Laboratory	Confirmed cases	Confirmation Serum	Molecular genetic testing
8	2	n.s.	1
12	1	n.s.	1
Total	**3***	**n.s.**	**2**

*including n=1 case without proper confirmation

7.1.11 Glutaric acidaemia type I

Laboratory	Confirmed cases	Confirmation Serum	Urinary organic acids
8	2	n.s.	1
11	1	n.s.	1
13	1	n.s.	n.s.
Total	**4**	**n.s.**	**2**

*including n=2 cases without proper confirmation

7.1.12 Isovaleric acidaemia

Laboratory	Confirmed cases	Molecular genetic testing	Urinary organic acids
5	3	1	3
6	1	1	1
8	3	1	3
10	1	n.s.	n.s.
12	1	n.s.	n.s.
13	1	1	1
Total	**10**	**4**	**8**

*including n=2 cases without proper confirmation

8 Laboratory Organisation

Paragraphs 13 to 15 verify organization issues like accreditation, period of sample custody, etc.

8.1 Demand for repeat screening due to insufficient sample quality

Laboratory*	Primary screening	Repeat demanded	Repeat received	received/ demanded (%)	Demanded repeats/ primary screening (%)
1	45963	359	350	97,49	0,78
3	14175	35	35	100	0,25
5	50667	403	403	100	0,80
6	12578	10	10	100	0,08
8	174015	1017	916	90,07	0,58
9	107433	329	328	99,70	0,31
10	33320	186	186	100	0,56
11	16833	5	5	100	0,03
12	82561	249	242	97,19	0,30
13	84588	191	189	98,95	0,23
14	20983	8	8	100	0,04
Total	**643116**	**2792**	**2672**	**95,70**	**0,43**

*Information from laboratories which are not listed cannot be given

8.2 Management of Test cards

Laboratory	Test card custody > 3 months	accreditation	Health insurance authorisation	Federal state screening centre
1	yes	DACH	01.08.2005	yes
3	yes	DACH / ZLG	April 2005 / 2006	no
5	yes	DACH	01.07.2005	yes
6	yes	DACH	2003	
7		ZLG	Feb 2006	no
8	no	ZLG	1978	no
9	yes	DACH		
10	no	ZLG	01.04.2005	no
11	yes	DACH	10.04.2006	no
12	no	DACH	1999	yes
13	no	DACH	1999	no
14	no	DACH	April 2003	yes
15	no	DACH	April 2003	no

8.3 Acquisition of completeness

Laboratory	No acquisition of completeness	Comparison with birth records	Name based Comparison with birth registry
1		yes	
3		yes	
5		yes	
6		yes	
7	yes		
8		yes	
9		yes	
10		yes	
11		yes	
12			yes
13	yes		
14		yes	yes
15	yes		
Total	**3**	**9**	**2**

8.4 Tracking

When necessary laboratories or regional screening centers do tracking in the listed situations.

Laboratory	Suspicious primary screening	Primary screening < 36.h.	Primary screening < 32 WoG	Empty cards	Bad sample quality	confirmation	Therapy
1	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
8	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	yes
14	yes	yes	yes		yes	yes	yes
15							

9 Methods and cut offs in the screening

9.1 Filter paper for sampling

Laboratory	Filter paper
1	WS 903
3	WS 903
5	WS 902
6	WS 903
7	WS 2992
8	WS 903
9	WS 903
10	WS 903
11	WS 903
12	WS 2992
13	WS 2992
14	WS 903
15	WS 903

9.2 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	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

9.3 Biotinidase Deficiency

Laboratory	Parameter	Cut off	Method
1	Biotinidase	30% board mean	Colorimetry qualitativee
3	Biotinidase	30 % daily mean	Colorimetry qualitativee
5	Biotinidase	n.s.	Colorimetry quantitativee
6	Biotinidase	30% daily mean	Colorimetry quantitativee
7	Biotinidase	2,7 U/g Hb	Colorimetry quantitativee
8	Biotinidase	< 30% daily mean	Colorimetry quantitativee
9	Biotinidase	0,2	Colorimetry qualitativee
10	Biotinidase	0,2	Colorimetry qualitativee
11	Biotinidase	n.s.	Colorimetry qualitativee
12	Biotinidase	< 30%	Fluorometry quantitativee
13	Biotinidase	< 30%	Fluorometry quantitativee
14	Biotinidase	< 30 %	Colorimetry quantitativee
15	Biotinidase	< 30 %	Colorimetry quantitativee

9.4 Galactosaemia

Laboratory	Parameter	Cut off	Method
1	galactose GALT	15 mg/dl 3,5 U/gHb	BIORAD Quantase Fluorometry(PE)
3	GALT galactose	2,3 Ug/Hb 20 mg/dl	BIORAD Quantase
5	GALT galactose	 n.s.	Colorimetry quantitative Fluorometry quantitative
6	GALT	3,5 U/g Hb	Fluorometry quantitative
7	GALT	3,5 U/g Hb	Fluorometry quantitative
8	GALT galactose	<20 % Tagesmittel >15 mg/dl (ab Juni >18 mg/dl)	Colorimetry non Kit Fluoro quant non kit
9	GALT galactose	<2,3U/gHb 20mg/dl	BiORAD Quantase BIORAD Quantase
9	GALT galactose	<2,3U/gHb 20mg/dl	BiORAD Quantase BIORAD Quantase
10	Galakrose GALT	1111µmol/l 2,3U/gHb	BiORAD Quantase BIORAD Quantase
12	GALT galactose	< 30% 15 mg/dl	Colorimtrie non Kit Fluoro. quant.(non-kit)
13	GALT galactose	< 30% 15 mg/dl	Colorimtrie non Kit Fluoro. quant.(non-kit)
14	GALT galactose	<2,3 U/g Hb >15mg/dl	BIORAD Quantase BIORAD Quantase
15	GALT galactose	<2,3 U/g Hb >15mg/dl	BIORAD Quantase BIORAD Quantase

9.5 MS/MS

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

9.6 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 in days)	
3	17 OHP	AutoDELFIA	yes			ln(OHP) = 2,90798 –0,40653* ln(Age in days)	
5	17 OHP	AutoDELFIA		yes		MeWoGert * 0,75 (17OHP test B015112)	40
6	17 OHP	DELFIA		yes			40
7	17 OHP	AutoDELFIA					40
8	17 OHP	DELFIA					50
9	17 OHP	AutoDELFIA		yes			50
10	17 OHP	AutoDELFIA					
11	17 OHP	DELFIA	yes				
12	17 OHP	AutoDELFIA	yes		yes		
13	17 OHP	AutoDELFIA	yes		yes		
14	17 OHP	AutoDELFIA	yes		yes		40
15	17 OHP	AutoDELFIA	yes		yes		40

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 in days)	
3	17 OHP	AutoDELFIA	Yes	Yes		ln(OHP) = 3,470 –0,121* ln(Age in days)	
5	17 OHP	AutoDELFIA		Yes		Before discharge, i.e. 36-38.corrected-WoG	40
6	17 OHP	DELFIA		Yes			
7	17 OHP	AutoDELFIA			Yes		
8*	17 OHP	DELFIA		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: Cut off depends on gestational age. If unknown, cut off depends on the birth weight

9.7 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.

9.7.1 PKU

Parameter /Cut off	1	3*	5	6	7	8	9	10	11	12	14
Phe	120	LW	150	150	150	150	123	150	128	120	120
Tyr								NW		NW	
Phe/Tyr	NW	NW	NW	NW	2,5	2,5	NW	NW	2,2	2,0	NW

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.2 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	239	LW	NW
Leu/Ile	263	LW	z >= 3,5	345	300	400	299	314	305	LW	300
Fischer-Q	NW			NW					3,6	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	

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.3 MCAD- Deficiency

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C0								NW			
C6	NW	NW	NW		0,18	NW	NW	NW	NW	LW	NW
C8	0,28	LW	z >= 3,5	0,230	0,40	0,3	0,28	0,3	0,24	LW	0,34
C8/C10	NW	LW	NW	NW		5,0	NW	NW	3,48	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	NW	LW	NW
C8/C2	NW			NW		0,02	NW				NW
C8/C6			NW				NW			LW	

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.4 LCHAD- Deficiency

Parameter / Cut off	1	3*	5**	6	7	8	9	10	11	12	14
C0								NW			
C14:1			NW	NW		NW		NW	NW	NW	
C14OH			NW	0,041			NW	NW	NW	LW	
C16OH	0,08	LW	z >= 3,5	0,07	0,11	0,1	0,1	0,15	0,058	LW	0,60
C16:1OH			NW	NW			NW	NW		LW	NW
C18OH	0,04	NW		0,04	0,1	NW	0,07	NW	0,031	LW	NW
C18:1OH	0,05	NW	z >= 3,5	NW	0,1	0,1	0,11	NW	0,048	LW	NW
C18:2OH						NW		NW			NW
C16OH/C16		NW	NW					NW	0,025		

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

** Z values based on > 10.000 card (s. MCAD)

9.7.5 VLCAD- Deficiency

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C0								NW			
C12										LW	
C14	NW	NW	NW	NW	0,65	NW	NW	NW	0,360	LW	NW
C14:1	0,43	LW	z >= 3,5	0,245	0,4	0,3	0,43	0,36	0,180	LW	0,25
C16:1							NW	NW			
C14:2	NW	NW		NW	NW	NW			0,030	LW	NW
C14:1/C16	NW	LW	NW	NW					0,073		
C14/C4								NW			NW
C14:1/C4			NW				NW	NW		LW	NW
C14:1/C12:1						NW					

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.6 CPT I Deficiency

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C0	NW	LW	NW	54,06	70	80	65,49	50	NW	NW	NW
C8											
C16	0,94	LW	NW	8,228	<0,6		LW	0,56	0,71	LW	<1
C18	0,24	NW	NW	2,249	<0,3		LW	0,21	0,19	LW	NW
C18:1	0,43			3,604				NW	0,26	LW	
C16/C2											
(C16+C18:1)/C2				NW							
C0/(C16+C18)	NW	NW	>= 70	NW		40	LW		16,1	LW	NW

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.7 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	4,5	NW	NW
C16	7,84	LW	NW	8,228	8,0	8	7,65	8,83	8,8	LW	>6
C16:1					0,6		0,67	NW		LW	NW
C18	2,27			2,249	2,6		2,34	3,65	2,2	LW	>2,5
C18:1	3	LW	NW	3,604	3,5	3,4	1,92	NW	3,02	LW	NW
(C16+C18:1)/C2	NW	NW	z >= 3,5			0,3	NW	20,3	NW		
C18:2								NW		LW	
C0/(C16+C18)				NW			NW	NW			

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.8 CACT- Deficiency

Parameter / Cut off	1	3*	10	5	6	7	8	9	11	12	14
AC ges			NW					NW			
C0	NW	NW	NW		NW		< 25	NW	4,5	LW	NW
C16	7,84	LW	8,83	NW	8,228	8,0	8,0	7,65	8,8	LW	>6
C16:1			NW					NW		LW	NW
C18	2,27		2,65		2,249	2,6	2,5	2,34	2,2	LW	NW
C18:1	3	LW	3,9	NW	3,604	3,5			3,02	LW	NW
(C16+C18:1)/C2	NW	NW	NW	z >= 3,5					NW		NW
C18:2										LW	
C0/AC ges			NW								
C0/(C16+C18)			NW		NW			NW			
C0/(C16+C18:1)			NW					NW			

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.9 Glutaric acidaemia type I

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C5DC (Glut)	0,12	LW	z >= 3,0	0,666	0,33	0,20	0,17	0,25	0,54	LW	<0,15
C5DC/C0	NW			NW		NW					
C5DC/C2	NW									LW	
C5DC/C4	NW		NW	NW				NW		LW	
C5DC/C8	NW	NW	NW	NW	5,9		NW	NW			NW
C5DC/C12	NW	NW	NW						NW	LW	
C5DC/C16			NW	NW			NW	NW	NW	LW	NW
C5DC/(C8+C10)		NW									

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

9.7.10 Isovaleric acidaemia

Parameter / Cut off	1	3*	5	6	7	8	9	10	11	12	14
C0								NW			
C5	0,38	LW	z >= 3,5	0,53	1	0,5	0,63	0,6	0,36	LW	0,6
C5/C2			NW	NW		0,02	NW				
C5/C3								NW			NW
C5/C8	NW	NW		NW	NW			NW	NW	LW	
C5/C4	NW	NW	NW	NW				NW	NW	LW	

* Quarterly adaptation of cut off values depending on kit charge and machine status on the basis of all results > 32 gestational age and > 36 hours.

10 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
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3. Nennstiel-Ratzel U, Liebl B, Zapf A. Modellprojekt zur Neuordnung des Neugeborenen-Screening in Bayern. Gesundheitswesen 2003 Mar;65 Suppl 1:S31-5.

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