



Biotinidase-Mangel

Regionaler Anstieg der Inzidenz

Ursachen ???

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Methoden der Biotinidase-Bestimmung im Neugeborenen-Screening

1. Klassische Methode

Biotinyl-p-Aminobenzoesäure



Biotinidase

p-Aminobenzoesäure



Natrium Nitrit & Naphtylethylendiamin



rotvioletter Azofarbstoff

2. Fluorimetrische Methode

Biotinyl-6-Aminoquinolin



Biotinidase

6-Aminoquinolin



1968 – 2009

Klassische Methode (visuell)



2009 – 2013

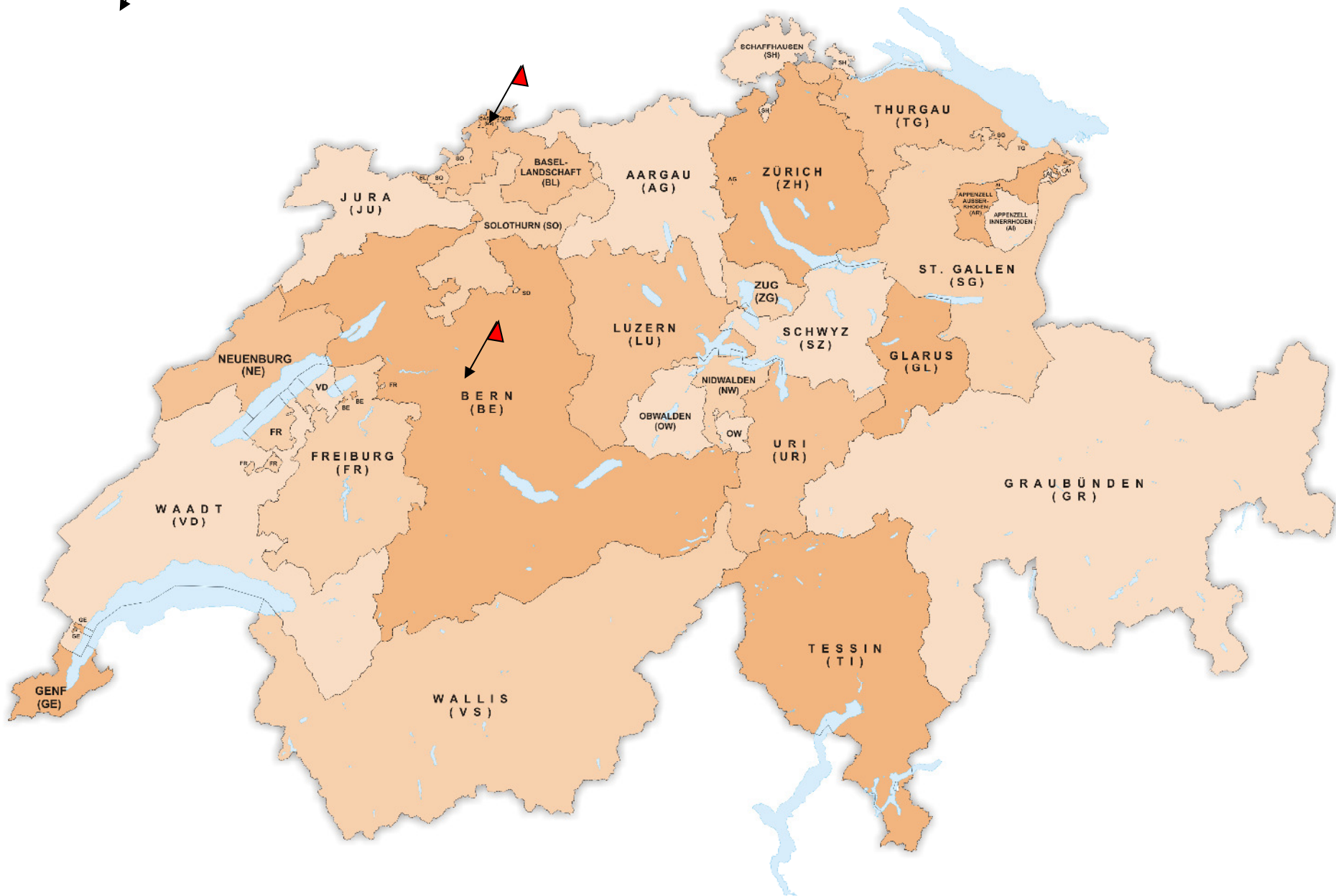
Flourimetrische Methode (Victor)





Seit 2013

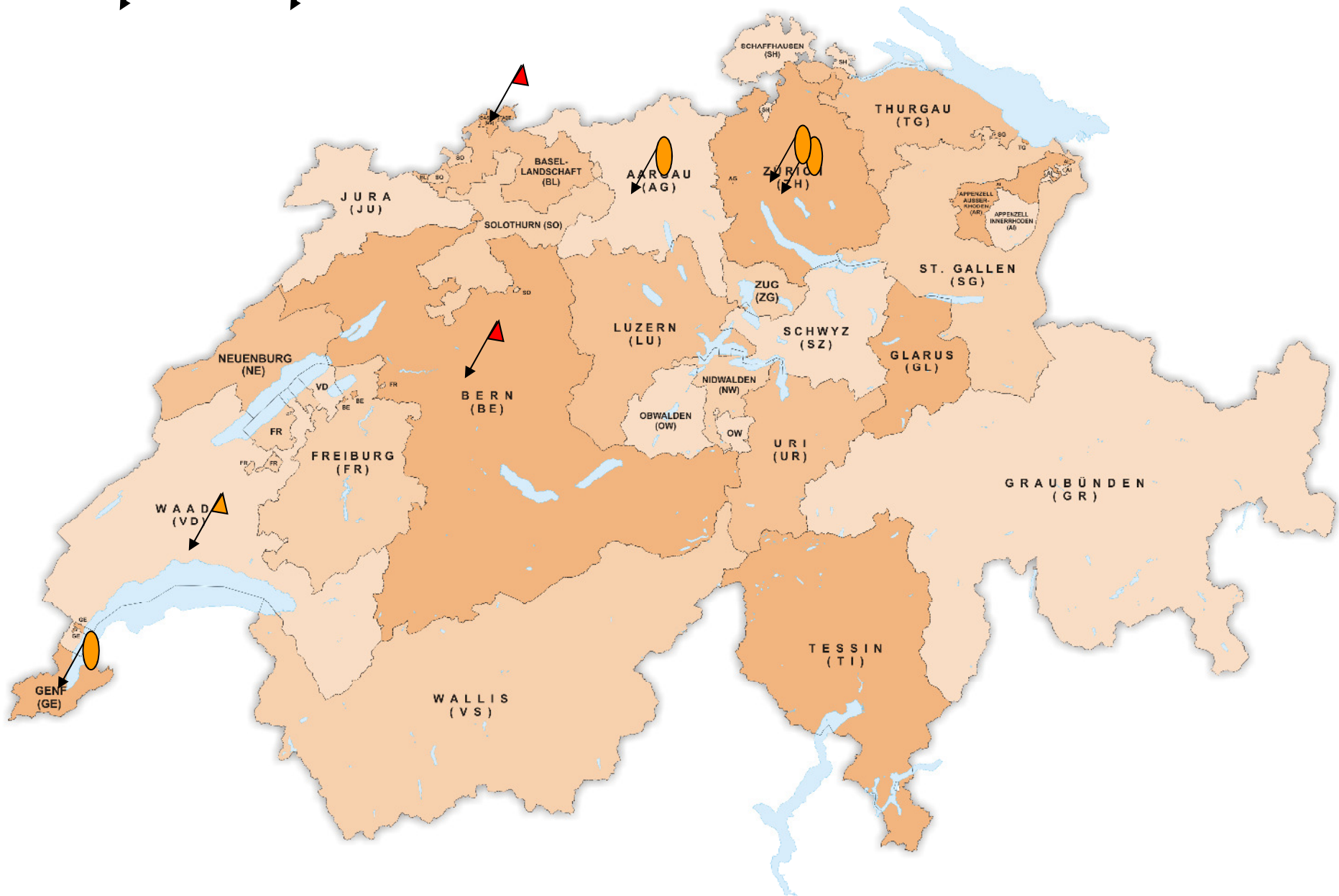
Immunologische (GSP)



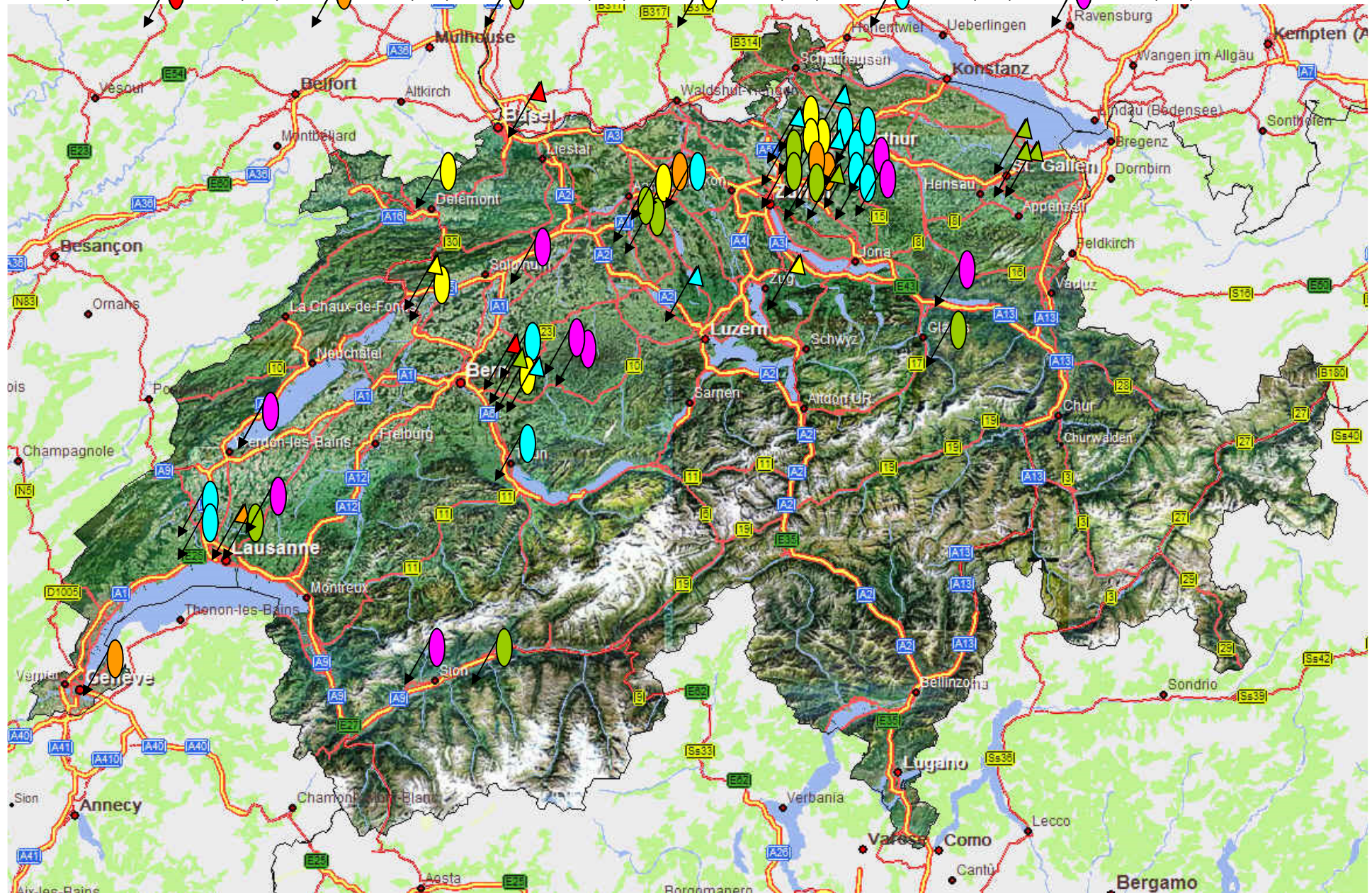
kompl.  2009 (n=2)
part.  2009 (n=0)



kompl.  2009 (n=2)  2010 (n=1)
 part.  2009 (n=0)  2010 (n=4)



kompl. \blacktriangle 2009 (n=2) \blacktriangle 2010 (n=1) \blacktriangle 2011 (n=5) \blacktriangle 2012 (n=2) \blacktriangle 2013 (n=5) \blacktriangle 2014 (n=0)
 part. \bullet 2009 (n=0) \bullet 2010 (n=4) \bullet 2011 (n=8) \bullet 2012 (n=7) \bullet 2013 (n=9) \bullet 2014 (n=9)





Jahr	n	MW	Median	0.1%	0.2%	75 U	30% dMW
1987-2004	1'548'151	-	-	-	-	-	-
2005	76'129	-	-	-	-	-	-
2006	76'209	-	-	-	-	-	-
2007	77'259	-	-	-	-	-	-
2008	79'736	-	-	-	-	-	-
2009	75'497	257	252	58	77	0.19%	77
2010	85'454	263	252	60	75	0.20%	79
2011	85'118	288	278	54	68	0.28%	86
2012	86'630	241	236	61	77	0.18%	72
2013	85'527	220	218	64	74	0.22%	66
<i>fluor.</i>	<i>27'431</i>	<i>226</i>	<i>224</i>	<i>73</i>	<i>89</i>	<i>0.11%</i>	<i>68</i>
<i>immun.</i>	<i>60'019</i>	<i>217</i>	<i>213</i>	<i>62</i>	<i>72</i>	<i>0.27%</i>	<i>65</i>
2014	86'339	230	228	64	74	0.21%	68



Jahr	n	part.	kompl.	(p & k)	Inz. (p-kum)	Inz. (k.-kum)	Inz (kum.)	n (kum)
1987-2004	1'548'151	2	19	21	774'076	81'482	73'721	1'548'151
2005	76'129	0	1	1	812'140	81'214	73'831	1'624'280
2006	76'209	0	0	0	850'245	85'024	77'295	1'700'489
2007	77'259	1	1	2	592'583	84'655	74'073	1'777'748
2008	79'736	0	1	1	619'161	84'431	74'299	1'857'484
2009	75'497	0	2	2	644'327	80'541	71'592	1'932'981
2010	85'454	4	1	5	288'348	80'737	63'076	2'018'435
2011	85'118	8	5	13	140'237	70'118	46'746	2'103'553
2012	86'630	7	2	9	99'554	68'443	40'559	2'190'183
2013	85'527	9	5	14	73'410	61'506	33'466	2'275'710
fluor.	27'431							
immun.	60'019							
2014	86'339	9	0	9	59'051	63'839	30'676	2'362'049
<i>Gesamt</i>	2'362'049	40	37	77	59'051	63'839	30'676	2'362'049
2011-2014							7'636	343'614



Lab.	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø / a	n / a (ca.)
1	-	1	1	1	1	2	-	2	-	2	0.8	52'000
2	-	-	-									
3	4	2	-	1	-	1	-	-	-	1	0.8	16'000
4	3	-										
5	-	1	-	1	1	1	-	-	-	-	0.4	53'000
6	-	-	-	1	-	1	1	1	-	-	0.4	13'000
7	-	-	2	2	1	1	-	2	1	-	0.9	45'000
8	24	27	18	11	23	21	17	13	26	15	18.0	160'000
9	-	3	4	1	1	2	2	-	4	-	1.7	110'000
10	1	-	-	-	2	1	2	2	1	-	0.9	35'000
11	-	-	-	-	-	-	-	-	1	-	0.1	17'000
12	-	1	2	-	2	1	4	-	1	-	1.1	80'000
13	4	-	1	-	-	2	1	-	3	1	1.1	65'000
14	-	1	1	-	-	-	1	-	-	-	0.3	25'000
15	-	-	-	-	-	-	-	1	1	2	0.2	9'000





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**IMPROVED IDENTIFICATION OF PARTIAL
BIOTINIDASE DEFICIENCY BY NEWBORN
SCREENING USING AGE-RELATED ENZYME
ACTIVITY CUTOFFS: REDUCTION OF THE FALSE-
POSITIVE RATE**

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Harry Hawkins¹, Bonita Taffe¹⁺





Michigan Newborn Screening Programm

Gesamt-Inzidenz des Biotinidase-Mangels

D444H

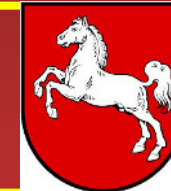
2008 → 1 : 15'000

2012 → 1 : 6'000



2011-2014 → 1 : 7'600

2004-2013 → 1 : 9'000





Wer hat Interesse an einer Studie teilzunehmen ?

Nachverfolgen bereits diagnostizierter Fälle ?

Mutationsanalytik möglichst aller Fälle

Zusammenstellung aller Daten

Ergebnisse:

Verbesserung / Vereinheitlichung

Müssen/Sollen wir den partiellen
Biotinidase-Mangel im NGS finden ?



