CAH Nomenclature Update 2024

The **CAH StripAssay®** (REF 4-380, 4-380-A, 4-380-TRIAL) is a qualitative genetic test for the targeted analysis of 11 common mutations in the CYP21A2 gene causing congenital adrenal hyperplasia (CAH). The test is used as an aid to confirm the presence of CYP21A2 mutations in patients with a suspected diagnosis of CAH and as a second-tier diagnostic test in newborn screening programs. In addition, approximately 50% of large deletions or conversions can be detected. CYP21A1P/CYP21A2 chimeric genes with a junction site downstream cluster E6 and complete heterozygous CYP21A2 deletions will not be detected.

The CYP21A2 gene may harbour polymorphisms affecting the numbering of oligonucleotides and codons. Thus, differences in nomenclature exist in the literature which result from different reference sequences. ViennaLab uses the RefSeq NM_000500.9 as it is recommended by the EMQN guidelines (Baumgartner-Parzer et al., 2020) for genetic testing of 21-OHP deficiency. Beginning with RefSeq NM_000500.7 there was a shift of three nucleotides, thus P30L (c.89C>T) became P31L (c.92C>T) etc.

Gene name: Steroid 21-hydroxylase
Gene abbreviation: CYP21A2

Legacy name			**HGVS nomenclature**		**RefSNP**
new		old	new (NM_000500.9)	old (NM_000500.6)	
P31L		(P30L)	c.92C>T	c.89C>T	rs9378251
I2 splice		I2 splice	c.293-13A/C>G	c.290-13A/C>G	rs6467
Del 8 bp E3		Del 8 bp E3	c.332_339del	c.329_336delGAGACTAC	rs387906510
I173N		(I172N)	c.518T>A	c.515T>A	rs6475
Cluster E6	I237N	(I236N)	c.707T>A	c.707T>A	rs111647200
	V238E	(V237E)	c.710T>A	c.710T>A	rs12530380
	M240K	(M239K)	c.716T>A	c.716T>A	rs6476
V282L		(V281L)	c.844G>T	c.841G>T	rs6471
L308fs		(L307fs)	c.923dup	c.920_921insT	rs267606756
Q319X		(Q318X)	c.955C>T	c.952C>T	rs7755898
R357W		(R356W)	c.1069C>T	c.1066C>T	rs7769409
P454S		(P453S)	c.1360C>T	c.1357C>T	rs6445
R484P		(R483P)	c.1451G>C	c.1448G>C	rs200005406

Twenty to 25% of pathogenic variants are large CYP21A2 deletions, duplications or chimeric genes. Therefore, assessment of the CYP21A2 copy number variation (CNV) is crucial for diagnosis. The combination of both, CAH StripAssay® and CAH RealFast™ CNV Assay, is a faster and more cost-efficient targeted analysis compared to sequencing the whole gene and CNV analysis by MLPA. In total, ViennaLab CAH assays have a detection rate of up to 94%.