

Variant Under Assessment (VUA)	Baseline computational/ predictive code applicable to VUA	Position of comparison variant relative to VUA	PS1 code applicable to VUA	
			with P comparison variant	with LP comparison variant
Located <u>outside</u> splice donor/ acceptor +/- 1,2 dinucleotide positions	PP3	same nucleotide	PS1	PS1_Moderate
	PP3	within same splice donor/acceptor motif (including at +/- 1,2 positions)	PS1_Moderate	PS1_Supporting
Located at splice donor/acceptor +/- 1,2 dinucleotide positions	PVS1	within same splice donor/ acceptor +/- 1,2 dinucleotide	PS1_Supporting	N/A
	PVS1	within same splice donor/acceptor region, but outside +/- 1,2 dinucleotide	PS1_Supporting	PS1_Supporting
	PVS1_Strong, PVS1_Moderate, or PVS1_Supporting	within same splice donor/ acceptor +/- 1,2 dinucleotide	PS1	N/A
	PVS1_Strong, PVS1_Moderate, or PVS1_Supporting	within same splice donor/acceptor motif, but outside +/- 1,2 dinucleotide	PS1_Moderate	PS1_Supporting

Table 2. PS1 code weights for variants with same predicted splicing event as a known (likely) pathogenic variant

Table taken from Walker et al, 2023. Using the ACMG/AMP framework to capture evidence related to predicted and observed impact on splicing: Recommendations from the ClinGen SVI Splicing Subgroup. Am J Hum Genet. 2023 Jul 6;110(7):1046-1067. PMID: 37352859