PP4

Patient's phenotype or family history is highly specific for a disease with a single genetic etiology.

- PP4 applicability and strength is determined by the total points accumulated by a single affected individual according to the table below and the following total point ranges:
  - <1 point: PP4 not met
  - 1-<2 points: PP4
  - ≥2-<4 points: PP4_Moderate
  - ≥4 points: PP4_Strong[1]

Evidence Description	Points
Diagnostic criteria met for SCID (Criteria 1 and 3 or Criterion 4 by itself) or Leaky SCID/Omenn syndrome (excluding Criterion 2)[1]	0.5
SCID gene panel or exome/genome sequencing conducted (only applicable if genetic testing did not provide an alternative genetic explanation for SCID/Leaky SCID/Omenn syndrome phenotype)	1
Family history of SCID (only applicable if SCID gene panel or exome/genome sequencing was conducted on proband and did not provide an alternative genetic explanation for phenotype)	0.5
Decreased presence of TCRVα7.2 (<2%) in CD3+ T lymphocytes and/or mucosa-associated invariant T-cells demonstrated by flow cytometry AND pathogenic or likely pathogenic variants in RAG2 and DCLRE1C have been excluded PMID: 39792639	1.5
Decreased presence of TCRVα7.2 (<2%) in CD3+ T lymphocytes and/or mucosa-associated invariant T-cells demonstrated by flow cytometry AND pathogenic or likely pathogenic variants in RAG2 and DCLRE1C have **NOT** been excluded PMID: 39792639	0.5
Increased presence of 9G4+ (>10%), 9G4int (>5%) or 9G4hi (>5%) cells in CD19+ B cells demonstrated by flow cytometry AND pathogenic or likely pathogenic variants in RAG2 have been excluded PMID: 39792639	1
Increased presence of 9G4+ (>10%), 9G4int (>5%) or 9G4hi (>5%) cells in CD19+ B cells demonstrated by flow cytometry AND pathogenic or likely pathogenic variants in RAG2 have **NOT** been excluded PMID: 39792639	0.5
SCID phenotype corrected by RAG1 gene therapy	4
T-B-NK+ lymphocyte subset profile* (See notes)	0.5

[1]The diagnostic criteria should follow the PIDTC 2022 specification, summarized here. *Notes: 1) If NK cells are not noted or are present, criteria may still be applied if SCID gene panel or exome/genome sequencing has ruled out alternative causes; 2) If maternal T cells are present, the T lymphocyte profile is still considered to be T- (autologous T cells are absent).