**Assigning copy number variant significance**

**QC validated CNV**

Known benign CNV or common CNV?

YES \*

NO

\*except 15q11.2 reported as UCS

UCS or CS

3 dup or 5 del cases in DGV/CHOP/ISCA benign?

YES

NO

Known microdeletion /duplication syndrome clinically relevant? OMIM, Gene Reviews?

NO

Same / similar

size?

YES

OMIM Genes present?

NO -

YES

YES

check ClinVar, ISCAPath,

UCSC, DECIPHER literature

Novel dup/del with clear human pathogenic evidence, (for example gene dosage)

Possible pathogenic association?

(gene function related to phenotype, or susceptibility locus)

NO -

NO -

YES

≥ 500kb, OMIM genes but no human pathogenic assoc

YES

UCS, likely pathogenic

Uncertain clinical significance, UCS.

(optional – LB, likely benign and LP, likely pathogenic)

Thought to be benign,

TBB

Clinically significant, CS