Exception variant reporting

In UK labs, there are certain genes in which only certain types of (likely) pathogenic variants are reported when the indication for testing is cancer predisposition, because of the underlying mechanism of disease or low associated disease penetrance.

The table here below outlines gene-specific reporting, indicating those variants, or regions of the gene in question that are explicitly included or excluded from analysis, when testing is undertaken in a UK laboratory.

It is not feasible to maintain a formal whitelist of exception variants, but laboratory teams are encouraged to communicate rationale for reporting of non-standard variants via CanVar-UK.

Gene	**Current expected practice in variant reporting**
APC	*APC* c.3920T>A; p.Ile1307Lys (I1307K) **excluded** from analysis/reporting
ATM	Reporting restricted to truncating variants and c.7271T>G[#]
CHEK2	Reporting restricted to truncating variants and c.349A>G p.(Arg117Gly)*
EPCAM	Reporting restricted to 3' CNV
GREM1	Copy number analysis only to check for duplication involving the 3' end of the *SCG5* gene & a region upstream of the *GREM1* gene
POLE	Reporting restricted to missense variants in exonuclease domain, exons 9-14 (cancer predisposition)
POLD1	Reporting restricted to missense variants in exonuclease domain, exons 6-13 (cancer predisposition)
RAD51C	Reporting restricted to truncating variants*
RAD51D	Reporting restricted to truncating variants*
RET	Reporting (for MEN2) restricted to exons 5, 7, 8, 10, 11,13-16

Please refer to UKCGG/CStAG statement on reporting practice for variants in ATM v.2.2 08/10/2025

Please refer to UKCGG/CStAG statement on reporting practice for variants in “moderate risk” breast cancer susceptibility genes v.1 08/10/2025