CLAIMS

1. A variant IgG4 antibody which has been modified in the heavy chain constant region, wherein the variant IgG4 antibody has a reduced level of binding to host cell protein (HCP), compared to an unmodified IgG4 antibody, wherein the modification comprises substitution of R222 to T or K; and/or replacement of YGPP (SEQ ID NO: 23) (Kabat residues 229 to 238) with CCVE (SEQ ID NO:25).

2. The variant IgG4 antibody according to claim 1, wherein the modification further comprises:

(a) substitution of one or more amino acids comprising K203 to R, E, or Q; R222 to Q; E226 to L or I; S227 to R, P, A, N, or T; Y229 to S, F, W, or H; G230 to C, A, N, or S; P237 to H, E, D, or V; and/or P238 to T, K, or E; and/or

(b) replacement of ESKYGPP (SEQ ID NO: 26) (Kabat residues 226 to 238) with EPKSCDKTHT (SEQ ID NO: 27), or ERKYGPP (SEQ ID NO: 28), or ERKCCVE (SEQ ID NO: 29), or ELKTPLGDTTHT (SEQ ID NO: 30); and/or

(c) replacement of YGPP (SEQ ID NO: 23) (Kabat residues 229 to 238) with SCDKTHT (SEQ ID NO: 24).

3. The variant IgG4 antibody according to claim 1 or 2, wherein the IgG4 antibody has reduced binding affinity and/or binding activity to host cell protein (HCP) in comparison to the unmodified IgG4 antibody.

4. The variant IgG4 antibody according to any one of claims 1 to 3, wherein the variant IgG4 antibody comprises a further substitution of S241 to P and/or L248 to E and/or replacement of EFLGGP (SEQ ID NO: 31) (Kabat residues 246 to 251) with PAAAP (SEQ ID NO: 33) or PAAAS (SEQ ID NO: 32).

5. The variant IgG4 antibody according to any one of claims 1 to 4, wherein the variant IgG4 antibody comprises the sequence CPPC (SEQ ID NO: 20) (Kabat residues 239 to 242).

6. The variant IgG4 antibody according to any one of claims 1 to 5, wherein no further modifications are made in the heavy chain constant region in comparison to the unmodified IgG4 antibody.

7. The variant IgG4 antibody according to any one of claims 1 to 6, wherein the host cell protein is putative phospholipase B-Like 2 (PLBL2).

8. A cell line encoding the variant IgG4 antibody of any one of claims 1 to 7.

9. A method of reducing binding of an IgG4 antibody to host cell protein (HCP) comprising modifying the antibody sequence in the heavy chain constant region, wherein the modification comprises:

(a) substitution of one or more amino acids comprising K203 to Q; R222 to T or K; E226 to L; S227 to R; P237 to H or E; and/or P238 to T; and/or

(b) replacement of ESKYGPP (SEQ ID NO: 26) (Kabat residues 226 to 238) with EPKSCDKTHT (SEQ ID NO: 27), or ERKYGPP (SEQ ID NO: 28), or ERKCCVE (SEQ ID NO: 29), or ELKTPLGDTTHT (SEQ ID NO: 30); and/or

(c) replacement of YGPP (SEQ ID NO: 23) (Kabat residues 229 to 238) with SCDKTHT (SEQ ID NO: 24), or CCVE (SEQ ID NO: 25).

10. The method according to claim 9, wherein the host cell protein is putative phospholipase B-Like 2 (PLBL2).

11. A composition comprising the variant IgG4 antibody according to any one of claims 1 to 7.

12. The composition according to claim 11, wherein the variant IgG4 antibody is at a concentration of at least 10mg/mL, at least 20 mg/mL, at least 50mg/mL, at least 75mg/mL or at least 100mg/mL.

13. The composition according to claim 11 or claim 12, wherein the concentration of putative phospholipase B-Like 2 (PLBL2) in the composition is less than 500ppm, less than 100ppm or less than 10ppm.

14. The composition according to any one of claims 11 to 13, which additionally comprises a buffer and/or a fatty acid ester; optionally wherein the fatty acid ester is Polysorbate 20 or Polysorbate 80.