Chapman, 2002, Advanced Drug Delivery Reviews, 54, 531-545). Thus, for example, where the product is intended to leave the circulation and penetrate tissue, for example for use in the treatment of a tumour, it may be advantageous to use a small molecular weight polymer, for example with a molecular weight of around 5000Da. For applications where the product remains in the circulation, it may be advantageous to use a higher molecular weight polymer, for example having a molecular weight in the range from 20000Da to 40000Da.

Suitable polymers include a polyalkylene polymer, such as a poly(ethyleneglycol) or, especially, a methoxypoly(ethyleneglycol) or a derivative thereof, and especially with a molecular weight in the range from about 15000Da to about 40000Da.

In one example an antibody for use in the present invention is attached to poly(ethyleneglycol) (PEG) moieties. In one particular example the PEG molecules may be attached through any available amino acid side-chain or terminal amino acid functional group located in the antibody, for example any free amino, imino, thiol, hydroxyl or carboxyl group. Such amino acids may occur naturally in the antibody or may be engineered into the antibody using recombinant DNA methods (see for example US 5,219,996; US 5,667,425; WO 98/25971). In one example the molecule of the present invention is a modified antibody wherein the modification is the addition to the C-terminal end of its heavy chain one or more amino acids to allow the attachment of an effector molecule. Multiple sites can be used to attach two or more PEG molecules.

In one embodiment a PEG molecule is linked to a cysteine 171 in the light chain, for example see WO2008/038024 ~~incorporated herein by reference~~.

Suitably PEG molecules are covalently linked through a thiol group of at least one cysteine residue located in the antibody. Each polymer molecule attached to the modified antibody may be covalently linked to the sulphur atom of a cysteine residue located in the antibody. The covalent linkage will generally be a disulphide bond or, in particular, a sulphur-carbon bond. Where a thiol group is used as the point of attachment appropriately activated effector molecules, for example thiol selective derivatives such as maleimides and cysteine derivatives may be used. An activated polymer may be used as the starting material in the preparation of polymer-modified antibody as described above. The activated polymer may be any polymer containing

8. The antibody according to any of claim 1 to 6, wherein the cysteine at position 239, numbered according to the Kabat numbering system, in the heavy chain is substituted with another amino acid.

9. The antibody according to any of claims 1 to 6, wherein the cysteine at position 242, numbered according to the Kabat numbering system, in the heavy chain is substituted with another amino acid.

~~10. An antibody of the class IgG4 comprising at least one heavy chain which comprises a $C_H1$ domain and a hinge region, wherein in each heavy chain:~~

~~a. the inter-chain cysteine at position 127, numbered according to the Kabat numbering system, is substituted with another amino acid; and~~

~~b. the cysteine at position 239 or the cysteine at position 242, numbered according to the Kabat numbering system, is substituted with another amino acid.~~

~~11.~~10. The antibody according to any of claims 7 to ~~10~~9, wherein the cysteine at position 239 and/or the cysteine at position 242 is substituted by a non-thiol containing amino acid.

~~12.~~11. The antibody according to claim ~~11~~10, wherein the non-thiol containing amino acid is serine.

~~13.~~12. The antibody according to any preceding claim, wherein the cysteine at position 127 is substituted by a non-thiol containing amino acid.

~~14.~~13. The antibody according to claim ~~13~~12, wherein the non-thiol containing amino acid is serine.

~~15.~~14. The antibody according to any preceding claim, wherein the heavy chain is mutated to insert three amino acids between amino acids 226-243, numbered according to the Kabat numbering system.

~~16.~~15. The antibody according to claim ~~15~~14, wherein the heavy chain is mutated to insert three amino acids between positions 238 and 239, numbered according to the Kabat numbering system.

~~17.~~16. The antibody according to claim ~~16~~15, wherein three alanines are inserted between positions 238 and 239, numbered according to the Kabat numbering system.

~~18.~~17. The antibody according to claim ~~16~~15, wherein a threonine, a histidine and a further theronine are inserted between positions 238 and 239, numbered according to the Kabat numbering system.

~~19.~~18. The antibody according to any preceding claim, wherein the serine at position 241, numbered according to the Kabat numbering system, is substituted with proline.

~~20.~~19. The antibody according to any preceding claim, wherein the glycine at position 230 is substituted with cysteine, the serine at position 227 is substituted with proline, the tyrosine at position 229 is substituted with serine, the proline at position 237 is substituted with aspartic acid, the proline at position 238 is substituted with lysine, the amino acid sequence threonine-histidine-threonine is inserted between positions 238 and 239 and the serine at position 241 is substituted with proline.

~~21.~~20. The antibody according to any preceding claim, wherein the heavy chain comprises a CH2 domain and a CH3 domain.

~~22.~~21. The antibody according to any preceding claim, wherein the antibody comprises two heavy chains and as defined in any preceding claim.

~~23.~~22. The antibody according to claim ~~22~~21, wherein the heavy chains are identical.

~~24.~~23. The antibody according to any one of claims 1 to ~~23~~22, wherein the heavy chain or each heavy chain comprises an upper hinge region and core region from residue 226 to residue 243 according to the Kabat numbering system of 12 to 17 amino acids in length.

~~25.~~24. The antibody according to claim ~~24~~23, wherein the upper hinge and core region is of 15 amino acids in length.

~~26.~~25. An expression vector comprising a sequence which encodes an antibody as defined in any one of claims 1 to ~~25~~24.

~~27.~~26. A host cell comprising a vector as defined in claim ~~26~~25.

~~28.~~27. An antibody as defined in any one of claims 1 to ~~25~~ 24 for use in the treatment of a disease or disorder.

~~29.~~28. Use of an antibody as defined in any one of claims 1 to 24 in the manufacture of a medicament ~~A method~~ for the treatment of a disease or disorder ~~comprising administering a therapeutically effective amount of an antibody as defined in any one of claims 1 to 25~~.

~~30. An IgG4 antibody, comprising a heavy chain with an upper hinge, core and lower hinge, and said upper hinge and core in the heavy chain or each heavy chain therein is 12 to 17, such as 15 amino acids in length.~~