CLAIMS

1. An immunoglobulin single variable domain which is a heavy-chain variable domain that has at its C-terminal region

   (i) the amino acid residue valine (V) at position 11, wherein the amino acid residues are numbered according to Kabat numbering; and

   (ii) 1 to 10 amino acid residues added to the C-terminal amino acid sequence VTVSS (SEQ ID NO: 33) of the immunoglobulin single variable domain, each independently chosen from any naturally occurring amino acids.

2. The immunoglobulin single variable domain according to claim 1 that has at its C-terminal region

   (i) in addition to the amino acid residue valine (V) at position 11, one or more amino acid residues selected from glutamine (Q) at position 110, glycine (G) at position 112 and glycine (G) at position 113, wherein the amino acid residues are numbered according to Kabat numbering; and

   (ii) 1 to 10 amino acid residues added to the C-terminal amino acid sequence VTVSS (SEQ ID NO: 33) of the immunoglobulin single variable domain, each independently chosen from any naturally occurring amino acids.

3. The immunoglobulin single variable domain according to claim 1 or claim 2, which has at its C-terminal region

   (i) in addition to the amino acid residue valine (V) at position 11, one or more amino acid residues selected from glutamine (Q) at position 110, glycine (G) at position 112 and glycine (G) at position 113, wherein the amino acid residues are numbered according to Kabat numbering; and

   (ii) 1, 2, 3, 4 or 5 amino acid residues added to the C-terminal amino acid sequence VTVSS (SEQ ID NO: 33) of the immunoglobulin single variable domain, each independently chosen from any naturally occurring amino acids.

4. The immunoglobulin single variable domain according to any one of claims 1 to 3, in which the naturally occurring amino acids are independently chosen from alanine, glycine, valine, leucine or isoleucine.

5. The immunoglobulin single variable domain according to any one of the preceding claims, which has the sequence VTVSS(X)n at its C-terminus, wherein

a) n = 1, 2 or 3 in which each X = Ala or Gly; or
b) n = 1, 2 or 3 in which each X = Ala; or
c) n = 1, 2 or 3 in which each X = Gly; or
d) n = 2 or 3 in which at least one X = Ala or Gly; or
e) n = 2 or 3 in which all but one X = Ala or Gly.

6. The immunoglobulin single variable domain according to any one of the preceding claims, which has the sequence VTVSS(X)n at its C-terminus, wherein:
   a) X is Ala and n is 1, 2 or 3; or
   b) X is Gly and n is 1, 2 or 3.

7. The immunoglobulin single variable domain according to any one of the preceding claims, which has the sequence VTVSS(X)n at its C-terminus, wherein X is Ala and n is 1.

8. An immunoglobulin single variable domain, which is a heavy-chain variable domain, having a valine (V) residue at position 11 and having the sequence VTVSS(X)n at its C-terminal end, wherein n = 1 to 10 and X represents amino acid residues that are independently chosen from naturally occurring amino acids, wherein the amino acid residues are numbered according to Kabat numbering.

9. The immunoglobulin single variable domain according to claim 8, wherein n = 1, 2, 3, 4 or 5.

10. The immunoglobulin single variable domain according to claim 8 or claim 9, wherein each X is independently chosen from alanine, glycine, valine, leucine or isoleucine.

11. The immunoglobulin single variable domain according to any one of claims 8 to 10, wherein
    a) n = 1, 2 or 3 in which each X = Ala or Gly; or
    b) n = 1, 2 or 3 in which each X = Ala; or
    c) n = 1, 2 or 3 in which each X = Gly; or
    d) n = 2 or 3 in which at least one X = Ala or Gly; or
    e) n = 2 or 3 in which all but one X = Ala or Gly.

12. The immunoglobulin single variable domain according to claim 11, wherein
    a) X is Ala and n is 1, 2 or 3; or

b) X is Gly and n is 1, 2 or 3.

13. The immunoglobulin single variable domain according to claim 12, wherein X is Ala and n is 1.

14. The immunoglobulin single variable domain according to any one of the preceding claims, that has a substantially reduced tendency (such as at least a statistically relevant reduced tendency) to give rise to protein interference, compared to the same ISV but without the modifications.

15. The immunoglobulin single variable domain according to any one of the preceding claims that has, in a surface plasmon resonance assay with a polyclonal antibody as the analytical antibody, substantially reduced ability to be bound by the polyclonal antibody, compared to the same ISV but without the modifications.

16. The immunoglobulin single variable domain according to any one of the preceding claims that has, in a bridging assay with a polyclonal antibody as the analytical antibody, substantially reduced ability to be bound by the polyclonal antibody, compared to the same ISV but without the modifications.

17. The immunoglobulin single variable domain according to any one of the preceding claims that is a humanized VHH or a camelized VH, such as a camelized human VH.

18. A protein or polypeptide which contains an ISV according to any one of claims 1 to 17 at its C-terminal end.

19. The protein or polypeptide according to claim 18, that is a bivalent, multivalent, bispecific, multispecific, biparatopic or multiparatopic ISV construct.

20. An ISV-based biological comprising one or more ISVs and further comprising one or more other therapeutic moieties and/or one or more other moieties that influence the pharmacokinetic or pharmacodynamics properties of the ISV-based biological, that has an ISV according to any one of claims 1 to 17 at its C-terminal end.

21. The ISV-based biological according to claim 20, in which the one or more other moieties influence the half-life of the ISV-based biological.

22. The ISV-based biological according to claim 20 or claim 21, in which the one or more other moieties increase the half-life of the ISV-based biological.

23. The ISV-based biological according to any one of claims 20 to 22, in which the one or more other moieties comprise a serum–albumin binding ISV.

24. An immunoglobulin single variable domain according to any one of claims 1 to 17, a protein or polypeptide according to claim 18 or claim 19, or an ISV-based biological according to any one of claims 20 to 23, for use in a method of therapy.

25. A pharmaceutical composition that comprises an immunoglobulin single variable domain according to any one of claims 1 to 17, a protein or polypeptide according to claim 18 or claim 19, or an ISV-based biological according to any one of claims 20 to 23, and at least one suitable carrier, diluent or excipient.

26. A protein, polypeptide or other biological drug that comprises at least one immunoglobulin single variable domain (ISV) at its C-terminal end, wherein said ISV is a heavy-chain variable domain that has at its C-terminal region (i) the amino acid residue valine (V) at position 11, wherein the amino acid residues are numbered according to Kabat numbering, and (ii) 1 to 5 amino acid residues added to the C-terminal amino acid sequence VTVSS (SEQ ID NO: 33) of the immunoglobulin single variable domain, each independently chosen from any naturally occurring amino acids, such that the ISV has a substantially reduced tendency to give rise to protein interference compared to the same ISV without the modifications.