

C L A I M S

1. A method for detecting and/or measuring, in a sample, anti-drug antibodies (ADA) against an ISV-based drug, in which said ISV-based drug comprises one or more immunoglobulin single variable domains (ISVs), in which each such ISV is comprised of framework regions (FRs) and complementarity determining regions (CDRs) and in which at least one of the ISVs present in the ISV-based drug is specific for one or more therapeutic targets, said method comprising performing a bridging anti-drug antibody assay in the presence of a variant of said ISV-based drug, which variant is such that it is non-functional with respect to binding to the therapeutic target(s) to which the ISV-based drug is intended to bind.
2. The method according to claim 1, wherein one or more ISVs in the variant that are intended to bind to the one or more therapeutic targets have CDR's that are different from the CDR's in the corresponding ISVs in the ISV-based drug.
3. The method according to claim 1 or 2, in which the variant has essentially the same amino acid sequence as the ISV-based drug, except for changes to the CDRs that, in the variant, remove the ability of the ISV(s) present in the variant to bind to the therapeutic target(s) of the ISV-based drug.
4. The method according to claim 3, in which the variant has a degree of sequence identity with the ISV-based drug of at least 90%, not taking into account the changes in the CDRs that, in the variant, remove the ability of the ISV(s) present in the variant to bind to the therapeutic target(s) of the ISV-based drug.
5. The method of claim 4, wherein the variant is at least 95% identical to the ISV-based drug, not taking into account the changes in the CDRs that, in the variant, remove the ability of the ISV(s) present in the variant to bind to the therapeutic target(s) of the ISV-based drug.

6. The method of claim 4, wherein the variant is at least 90% identical to the ISV-based drug, not taking into account the changes in the CDRs that, in the variant, remove the ability of the ISV(s) present in the variant to bind to the therapeutic target(s) of the ISV-based drug.
7. The method of claim 4, wherein the variant is 100% identical to the ISV-based drug, not taking into account the changes in the CDRs that, in the variant, remove the ability of the ISV(s) present in the variant to bind to the therapeutic target(s) of the ISV-based drug.
8. The method according to any one of claims 1 to 7, in which performing the bridging anti-drug antibody assay comprises the steps of:
 - a) contacting said sample with a capturing agent that is immobilized on a support, wherein said capturing agent is or essentially consists of said ISV-based drug, under conditions such that any anti-drug antibodies against the ISV-based drug binds to said capturing agent;
 - b) detecting or measuring any anti-drug antibodies that have bound to the capturing agent, by contacting the complex of the capturing agent and any captured anti-drug antibodies with a detection agent, which detection agent is or essentially consists of said ISV-based drug which is linked to a detectable label, under conditions such that said detection agent binds to any captured anti-drug antibodies and/or the complex of the capturing agent with any of the captured anti-drug antibodies.
9. The method of claim 8, in which the method comprises, prior to step b), a step of removing any components or constituents present in said sample that do not bind to the capturing agent.
10. The method according to claim 8 or 9, in which in step b), essentially only neutralizing ADAs against the ISV-based drug are detected or measured.
11. The method according to any one of claims 1 to 10, which is performed on a sample that contains, both neutralizing and non-neutralizing ADAs against the ISV-based drug.

12. The method according to any one of claims 1 to 10, which is performed on a sample that is suspected to contain both neutralizing and non-neutralizing ADAs against the ISV-based drug.
13. The method according to any one of claims 1 to 12, which is performed on a sample obtained from a human subject.
14. The method according to any one of claims 1 to 13, which is performed on a biological fluid.
15. The method according to any one of claims 1 to 14, which is performed on a sample of whole blood, serum, plasma, lymph fluid, ocular fluid, bronchoalveolar fluid/BALF, or cerebrospinal fluid.
16. The method of claim 14, in which the biological fluid comprises sputum or nasal washes.
17. The method of claim 14, in which the biological fluid comprises whole blood, serum or plasma.
18. The method according to any one of claims 1 to 17, in which the ISV-based drug has a half-life in man, expressed as $t_{1/2\beta}$, of at least 3 days.
19. The method according to any one of claims 1 to 18, in which the ISV-based drug comprises at least two ISVs.
20. The method according to any one of claims 1 to 18, in which the ISV-based drug comprises 2 ISVs.
21. The method according to any one of claims 1 to 18, in which the ISV-based drug comprises 3 ISVs.

22. The method according to any one of claims 1 to 18, in which the ISV-based drug comprises 4 ISVs.
23. The method according to any one of claims 1 to 18, in which the ISV-based drug comprises 5 ISVs.
24. The method according to any one of claims 19 to 23, in which the ISV-based drug comprises at least one ISV against serum albumin.