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(54) **Title**: SOLUBLE "HEAVY-CHAIN ONLY " ANTIBODIES

(57) **Abstract**: The present invention provides a high affinity, antigen-specific, soluble heavy chain-only antibody which: lacks hallmark camelid-related amino acid substitutions and has FR2 substitutions which are not found in antibodies which comprise heavy and light chain; shows increased net hydrophobicity within CDR1 and an increased number of charged amino acids present in CDR3; and comprises one or more amino acid substitutions within the framework β-pleated sheet leading to increased net hydrophobicity within FR1 and an increased number of charged amino acids present in FR3. Also provided are VH domains having the same properties, gene segments for their production, methods for their production, transgenic animals and uses of the antibody of the VH domains in therapy.

WO 2010/109165 A8