CLAIMS

1. An *in vitro* method for inactivating lipid-enveloped virus contaminants in a protein solution in the purification of a therapeutic protein composition, said method comprising:

providing a protein solution comprising a therapeutic protein and possibly comprising lipid-enveloped virus contaminants;

immobilizing said therapeutic protein on an ion exchange resin *in vitro*, wherein said protein is directly immobilized on said ion exchange resin;

wherein said immobilization is not in the presence of a solvent-detergent mixture, said mixture comprising a non-ionic detergent and an organic solvent; and

subsequently treating said therapeutic protein, while said therapeutic protein remains immobilized on said ion exchange resin, with a solvent-detergent mixture comprising a non-ionic detergent and an organic solvent at concentrations and for a time period suitable to effect inactivation of said lipid-enveloped virus contaminants;

wherein said solvent-detergent treatment results in reduced formation of aggregates of said therapeutic protein compared to solvent-detergent treatment when the therapeutic protein is not immobilized;

whereby said lipid-enveloped virus contaminants are inactivated.

2. The method according to claim 1, wherein said therapeutic protein is at least one selected from ADAMTS13, Factor VIII, Factor VIIa. Factor IX, von Willebrand factor, and anti-MIF antibody.

3. The method according to claim 1, wherein said ion exchange resin is selected from the group consisting of cation exchange resin, anion exchange resin, and mixed mode resin.

4. The method according to claim 1, wherein said solvent-detergent mixture comprises 1% Triton X-100, 0.3% Tri-N-butyl phosphate, and 0.3% Polysorbate 80.

5. The method according to claim 1, wherein incubation in said solvent-detergent mixture continues for 30 minutes to 1 hour.

6. The method according to claim 1, further comprising eluting said therapeutic protein from said ion exchange resin with a storage buffer.

7. The method according to claim 6, wherein said storage buffer has a pH of greater than 7.0 and comprises less than 10 mM calcium ions, a buffering compound, 0.05% non-ionic detergent, and a salt.

8. The method according to claim 1, wherein said ion exchange resin is a cation exchange resin; and

wherein there is no ultrafiltration, diafiltration, or buffer exchange step subsequent to the eluting step from the cation exchange resin with the storage buffer.

9. The method according to claim 1, wherein said ion exchange resin is an anion exchange resin.