CLAIMS

1. A method of producing a viral vaccine, the method comprising the steps of:

    a. purifying viral particles from harvested cell culture;
    b. inactivating and splitting the viral particles to produce sub-virions; and
    c. purifying the sub-virions;

wherein inactivating and splitting the viral particles of step b comprises treating the viral particles with a reagent comprising at least polysorbate 80 and at least cetrimonium bromide (CTAB), and wherein the polysorbate 80 and the CTAB are present in an amount effective to reduce particle size of the viral particles.

2. The method of claim 1, wherein the reagent further comprises at least one salt, wherein the at least one salt is present in an amount effective to reduce particle size of the viral particles.

3. The method of claim 1, wherein an average hydrodynamic radius of the sub-virions ranges from 150 nm to 350 nm.

4. The method of claim 1, wherein a concentration of the polysorbate 80 is at least 1.0 g/L.

5. The method of claim 1, wherein a concentration of the CTAB ranges from 1.25 g/L to 3.0 g/L.

6. The method of claim 2, wherein the at least one salt comprises sodium chloride (NaCl).

7. The method of claim 2, wherein the at least one salt comprises 0.1 - 200 mM NaCl.

8. The method of claim 1, wherein the particle size of the sub-virions is less than 500 nm.

9. The method of claim 1, wherein the particle size of the sub-virions is the hydrodynamic radius.

10. The method of claim 1, wherein the viral particles are from influenza virus.

11. The method of claim 1, wherein the concentration of the polysorbate 80 is 0.3 g/L prior to splitting.

12. The method of claim 1, wherein the concentration of the polysorbate 80 increases in an amount that ranges from 0.1 - 2.2 g/L during splitting.

13. The method of claim 1, wherein the concentration of the polysorbate 80 is 0.3 g/L, 1.4 g/L, or 2.5 g/L during splitting.

14. The method of claim 6, wherein a concentration of the NaCl ranging from 0.1 - 25 mM is associated with increased filtration throughput.

15. A method of reducing viral particle size in a virus manufacturing process, the method comprising the steps of:

a. purifying viral particles harvested from cell culture;
b. inactivating and splitting the viral particles to produce sub-virions; and
c. purifying the sub-virions;

wherein inactivating and splitting the viral particles of step b comprises treating the viral particles with a reagent comprising at least polysorbate 80 and at least cetrimonium bromide (CTAB), and wherein the polysorbate 80 and the CTAB are present in an amount effective to reduce particle size of the viral particles.

16. A method of producing an influenza viral vaccine formulation comprising purified viral proteins, the method comprising the steps of:

a. purifying viral particles from a harvested cell culture of MDCK cells;
b. treating the purified viral particles with at least one alkylating agent to inactivate the viral particles;
c. treating the inactivated viral particle with at least cetrimonium bromide (CTAB)to split the inactivated viral particles to produce subvirions; and

d. purifying the sub-virions to produce purified influenza viral proteins; wherein inactivating and splitting the viral particles of step b and/or c further comprises treating the viral particles with a reagent comprising polysorbate 80 and the CTAB, and wherein the polysorbate 80 and the CTAB are present in an amount effective to reduce particle size of the viral particles.

17. The method of claim 1, wherein the viral vaccine is formulated in a sub-virion form.

18. The method of claim 1, wherein the particle size of the sub-virions ranges from greater than 150 nm to less than 500 nm.

19. The method of claim 15 or 16, wherein the reagent further comprises at least one salt, wherein the at least one salt is present in an amount effective to reduce the particle size of the viral particles.

20. The method of claim 19, wherein the at least one salt comprises sodium chloride (NaCl).

21. The method of claim 19 or 20, wherein the at least one salt comprises 0.1 - 200 mM NaCl.