CLAIMS

1. A method for manufacture of an oil-in-water emulsion vaccine adjuvant comprising squalene and a surfactant, said method comprising steps of:

(i) mixing emulsion components to form a first emulsion comprising squalene and a surfactant and having an average oil droplet size of 5000 nm or less;

(ii) microfluidizing the first emulsion to form a second emulsion having an average oil droplet size which is 500 nm or less; an

(iii) filtering the second emulsion using a hydrophilic polyethersulfone asymmetric membrane, thereby providing a vaccine adjuvant.

2. The method of claim 1, further comprising prefiltering the second emulsion through a polyethersulfone membrane prior to step (iii).

3. The method of claim 2, wherein the prefiltration membrane is porous.

4. The method of claim 2, wherein the prefiltering step(s) are carried out using a double-layer filter comprising first and second layers.

5. The method of claim 4, where (a) the first layer has pore size ≥ 0.3 µm, and/or (b) the second layer has a pore size < 0.3 µm.

6. The method according to claim 1, wherein the number of oil droplets having a size of > 1.2 µm in the first emulsion is $5x10^{11}$/ml or less.

7. The method according to claim 1, wherein the second average oil droplet size is 500 nm or less.

8. The method according to claim 1, wherein the number of oil droplets having a size of > 1.2 µm in the second emulsion is $5x10^{10}$/ml or less.

9. The method according to claim 1, wherein the average oil droplet size after filtration is less than 220 nm.

10. The method according to claim 1, wherein the number of oil droplets having a size of > 1.2 µm after filtration is $5x10^{8}$/ml or less.

11. A method for preparing a vaccine composition, comprising preparing an emulsion adjuvant according to claim 1 and combining the emulsion adjuvant with an antigen.

12. The method of claim 11, wherein the emulsion adjuvant is a bulk adjuvant and the method comprises extracting unit doses from the bulk adjuvant for packaging as kit components.

13. The method of claim 11, wherein the antigen is an influenza virus antigen.

14. The method of claim 13, wherein the combination of the emulsion and the antigen forms a vaccine composition, said composition comprising about 15 µg, about 10 µg, about 7.5 µg, about 5 µg, about 3.8 µg, about 3.75 µg, about 1.9 µg, or about 1.5 µg of hemagglutinin per influenza virus strain.

15. The method of claim 13, wherein the combination of the emulsion and the antigen forms a vaccine composition, wherein the vaccine composition comprises thiomersal or 2-phenoxyethanol preservative.

16. A method of preparing a vaccine kit comprising preparing an emulsion adjuvant according to claim 1 and packaging the emulsion adjuvant into a kit as a kit component together with an antigen component.

17. The method of claim 16, wherein the kit components are in separate vials.

18. The method of claim 17, wherein the vials are made from borosilicate glass.

19. A method for manufacture of an oil-in-water emulsion vaccine adjuvant comprising squalene and a surfactant, said method comprising steps of:

(i) mixing emulsion components to form an emulsion comprising squalene and a surfactant and having an average oil droplet size of 500 nm or less;

(ii) filtering the emulsion using a hydrophilic polyethersulfone double-layer filter which has a first membrane layer with larger pores and a second membrane layer with smaller pores, thereby providing a vaccine adjuvant.

20. A method for manufacturing a pharmaceutically acceptable composition comprising an oil-in-water emulsion, said method comprising:

(a) mixing emulsion components to form an oil-in-water emulsion having an average oil droplet size below 1 μm;

(b) prefiltering the oil-in-water emulsion using a hydrophilic polyethersulfone filtration membrane; and

(c) filtering the prefiltered oil-in-water emulsion obtained in step (b) using a hydrophilic polyethersulfone filtration membrane.