CLAIMS (JULY 2012)

1. A method for the manufacture of a vaccine adjuvant oil-in-water emulsion comprising squalene, the method comprising the step of: (b) microfluidization of a first emulsion having a first average oil droplet size to form a second emulsion having a second average oil droplet size which is less than the first average oil droplet size, wherein the second emulsion is formed by circulating the second emulsion components by transferring them from a first emulsion container, through a first microfluidization device to a second emulsion container, and then again through the same microfluidization device, wherein substantially all of the emulsion components from the first container are passed through the microfluidization device into the second container, and then substantially all of the emulsion components from the second container are passed through the microfluidization device back into the first container.

2. The method according to claim 1, comprising before step (b): (a) formation of a first emulsion having a first average oil droplet size.

3. The method according to claim 1 or claim 2, comprising after step (b): (c) filtration of the second emulsion.

4. A method for the manufacture of a squalene-containing oil-in-water emulsion vaccine adjuvant, the method comprising the step of: (i) formation of a first emulsion having a first average oil droplet size using a homogenizer, wherein the first emulsion is formed by transferring its components from a first container to a second container through a homogenizer, and then returning them from the second container to the first container through the same homogenizer, wherein substantially all of the emulsion components from the first container are passed through the homogenizer into the second container, and then substantially all of the emulsion components from the second container are passed through the homogenizer back into the first container.

5. The method according to claim 4, comprising: (ii) microfluidization of the first emulsion to form a second emulsion having a second average oil droplet size which is less than the first average oil droplet size.

6. The method of claim 5, wherein the homogenizer provides a shear rate of up to $1x10^6$ s^{-1}, and wherein the microfluidization occurs an interaction chamber that provides a shear rate $>2.5x10^6$ s^{-1}.

7. The method according to claim 5 or claim 6, comprising: (iii) filtration of the second emulsion.

8. The method of any one of claims 4 to 7, wherein step (i) comprises two or more cycles of transferring the first emulsion's components from the first container to the second container and back again.

9. The method of any one of claims 5 to 8, wherein during step (ii), the second emulsion is formed by circulating the second emulsion components through a microfluidization device a plurality of times.

10. The method of claim 9, wherein the circulation of the second emulsion components comprises transferring the second emulsion components between a first emulsion container and a microfluidization device.

11. The method of claim 9 or claim 10, wherein the circulation of the second emulsion components comprises transferring the second emulsion components from a first emulsion container, through a first microfluidization device to a second emulsion container, and then through a second microfluidization device, wherein the first and second microfluidization devices are the same.

12. The method of any one of claims 8 to 11, wherein after passing through the second microfluidization device, the second emulsion components are returned to the first emulsion container and the circulation of claim 8 or claim 9 is repeated one or more times.

13. The method of any one of the preceding claims, wherein the first average oil droplet size is 5000 nm or less.

14. The method according to any one of the preceding claims, wherein the number of oil droplets having a size of > 1.2 μm in the first emulsion is 5×10^{11} /ml or less.

15. The method of any one of the preceding claims, wherein the second average oil droplet size is 500 nm or less.

16. The method according to any one of the preceding claims, wherein the number of oil droplets having a size of > 1.2 μm in the second emulsion is 5×10^{10} /ml or less.

17. A method for preparing a vaccine composition, comprising preparing an emulsion according to any one of claims 1 to 16 and combining the emulsion with an antigen.

18. A method for preparing a vaccine kit comprising preparing an emulsion according to any one of claims 1 to 16 and packaging the emulsion into a kit as a kit component together with an antigen component.

19. The method of claim 18, wherein the kit components are in separate vials.

20. The method of claim 19, wherein the vials are made from borosilicate glass.

21. The method of any of claims 18 to 20, wherein the adjuvant is a bulk adjuvant and the method comprises extracting unit doses from the bulk adjuvant for packaging as kit components.

22. The method of any one of claims 17 to 21, wherein the antigen is an influenza virus antigen.

23. The method of claim 22, wherein the combination of the emulsion and the antigen forms a vaccine composition and wherein the vaccine composition includes about 15μg, about 10μg, about 7.5μg, about 5μg, about 3.8μg, about 1.9μg, about 1.5μg of hemagglutinin per influenza virus strain.

24. The method of claim 22 or claim 23, wherein the combination of the emulsion and the antigen forms a vaccine composition and wherein the vaccine composition includes a thiomersal or 2-phenoxyethanol preservative.

Claims

1. An invention not claimed in any divisional application.