What is Claimed is:

1. A method of producing an immunogenic polysaccharide-protein conjugate comprising an isolated *Staphylococcus aureus* capsular polysaccharide conjugated to a carrier protein, the method comprising the steps of:

a) reacting an isolated *S. aureus* capsular polysaccharide with carbonyl ditriazole (CDT) in an organic solvent to produce an activated polysaccharide;

b) reacting the activated polysaccharide with a carrier protein in an organic solvent to produce a polysaccharide-carrier protein conjugate; and

c) isolating the capsular polysaccharide-carrier protein conjugate.

2. The method of claim 1, wherein the capsular polysaccharide is a serotype 5 or a serotype 8 capsular polysaccharide

3. The method of claim 1 or claim 2, which further comprises lyophilizing the isolated polysaccharide and re-suspending the lyophilized polysaccharide in an organic solvent.

4. The method of any one of claims 1-3, wherein the activated polysaccharide is isolated from the activation reaction prior to reacting with the carrier protein.

5. The method of claim 4, wherein step b) comprises:

i) lyophilizing the activated isolated polysaccharide to produce a lyophilized activated isolated polysaccharide;

ii) lyophilizing the carrier protein to produce a lyophilized carrier protein; and

iii) re-suspending the lyophilized activated isolated polysaccharide and the lyophilized carrier protein in an organic solvent to produce an activated isolated polysaccharide mixed with a carrier protein.

6. The method of any one of claims 1-5, which further comprises dilution of the reaction mixture of step b) into a buffer and maintaining a pH of about 8.8 to about 9.2, such as about 9.0, for at least 4 hours at about 20°C to about 26°C, such as about 23°C.

7. The method of any one of claims 1-6, wherein the organic solvent is a polar aprotic solvent.

8. The method of claim 7, wherein the polar aprotic solvent is selected from the group consisting of dimethyl sulfoxide (DMSO), dimethylformamide (DMF), dimethylacetamide, N methyl 2 pyrrolidone, and hexamethylphosphoramide (HMPA).

9. The method of claim 8, wherein the organic solvent is dimethyl sulfoxide (DMSO).

10. The method of any one of claims 1-9, wherein the step of reacting the polysaccharide with CDT comprises determining the water present in the *S. aureus* serotype 8 capsular polysaccharide and adjusting the CDT concentration to about 1:1 about 0.5:1, or about 0.75:1 molar ratio of CDT:water in the organic solvent.

11. The method of any one of claims 1-9, wherein the step of reacting the *S. aureus* serotype 5 polysaccharide with CDT comprises providing about 20-fold molar excess of CDT compared to the polysaccharide.

12. The method of any one of claims 1-9 and 11, wherein the serotype 5 polysaccharide CDT in an organic solvent mixture is adjusted to a water concentration between 0.1 and 0.3%, such as 0.2%.

13. The method of any one of claims 1-12, wherein the step of isolating the activated polysaccharide comprises diafiltration.

14. The method of any one of claims 1-13, wherein prior to lyophilization the carrier protein is diafiltered against NaCl and the w/w ratio of NaCl/protein carrier protein is adjusted to about 0.5 to about 1.5.

15. The method of any one of claims 1-14, wherein the carrier protein is CRM_{197}.

16. The method of claim 15, wherein the activated polysaccharide is reacted with the CRM_{197} in a ratio by weight of about 1:1.

17. The method of any one of claims 1-16, wherein the isolated *S. aureus* capsular polysaccharide is mixed with imidazole or triazole prior to mixing with CDT in an organic solvent.

18. The method of any one of claims 1-17, which further comprises hydrolyzing the polysaccharide-carrier protein conjugate to remove unreacted activation groups.

What is Claimed is:

1. An immunogenic polysaccharide-protein conjugate comprising a *Staphylococcus aureus* capsular polysaccharide conjugated to a carrier protein, wherein the polysaccharide has a molecular weight of between 70 kDa and 800 kDa.

2. The immunogenic conjugate of claim 1, wherein the immunogenic conjugate has a molecular weight of between 200 kDa and 5000 kDa or between 500 kDa and 2500 kDa.

3. The immunogenic polysaccharide protein conjugate of claim 1 or 2, wherein the capsular polysaccharide is a serotype 5 or a serotype 8 capsular polysaccharide.

4. The immunogenic conjugate of any one of claims 1-3, wherein the polysaccharide has a molecular weight range of between 70 kDa and 300 kDa.

5. The immunogenic conjugate of any one of claims 1-4, wherein the polysaccharide has a degree of O-acetylation between 10-100%, between 50-100%, or between 75-100%.

6. The immunogenic conjugate of any of claims 1-5, wherein the carrier protein is CRM197 or pneumolysin.

7. The immunogenic conjugate of claim 6, wherein the CRM197 is covalently linked to the polysaccharide through a carbamate linkage, an amide linkage, or both.

8. The immunogenic conjugate of claim 6 or 7, wherein the molar ratio of conjugated lysines to CRM197 is about 10:1 to about 25:1.

9. The immunogenic conjugate of claim 8, wherein at least one covalent linkage between CRM197 and polysaccharide occurs at least at every 5 to 10 saccharide repeat units of the polysaccharide or every 5 saccharide repeat units of the polysaccharide.

10. The immunogenic conjugate of any of claims 6-9, wherein the CRM197 comprises 5 to 25, 5 to 20, or 10 to 25 lysines covalently linked to the polysaccharide.

11. An immunogenic composition comprising the immunogenic conjugate of any of claims 1-10 and at least one of an adjuvant, diluent, or carrier.

12. The immunogenic composition of claim 11, wherein the immunogenic composition comprises less than 30% or less than 20% free type 5 or 8 polysaccharide compared to the total amount of type 5 or 8 polysaccharide.

13. A method of producing the immunogenic conjugate of any of claims 1-10 comprising the steps of:

a) reacting an isolated *S. aureus* capsular polysaccharide with carbonyl ditriazole (CDT) in an organic solvent to produce an activated polysaccharide;

b) reacting the activated polysaccharide with a carrier protein in an organic solvent to produce a polysaccharide-carrier protein conjugate; and

c) isolating the capsular polysaccharide-carrier protein conjugate.

14. The method of claim 13, which further comprises lyophilizing the isolated polysaccharide and re-suspending the lyophilized polysaccharide in an organic solvent.

15. The method of claim 13 or 14, wherein the activated polysaccharide is isolated from the activation reaction prior to reacting with the carrier protein.

16. The method of claim 15, wherein step b) comprises:

i) lyophilizing the activated isolated polysaccharide to produce a lyophilized activated isolated polysaccharide;

ii) lyophilizing the carrier protein to produce a lyophilized carrier protein; and

iii) re-suspending the lyophilized activated isolated polysaccharide and the lyophilized carrier protein in an organic solvent to produce an activated isolated polysaccharide mixed with a carrier protein.

17. The method of any of claims 13-16, which further comprises dilution of the reaction mixture of step b) into a buffer and maintaining a pH of about 8.8 to about 9.2, such as about 9.0, for at least 4 hours at about 20°C to about 26°C, such as about 23°C.

18. The method of any of claims 13-17 wherein the step of reacting the polysaccharide with CDT comprises determining the water present in the *S. aureus* serotype 8 capsular polysaccharide and adjusting the CDT concentration to about 1:1, about 0.5:1, or about 0.75:1 molar ratio of CDT:water in the organic solvent.

19. The method of any of claims 13-17, wherein the step of reacting the *S. aureus* serotype 5 polysaccharide with CDT comprises providing about 20-fold molar excess of CDT compared to the polysaccharide.

20. The method of any of claims 13-17 or 19, wherein the serotype 5 polysaccharide CDT in an organic solvent mixture is adjusted to a water concentration between 0.1 and 0.3%, such as 0.2%.

21. The method of any of claims 13-20, wherein the isolated *S. aureus* serotype capsular polysaccharide is mixed with imidazole or triazole prior to mixing with CDT in an organic solvent.

22. The method of any of claims 13-21, which further comprises hydrolyzing the serotype polysaccharide-carrier protein conjugate to remove unreacted activation groups.

23. A method of producing the immunogenic conjugate of any of claims 1-10 comprising the steps of:

a) reacting a *S. aureus* polysaccharide with 3 (2 pyridyldithio) propionyl hydrazide (PDPH) and a carbodiimide in an organic solvent to produce a PDPH linked polysaccharide;

b) reacting the PDPH-linked polysaccharide with a reducing agent to produce an activated polysaccharide;

c) isolating the activated polysaccharide to produce an isolated activated polysaccharide;

d) providing an activated carrier protein;

e) reacting the isolated activated polysaccharide with the activated carrier protein to produce the polysaccharide-carrier protein conjugate; and

f) isolating the polysaccharide-carrier protein conjugate.

24. The method of claim 23, wherein the activated carrier protein is isolated prior to reacting the activated carrier protein with the activated polysaccharide.

25. The method of claim 23 or 24, wherein step c) further comprises lyophilizing the isolated activated polysaccharide to produce a lyophilized activated polysaccharide.

26. The method of any of claims 13-25, wherein the organic solvent is a polar aprotic solvent.

27. The method of claim 26, wherein the polar aprotic solvent is selected from the group consisting of dimethyl sulfoxide (DMSO), dimethylformamide (DMF), dimethylacetamide, N methyl 2 pyrrolidone, and hexamethylphosphoramide (HMPA).

28. The method of any of claims 23-27, wherein the carbodiimide is 1 Ethyl 3 (3 dimethylaminopropyl) carbodiimide (EDAC).

29. The method of claim 28, wherein the step of reacting the serotype capsular polysaccharide with PDPH and EDAC in an organic solvent comprises maintaining a polysaccharide:PDPH:EDAC ratio by weight of about 1:5:3.

30. The method of any of claims 23-29, wherein the reducing agent is dithiothreitol (DTT).

31. The method of any of claims 23-30, wherein activation of the carrier protein comprises reacting the carrier protein with a bromoacetic acid.

32. The method of any of claims 23-31, which further includes the step of hydrolyzing the serotype polysaccharide carrier protein conjugate to remove unreacted activation groups.

33. The method of claim 32, wherein the step of hydrolyzing the serotype polysaccharide carrier protein conjugate comprises the addition of cysteamine hydrochloride.