We claim:

1. An immunogenic composition comprising 28µg-35µg (for example around 30µg) of detoxified pneumolysin (dPly), per human dose for use in the treatment or prevention of disease caused by *Streptococcus pneumoniae* infection wherein the immunogenic composition further comprises *Streptococcus pneumoniae* capsular saccharide conjugates comprising a conjugated serotype 4 saccharide, a conjugated serotype 6B saccharide, a conjugated serotype 9V saccharide, a conjugated serotype 14 saccharide, a conjugated serotype 18C saccharide, a conjugated serotype 19F saccharide and a conjugated serotype 23F saccharide.

2. The immunogenic composition of claim 1 wherein the pneumolysin has been chemically detoxified.

3. The immunogenic composition of any claim 1 or 2 wherein the pneumolysin has been genetically detoxified.

4. The immunogenic composition of any one of claims 1-3 wherein the immunogenic composition further comprises PhtD (poly histidine triad family D).

5. The immunogenic composition of claim 4 wherein the immunogenic composition comprises 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of PhtD, per human dose.

6. An immunogenic composition comprising 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of PhtD, per human dose for use in the treatment or prevention of disease caused by *Streptococcus pneumoniae* infection wherein the immunogenic composition further comprises *Streptococcus pneumoniae* capsular saccharide conjugates comprising a conjugated serotype 4 saccharide, a conjugated serotype 6B saccharide, a conjugated serotype 9V saccharide, a conjugated serotype 14 saccharide, a conjugated serotype 18C saccharide, a conjugated serotype 19F saccharide and a conjugated serotype 23F saccharide.

7. The immunogenic composition of any one of claims 4-6 wherein the PhtD (poly histidine triad family D) comprises an amino acid sequence at least 85%, 90%, 95%, 98%, 99% or 100% identical to the sequence at amino acids 21-838 of Sequence ID No.4 of WO00/37105.

8. The immunogenic composition of claim 6 or 7 wherein the composition further comprises detoxified pneumolysin (dPly).

9. The immunogenic composition of claim 8 wherein the composition comprises 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of detoxified pneumolysin (dPly), per human dose.

10. The immunogenic composition of any preceding claim wherein the immunogenic composition has a dose volume between 0.2 and 1.0 ml.

11. The immunogenic composition of any preceding claim wherein the immunogenic composition has a dose volume of 0.5ml.

12. The immunogenic composition of any preceding claim which comprises at least one further unconjugated or conjugated *Streptococcus pneumoniae* protein.

13. The immunogenic composition of claim 12 wherein the at least one further unconjugated or conjugated *Streptococcus pneumoniae* protein is selected from the group consisting of Poly Histidine Triad family (PhtX), Choline Binding Protein Family (CbpX), CbpX truncates, LytX (autolytic enzyme) family, LytX truncates, CbpX truncate-LytX truncate chimeric proteins, PcpA (pneumococcal choline binding protein A), PspA (Pneumococcal surface protein A), PsaA (pneumococcal surface adhesion A), Sp128 (*Streptococcus pneumoniae*

128), Sp101 (*Streptococcus pneumoniae* 101), Sp130 (*Streptococcus pneumoniae* 130), SP125 (*Streptococcus pneumoniae* 125) and SP133 (*Streptococcus pneumoniae* 133).

14. The immunogenic composition of claim 13 wherein the at least one further unconjugated or conjugated *Streptococcus pneumoniae* protein comprises a Poly Histidine Triad family (PhtX) protein selected from the group consisting of PhtB, PhtE, PhtA or a PhtBD or PhtDE fusion protein.

15. The immunogenic composition of any one of claims 12-14 wherein the composition comprises 1µg-100µg, 1µg-50µg, 1µg-20µg, 28µg-35µg, around 10µg or around 30µg of the at least one further unconjugated or conjugated *Streptococcus pneumoniae* protein, per human dose.

16. The immunogenic composition of any preceding claim wherein the immunogenic composition does not comprise an oil in water adjuvant.

17. The immunogenic composition of any preceding claim wherein the immunogenic composition does not comprise an adjuvant comprising QS21, Monophosphoryl lipid A (MPL), phospholipid and sterol, presented in the form of a liposome.

18. The immunogenic composition of any preceding claim wherein the immunogenic composition does not comprise an adjuvant comprising QS21.

19. The immunogenic composition of any preceding claim wherein the immunogenic composition does not comprise an adjuvant comprising Monosphosphoryl lipid A (MPL)

20. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 1 saccharide.

21. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 5 saccharide.

22. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 7F saccharide.

23. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 3 saccharide.

24. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 6A saccharide.

25. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 19A saccharide.

26. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 33F saccharide.

27. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 22F saccharide.

28. The immunogenic composition of any one of the preceding claims wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates are conjugated to a carrier protein independently selected from the group consisting of tetanus toxoid (TT), fragment C of TT, diphtheria toxoid, CRM197 (cross reacting material 197), detoxified pneumolysin,

protein D (from *H.influenzae*), PhtD (Poly Histidine Triad D), PhtDE (fusion protein between Poly Histidine Triad D and Poly Histidine Triad E) and N19.

29. The immunogenic composition of any one of the preceding claims wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates are all independently conjugated to CRM197.

30. The immunogenic composition of claim 20 wherein the conjugated serotype 1 saccharide is conjugated to protein D or CRM197.

31. The immunogenic composition of any one of the preceding claims wherein the conjugated serotype 4 saccharide is conjugated to protein D or CRM197.

32. The immunogenic composition of claim 21 wherein the conjugated serotype 5 saccharide is conjugated to protein D or CRM197.

33. The immunogenic composition of any one of the preceding claims wherein the conjugated serotype 6B saccharide is conjugated to protein D or CRM197.

34. The immunogenic composition of claim 22 wherein the conjugated serotype 7F saccharide is conjugated to protein D or CRM197.

35. The immunogenic composition of any one of the preceding claims wherein the conjugated serotype 9V saccharide is conjugated to protein D or CRM197.

36. The immunogenic composition of any one of the preceding claims wherein the conjugated serotype 14 saccharide is conjugated to protein D or CRM197.

37. The immunogenic composition of any one of the preceding claims wherein the conjugated serotype 18C saccharide is conjugated to tetanus toxoid or CRM197.

38. The immunogenic composition of any one of the preceding claims wherein the conjugated 19F saccharide is conjugated to diphtheria toxoid or CRM197.

39. The immunogenic composition of any one of the preceding claims wherein the conjugated 23F saccharide is conjugated to protein D or CRM197.

40. The immunogenic composition of claim 24 wherein the conjugated 6A saccharide is conjugated to CRM197.

41. The immunogenic composition of claim 25 wherein the conjugated 19A saccharide is conjugated to CRM197.

42. The immunogenic composition of any one of the preceding claims wherein a minority of the1 or more *Streptococcus pneumoniae* capsular saccharide conjugates are conjugated to protein D.

43. The immunogenic composition of any one of claims 1-28 or 30-42 wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises a serotype 1 saccharide conjugated to protein D, a serotype 4 saccharide conjugated to protein D, a serotype 5 saccharide conjugated to protein D, a serotype 6B saccharide conjugated to protein D, a serotype 7F saccharide conjugated to protein D, a serotype 9V saccharide conjugated to protein D, a serotype 14 saccharide conjugated to protein D, a serotype 23F saccharide conjugated to protein D, a serotype 18C saccharide conjugated to tetanus toxoid and a serotype 19F saccharide conjugated to diphtheria toxoid.

44. The immunogenic composition of any one of the preceding claims wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 saccharides conjugated to a carrier protein through reductive amination.

45. The immunogenic composition of any one of the preceding claims wherein the 1 or more capsular saccharides from *S.pneumoniae* are conjugated to a carrier protein through reductive amination.

46. The immunogenic composition of any one of claims1-44 wherein all of the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 saccharides conjugated to a carrier protein through CDAP chemistry.

47. The immunogenic composition of any one of claims 1-3 or 46 wherein all of the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates are conjugated to a carrier protein through CDAP chemistry.

48. The immunogenic composition of any one of claims 1-44 or 46 wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 saccharides conjugated to a carrier protein through reductive amination and comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 saccharides conjugated to a carrier protein through a chemistry other than reductive amination for example CDAP chemistry.

49. The immunogenic composition of any one of the preceding claims wherein the dose of the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates is between 1 and 10µg, 1 and 5µg, or 1 and 3µg of saccharide per conjugate.

50. The immunogenic composition of any one of the preceding claims wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises conjugates of saccharides from serotypes 1, 5, 6B, 7F, 9V, 14 and 23F (and optionally 6A and/or 3) at dosages of 1µg of saccharide per conjugate.

51. The immunogenic composition of any one of the preceding claims wherein the 1 or more *Streptococcus pneumoniae* capsular saccharide conjugates comprises conjugates of saccharides from serotypes 4, 18C, and 19F(and optionally 22F and/or 19A) at dosages of 3µg of saccharide per conjugate.

52. The immunogenic composition of any one of the preceding claims wherein the immunogenic composition comprises less than 23, 22, 21, 20, 19, 18, 17, 16, 15, 14 or 13 *Streptococcus pneumoniae* capsular saccharide conjugates.

53. The immunogenic composition of any one of the preceding claims wherein the immunogenic composition further comprises unconjugated *S.pneumoniae* saccharides of serotypes different from those conjugated, such that the number of conjugated and unconjugated saccharide serotypes is less than or equal to 23.

54. The immunogenic composition of any preceding claim which further comprises an adjuvant.

55. The immunogenic composition of claim 54 wherein the adjuvant is aluminium phosphate.

56. The immunogenic composition of claim 53 wherein the adjuvant is aluminium hydroxide.

57. The immunogenic composition of claim 55 wherein the adjuvant comprises 100-750, 200-500, or 300-400 µg Al as aluminium phosphate per human dose.

58. A vaccine comprising the immunogenic composition of any preceding claim and a pharmaceutically acceptable excipient.

59. The immunogenic composition of any one of the preceding claims wherein the use comprises administration of the immunogenic composition to an adult human host.

60. The immunogenic composition of any one of the preceding claims wherein the use comprises administration of the immunogenic composition to an elderly human host.

61. The immunogenic composition of any one of claims 1-58 wherein the use comprises administration of the immunogenic composition to an infant or toddler human host.

62. The immunogenic composition of any one of the preceding claims wherein the diseases comprise at least one disease selected from the group consisting of pneumonia, invasive pneumococcal disease (IPD), exacerbations of chronic obstructive pulmonary disease (COPD), otitis media, recurrent otitis media, meningitis, bacteraemia, and conjunctivitis.

We claim:

1. An immunogenic composition comprising 28µg-35µg (for example around 30µg) of detoxified pneumolysin (dPly), per human dose for use in the treatment or prevention of disease caused by *Streptococcus pneumoniae* infection wherein the immunogenic composition further comprises *Streptococcus pneumoniae* capsular saccharide conjugates comprising a conjugated serotype 4 saccharide, a conjugated serotype 6B saccharide, a conjugated serotype 9V saccharide, a conjugated serotype 14 saccharide, a conjugated serotype 18C saccharide, a conjugated serotype 19F saccharide and a conjugated serotype 23F saccharide.

2. The immunogenic composition of claim 1 wherein the immunogenic composition further comprises PhtD (poly histidine triad family D).

3. The immunogenic composition of claim 2 wherein the immunogenic composition comprises 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of PhtD, per human dose.

4. An immunogenic composition comprising 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of PhtD, per human dose for use in the treatment or prevention of disease caused by *Streptococcus pneumoniae* infection wherein the immunogenic composition further comprises *Streptococcus pneumoniae* capsular saccharide conjugates comprising a conjugated serotype 4 saccharide, a conjugated serotype 6B saccharide, a conjugated serotype 9V saccharide, a conjugated serotype 14 saccharide, a conjugated serotype 18C saccharide, a conjugated serotype 19F saccharide and a conjugated serotype 23F saccharide.

5. The immunogenic composition of claims 2-4 wherein the PhtD (poly histidine triad family D) comprises an amino acid sequence at least 85%, 90%, 95%, 98%, 99% or 100% identical to the sequence at amino acids 21-838 of Sequence ID No.4 of WO00/37105.

6. The immunogenic composition of claim 4 or 5 wherein the composition comprises 26µg-45µg (for example 26µg-40µg, 28µg-35µg or around 30µg) of detoxified pneumolysin (dPly), per human dose.

7. The immunogenic composition of any preceding claim wherein the immunogenic composition has a dose volume of 0.5ml.

8. The immunogenic composition of any preceding claim which comprises at least one further unconjugated or conjugated *Streptococcus pneumoniae* protein selected from the group consisting of Poly Histidine Triad family (PhtX), Choline Binding Protein Family (CbpX), CbpX truncates, LytX (autolytic enzyme) family, LytX truncates, CbpX truncate-LytX truncate chimeric proteins, PcpA (pneumococcal choline binding protein A), PspA (Pneumococcal surface protein A), PsaA (pneumococcal surface adhesion A), Sp128 (*Streptococcus pneumoniae* 128), Sp101 (*Streptococcus pneumoniae* 101), Sp130 (*Streptococcus pneumoniae* 130), SP125 (*Streptococcus pneumoniae* 125) and SP133 (*Streptococcus pneumoniae* 133).

9. The immunogenic composition of any preceding claim wherein the immunogenic composition does not comprise an oil in water adjuvant.

10. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 1 saccharide, a conjugated serotype 5 saccharide and a conjugated serotype 7F saccharide.

11. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 6A saccharide and a conjugated serotype 19A saccharide.

12. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates further comprise a conjugated serotype 33F saccharide, and a conjugated serotype 22F saccharide.

13. The immunogenic composition of any one of the preceding claims wherein the *Streptococcus pneumoniae* capsular saccharide conjugates are conjugated to a carrier protein independently selected from the group consisting of tetanus toxoid (TT), fragment C of TT, diphtheria toxoid, CRM197 (cross reacting material 197), detoxified pneumolysin, protein D (from *H.influenzae*), PhtD (Poly Histidine Triad D), PhtDE (fusion protein between Poly Histidine Triad D and Poly Histidine Triad E) and N19.

14. The immunogenic composition of any one of claims 1-13 wherein the *Streptococcus pneumoniae* capsular saccharide conjugates comprise a serotype 1 saccharide conjugated to protein D, a serotype 4 saccharide conjugated to protein D, a serotype 5 saccharide conjugated to protein D, a serotype 6B saccharide conjugated to protein D, a serotype 7F saccharide conjugated to protein D, a serotype 9V saccharide conjugated to protein D, a serotype 14 saccharide conjugated to protein D, a serotype 23F saccharide conjugated to protein D, a serotype 18C saccharide conjugated to tetanus toxoid and a serotype 19F saccharide conjugated to diphtheria toxoid.

15. The immunogenic composition of any preceding claim which further comprises an adjuvant.

16. A vaccine comprising the immunogenic composition of any preceding claim and a pharmaceutically acceptable excipient.

17. The immunogenic composition of any one of the preceding claims wherein the use comprises administration of the immunogenic composition to an adult human host, an elderly human host, or to an infant or toddler human host and wherein the diseases comprise at least one disease selected from the group consisting of pneumonia, invasive pneumococcal disease (IPD), exacerbations of chronic obstructive pulmonary disease (COPD), otitis media, recurrent otitis media, meningitis, bacteraemia, and conjunctivitis.

18. Use of an immunogenic composition of any one of claims 1-15 or a vaccine of claim 16, in the manufacture of a medicament for the treatment or prevention of disease caused by *Streptococcus pneumonia* infection.

19. The use according to claim 18, wherein the disease comprise at least one selected from the group consisting of of pneumonia, invasive pneumococcal disease (IPD), exacerbations of chronic obstructive pulmonary disease (COPD), otitis media, recurrent otitis media, meningitis, bacteraemia, and conjunctivitis.