serotypes present in Prevnar®. See Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep 2005, 54(36):893-7. However, there are limitations in serotype coverage with Prevnar® in certain regions of the world and some evidence of certain emerging serotypes in the United States (for example, 19A and others). See O'Brien *et al.*, 2004, Am J Epidemiol 159:634-44; Whitney *et al.*, 2003, N Engl J Med 348:1737-46; Kyaw *et al.*, 2006, N Engl J Med 354:1455-63; Hicks *et al.*, 2007, J Infect Dis 196:1346-54; Traore *et al.*, 2009, Clin Infect Dis 48:S181-S189.

U.S. Patent Application Publication No. US 2006/0228380 A1 describes a 13-valent pneumococcal polysaccharide-protein conjugate vaccine including serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. Chinese Patent Application Publication No. CN 101590224 A describes a 14-valent pneumococcal polysaccharide-protein conjugate vaccine including serotypes 1, 2, 4, 5, 6A, 6B, 7F, 9N, 9V, 14, 18C, 19A, 19F and 23F.

Other PCVs have covered 7, 10, 11, or 13 of the serotypes contained in PCV-15, but immune interference has been observed for some serotypes (e.g. lower protection for serotype 3 in GSK's PCV-11) and lower response rates to serotype 6B in Pfizer's PCV-13. See Prymula *et al.*, 2006, Lancet 367:740-48 and Kieninger *et al.*, Safety and Immunologic Non-inferiority of 13-valent Pneumococcal Conjugate Vaccine Compared to 7-valent Pneumococcal Conjugate Vaccine Given as a 4-Dose Series in Healthy Infants and Toddlers, presented at the 48th Annual ICAAC/ISDA 46th Annual Meeting, Washington DC, October 25-28, 2008.

SUMMARY

The present disclosure provides an immunogenic composition comprising (1) a multivalent polysaccharide-protein conjugate mixture consisting of capsular polysaccharides from 15 different serotypes of *S. pneumoniae* conjugated to a carrier protein, and (2) a pharmaceutically acceptable carrier. More specifically, the present disclosure provides a 15-valent pneumococcal conjugate vaccine (PCV-15) composition comprising a multivalent polysaccharide-protein conjugate mixture consisting of capsular polysasccharides from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F of *S. pneumoniae* conjugated to a carrier protein; and a pharmaceutically acceptable carrier. In one aspect, the present disclosure provides an immunogenic composition comprising: (1) a multivalent polysaccharide-protein conjugate mixture consisting of capsular polysaccharides from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F of *Streptococcus pneumoniae* conjugated to a CRM_{197}; and (2) a pharmaceutically acceptable

carrier. In one specific embodiment, the immunogenic composition contains capsular polysaccharides from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F and the carrier protein is CRM_{197}.

In certain embodiments, the composition further comprises an adjuvant. In certain embodiments, the adjuvant is an aluminum-based adjuvant, such as aluminum phosphate,

aluminum sulfate or aluminum hydroxide. In a particular embodiment of the disclosure, the adjuvant is aluminum phosphate.

The present disclosure also provides a method of inducing an immune response to a *S. pneumoniae* capsular polysaccharide, comprising administering to a human an immunologically effective amount of the above immunogenic composition.

The present disclosure further provides an immunogenic composition administered as a single 0.5 mL dose formulated to contain: 2 μg of each polysaccharide, except for 6B at 4 μg; about 32 μg CRM_{197} carrier protein; 0.125 mg of elemental aluminum (0.5 mg aluminum phosphate) adjuvant; 150 mM sodium chloride and 20 mM L-histidine buffer.

In another aspect, the present disclosure provides use of the immunogenic composition as defined herein in the manufacture of a medicament for inducing an immune response to a *Streptococcus pneumoniae* capsular polysaccharide.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: Comparison of GMCs for PCV-15 relative to Prevnar® in Infant Rhesus Monkeys (Prevnar serotypes, PD-2 and PD-3). Error bars denote 2 standard errors.

Figure 2: Serotype-specific GMCs to non- Prevnar® serotypes in infant rhesus monkeys immunized with PCV-15. Error bars denote 2 standard errors.

Figure 3: NZWR-1: Comparison of geometric mean titers in rabbits immunized with PCV-15 without (0xA) or with APA (B1) (Post-dose 2). Error bars denote 95% CI on the geometric mean fold-difference (PCV-15 without APA / PCV-15 with APA).

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a multivalent immunogenic composition comprising, consisting essentially of, or alternatively, consisting of 15 distinct polysaccharide-protein conjugates, wherein each of the conjugates contains a different capsular polysaccharide conjugated to a carrier protein, and wherein the capsular polysaccharides are prepared from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F of *S. pneumoniae*, together with a pharmaceutically acceptable carrier. In certain embodiments, the carrier protein is CRM_{197}. The immunogenic composition may further comprise an adjuvant, such as an aluminum-based adjuvant, such as aluminum phosphate, aluminum sulfate and aluminum hydroxide. The present invention also provides a method of inducing an immune response to a *S. pneumoniae* capsular polysaccharide conjugate, comprising administering to a human an immunologically effective amount of the above multivalent immunogenic composition.

As illustrated in the Examples, *infra.*, preclinical studies in infant rhesus monkeys demonstrated robust antibody responses to all 15 serotypes in PCV-15 which are comparable to the responses for the 7 common serotypes in Prevnar®. Applicants' finding that a 15 valent

WHAT IS CLAIMED IS:

1. An immunogenic composition comprising:

(1) a multivalent polysaccharide-protein conjugate mixture consisting of capsular polysaccharides from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F of *Streptococcus pneumoniae* conjugated to a CRM_{197}; and

(2) a pharmaceutically acceptable carrier.

2. The immunogenic composition of claim 1, further comprising an adjuvant.

3. The immunogenic composition of claim 2, wherein the adjuvant is an aluminum-based adjuvant.

4. The immunogenic composition of claim 3, wherein the adjuvant is selected from the group consisting of aluminum phosphate, aluminum sulfate and aluminum hydroxide.

5. The immunogenic composition of claim 4, wherein the adjuvant is aluminum phosphate.

6. The immunogenic composition of any one of the preceding claims formulated as a single 0.5 mL dose containing 2 μg of each saccharide, except for 6B at 4 μg; about 32 μg CRM_{197} carrier protein; 0.5 mg aluminum phosphate adjuvant; 150 mM sodium chloride and 20 mM L-histidine buffer.

7. Use of the immunogenic composition of any one of the preceding claims in the manufacture of a medicament for inducing an immune response to a *Streptococcus pneumoniae* capsular polysaccharide.

8. The use of claim 7, wherein the immunogenic composition is to be administered as a single 0.5 mL dose containing: 2 μg of each saccharide, except for 6B at 4 μg; about 32 μg CRM_{197} carrier protein; 0.5 mg aluminum phosphate adjuvant; 150 mM sodium chloride and 20 mM L-histidine buffer.