A Method with Increased Yield for Production of Polysaccharide-Protein Conjugate Vaccines Using Hydrazide Chemistry

Technology Summary

Current methods for synthetically manufacturing polysaccharide-protein conjugate vaccines use conjugation reactions with low efficiency (~20%) that waste up to 80% of the activated polysaccharide (PS) reactant.

FDA inventors have developed a method to improve yields by ~60% for conjugating hydrazide groups to aldehyde or cyanate ester groups, the reaction underlying polysaccharide-protein conjugation. Higher conjugation efficiency minimizes the need to remove residual unconjugated protein and polysaccharide reactants, thereby simplifying the purification of the conjugate product to remove small molecule by-products. The new conjugation reaction can be carried out within one or two days with reactant concentrations between 1 and 25 mg/mL at PS/protein ratios from 1:2 to 3:1, at temperatures between 4 and 40 degrees Centigrade, and in a pH range of 5.5 to 7.4, optimal conditions varying from PS to PS.

Potential Commercial Applications

- Vaccine manufacturing

Competitive Advantages

- Reduced manufacturing times
- Increased yield and efficacy manufacturing conjugate vaccines

Inventors: Che-Hung Robert Lee, Carl Frasch

Publications:

Preparation of bacterial polysaccharide-protein conjugates: analytical and manufacturing challenges. Vaccine. 2009 Oct 30;27(46):6468-70. doi: 10.1016/j.vaccine.2009.06.013. PMID: 19555714

Intellectual Property:

United States Patent: No. 8,048,432 issued 11.01.2011
United States Patent: No. 8,465,749 issued 06.18.2013
United States Patent: No. 8,753,649 issued 06.17.2014
United States Patent No. 10,566,899 issued 01.11.2011
United States Patent No. 10,566,898 issued 11.03.2015
United States Patent No. 9,173,931 issued 11.03.2015
United States Patent No. 9,198,976 issued 12.01.2015

Product Area: vaccine, polysaccharide, protein, manufacturing, conjugate, manufacturing, method, procedure, bacterial

FDA Reference No: E-2003-025; E-2003-026

Licensing Contact:
Ken Millburne, J.D.
FDA Technology Transfer Program
Email: FDAInventionlicensing@fda.hhs.gov
Phone:301-346-3964