

ABSTRACT

Provided is a liquid formulation of a six combined vaccine containing DPT-IPV-Hib-HBs, in which a HBs antigen is stably adsorbed and retained to an aluminum adjuvant, and PRP as a Hib antigen is stably coupled and retained to a carrier protein. A method for producing a stable liquid formulation of a six combined vaccine against diphtheria, pertussis, tetanus, polio, *Haemophilus influenzae* type b (Hib), and hepatitis B (HepB), the method comprising the following steps of: (1) mixing diphtheria toxoid (D) and tetanus toxoid (T) with an aluminum adjuvant to produce a DT adjuvant; (2) mixing a hepatitis B surface (HBs) antigen with the DT adjuvant obtained in step (1) to produce a DT-HBs adjuvant; (3) mixing a pertussis antigen (P) with the DT-HBs adjuvant obtained in step (2) to produce a DPT-HBs adjuvant; (4) mixing inactivated poliovirus (IPV) with the DPT-HBs adjuvant obtained in step (3) to produce a DPT-IPV-HBs adjuvant; (5) adding a succinate phosphate buffer to the DPT-IPV-HBs adjuvant obtained in step (4), and then adding PRP (PRP-T conjugate) as a Hib antigen to produce a mixture of DPT-IPV-Hib-HBs adjuvant and PRP-T conjugate; and (6) adjusting pH of the mixture of DPT-IPV-Hib-HBs adjuvant and PRP-T conjugate obtained in step (5) to 5.4 to 5.9.