

COMBINATION VACCINES



- Combinations vaccines are indispensable to reduce the number of routine injections in vaccination programs to the absolute minimum. They have been shown to significantly reduce reactogenicity, completion and compliance.
- Combination vaccines are products that protect either against several serotypes/strains of one microorganism (e.g., trivalent influenza, multivalent pneumococcal) or against 2 or more different pathogens in a single injection (e.g., DTP based combinations).
- They have been used since the mid 1940s (trivalent influenza 1945, early pneumococcal combinations 1947, DTWP 1948) and have become central to pediatric schedules, especially DTaP and DTWP based combinations that can cover up to six diseases in one shot.
- Live combination vaccines include MR, MMR, MMRV and trivalent OPV.
- Travel vaccines include HAV–HBV and HAV–typhoid.
- High valency pneumococcal polysaccharide (23 serotypes) and conjugate vaccines (20 serotypes to date) illustrate the extremes of current combinations.

Key challenges include	Major benefits include:
• Chemical/physical incompatibilities	• Simplified logistics
• More complex manufacturing with a higher risk of production failures	• Fewer injections and clinic visits
• Reduced program flexibility (issues with one antigen affect the whole product)	• Higher acceptance and completion/compliance
• Difficulty attributing adverse events to a single component	• Fewer administration errors
• Immunologic interference between components	• Reduced local reactogenicity compared to separate injections
• Limited interchangeability between different brands	• Overall cost savings for health systems, families, and society

- Each new combination requires a full development and licensure program (preclinical plus phase 1–3 trials) and ongoing post-marketing monitoring, because immunologic interactions and program-level effects cannot be predicted reliably from single-component data alone. It is dangerous and illegal to simply mix different licensed products.

Combination vaccines: Relevant examples (list not complete)

Abbreviation	Antigens included	Example manufacturer(s) and regions
Td	Tetanus toxoid, reduced dose diphtheria toxoid	Various global; India: Serum Institute of India (SII), Biological E; China: CNBG; LatAm: Bio Manguinhos/Fiocruz (Brazil)
Tdap	Tetanus toxoid, reduced dose diphtheria toxoid, acellular pertussis (3–5 components)	GSK, Sanofi (SP, SPMSD); India: SII, Biological E (similar aP based products); China: CNBG adult pertussis containing vaccines; LatAm: Fiocruz (under licence)
Td-IPV	Tetanus toxoid, reduced dose diphtheria toxoid, inactivated poliovirus types 1, 2, 3	Sanofi Pasteur (SP, SPMSD); used in Europe and some Latin American markets
Tdap-IPV	Tetanus toxoid, reduced dose diphtheria toxoid, acellular pertussis, inactivated poliovirus types 1, 2, 3	GSK, Sanofi (SP, SPMSD); used in Europe, parts of Latin America, some high income Asia Pacific markets
DTwP-Hib	Diphtheria toxoid, tetanus toxoid, whole cell pertussis, Hib conjugate	GSK; India: SII; other Indian suppliers for domestic/EPI markets
DTwP-HBV	Diphtheria toxoid, tetanus toxoid, whole cell pertussis, hepatitis B surface antigen	Bio Farma (Indonesia), Biological E (India), SII; widely used in Asia and some African/LatAm programmes via UNICEF tenders
DTwP-HBV-Hib	Diphtheria toxoid, tetanus toxoid, whole cell pertussis, hepatitis B surface antigen, Hib conjugate	Bio Farma, Biological E, Janssen (J&J), GSK, LG Life Sciences, Panacea Biotec, SII, Sanofi (SP); used in India and other LMICs, some uptake in Latin America via PAHO/UN procurement
DTaP	Diphtheria toxoid, tetanus toxoid, acellular pertussis (2–5 components)	GSK, Sanofi (SP, SPMSD), Statens Serum Institut (SSI); paediatric use in EU, US, some LatAm markets
DTaP-Hib	Diphtheria toxoid, tetanus toxoid, acellular pertussis, Hib conjugate	GSK; used in Europe and some middle income countries; analogous combinations by Indian manufacturers for domestic use
DTaP-Hib-IPV	Diphtheria toxoid, tetanus toxoid, acellular pertussis, Hib conjugate, inactivated poliovirus types 1, 2, 3	GSK, Sanofi (SP, SPMSD), SSI; used in Europe, high income markets and selected middle income countries including some in Latin America
DTaP-Hib-IPV	Diphtheria toxoid, tetanus toxoid, acellular pertussis, Hib conjugate, inactivated poliovirus types 1, 2, 3	GSK, Sanofi (SP, SPMSD), SSI; used in Europe, high income markets and selected middle income countries including some in Latin America
DTaP-Hib-IPV-HBV (hexavalent)	Diphtheria toxoid, tetanus toxoid, acellular pertussis, Hib conjugate, inactivated poliovirus types 1, 2, 3, hepatitis B surface antigen	GSK, MCM, Sanofi (SP, SPMSD); widely used in the EU and some Latin American and Asia Pacific markets; India has domestically produced hexavalent analogues entering the market
MMR	Measles, mumps, rubella live attenuated viruses	GSK, Sanofi (SPMSD), Merck; produced locally or under licence in China (CNBG) and in several LatAm producers (e.g., Fiocruz)
MMRV	Measles, mumps, rubella, varicella live attenuated viruses	GSK, Sanofi (SPMSD), Merck; used in Europe, North America, parts of Latin America and some high income Asian settings
MenC-Hib	Meningococcal C conjugate, Hib conjugate	GSK; mainly Europe; similar Men Hib combinations developed by Indian manufacturers for domestic/export markets
MenCY-Hib	Meningococcal C conjugate, Hib conjugate	GSK; mainly Europe; similar Men Hib combinations developed by Indian manufacturers for domestic/export markets
MenACWY (quadrivalent)	Neisseria meningitidis serogroups A, C, W, Y (polysaccharide or conjugate)	Sanofi, GSK; used in US, EU, Gulf, parts of Latin America; India (SII) and China (e.g., Walvax) produce MenA/C or ACWY conjugates for domestic/regional use
MenAC (China)	Neisseria meningitidis serogroups A, C, W, Y (polysaccharide or conjugate)	Sanofi, GSK; used in US, EU, Gulf, parts of Latin America; India (SII) and China (e.g., Walvax) produce MenA/C or ACWY conjugates for domestic/regional use
MenA (Africa)	Neisseria meningitidis serogroup A conjugate	Serum Institute of India MenAfriVac; used across the African meningitis belt through mass campaigns and routine programmes
HAV-HBV	Inactivated hepatitis A virus, hepatitis B surface antigen	GSK (Twinrix and generics); used for travellers and at risk groups in EU, US, LatAm; Indian and Chinese manufacturers have analogous combined HAV-HBV products for domestic markets
HAV-HBV	Inactivated hepatitis A virus, hepatitis B surface antigen	GSK (Twinrix and generics); used for travellers and at risk groups in EU, US, LatAm; Indian and Chinese manufacturers have analogous combined HAV-HBV products for domestic markets
HAV-Ty	Inactivated hepatitis A virus, Vi polysaccharide typhoid antigen	GSK, Sanofi (SP, SPMSD); used in Europe, Asia and Latin America for travellers and residents in endemic areas; India and China also supply separate HAV and typhoid vaccines that are co administered.
TIV/QIV (trivalent/quadrivalent influenza)	Inactivated influenza viruses: 2 A subtypes + 1 (TIV) or 2 (QIV) B lineages	GSK, Sanofi, CSL Seqirus; China: CNBG, Sinovac; India: SII; widely used globally, including Latin America via PAHO revolving fund
LAIV (quadrivalent)	Live attenuated influenza viruses: 2 A subtypes + 2 B lineages	AstraZeneca (FluMist/Fluenz); used in some EU countries and the US paediatric programmes; limited uptake in LMICs
OPV (trivalent)	Oral live attenuated poliovirus types 1, 2, 3	Various including Sanofi, GSK historically; India and China have domestic OPV producers; widely used in many LMICs and Latin America through GPEI/UNICEF
IPV (trivalent)	Inactivated poliovirus types 1, 2, 3	Sanofi, GSK, Bilthoven Biologicals; India (Panacea, SII) and China (CNBG) produce IPV; used globally in stand alone form and within combinations

References

Esteves Jaramillo A, Schmitt HJ. Combination vaccines. In: Schmitt HJ, ed. Essentials in Vaccinology. Singapore: Global Health Press; 2021. VacciTUTOR, Chapter 28. doi:10.33442/vt202128. See individual [VacciTUTOR](#) chapters for details.

[READ MORE](#)