Hexavalent vaccines indicator

Benefits of the intervention

Serogroup or serotype coverage by vaccines considered (for serogroup- or serotype-specific vaccines)

Serogrouping is not a relevant concept for diphtheria, tetanus, pertussis, or hepatitis B in the context of vaccine coverage

There are 6 serotypes of Haemophilus influenzae (a to f) of which type b was the commonest cause of severe disease in children. Disease due to other serotypes and non-typeable Haemophilus influenzae can cause disease. 1, 2, 3, 4, 5

Poliovirus exists in three distinct serotypes: types 1, 2, and 3. Immunity to one serotype does not confer protection against the others, necessitating vaccines that target all three (trivalent vaccine). All the available Hexavalent vaccines contains all the three Polio serotypes. 6, 7

Efficacy and effectiveness estimates (e.g. against infection, disease, hospitalization, death), including in different populations

Clinical studies consistently show that hexavalent vaccines are highly effective in generating protective immune responses against all six targeted diseases3, 8, 9, 10, 11, 12, 13, 14, 15 :

- Diphtheria - Nearly all children achieve seroprotective antibody levels after vaccination and booster doses with non-inferior protection compared to monovalent or pentavalent vaccines. 9
- Tetanus - 100% seroprotection rates reported post-booster; strong and persistent antibody

responses with no evidence of reduced efficacy compared to monovalent or other combination vaccines. 9

- Pertussis - High seroconversion rates (94–95% for Bordetella pertussis, 77–87% for pertussis toxin). Head-to-head studies and clinical trials confirm that the immune response to pertussis antigens in hexavalent vaccines is non-inferior to that of other licensed combination vaccines, including pentavalent and monovalent formulations. Some differences in antibody levels (e.g., anti-pertussis toxin, anti-pertactin) exist, but these have not shown clear clinical relevance. Hexavalent vaccines may contain either whole cell pertussis (wP) or acellular pertussis (aP) antigens, which influence immunogenicity and reactogenicity profiles, with aP generally associated with lower reactogenicity. 15

- Hepatitis B - >99% seroprotection post-booster with no significant reduction compared to the monovalent vaccine. 12

- Hib - 96–100% achieve protective antibody levels post-primary and booster doses. There is some evidence that Hib conjugate vaccine in combination with acellular pertussis (DTaP-Hib) induces a lower antibody response than Hib conjugate in combination with whole cell pertussis (DTwP-Hib) or separately administered DTaP and Hib conjugate vaccines. 14

- Poliomyelitis - 98–100% seroprotection for all three poliovirus types post-booster. Non inferiority (as measures by antibody titers) has been demonstrated for wP containing Hexavalent and IPV/OPV. 10, 11, 13

Duration of protection and waning of immunity in general and risk groups

The duration of protection varies by disease component, but evidence shows that these vaccines provide strong initial immunity and long-lasting immune memory, especially when booster doses are included . 16, 17, 18, 19, 5, 6, 20, 21, 22, 23, 24, 25, 26, 27 .

Diphtheria - Data on the duration of seroprotection from 2 large representative population studies from the Netherlands, using a complete 3-dose primary series plus 3-dose booster series prior to adolescence, indicate that this schedule results in very high seroprevalence above the threshold for basic protection (≥0.01 IU/mL) up to 39 years of age and potentially longer. 16, 22, 25

Tetanus - Data from serological studies suggest that a primary series of 3 TTCV doses in infancy plus a booster during the second year of life will provide 3–5 years of protection. A further booster dose (e.g. in early childhood) provides protection into adolescence, and another booster

during adolescence induces immunity that lasts through much of adulthood, providing protection to women of reproductive age. 17, 21, 25

Pertussis - Whereas little is known about the duration of protection following pertussis vaccination in LMICs countries, several studies in HICs show that protection wanes after 4-12 years. 18, 20

Hepatitis B - In a study in Alaska, USA, a 3-dose vaccination schedule prevented all clinically appparent and chronic HepB infection for at least 30 years. 19, 23, 24, 26

Hib - Although there is some evidence of a decrease over time in the proportion of Hib vaccine recipients with antibody levels higher than the set thresholds, there is only limited evidence to suggest that this decline is associated with an increase in clinical disease. 5, 25

Poliomyelitis - The exact duration of immunity following a complete IPV series is not fully determined; however, it is believed to confer protection for many years. 6

Sources

1.

Shuel M, Hoang L, Law DKS, Tsang R (2011). Invasive Haemophilus influenzae in British Columbia: non-Hib and non-typeable strains causing disease in children and adults. Int J Infect Dis. 15:e167–e173. doi:10.1016/j.ijid.2010.10.005.

2.

Knuf M et al. (2021). Hexavalent vaccines: what can we learn from head-to-head studies? Vaccine. 39(41):6025–6036. doi:10.1016/j.vaccine.2021.08.086.

3.

Boisnard F, Manson C, Serradell L, Macina D (2023). DTaP-IPV-HB-Hib vaccine (Hexaxim): an update 10 years after first licensure. Expert Rev Vaccines. 22:1196–1213. doi:10.1080/14760584.2023.2280236.

4.

Vesikari T, Borrow R, Da Costa X, Richard P, Eymin C, Boisnard F, Lockhart S (2017). Concomitant administration of a fully liquid, ready-to-use DTaP-IPV-HB-PRP-T hexavalent vaccine with a meningococcal serogroup C conjugate vaccine in infants. Vaccine. 35(3):452–458. doi:10.1016/j.vaccine.2016.11.053.

5.
Haemophilus influenzae type b (Hib) vaccine: WHO position paper, July 2013. Weekly Epidemiological Record. 2013; 88(39): 413–426.

6.
Polio vaccines: WHO position paper, June 2022. Weekly Epidemiological Record. 2022; 97(25): 277–296.7.

7.
Centers for Disease Control and Prevention (CDC) (no date). Polio vaccines [website]. Atlanta: CDC. Available at: https://www.cdc.gov/polio/vaccines/index.html (accessed 24 June 2025).

8.
Dakin A, Borrow R, Arkwright P (2022). A review of the DTaP-IPV-HB-PRP-T Hexavalent vaccine in pediatric patients. Expert Rev Vaccines. 22:104–117. doi:10.1080/14760584.2023.2161519.

9.
Wanlapakorn N, Sarawanangkoor N, Srimuan D, Thatsanathorn T, Thongmee T, et al. (2024). Antibody persistence to diphtheria toxoid, tetanus toxoid, Bordetella pertussis antigens, and Haemophilus influenzae type b following primary and first booster with pentavalent versus hexavalent vaccines. Hum Vaccin Immunother. 20. doi:10.1080/21645515.2024.2352909.

10.
Knuf M, Haas H, García-Corbeira P, Turriani E, Mukherjee P, et al. (2021). Hexavalent vaccines: what can we learn from head-to-head studies? Vaccine. doi:10.1016/j.vaccine.2021.08.086.

11.
Sharma H, Parekh S, Pujari P, Shewale S, Desai S, et al. (2024). A randomized, active-controlled, multi-centric, phase-II clinical study to assess safety and immunogenicity of a fully liquid DTwP-HepB-IPV-Hib hexavalent vaccine (HEXASIIL®) in Indian toddlers. Vaccine. 42(26):126380. doi:10.1016/j.vaccine.2024.126380.

12.
Steiner M, Ramakrishnan G, Gartner B, Van Der Meeren O, Jacquet J, et al. (2010). Lasting immune memory against hepatitis B in children after primary immunization with 4 doses of DTPa-

HBV-IPV/Hib in the first and 2nd year of life. BMC Infect Dis. 10:9. doi:10.1186/1471-2334-10-9.

13.
Sanchez L, Rungmaitree S, Kosalaraksa P, Jantarabenjakul W, Leclercq J, Yaiprayoon Y, Midde VJ, Varghese K, Mangarule S, Noriega F (2023). Immunogenicity and safety of a hexavalent DTwP-IPV-HB-PRPT vaccine versus separate DTwP-HB-PRPT, bOPV, and IPV vaccines administered at 2, 4, 6 months of age concomitantly with rotavirus and pneumococcal conjugate vaccines in healthy infants in Thailand. Pediatr Infect Dis J. 42(8):711–718. doi:10.1097/INF.0000000000003975.

14.
Haemophilus influenzae type b (Hib) vaccine: WHO position paper, July 2013. Weekly Epidemiological Record. 2013;88(39):413–426.

15.
Patterson J, Kagina BM, Gold M, Hussey GD, Muloiwa R (2018). Comparison of adverse events following immunisation with acellular and whole-cell pertussis vaccines: a systematic review. Vaccine. 36:6007–6016. doi:10.1016/j.vaccine.2018.08.022.

16.
Diphtheria vaccine: WHO position paper, August 2017. Weekly Epidemiological Record. 2017; 92(31): 417–435.

17.
Tetanus vaccine: WHO position paper, February 2017. Weekly Epidemiological Record. 2017; 92(6): 53–76.

18.
Pertussis vaccine: WHO position paper, August 2015. Weekly Epidemiological Record. 2015; 90(35): 433–460.

19.
Hepatitis B vaccines: WHO position paper, July 2017. Weekly Epidemiological Record. 2017; 92(27): 369–392.

20.

Wendelboe, A.M., et al. (2005) ‘Duration of immunity against pertussis after natural infection or vaccination’, Pediatric Infectious Disease Journal, 24(Suppl. 5), pp. S58–S61.

21.

Borrow, R., Balmer, P. and Roper, M.H. (2007) The immunologic basis for immunization: module 3: tetanus. Geneva: World Health Organization. Available at: http://apps.who.int/iris/bitstream/10665/43687/1/9789241595551_eng.pdf (accessed 30 June 2025).

22.

Swart, E.M., et al. (2016) ‘Long-term protection against diphtheria in the Netherlands after 50 years of vaccination: results from a seroepidemiological study’, PLoS ONE, 11(2), e0148605. doi: 10.1371/journal.pone.0148605.

23.

Bruce, M.G., et al. (2016) ‘Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose’, Journal of Infectious Diseases, 214, pp. 16–22. doi: 10.1093/infdis/jiw144.

24.

Wanlapakorn, N., Sarawanangkoor, N., Srimuan, D., Thatsanathorn, T., Klinfueng, S. and Poovorawan, Y. (2024) ‘Persistence of hepatitis B surface antibody until 7 years of age following administration of hexavalent and pentavalent vaccines in children at 2, 4, 6, and 18 months’, Vaccine: X, 20. doi: 10.1016/j.jvacx.2024.100561.

25.

Wanlapakorn, N., Sarawanangkoor, N., Srimuan, D., Thatsanathorn, T., Thongmee, T. and Poovorawan, Y. (2024) ‘Antibody persistence to diphtheria toxoid, tetanus toxoid, Bordetella pertussis antigens, and Haemophilus influenzae type b following primary and first booster with pentavalent versus hexavalent vaccines’, Human Vaccines & Immunotherapeutics, 20. doi: 10.1080/21645515.2024.2352909.

26.

Avdičová, M., Crasta, P., Hardt, K. and Kovac, M. (2015) ‘Lasting immune memory against hepatitis B following challenge 10-11 years after primary vaccination with either three doses of

hexavalent DTPa-HBV-IPV/Hib or monovalent hepatitis B vaccine at 3, 5 and 11-12 months of age', Vaccine, 33(23), pp. 2727–2733. doi: 10.1016/j.vaccine.2014.06.070.

27.

Mangarule, S., Sapru, A., Bavdekar, A., Kawade, A., Lalwani, S., et al. (2023) 'Antibody persistence following administration of a hexavalent DTwP-IPV-HB-PRPT vaccine versus separate DTwP-HB-PRPT and IPV vaccines and safety and immunogenicity of a booster dose of DTwP-IPV-HB-PRP~T administered with an MMR vaccine in healthy infants in India', Pediatric Infectious Disease Journal, 42(12), pp. 1128–1135.