Pentavalent to Hexavalent Vaccine Evidence to Recommendation Evidence for National Immunization Technical Advisory Groups (NITAGs)

Since 2011, Gavi, the Vaccine Alliance (Gavi) has supported the use of pentavalent (penta) (DTwP-HepB-Hib) vaccine, safeguarding millions of children from five major illnesses (diphtheria, Hib, Hepatitis B, pertussis and tetanus). In 2023, a new Gavi program began to support countries in switching from the penta to hexavalent (hexa)(DTwP-HepB-Hib-IPV) vaccines, which added the inactivated polio vaccine (IPV). The switch aimed to reduce the number of injections and healthcare professional workload, cut costs through combination, and boost polio eradication efforts by improving IPV coverage among zero-dose and under-vaccinated children.

National Immunization Technical Advisory Groups (NITAGs) play a crucial role in new vaccine introduction and in the applications for Gavi support as they gather and organize available evidence to provide timely vaccine policy recommendations to their Ministries of Health (MoH).

The purpose of this document is to summarize and catalogue key findings of existing evidence for the penta to hexa switch through the lens of Population, Intervention, Comparison, Outcomes (PICO) questions and the Evidence to Recommendation Framework (EtR) and can be used as a starting point for NITAGs to develop context-specific recommendations in their countries.

This document has been compiled and reviewed by experts and will provide:

1. A PICO Question
2. The Evidence to Recommendation Framework separated by domain
3. Broad and PICO-specific evidence to collect by domain
4. Key sources of evidence for NITAGs for each element of each domain
5. Additional resources and tools for each domain

Note that in the criteria tables for each domain, the column “Priority” has been left blank. It is recommended that each NITAG complete this column according to its own considerations, using the categories “Critical”, “Important”, or “Of Limited Importance”

PICO-Specific Evidence Tables for Hexavalent Vaccine

Policy Question: Should hexa vaccine be recommended for young children in the routine immunization programme, to replace penta and IPV doses in the first year of life?

Broad policy question: *Should hexavalent vaccine be recommended for young children in the routine immunization program, to replace pentavalent vaccine plus IPV in the first year of life?*		
P	Target **Population**	Infants < 1 yr of age
I	Vaccine **Intervention**	Three doses of hexavalent (DTP-HepB-Hib-IPV), given at same schedule as current pentavalent (i.e. 6, 10, and 14 weeks age)
C	**Comparison** Intervention	Pentavalent (DTP-HepB-Hib) at 6, 10, and 14 weeks and IPV (1 dose) at 9 months of age
O	**Outcomes** - Anticipated benefits or harms	Anticipated benefits: Sustained protection against diphtheria, tetanus, pertussis, hepB, H influenza B and polio. Anticipated harms: Serious adverse events (e.g. anaphylaxis)
Focused PICO Question: *In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine is safe and provides similar protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?*		

Draft - PICO-Specific Evidence Tables for Hexavalent Vaccine (*Jan 7, 2026*)

Policy Question: Should hexavalent vaccine be recommended for young children in the routine immunization programme, to replace pentavalent and IPV doses in the first year of life?

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine is safe and provides similar protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Domain 1: Problem – PICO Specific Criteria Table

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
1.1 Burden of disease	• Incidence and prevalence of morbidity and mortality • Age-specific morbidity and mortality • Risk group • Disease occurrence over time • Changes in epidemiology over time	• Incidence, morbidity, mortality and prevalence of 6 diseases (diphtheria, tetanus, pertussis, Hepatitis B, H influenza type b, Poliomyelitis) • Age-specific morbidity and mortality for each of these diseases (focused on children < 5 yrs) • Risk groups – immunodeficiency, malnutrition, HIV, asplenia, complement deficiency, • Disease occurrence, changes in epidemiology over time (each of the diseases) • Registered outbreaks over the past 3 years (Diphtheria, Pertussis, Poliomyelitis)		• Country Disease Surveillance Data • Global – WHO UNICEF JRF Immunization Data Portal * – Annual reported cases of Vaccine preventable diseases • Global - WHO Vaccine Position papers (SAGE Polio, Diphtheria, Pertussis, Tetanus, etc)
1.2 Clinical characteristics of the disease	• Signs and symptoms of disease • Severe forms • Long-term complications of disease • Medical management of disease	• Signs and symptoms of the 6 diseases • Severe forms of the diseases • Long-term complications of disease (sequelae) – paralytic polio, diphtheria • Medical management of diseases • Antibiotics use and antimicrobial resistance for treating Diphtheria, Pertussis, H. influenza		• WHO Vaccine Position papers • WHO Health Topics (ex Diphtheria, Hepatitis, Pertussis, Poliomyelitis, Tetanus • General Medical literature, textbooks
1.3 Use and Costs of Health Care	• Primary/secondary/tertiary care implications • Short- and long-term use of healthcare (e.g., treatments, hospitalization)	• Primary/secondary/tertiary care implications for each disease • Short-and long-term use of health care (e.g. hygiene, health education) and their effectiveness, costs, practicality • Antibiotic susceptibility and resistance		• Global data gathered from WHO, CDC, ECDC, WHO Regional sites. • Local data for a specific country (Literature search in PUBMED or other search databases) • Local data from Ministry of Health
1.4 Alternative preventive and	• Alternative preventive and control measures (e.g., health education,	• Vs. current vaccine schedule - 3 doses of Penta + 1 or 2 doses IPV		• Global data - WHO Vaccine Position papers

control measures	hygiene) and their effectiveness, costs, practicality	• Other preventive and control measures (e.g. antibiotic prophylaxis for contacts)		
1.5 Regional & international considerations	• Existence of regional and global recommendations • Disease potential for international spread and pandemic risk	• WHO SAGE and regional recommendations and guidance for prevention and epidemic response • SAGE and RITAG guidance of switching from penta to hexa vaccines, and for OPV to IPV, and for DT(P) booster doses • Disease potential for international spread (Polio, Diphtheria, Pertussis)?		• Global data - WHO Vaccine Position papers • Data from Regional TAG and country NITAG recommendations (available at the NITAG Resource Center on vaccines and hexa switch

*WHO UNICEF Joint Reporting Form on Immunization

Resources and Tools: Domain 1 - Problem

1. World Health Organization – WHO UNICEF Joint Reporting Form – Annual reported cases of Vaccine preventable diseases WHO UNICEF JRF Immunization Data Portal
2. Global Polio Eradication Initiative - Poliomyelitis –
    a. Wild virus https://polioeradication.org/wild-poliovirus-count/
    b. Vaccine Derived - https://polioeradication.org/circulating-vaccine-derived-poliovirus-count/
3. WHO Vaccine Position Papers (SAGE Polio, Diphtheria, Tetanus, Pertussis, HepB, H. influenzae) WHO Vaccine Position papers
4. WHO Health Topics (ex Diphtheria, Hepatitis, Pertussis, Poliomyelitis , Tetanus)
5. NITAG Resource Center - Data from Regional TAG and country NITAG recommendations (available at the NITAG Resource Center) on vaccines and hexavalent switch

Domain 2: Benefits and Harms of the Options

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
2.1 Vaccine characteristic	• Vaccine presentation, formulation, dosage, and route of administration • Administration schedule and possibility of co-administration with other vaccines and drugs • Flexibility of vaccination schedule • Cold chain and logistic requirements	• Presentation, formulation, dose and route of administration of WHO pre-qualified Penta and Hexa vaccines • Current recommended schedules– Penta + IPV vs Hexa, if it will be introduced. • Interaction of Penta vs Hexa when co-administered with other vaccines • Age constraints for Hexa vs Penta vaccines. • Cold chain requirements for use of Penta vs Hexa		• GAVI. Hexavalent vaccine programme information. Gavi Hexa Support • WHO and UNICEF Hexa Introduction Guidance -FAQs Hexa Introduction • Manufacturers vaccine package insert - Hexasiil Package Insert • Primary vaccine studies – Sharma (2024), Mangarule (2022, 2024) • Global - WHO Position Paper - Polio 2022 • Country vaccination schedules: Penta, IPV, DTP boosters
2.2 Safety	• Type, consequences and frequency of short and long-term adverse events following vaccination • Risk groups or risk factors for adverse events • Contraindications or precautions	• Differences in safety profile of Penta + IPV vs Hexa • Serious adverse events following immunization in target populations • Any known contraindications or precautions for both vaccines		• Hexasiil Package Insert • Primary vaccine studies - – Sharma (2024), Mangarule (2024) • Global - WHO Vaccine Position Papers (SAGE) • The Global Advisory Committee on Vaccine Safety (who.int) - statements and background documents:
2.3 Efficacy and effectiveness	• Vaccine efficacy/effectiveness and types of specific protection afforded • Critical determinants of the immune response associated with protection • Duration of protection and waning of immunity in general and risk groups • Interference in protection or immunity with other vaccines	• Comparison of immune response/ immunogenicity between Penta + IPV vs Hexa vaccines for each of the vaccine components • What is the difference in duration of protection and waning of immunity between Penta (3 doses)+ IPV vs Hexa (4 doses - one booster included) for each of components?		Immunogenicity • WHO SAGE proceedings (Polio 2025) • Hexasiil Package Insert • Primary vaccine studies – Sharma (2024), Mangarule (2024)

		• Is there any interference regarding protection or immunity with other vaccines		
2.4 Vaccine indirect effects	• Herd immunity/protection • Potential negative population impact of emergence of non-vaccine serotypes	• Is there any difference in the degree of herd immunity/protection produced by Penta + IPV vs. Hexa, particularly for polio (polio type 1 and cVDPV)? • Impact on cVDPV outbreaks and potential impact on bOPV withdrawal?		Global - WHO Position Paper - Polio 2022

Resources and Tools: Domain 2 - Benefits and Harms

1. WHO Position Paper - Polio 2022
2. WHO Meeting of the Strategic Advisory Group of Experts on Immunization, March 2025: conclusions and recommendations. WER No 23, 2025, 100, 219–238 *see. P 235*. WER10023-eng-fre.pdf
3. World Health Organization (2025). Frequently asked questions and considerations for the introduction of hexavalent vaccine DTwP-HepB-Hib-IPV in routine immunization programmes. In: World Health Organization [website]. Geneva: World Health Organization; FAQs Hexa Introduction
4. Gavi (2023). Hexavalent vaccine programme information. Gavi Hexa Support
5. The Global Advisory Committee on Vaccine Safety (who.int) - Full report of GACVS meeting of 2-3 December 2004, published in the WHO Weekly Epidemiological Record on 7 January 2005
6. Serum Institute of India – Hexasiil Package Insert
7. WHO –HEXASIIL | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Primary Vaccine Studies

8. Mangarule S et al. (2022) Safety and immunogenicity of a hexavalent DTwP-IPV-HB-PRP_T vaccine versus separate DTwP-HB-PRP_T and IPV vaccines in healthy infants in India. Vaccine: X 10 100137. https://doi.org/10.1016/j.jvacx.2021.100137
9. Sharma H et al (2024) A phase III randomized-controlled study of safety and immunogenicity of DTwPHepB-IPV-Hib vaccine (HEXASIIL®) in infants. NPJ Vaccines 9:41 1-9 https://doi.org/10.1038/s41541-024-00828-w
10. Sharma H 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 Vaccine 42(26) 126380 https://doi.org/10.1016/j.vaccine.2024.126380
11. Mangarule S et al. (2023) Antibody Persistence Following Administration of a Hexavalent DTwP-IPV-HB-PRP~T Vaccine Versus Separate DTwP-HB-PRP~T 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. The Pediatric Infectious Disease Journal 42(12):1128-1135. doi: 10.1097/INF.0000000000004118. Epub 2023 Oct 13.
12. Sanchez L et al. (2023) . Immunogenicity and Safety of a Hexavalent DTwP-IPV-HB-PRP~T Vaccine Versus Separate DTwP-HB-PRP~T, bOPV, and IPV Vaccines Administered at 2, 4, 6 Months of Age Concomitantly With Rotavirus and Pneumococcal Conjugate Vaccines in Healthy Infants in Thailand - PMC. The Pediatric Infectious Disease Journal 42(8), 711-18.

Other Resources

13. WHO/Gavi: Hexavalent Vaccine Programme Information
14. WHO hexa switch training module: Key facts on polio vaccination and rationale for switching to hexavalent vaccine

15. UNICEF Product menu (Sept 2025) - UNICEF Vaccine Prices Sept 2025
16. WHO. Hexavalent Compendium – Hexavalent Vaccine Comparison (DTaP-HepB-Hib-IPV and DTwP-HepB-Hib-IPV NITAG Resource Center Hexa Compendium

Domain 3: Values & Preferences

PICO Question In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
3.1 Benefits and harms	• Relative importance the target population attributes to the benefits and harms of the intervention as well as the comparison	• Perception of mothers and caregivers to accept Hexa compared to Penta + IPV? Any anticipated differences – an extra appointment? • Perceptions of reducing number of injections in 1st year with Hexa • Relative importance the target population attributes to the benefits and harms of the intervention as well as the comparison		Local data • KAP Studies • Focus groups • BeSD Study • Interviews Countries may use published evidence from other countries (eg Senegal, Mauritania – Hexa Early Adopters meeting Nov 2025)
3.2 Differences by segments of target population	• Differences in values and preferences (ethical, religious, financial) for different segments of the target population (disadvantaged, religious)	• Differences in values and preferences among different populations about additional antigen (added to the vaccine), reduced injections, additional dose in 2nd year (per above)		
3.3 Demand	• Demand for vaccine of target populations	• Demand for Hexa vaccine and reduced injections by target population/caregivers		

Resources and Tools: Domain 3 – Values and Preferences

1. Andrade C et al. Designing and Conducting Knowledge, Attitude, and Practice Surveys in Psychiatry: Practical Guidance. Indian J Psychol Med 2020 Aug 27;42(5):478–481. doi: 10.1177/0253717620946111 KAP Studies
2. Focus groups
3. WHO UNICEF. Behavioural and social drivers of vaccination: tools and practical guidance for achieving high uptake. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. BeSD Study
4. Al Bashar L, et al. (2023) Parents' and healthcare professionals' perception toward the introduction of a new fully liquid hexavalent vaccine in the Malaysian national immunization program: a cross-sectional study instrument development and its application. Frontiers in Immunology, 14. https://doi.org/10.3389/fimmu.2023.1052450.
5. Mauritania/Senegal – presentations from Hexa Early Adopters Meeting Nov 2025

Domain 4: Resource Use

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
4.1 Resource use and cost related to the vaccine	• Direct and indirect costs to administer the vaccine as they compare to other prevention or control measures • Cost using different strategies	• Current cost for purchasing Penta + IPV vs. added purchasing cost if programme switches to Hexavalent vaccine formulation. • Other direct or indirect cost related to switching from Penta + IPV to Hexa (training, cold chain modifications, staff cost for additional appointment, reduced injections, etc) • Are delivery strategies different or similar? In case of any difference what is the cost?		National • Size of population estimated for each dose, including booster dose; vaccine wastage rate • Estimated cost to vaccinate each age group Global/Regional • UNICEF Vaccine Prices Sept 2025 • UNICEF Supply Costs • GAVI Hexa costing guidance GAVI Hexa Funding Guidance • Gavi Hexa Assessment Support Tool GAVI Hexa Support Tool
4.2 Vaccine availability	• Availability of vaccine and long-term supply • Available suppliers and competition dynamic in the market	• Market availability of Penta and Hexa in the short and long term • Future suppliers and availability post-Gavi		National • Licensure - Natl Vaccine Regulatory Authority • MOH, Ministry of Finance Global/Regional • WHO –HEXASIIL | WHO Prequalification • UNICEF Vaccine Prices Sept 2025 • GAVI Hexavalent Funding
4.3 Vaccine affordability	• Availability of fiscal space to effectively implement and sustain the recommendation in the programme • Prevailing prices for the vaccine in the market and price	• Annual fiscal implications to the government contribution to Gavi for sustainability of government funding • Overall trend in increase in co-financing cost for all Gavi co-financed vaccines in case of Hexa introduction • When does Gavi eligibility end and how does the government intend to ensure sustainability?		National • Ministry of Finance • Vaccination cost data Global • Unit price for Hexa (UNICEF) – including expected trends - UNICEF Vaccine Prices Sept 2025 • GAVI Hexa Support Guidance

	estimations for the local community			• Countries may use published evidence from other countries if national data not available (eg Senegal, Mauritania – Hexa Early Adopters meeting Nov 2025)
4.4 Socio-economic	• School and work absenteeism • Indirect cost to patients and families • Productivity losses	• Possible reduced (or increased) absenteeism from patients and caregivers due to better protection (IPV) • Possible reduced productivity loss from sequelae due to Poliomyelitis, Diphtheria, Pertussis		National • MOH, Ministry of Finance
4.5 Economic impact of intervention on immunization program and health sector	• Reduction in healthcare costs • Cost-effectiveness ratio of vaccination program	• Reduction in healthcare costs for patients, including costs of acute care and of sequelae due to the targeted diseases if Hexa introduced vs Penta + IPV • Incremental Cost effectiveness of Hexa vaccine vs. Penta		National - If available Global/Regional • Countries may use published evidence from global, regional or other countries if national data not available; • Literature search in PUBMED or other search databases Hexa economic articles available (see economic study list)

Resources and Tools: Domain 4 – Resources

Vaccine Cost

1. UNICEF Product menu (Sept 2025) - UNICEF Vaccine Prices Sept 2025
2. Pan American Health Organization (PAHO) (2025). Revolving fund vaccine prices. Available at: https://www.paho.org/en/documents/revolving-fund-vaccine-prices-2025

Vaccine Purchase

1. World Health Organization (WHO) (2025). MI4A vaccine purchase data. Available at: https://www.who.int/teams/immunization-vaccines-and-biologicals/vaccine-access/mi4a/mi4a-vaccine-purchase-data

Vaccine Administration Supply Costs

1. UNICEF (2025). Auto-disable (AD) syringe price data. Available at: https://www.unicef.org/supply/documents/auto-disable-ad-syringe-price-data
2. UNICEF (2025). Safety boxes price data. Available at: https://www.unicef.org/supply/documents/safety-UNICEF Vaccine Prices Sept 2025boxes-price-data
3. UNICEF (2025). Syringe and safety box bundles price data. Available at: https://www.unicef.org/supply/documents/syringe-and-safety-box-bundles-price-data

Vaccine Prequalification

1. WHO –HEXASIIL | WHO Prequalification

GAVI Support and Financing

1. GAVI Gavi (2024). Gavi vaccine funding guidelines. Available at: https://www.gavi.org/news/document-library/gavi-vaccine-funding-guidelines
2. Gavi (2023). Hexavalent vaccine programme information. GAVI Hexavalent Funding
3. Gavi Hexa Assessment Support Tool GAVI Hexa Support Tool

Economic Studies

1. Seinfeld, J., et al. (2022). Economic assessment of incorporating the hexavalent vaccine as part of the National Immunization Program of Peru. BMC Health Services Research, 22, 651. https://doi.org/10.1186/s12913-022-08006-1
2. Seinfeld, J., et al. (2024). Introduction of a hexavalent vaccine containing acellular pertussis into the national immunization program for infants in Peru: a cost-consequence analysis of vaccination coverage. BMC Health Serv Res. 2024 Oct 10;24(1):1216. https://doi.org/10.1186/s12913-024-11684-8
3. Olivera, I., et al. (2023). Cost minimization analysis of a hexavalent vaccine in Argentina. BMC Health Services Research, 23(1), 1067. https://doi.org/10.1186/s12913-023-10038-0 .
4. Olivera, I., et al. (2020). Valuing the cost of improving Chilean primary vaccination: a cost minimization analysis of a hexavalent vaccine. BMC Health Serv Res. 2020;20(1):295. doi: 10.1186/s12913-020-05115-7
5. Romero, M., et al. (2021). Cost-Minimization and Budget Impact Analysis of a Hexavalent Vaccine (Hexaxim®) in the Colombian Expanded Program on Immunization. Value in Health Regional Issues, 26, 150–159. https://doi.org/10.1016/j.vhri.2021.06.001
6. Min, S., et al. (2023). Estimating the Total Societal Cost of a Hexavalent Vaccine versus a Pentavalent Vaccine with Hepatitis B in South Korea. Vaccines (Basel), 11(5), 984. https://doi.org/10.3390/vaccines11050984
7. Aljunid, S.M., Ismail, A., Nor, N.M., Zafar, A., Suleiman, A., et al. (2022) 'Economic impact of switching from partially combined vaccine "Pentaxim® and hepatitis B" to fully combined vaccine "Hexaxim®" in the Malaysian National Immunization Program', BMC Health Services Research, 22, p. 34. https://doi.org/10.1186/s12913-021-07428-7
8. Mogale, M., Burnett, R.J., Olivier, D., Mphahlele, J. (2014) 'Economic assessment of implementing Hexaxim® vaccine within the South African Expanded Programme on Immunisation (EPI-SA)',
9. International Journal of Infectious Diseases, 21(Suppl.), pp. 1–460 (Abstract, 16th ICID). April 2014 DOI:10.1016/j.ijid.2014.03.1307
10. Gavi Hexa Assessment Support Toolhttps://docs.google.com/spreadsheets/d/1A29atG6Mb4eCM7ApcNLxa4bekn26mE-x/edit?gid=249309308#gid=249309308
11. Senegal, Mauritania – presentations from the Hexa Early Adopters meeting Nov 2025

Domain 5: Equity

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
5.1 Equal access	• Universality, accessibility, and affordability of services for all the inhabitants in the country, including vulnerable, hard to reach and immigrant populations	• Are all communities reached with Penta? Will there be any difference is Hexa is used? • Are there communities or geographies with high burden of the targeted diseases but with limited access to service provision?		Local data. Countries may use published evidence from other countries (eg Senegal, Mauritania – Hexa Early Adopters meeting Nov 2025) (link?) Literature search in PUBMED or other search databases
5.2 Ethics, legality	• Non-health related effects of vaccination • Ethical considerations • Legal implications	• Legal implications of inaction if high incidence of targeted diseases (wild polio or cVDPV outbreaks) • Any ethical/legal implications with switching from Penta to Hexa?		
5.3 Stigma	• Stigma around the disease or around vaccination	• Stigma around the targeted diseases (including polio) and/or sequelae due to the specific diseases		

Domain 6: Acceptability

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
6.1 Related to disease and vaccine	• Perception of the public, stakeholders, and medical community about disease and vaccine (balances of benefits and harms)	• Perception of the public, stakeholders, and medical community about adding an antigen against polio (Hexa) vs continuously using Penta? • Perception about reducing number of injections in 1st year of life • Potential for higher or lower vaccination coverage with respect to polio eradication efforts		Local data • KAP Studies • Focus groups • BeSD Study • Interviews Countries may use published evidence from other countries (eg Senegal, Mauritania – Hexa Early Adopters meeting Nov 2025) Literature search in PUBMED or other search databases
6.2 Related to other interventions	• Impacts of program on efficacy and safety of other vaccines and health care interventions	• Will switching from Penta to Hexa affect the safety of other vaccines and other health care interventions? • Possible impact on occurrence of polio outbreaks (wild type 1 and cVDPV)		
6.3 Related to ethics, program, finances	• Ethical, programmatic, or financial issues that may affect acceptability of intervention by stakeholders	• Will switching from Penta to Hexa give rise to any ethical, programmatic, or financial issues that may affect stakeholders' acceptability?		

Resources and Tools: Domain 6 – Acceptability

1. Andrade C et al. Designing and Conducting Knowledge, Attitude, and Practice Surveys in Psychiatry: Practical Guidance. Indian J Psychol Med 2020 Aug 27;42(5):478–481. doi: 10.1177/0253717620946111 KAP Studies
2. Focus groups
3. WHO UNICEF. Behavioural and social drivers of vaccination: tools and practical guidance for achieving high uptake. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. BeSD Study
4. Al Bashar L, et al. (2023) Parents' and healthcare professionals' perception toward the introduction of a new fully liquid hexavalent vaccine in the Malaysian national immunization program: a cross-sectional study instrument development and its application. Frontiers in Immunology, 14. https://doi.org/10.3389/fimmu.2023.1052450.
5. Mauritania/Senegal – presentations from Hexa Early Adopters Meeting Nov 2025

Domain 7: Feasibility

PICO Question: In young children < 1 years, what is the scientific evidence that 3 doses of hexavalent vaccine at 6, 10 and 14 weeks, is safe and provides equal or better protection as 3 doses of pentavalent vaccine plus one dose of IPV, to prevent diphtheria, pertussis tetanus, hepatitis B, H. influenzae B and polio disease?

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
7.1 Accessibility	• Accessibility of target population	• Current coverage with each dose of pentavalent and IPV vaccine; dropout; zero dose children • Does the change from Penta to Hexa involve a change in RI target population and vaccine delivery strategies? • Reaching children who are not –up-to date or unvaccinated and in the 2nd year of life • Planning for transition from penta-hexavalent – national vs sub-national rollout; transition period to use Penta stocks		National • MOH EPI Program – local data • MOH EPI Multiyear Program plan – Operational and strategic • Other National program planning documents Global • GAVI Hexavalent Funding • WHO UNICEF FAQs Hexa Introduction
7.2 Resources for vaccine storage, distribution, and administration	• Availability of resources for vaccine storage, distribution, and administration —physical (cold chain storage), human, technical, and financial	• Adequacy of existing cold chain storage volume, transportation etc. • Any additional logistics and workforce required to accommodate changing from Penta + IPV to Hexa • Planning for transition from Penta to Hexavalent – national vs sub-national rollout; transition period to use Penta stocks		National • MOH EPI Program – local data • MOH EPI Multiyear Program plan – Operational and strategic Global • NITAG Resource Center Hexa Compendium • WHO UNICEF FAQs Hexa Introduction
7.3 Licensing of vaccine	• National Regulatory Authority (NRA) requirements to register available vaccines for use in target population and/or use in a different schedule as originally recommended	• Requirements and timeline of NRA (National Regulatory Authority) approval of vaccine and annual updates in vaccine formulation		National • Data from National regulatory bodies
7.4 Information management	• Availability of information systems to manage the vaccine supply chain measure related performance metrics,	• Program capacity to carry out monitoring of doses used and vaccine coverage		National • MOH EPI Program – local data

	i.e., coverage and vaccine utilization	• Capacity to monitor 4th dose in 2nd year of life • Existence, reliability, and sustainability of information and/or surveillance systems to measure outcomes and/or disease impact for targeted diseases (Diphtheria, Tetanus, Pertussis, Hepatitis B, H. influenzae, Poliomyelitis)		• MOH EPI Multiyear Program plan – Operational and strategic
7.5 Disease and AEFI surveillance	• Existence and reliability of surveillance systems to monitor disease and AEFI	• Laboratory capacity to confirm targeted diseases ((Diphtheria, Tetanus, Pertussis, Hepatitis B, H influenzae, Poliomyelitis)? • Systems for ongoing monitoring of AEFI and Adverse Events of Special Interest (AESI) following vaccination ? • Are there protocols/resources for clinical management of AEFIs?		National • National disease and AEFI surveillance programs Global • WHO UNICEF FAQs Hexa Introduction • NITAG Resource Center Hexa Compendium

Resources and Tools: Domain 7 - Feasibility

1. Gavi (2023). Hexavalent vaccine programme information. Available at: GAVI Hexavalent Funding
2. NITAG Resource Center Hexavalent Compendium NITAG Resource Center Hexa Compendium
3. World Health Organization (2025). Frequently asked questions and considerations for the introduction of hexavalent vaccine DTwP-HepB-Hib-IPV in routine immunization programmes. In: World Health Organization [website]. Geneva: World Health Organization; FAQs Hexa Introduction
4. Mauritania/Senegal – presentations from Hexa Early Adopters Meeting Nov 2025