Hexavalent vaccine

(DTaP-HBV-IPV-Hib)

Health Technology Assessment Philippines

OVERVIEW AND CONTEXT

Generic Name	Diphtheria, Tetanus and Pertussis (acellular component), Hepatitis B (rDNA), Poliomyelitis (inactivated) and Haemophilus influenzae Type B Conjugate Vaccine (adsorbed)
Applied dosing regimen	**Full term infants** ● **Primary:** 2 to 3 doses (at least 1 month interval between doses) ● **Booster:** ○ 3-dose primary: *A booster dose must be given at least 6 mos after last priming dose and preferably before 18 months of age* ○ 2-dose primary: *A booster dose must be given at least 6 mos after last priming dose and between 11 to 13 months of age* **Preterm infants (at least 24 weeks of gestational age)** ● **Primary:** 3-dose (at least 1 month interval between doses) ● **Booster:** *A booster dose must be given at least 6 mos after last priming dose and preferably before 18 months of age*
Products with Philippine FDA CPR	1. ***DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)*** 2. ***DTaP-HBV-IPV-Hib (pre-filled glass syringe)***
Drug/ Therapeutic class	Prophylactic vaccines
FDA approved/ Nominated indication	Primary and booster vaccination of infants and toddlers against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis, and invasive diseases due to haemophilus influenzae type B
Dosage strength and form	0.5 mL suspension for Injection
Mode of administration	Injected intramuscularly (IM)

Reference: Product insert; Topic Nomination Form

Hexavalent vaccine (DTaP-HBV-IPV-Hib)

Nominator	Department of Health – Disease Prevention and Control Bureau (DOH-DPCB)
Date of submission	16 November 2023
FDA CPR Status/ Expiry	DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial) - *February 2030 (for renewal)* DTaP-HBV-IPV-Hib (pre-filled glass syringe) - August 2028 *(for renewal)*

Reference: Topic Nomination Form

Rationale of Assessment

DPCB: the National Immunization Program (NIP) of the Department of Health procures Pentavalent (DTwP-HepB-Hib) vaccine, Oral Polio Vaccine (OPV), and Inactivated poliovirus vaccine (IPV) separately in line with the Omnibus Health Guidelines for Children. **However, given the evidence on the safety, efficacy, and ease of use of Hexavalent (DTaP-Hib-IPV-HepB) *(UK Health Security Agency, 2023)*, the program is considering streamlining the procurement of vaccines and adopt the said health technology.**

Hexavalent vaccine is not included in any of the following:

- DOH National Immunization Program
- Philippine National Formulary

Rationale of Assessment

PNF-included Counterpart Vaccine (Current Routine Immunization)	Nominated Health Technology
Pentavalent (DTwP-HepB-Hib) vaccine, Oral Polio Vaccine (OPV), and Inactivated poliovirus vaccine (IPV)	Hexavalent (DTaP-HBV-IPV-Hib) vaccine
Diphtheria Tetanus Pertussis (whole-cell) Hepatitis B (Recombinant), and Haemophilus Influenzae Type B (Hib) Combined Vaccine	Diphtheria Tetanus Pertussis (acellular component), Hepatitis B (rDNA), **Poliomyelitis (inactivated)** and Haemophilus influenzae Type B Conjugate Vaccine (adsorbed)
PLUS	
Inactivated Polio Vaccine (IPV)	

Note: OPV is not included as a comparator as it is part of the routine immunization, separate from IPV. Thus, it may also be administered to eligible population along with the hexavalent vaccine (GAVI The Vaccine Alliance 2023).

Considerations for the assessment

- Components of the hexavalent vaccine are all recommended by the local society (PIDSP)
- Inclusion of hexavalent vaccine will not displace other vaccines (e.g. pentavalent vaccine, IPV) in the PNF
- WHO recommends shifting from Oral Polio Vaccine (OPV) to Inactivated Polio Vaccine (IPV) as live-attenuated vaccine may also cause clinical polio. OPV will soon be phased out.
- Use of acellular pertussis *(hexavalent vaccine)* vs whole cell pertussis *(pentavalent vaccine)* has less adverse effects
    - Additional safety surveillance data from implementing countries were added as supplementary evidence
- No additional cold chain management concerns
- 6-in-1 vaccine reduces the number of injections and visits, improving compliance

Hexavalent vaccine (DTaP-HepB-IPV-Hib) for children <1 yo

Is there a DOH-approved/ local society CPG recommending this HT?	**NO** but the separate formulation of pentavalent vaccine + IPV is recommended **OHG (2023)**: **all infants on or before 1 year of age** are recommended to get the following: ○ pentavalent vaccine ○ inactivated polio vaccine (IPV) • Additionally, **infants aged 13 to 23 months** are also recommended to get these vaccines during **catch-up immunization** in public health facility or as part of catch-up program
Is there a local society certifying the HT as standard of care?	**PIDSP (2025):** DTwP-HiB-HepB and other DTaP combinations Given at a minimum age of 6 weeks
Is the HT in the WHO EML?	**NO** Previous listing for diphtheria-pertussis-tetanus combination vaccine was removed BUT hexavalent vaccine components as monovalent vaccines are listed in the EML WHO Routine Immunization Program (2024): • DTP containing vaccines are recommended for children with minimum age of 6 weeks

Vaccine profile (1 of 3)

	DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)	DTaP-HBV-IPV-Hib prefilled glass syringe	Pentavalent vaccine + Oral Polio vaccine + Inactivated Polio Vaccine	
			Pentavalent vaccine	IPV
Contents	DTaP-HBV-IPV-Hib *(pre-filled glass syringe; Hib component in glass vial)*	DTaP-HBV-IPV-Hib *(pre-filled glass syringe)*	DTwP-HepB-Hib	Inactivated Poliomyelitis Vaccine (Types 1, 2 And 3)
Dosage form/ Route	Suspension for injection (IM)	Suspension for injection (IM)	Suspension for injection (IM)	Suspension for injection (IM/SC)
Dose	0.5 mL	0.5 mL	0.5 mL	0.5 mL
Dosing regimen	2 to 3 doses	2 to 3 doses	3 doses	2 to 3 doses
Storage	2°C - 8°C	2°C - 8°C	must be stored and transported at 5°C ± 3°C; do not freeze	2°C - 8°C; do not freeze

Vaccine profile (2 of 3)

Pentavalent vaccine + Inactivated Polio Vaccine	
Pentavalent vaccine	**IPV**
Glass Vial x 0.5mL (single dose)	Type I Clear Vial x 0.5 mL

DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)	DTaP-HBV-IPV-Hib prefilled glass syringe
1 ml Type I glass pre-filled syringe (DTPa-HBV-IPV component) + 3 mL type I glass vial (Hib component) + 2 sterile needles (256 x 1")	0.5 mL in 1 mL pre-filled glass syringe with 2 separate needles (Box of 1's)

Vaccine profile (3 of 3)

Vaccine	DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)	OR	DTaP-HBV-IPV-Hib prefilled glass syringe	OR	Pentavalent	+	IPV
Platforms	●Diphtheria Toxoid ●Tetanus Toxoid ●Bordetella pertussis antigens ○Pertussis Toxoid (PT) ○Filamentous Haemagglutinin (FHA) ○Pertactin (PRN) ●Hepatitis B surface antigen (HBs) ●Poliovirus (inactivated) (IPV) ○Type 1 (Mahoney strain) ○Type 2 (MEF-1 strain) ○Type 3 (Saukett strain) ●Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate, PRP) conjugated to Tetanus Toxoid as carrier protein		• Diphtheria Toxoid • Tetanus Toxoid • Bordetella pertussis antigens ○ PT ○ FHA • Hepatitis B surface antigen • Poliovirus (Inactivated) ○ Type 1 (Mahoney) ○ Type 2 (MEF-1) ○ Type 3 (Saukett) • H. influenzae type b polysaccharide (Polyribosylribitol Phosphate) conjugated to Tetanus protein		• Diphtheria Toxoid • Tetanus Toxoid • Inactivated w-B. pertussis • Recombinant Hepatitis B surface antigen (HBsAg) • H. influenzae type b (PRP-TT-Purified capsular antigen i.e., Polyribosylribitol phosphate [PRP]) conjugated to Tetanus Toxoid		• Poliovirus (Inactivated) ○ Type 1 (Mahoney) ○ Type 2 (MEF-1) ○ Type 3 (Saukett)

Potential implications to health systems

Vaccine	DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial) OR	DTaP-HBV-IPV-Hib prefilled glass syringe OR	Pentavalent +	IPV
Implications	➢May take longer to administer compared to DTaP-HBV-IPV-Hib prefilled glass syringe *(has an extra step for reconstitution of Hib component)* ➢Simplified immunization schedule: fewer injections lead to better compliance ➢More expensive per dose than pentavalent ➢More expensive than DTaP-HBV-IPV-Hib prefilled glass syringe ➢Requires more storage space than *DTaP-HBV-IPV-Hib prefilled glass syringe* due to its packaging size (1 carton 5.5x2.4x13.3cm = box of 1 [1 dose])	➢ Ease of administration due to prefilled glass syringe ➢ Simplified immunization schedule: fewer injections lead to better compliance ➢ More expensive per dose than pentavalent ➢ Requires less storage space than DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial) (1 carton 7.7x3.5x4.2cm = box of 10 [10 doses])	➢ Requires more storage space in the cold chain due to separate packaging of two vaccines compared to *DTaP-HBV-IPV-Hib prefilled glass syringe* ➢ Separate IPV shot may lead to missed doses and incomplete immunization ➢ Lower compliance due to more injections required *(5 injections vs 3 injections)*` ➢ Cost-saving (cheaper than both hexavalent brands)	

Other PNF-listed vaccines

Indication	Other vaccine formulations available in the Philippine National Formulary:
Diphtheria Tetanus Pertussis	• Diphtheria-Tetanus Toxoids (DT) • Diphtheria-Tetanus Toxoid (Td) • Diphtheria-Tetanus Toxoids And Pertussis Vaccine (DTP) • Diphtheria-Tetanus Toxoids And Acellular Pertussis Vaccine (DTaP) • Diphtheria, tetanus, and pertussis (DTaP) + Haemophilus Influenzae Type B (Hib) • Diphtheria, tetanus, pertussis (DTP) + Hepatitis B Vaccine (Recombinant) • DTP + Inactivated Polio Vaccine (IPV) • DTP + IPV + Hib • Diphtheria, Tetanus, Pertussis, Hepatitis B (Recombinant), and Haemophilus Influenzae Type B (Hib) Combined Vaccine **[PENTAVALENT VACCINE]** • Tetanus Toxoid
Hepatitis B	• Hepatitis B Vaccine (Recombinant DNA) • Diphtheria, tetanus, pertussis (DTP) + Hepatitis B Vaccine (Recombinant) • Diphtheria, Tetanus, Pertussis, Hepatitis B (Recombinant), and Haemophilus Influenzae Type B (Hib) Combined Vaccine **[PENTAVALENT VACCINE]**
Invasive disease due to Haemophilus Influenzae type B	• Hemophilus Infuenzae Type B Conjugated Vaccine (Hib) • Hemophilus Infuenzae Type B Conjugated Vaccine (Hib) • DTaP + Haemophilus Influenzae Type B (Hib) • DTP + IPV + Hib • Diphtheria, Tetanus, Pertussis, Hepatitis B (Recombinant), and Haemophilus Influenzae Type B (Hib) Combined Vaccine **[PENTAVALENT VACCINE]**
Polio	• Poliomyelitis Vaccine (Type 1, 2, 3) (Inactivated) • Oral Polio Vaccine, Bivalent (Live Attenuated) (Type 1 And 3) • Dtp + Inactivated Polio Vaccine (IPV)

Policy Question

Should ***Hexavalent (DTaP-HBV-IPV-Hib) vaccine*** for active immunization to prevent diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive disease due to Haemophilus influenzae type b among ***all infants on or before 1 year of age*** be included in the Philippine National Formulary and National Immunization Program?

BACKGROUND

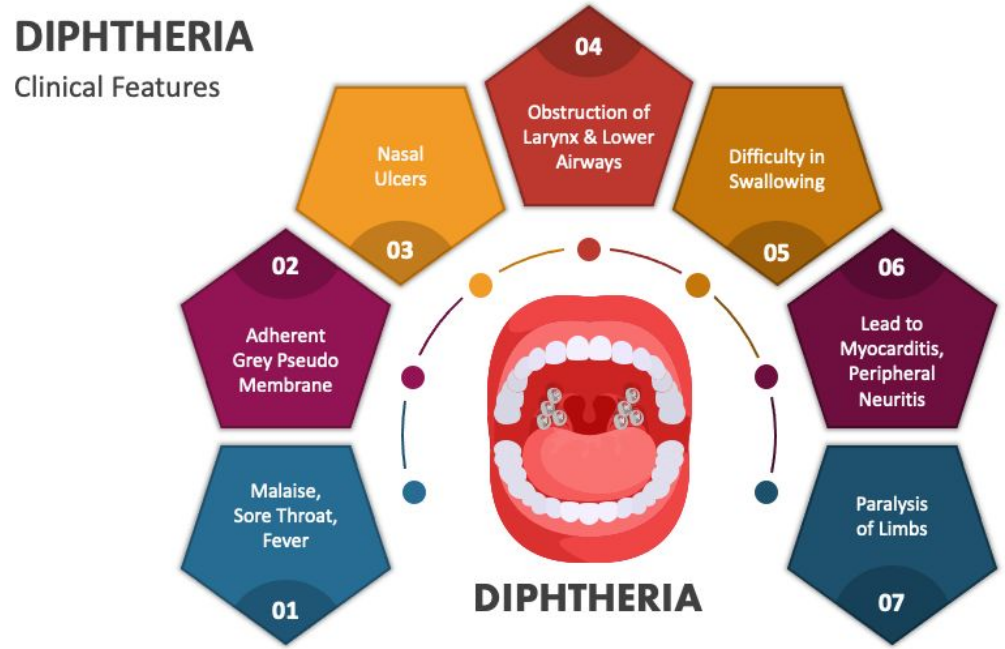
FDA-approved indication of DTaP-HBV-IPV-Hib

Primary and booster vaccination of infants and toddlers against:

- Diphtheria
- Tetanus
- Pertussis
- hepatitis B
- Poliomyelitis
- invasive diseases due to haemophilus influenzae type B

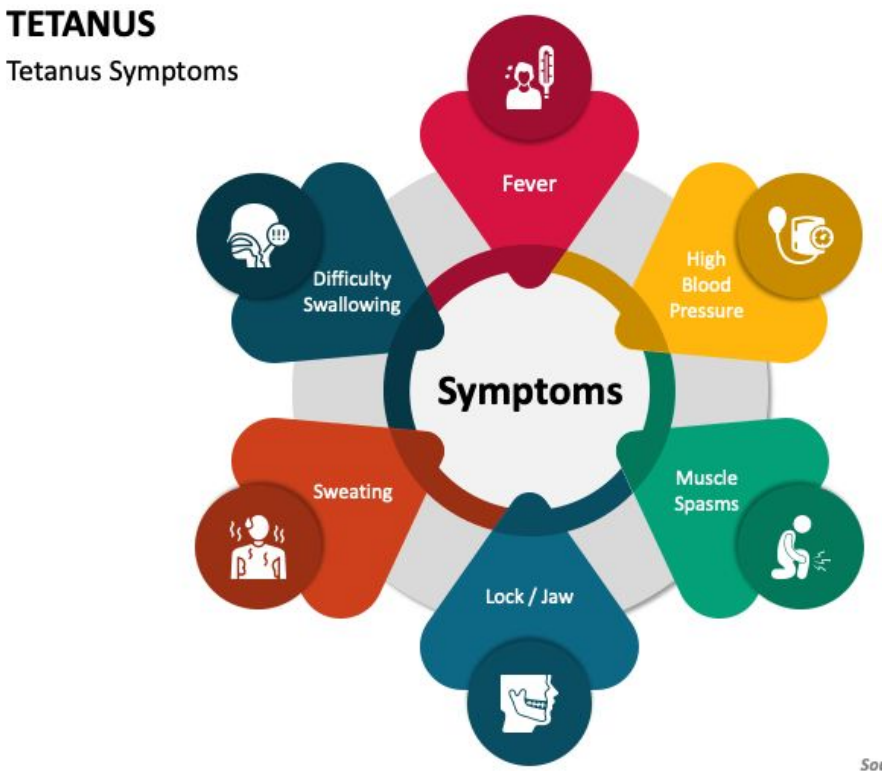
DIPHTHERIA

- is a disease caused by *Clostridium diphtheriae* that affects the upper respiratory tract and less often the skin. It also produces a toxin that damages the heart and the nerves
- Symptoms of diphtheria usually begin 2–5 days after exposure to the bacteria. Typical symptoms include:
  - sore throat
  - fever
  - swollen neck glands
  - weakness (WHO, 2024)



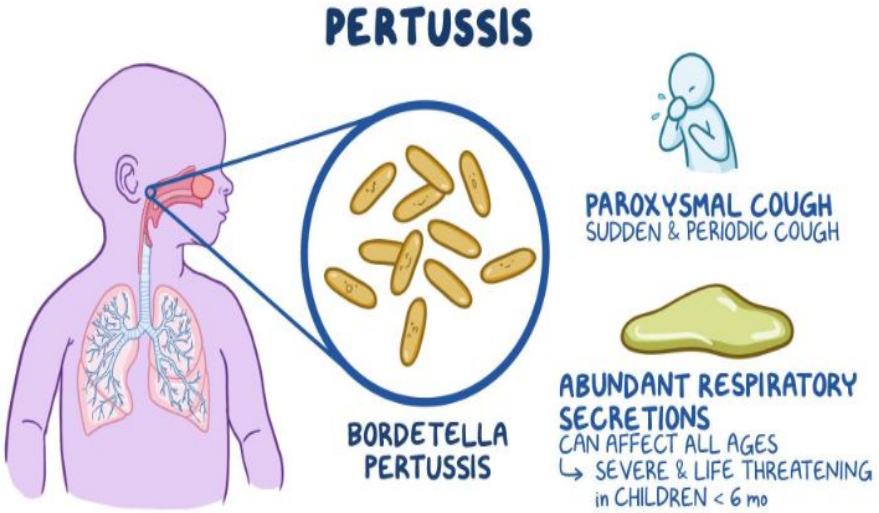
TETANUS

- Tetanus is a serious illness contracted through exposure to the spores of the bacterium, *C. tetani,* which live in soil, saliva, dust and manure.
- The bacteria can enter the body through a deep cuts, wounds or burns affecting the nervous system (WHO, n.d.)



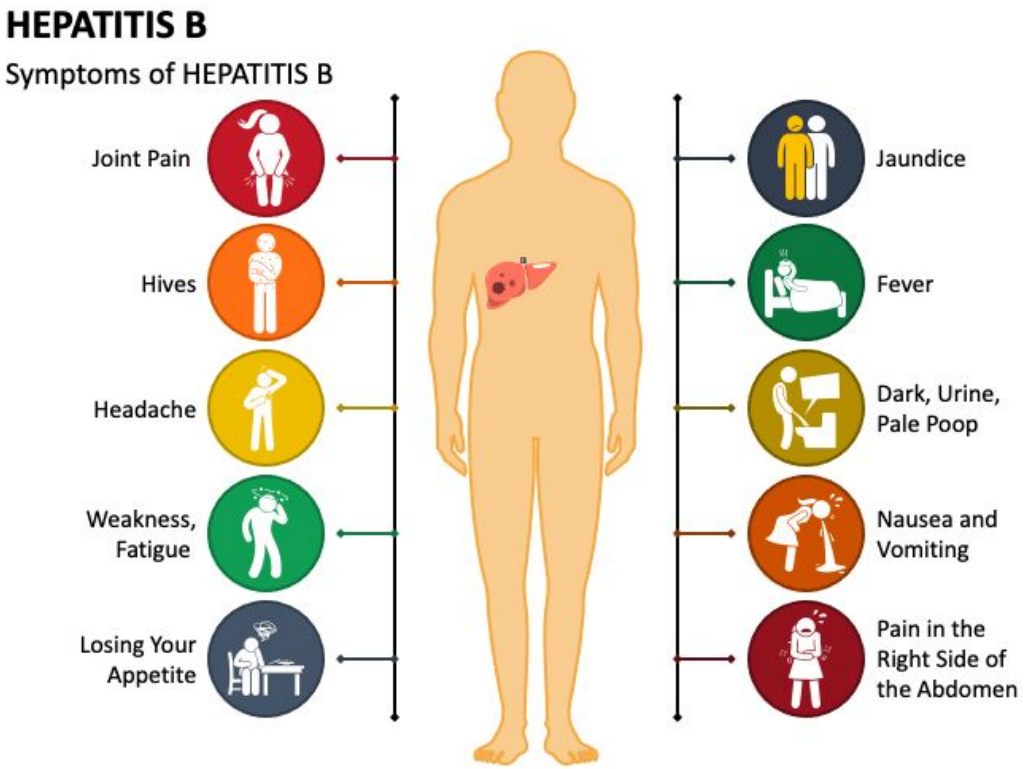
PERTUSSIS

- Pertussis, also known as whooping cough, is a highly contagious respiratory infection caused by the bacterium *Bordetella pertussis*.
- The first symptoms generally appear 7 to 10 days after infection. Symptoms include:
  - mild fever
  - runny nose
  - cough, which in typical cases gradually develops into a hacking cough followed by whooping (WHO, n.d.)



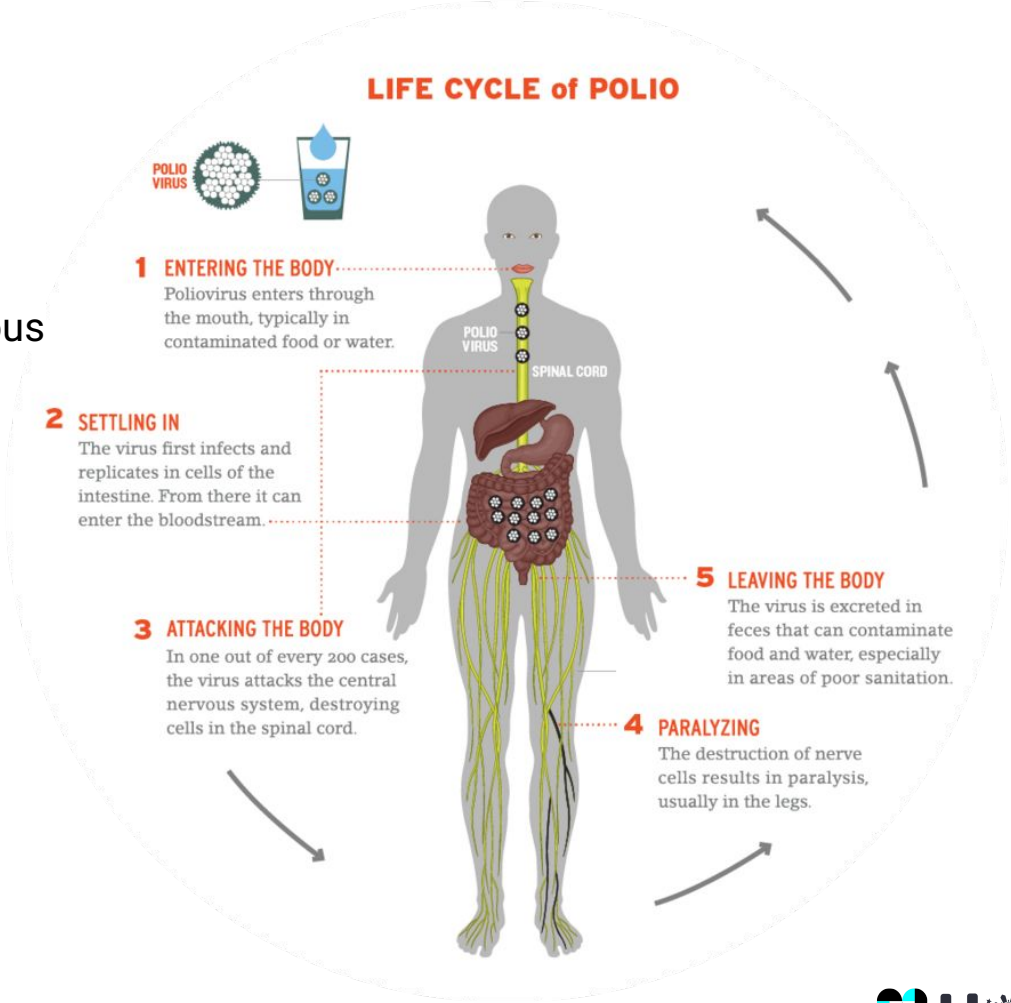
HEPATITIS B

- Hepatitis B is an infection of the liver caused by the hepatitis B virus. The infection can be acute (short and severe) or chronic (long term).
- It can spread through contact with infected body fluids like blood, saliva, vaginal fluids and semen. It can also be passed from a mother to her baby (WHO, 2024)



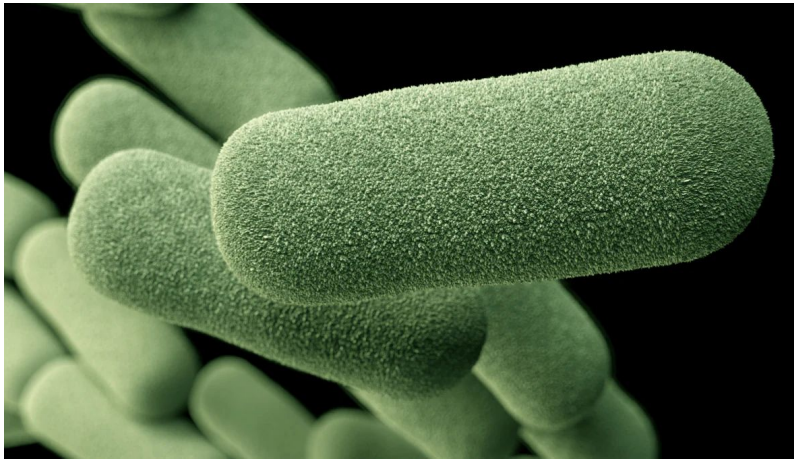
POLIOMYELITIS

- Polio is a highly infectious disease caused by a virus. It invades the nervous system and can cause total paralysis (WHO, 2024)
- Initial symptoms include:
  - fever
  - fatigue
  - headache
  - vomiting
  - stiffness of the neck
  - pain in the limbs



HAEMOPHILUS INFLUENZAE TYPE B (HIB)

- *Haemophilus influenzae* are bacteria commonly found in the upper respiratory tract, which are transmitted by droplets from people who are infected (but not necessarily symptomatic) to those who are susceptible.
- Over 90% of cases of invasive Hib disease occur in children <5 years of age (WHO, 2017)
- The most common serious infections caused by *H. influenzae* are:
  - Pneumonia
  - Bloodstream infection
  - Meningitis
  - Epiglottitis
  - Cellulitis
  - Infectious arthritis (CDC, n.d.)



CI: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

- **Global burden**
- Local epidemiological data
  - Cases among age groups
    - Number of diphtheria cases in the Philippines among different age groups (2014-2023)
    - Number of pertussis cases in the Philippines among different age groups (2014-2023)
    - Number of tetanus (non-neonatal) cases in the Philippines among different age groups (2014-2023)
    - Number of viral hepatitis cases in the Philippines among different age groups (2014-2023)
    - Number of influenza cases in the Philippines among different age groups (2020-2023)
  - Cases per region
  - Disease outbreaks in the last 5 years
- Vaccine Coverage

GLOBAL BURDEN

WHO reported cases and incidence		
	No. of cases in 2023 Total cases (all ages)	Total rate per 1,000,000 (total cases for all ages)
Diphtheria	24,779	4.5
Pertussis	159,832	23.6
Tetanus (non-neonatal)	21,830	3.8
Poliovirus	538	0.7

- **Hepatitis B:** The WHO (2022) reported that 254 million people are infected with Hepatitis B which is 3.3% of the world's population. The incidence was at 1.23 million (16 per 100,000 people) and the recorded deaths were 1.10 million (14 per 100,000 people).
- **Haemophilus influenzae:** Worldwide in 2015, there were an estimated 934,000 cases of Hib pneumonia in children aged 1-59 months and 31,400 cases of meningitis, resulting in 22,600 and 7,300 deaths respectively. Among children less than 5 years of age, 22% of reported pneumonia cases were caused by HiB while HiB caused 57% of the reported meningitis cases (PAHO).

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

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    - Number of viral hepatitis cases in the Philippines among different age groups (2014-2023)
    - Number of influenza cases (not specific to H. influenzae type B) in the Philippines among different age groups (2020-2023)
  - Cases per region
  - Disease outbreaks in the last 5 years
- Vaccine Coverage
  - Pentavalent vaccine national coverage and by region (2014 to 2023)
  - Inactivated polio vaccine national coverage and by region (2019 to 2023)

Vaccine Coverage vs Cases (all ages)

Diphtheria, Pertussis, Tetanus (non-neonatal), Viral Hepatitis, Influenza

Year	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Pentavalent Vaccine [3-dose] Coverage (%)	71.88	55.33	84.86	68.65	65.1	71.08	74.8	68.34	74.64	76.81
Diphtheria cases	3	1	29	36	97	86	189	113	90	250
Pertussis cases	1,283	164	178	96	4,383	4,372	3,862	3,171	2,255	1,388
Non-neonatal Tetanus cases	219	357	343	236	239	722	150	277	188	126
Viral hepatitis cases	1,571	1,551	1,956	1,348	1,292	1,047	3,941	1,317	746	1,373
Influenza cases ((not specific to H. influenzae type B)	NO DATA						27,500	31,672	87,135	65,841

Key findings: The association between the vaccine coverage and number of cases alone cannot be established as there were no inverse relationship observed between the vaccination rates and cases. For example, in 2015, the vaccination coverage was at its lowest (55.33%) while cases for diphtheria, pertussis, non-neonatal tetanus and viral hepatitis were relatively low compared to years with high vaccination rates (e.g., 2018 having the highest number of cases despite having a relatively high vaccination coverage). Further, since 2019, the vaccination coverage showed increasing trend. However, viral hepatitis, influenza, and diphtheria cases also increased in 2020, 2022 and 2023, respectively.

Vaccine Coverage vs Cases (all ages)

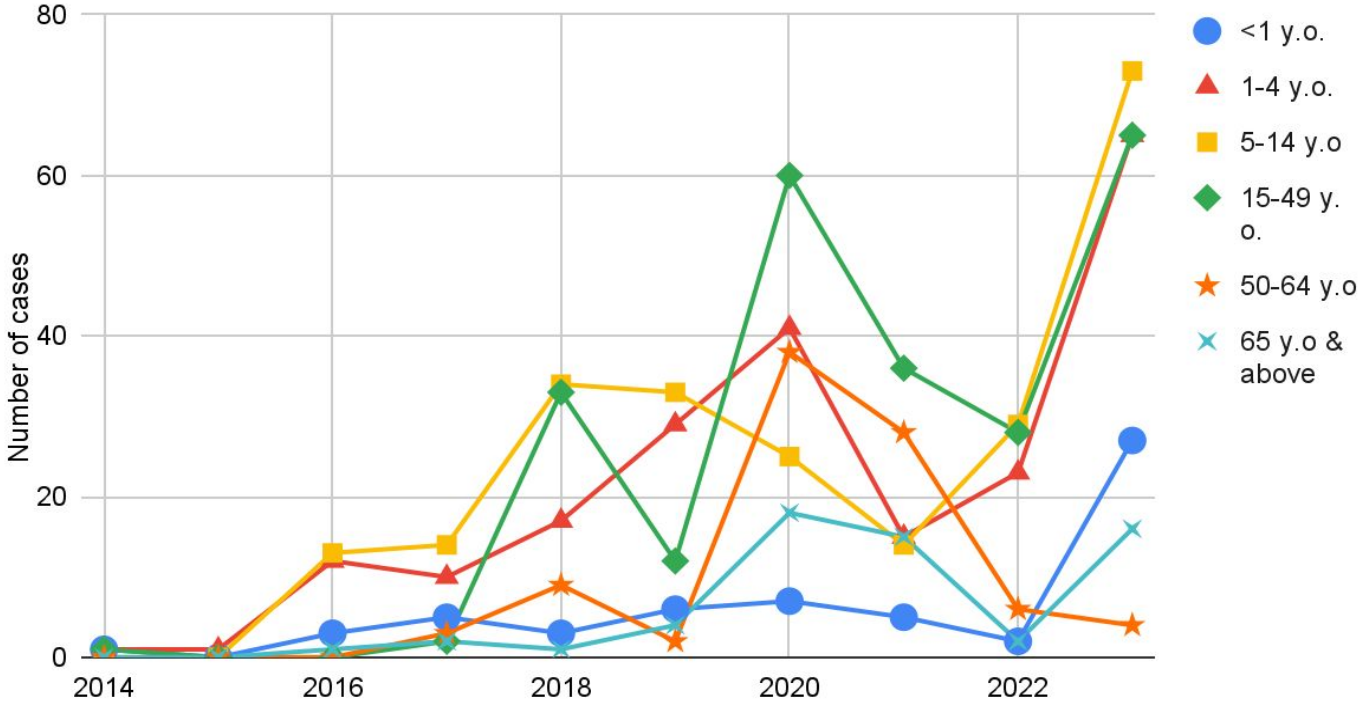
Polio

Year		2019	2020	2021	2022	2023
Vaccine Coverage (%)	IPV 1-dose	70.77	73.00	67.18	74.05	72.23
	IPV 2-dose		NO DATA		45.86	58.66
Cases		No data in FHSIS Note: *Polio outbreak: 2019 → officially closed: June 2021*				

Key findings: Vaccine coverage for polio was consistent from 2019 to 2023, with a minimal decline in 2021. Polio outbreak was reported in 2019 to 2021 but based on the 5 year data on vaccine coverage, association between outbreak and coverage cannot be established.

LOCAL EPIDEMIOLOGICAL DATA AMONG AGE GROUPS *(1 of 5)*

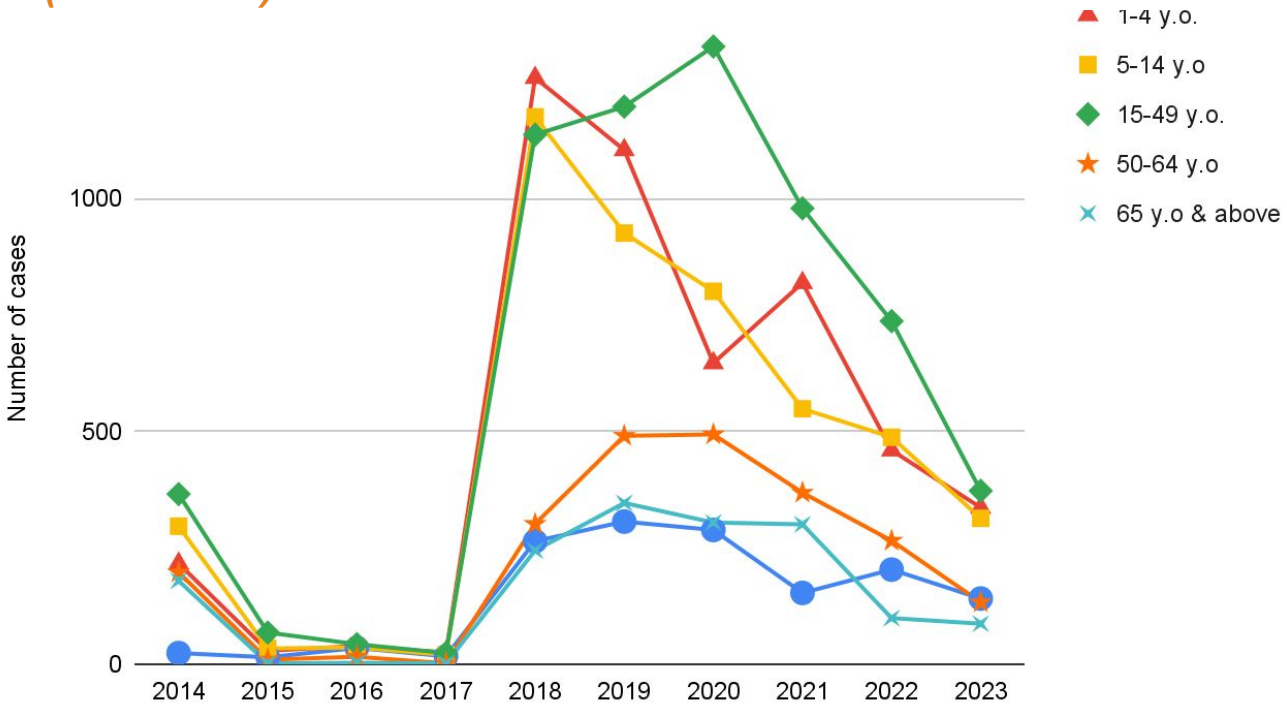
I. Number of diphtheria cases in the Philippines among different age groups (2014-2023)



Key Findings:
Most age groups showed a rise in diphtheria cases between 2017 and 2020, which was followed by a gradual decline in 2020 to 2022. In 2023, the number of cases increased across all age groups, except adults aged 50–64 years old. Further, surveillance reports have noted clustering and increase cases of diphtheria in areas that previously had no report of cases, indicating **pockets of local outbreaks** in 2023 (DOH DM 2023-0284).

LOCAL EPIDEMIOLOGICAL DATA AMONG AGE GROUPS *(2 of 5)*

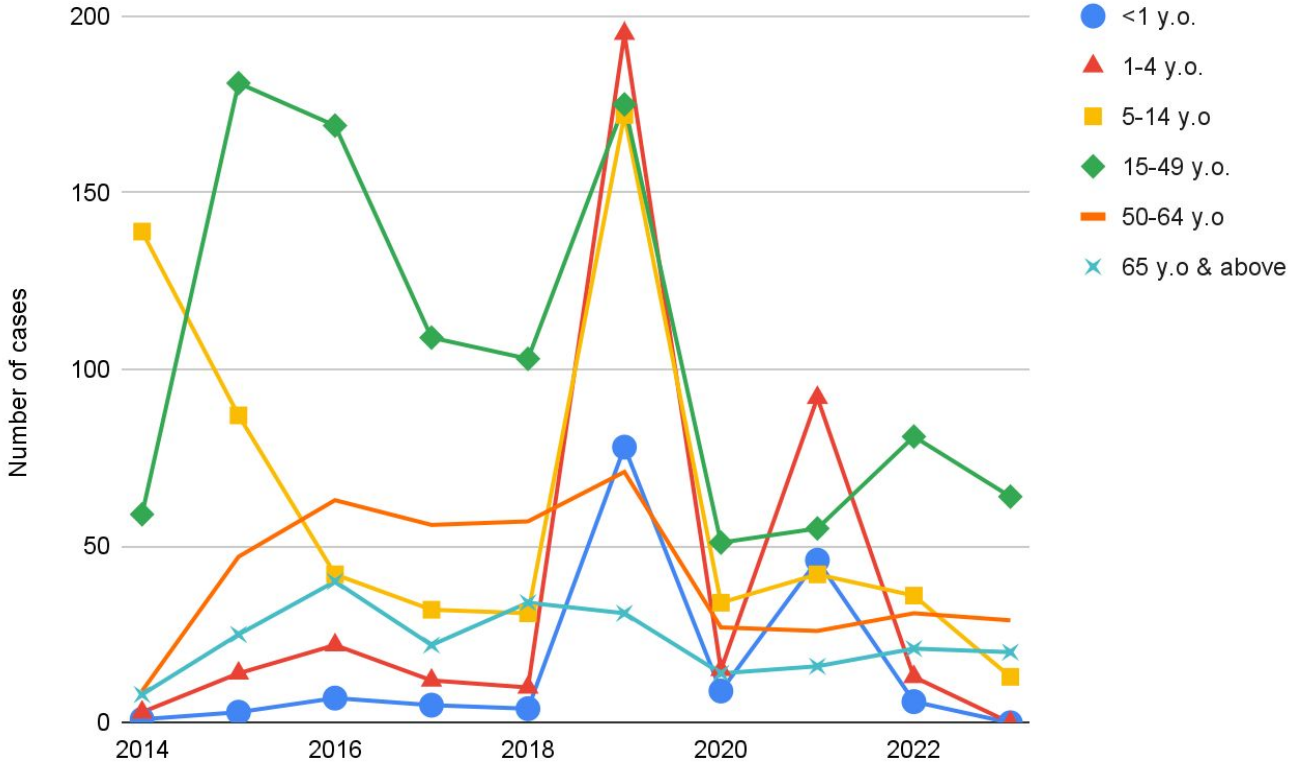
II. Number of pertussis cases in the Philippines among different age groups (2014-2023)



Key Findings:
From 2017 to 2018, reported cases of pertussis sharply increased in 1-49 y.o., while a gradual increase was observed in individuals <1 and 50 y.o. and above. Cases began to decline across all age groups from 2020 onwards. Additionally, pertussis outbreaks were reported in parts of Luzon and Visayas in 2024 (UNICEF, 2024)

LOCAL EPIDEMIOLOGICAL DATA AMONG AGE GROUPS *(3 of 5)*

III. Number of tetanus (non-neonatal) cases in the Philippines among different age groups (2014-2023)

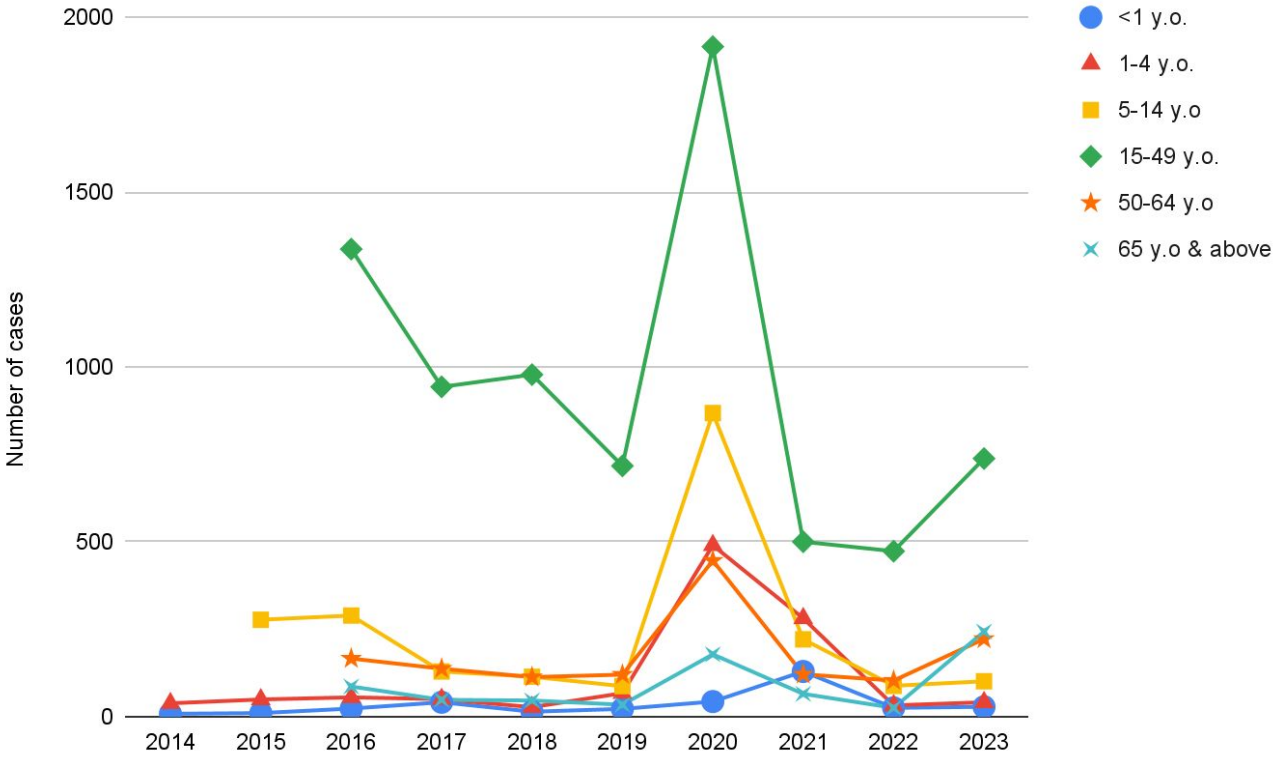


Key Findings:
In 2019, all age groups showed an increase in number of non-neonatal tetanus cases as compared with the previous years, with children aged 1-4 years having the highest number of cases (195).

(DTaP-HBV-IPV-Hib)

LOCAL EPIDEMIOLOGICAL DATA AMONG AGE GROUPS *(4 of 5)*

IV. Number of viral hepatitis cases in the Philippines among different age groups (2014-2023)

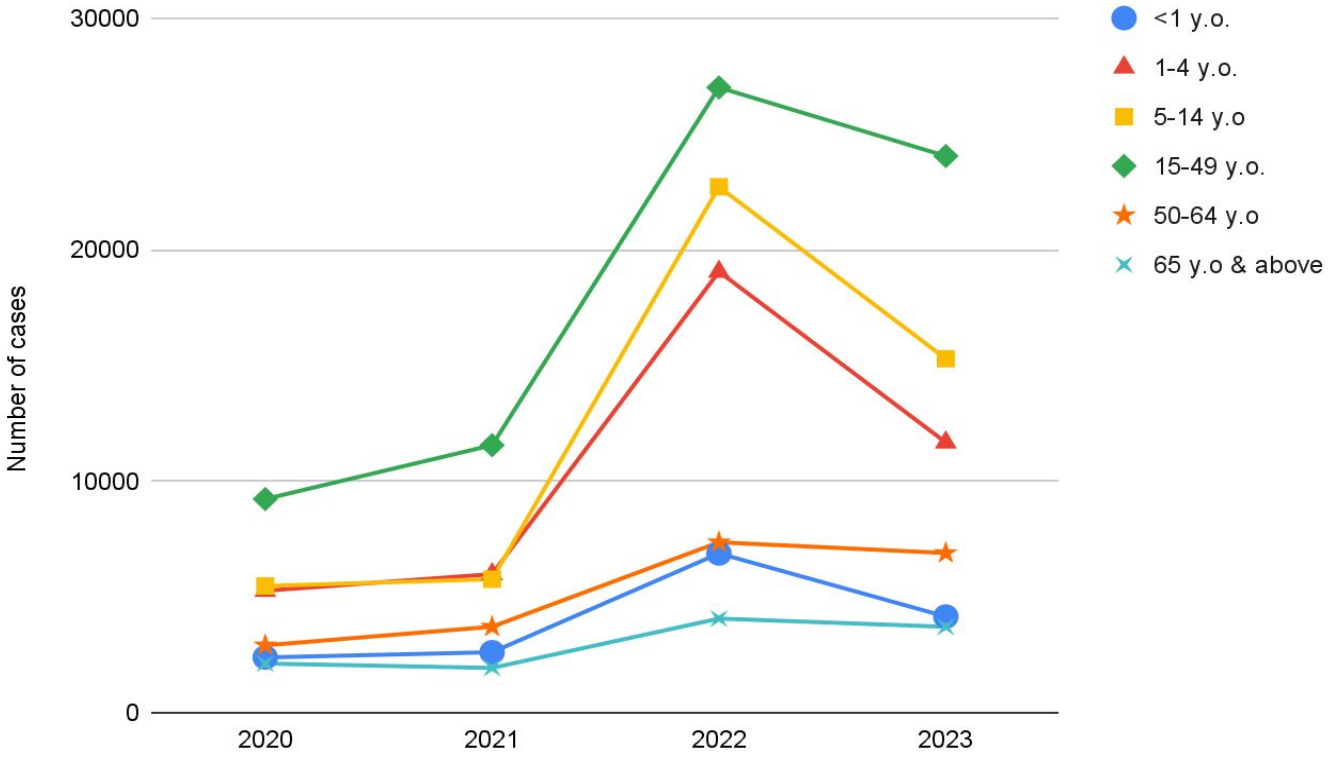


Key Findings:
The number of viral hepatitis cases increased for the majority of age groups in 2020, and then declined in 2021 and 2022. Most of the age groups saw a slight rise in cases in 2023.

ıe (DTaP-HBV-IPV-Hib)

LOCAL EPIDEMIOLOGICAL DATA AMONG AGE GROUPS *(5 of 5)*

V. Number of influenza (not specific to H. influenzae type B) cases in the Philippines among different age groups (2020-2023)



Key Findings:
Influenza cases showed an increasing trend across all age groups from 2020 to 2022 followed by a gradual decrease in 2023.

Note: FHSIS did not report influenza cases in the Philippines from 2019 and earlier.

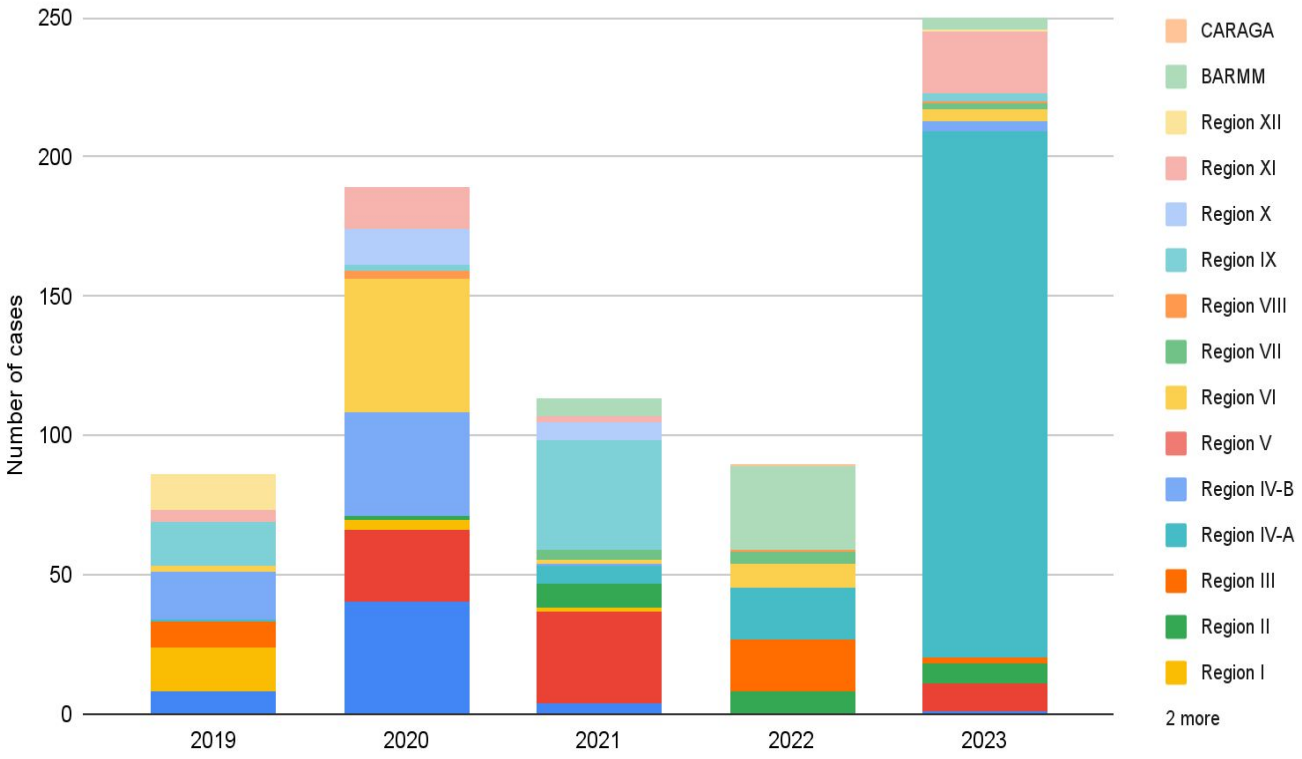
(DTaP-HBV-IPV-Hib)

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

- Global burden
- **Local epidemiological data**
  - Cases among age groups
  - **Cases per region**
    - **Diphtheria cases reported by region (2019-2023)**
    - **Pertussis cases reported by region (2019-2023)**
    - **Tetanus (non-neonatal) cases reported by region (2019-2023)**
    - **Viral hepatitis cases reported by region (2019-2023)**
    - **Influenza cases *(not specific to H. influenzae type B)* reported by region (2019-2023)**
  - Disease outbreaks in the last 5 years
- Vaccine Coverage
  - Pentavalent vaccine national coverage and by region (2014 to 2023)
  - Inactivated polio vaccine national coverage and by region (2019 to 2023)

LOCAL EPIDEMIOLOGICAL DATA PER REGION *(1 of 5)*

I. Diphtheria cases in all ages reported by region (2019-2023)

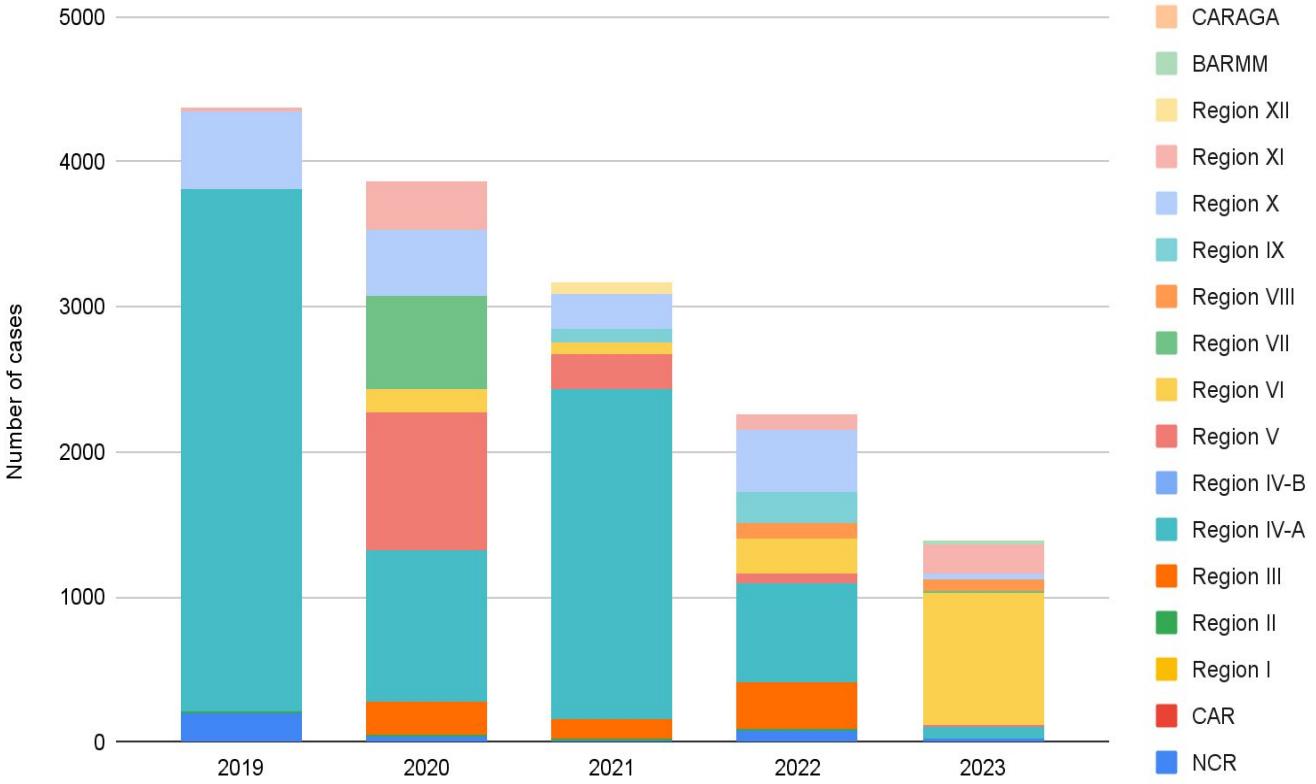


Key Findings:
Highest number of reported cases of diphtheria for all ages were observed in 2023, with Region IV-A (189) having the highest number of cases, followed by Region XI (22), and CAR (10).

(DTaP-HBV-IPV-Hib)

LOCAL EPIDEMIOLOGICAL DATA PER REGION *(2 of 5)*

II. Pertussis cases in all ages reported by region (2019-2023)



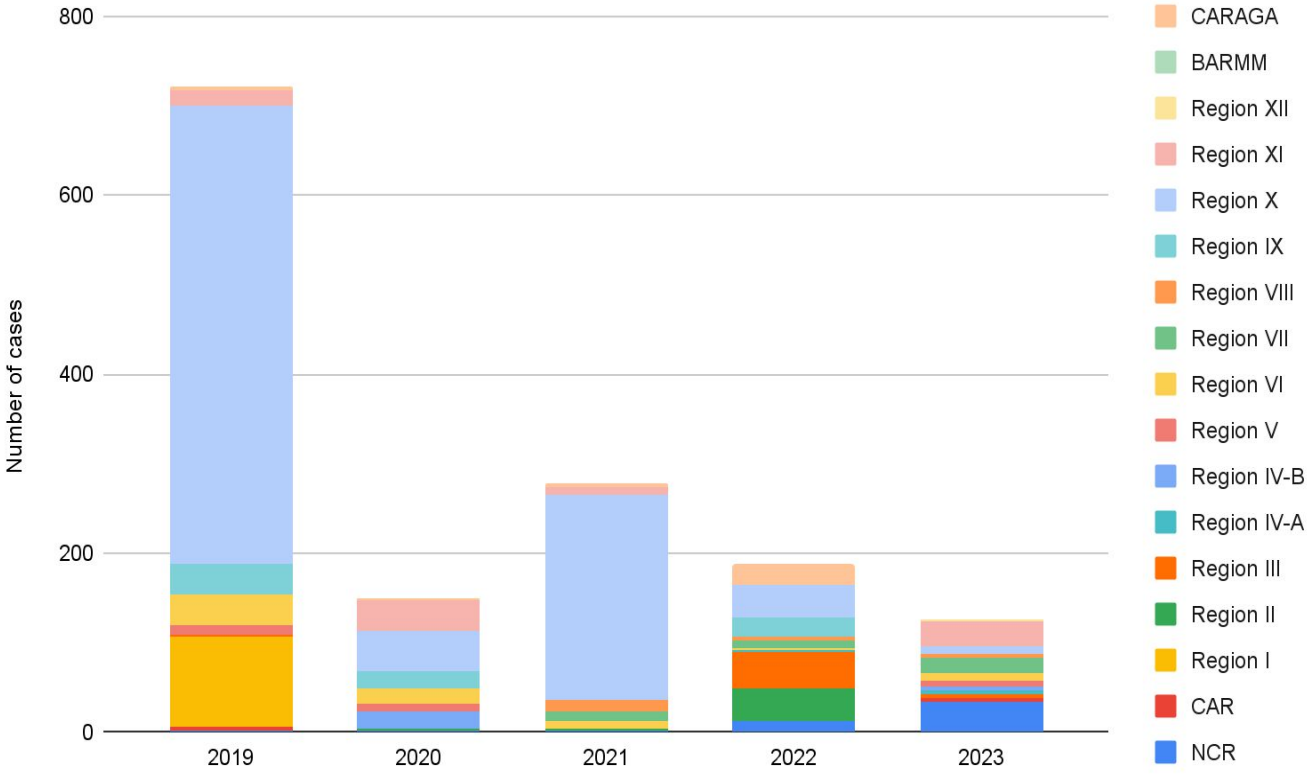
Key Findings:
From 2019 to 2023, the highest number of pertussis cases was observed in 2019 (4,372), with Region IV-A (3,610) having the highest proportion of cases. In the following years, Region IV-A also reported the highest number of cases: 1,045 (2020), 2,281 (2021), and 675 (2022).

(DTaP-HBV-IPV-Hib)

DOST PHILIPPINES

LOCAL EPIDEMIOLOGICAL DATA PER REGION *(3 of 5)*

III. Tetanus (non-neonatal) cases in all ages reported by region (2019-2023)



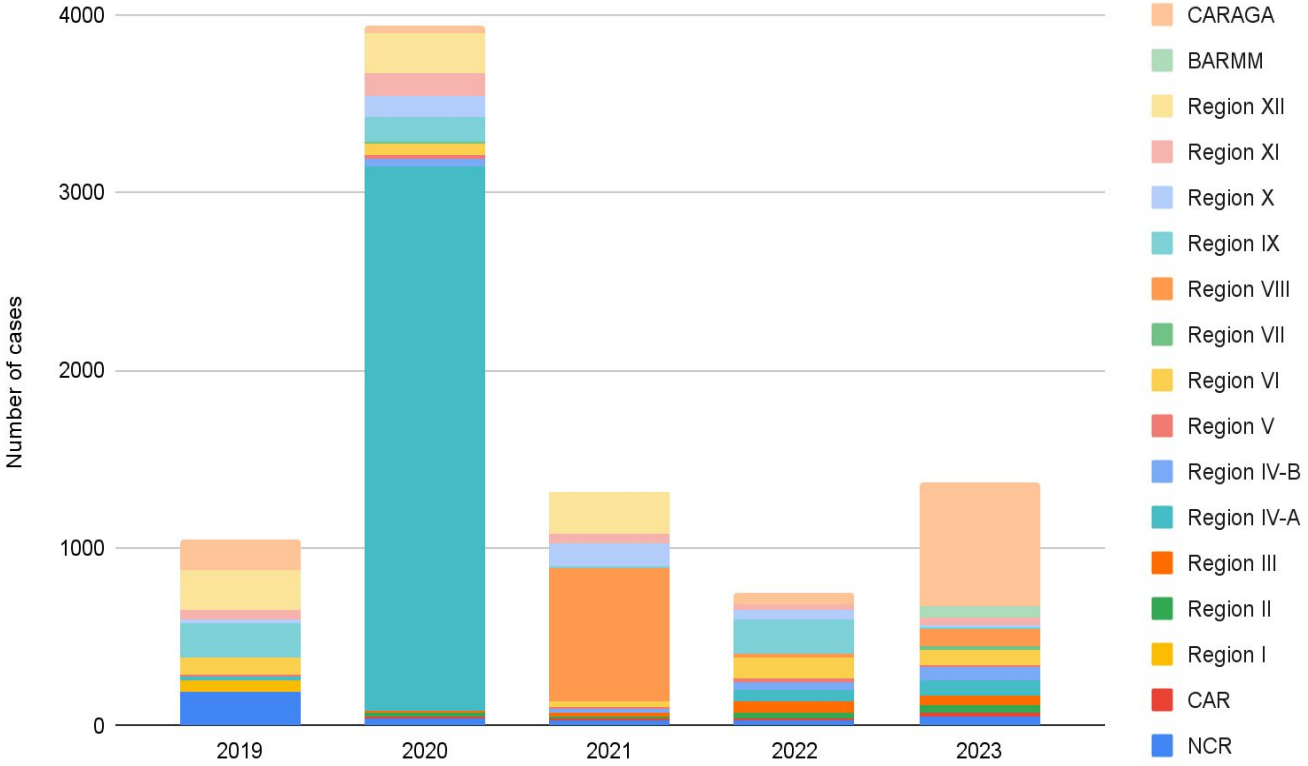
Key Findings:
From 2019 to 2021, Region X consistently had the highest reported cases of non-neonatal tetanus among all ages. Starting 2022, an overall decline in cases was reported.

(DTaP-HBV-IPV-Hib)

DOST PHILIPPINES

LOCAL EPIDEMIOLOGICAL DATA PER REGION *(4 of 5)*

IV. Viral hepatitis cases in all ages reported by region (2019-2023)



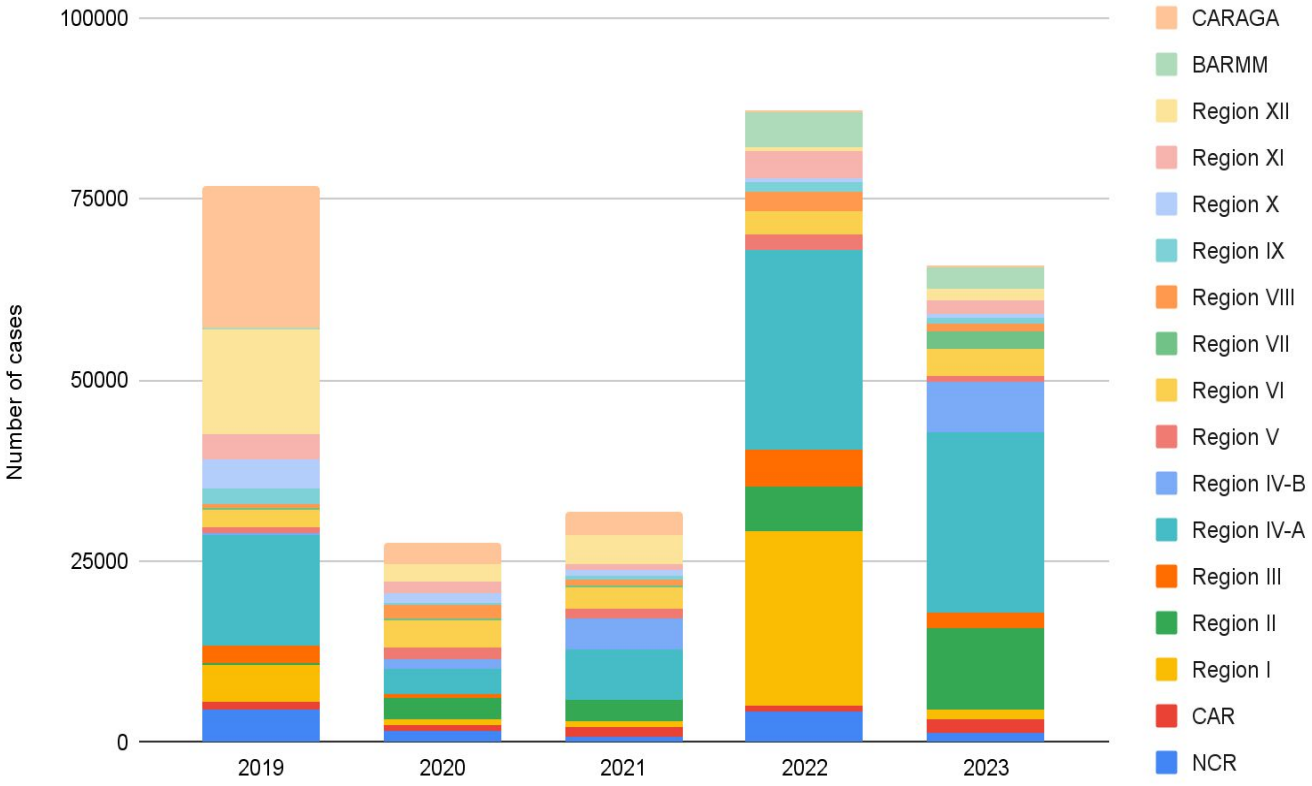
Key Findings:
From 2019 to 2023, a significant increase in number of viral hepatitis cases was observed in 2020. In the same year, Region IV-A reported the highest number of cases (3,061) followed by Region XII (228).

(DTaP-HBV-IPV-Hib)

DOST PHILIPPINES

LOCAL EPIDEMIOLOGICAL DATA PER REGION *(5 of 5)*

V. Influenza (not specific to H. influenzae type B) cases in all ages reported by region (2019-2023)



Key Findings:
2022 reported the highest cases of influenza in all ages in the country, with Region IV-A (27,664), Region I (24,214), and Region IV-B (6,186) having the highest number of cases. Additionally, Region IV-A consistently had the highest cases from 2021 to 2023.

(DTaP-HBV-IPV-Hib)

SUMMARY OF LOCAL EPIDEMIOLOGICAL DATA

By age group	By region
Diphtheria	
Increasing trend from 2021 to 2023 among all age groups was observed	No trends were observed in the number of cases per region. In 2023, Region IV-A (189) had the highest number of cases, followed by Region XI (22), and CAR (10).
Pertussis	
Decreasing trend from 2019 to 2023 among all age groups was observed	Region IV-A consistently had the highest cases from 2019 to 2022
Non-neonatal tetanus	
Decreasing trend from 2021 to 2023 among all age groups was observed	Region X consistently had the highest cases from 2019 to 2021
Viral Hepatitis	
Majority of age groups had an increase in cases in 2020, and declined from 2021 to 2022. Most of the age groups saw a slight rise in cases in 2023.	Region IV-A reported the highest number of cases (3,061) followed by Region XII (228) in 2020 (year with the highest reported cases)
Influenza (not specific to H. influenzae type B)	
Increasing trend across all age groups from 2020 to 2022, followed by a gradual decrease in 2023 was observed.	Region IV-A consistently had the highest cases from 2021 to 2023.

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

- Global burden
- **Local epidemiological data**
  - Cases among age groups
  - Cases per region
  - **Disease outbreaks in the last 5 years**
- Vaccine Coverage
  - Pentavalent vaccine national coverage and by region (2014 to 2023)
  - Inactivated polio vaccine national coverage and by region (2019 to 2023)

DISEASE OUTBREAKS IN THE PHILIPPINES IN THE LAST 5 YEARS

POLIO

- Polio outbreak: 2019 → officially closed: June 2021 (International Federation of Red Cross and Red Crescent; Polio Global Eradication Initiative Societies, 2021).
- Philippines remain at medium high risk for polio in 2022 (Global Polio Surveillance 2022-2024)

PERTUSSIS

- Pertussis outbreaks in parts of Luzon and Visayas in 2024 (UNICEF, 2024)

DIPHTHERIA

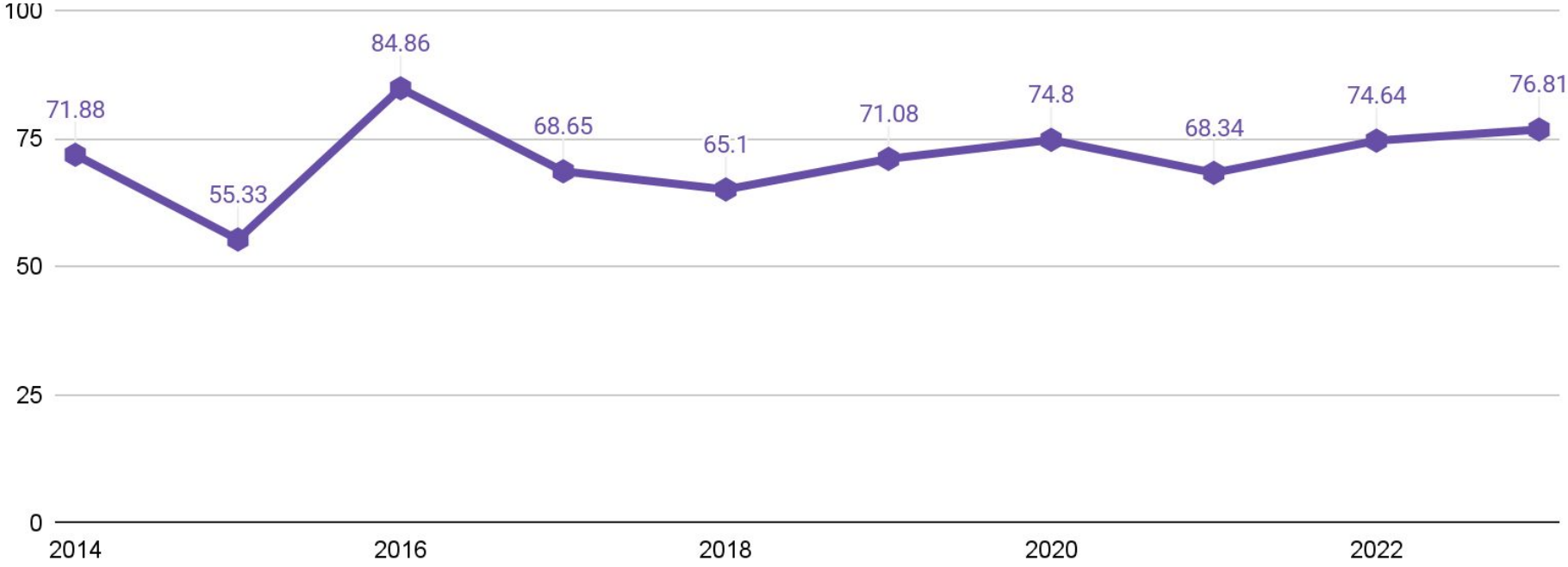
- 2023: As of morbidity week 29 (01 January 2023 - 22 July 2023), a total of 97 cases have been reported. Surveillance reports have noted clustering and increase cases of Diphtheria and Pertussis in areas that previously had no report of cases, indicating **pockets of local outbreaks** (DOH DM 2023-0284). Additionally, the U.S. Centers for Disease Control and Prevention (CDC) issued a Level 2 Travel Health Notice on May 1, 2023, for Diphtheria in the Philippines (PH US Embassy)
  [Note: Level 2 Travel Health Notice - sporadic cases of a disease in an unusual or new geographic location (to practice enhanced precautions) (US CDC)]

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

- Global burden
- Local epidemiological data
  - Cases among age groups
  - Cases per region
  - Disease outbreaks in the last 5 years
- **Vaccine Coverage**
  - **Pentavalent vaccine national coverage and by region (2014 to 2023)**
  - **Inactivated polio vaccine national coverage and by region (2019 to 2023)**

VACCINE COVERAGE *(1 of 5)*

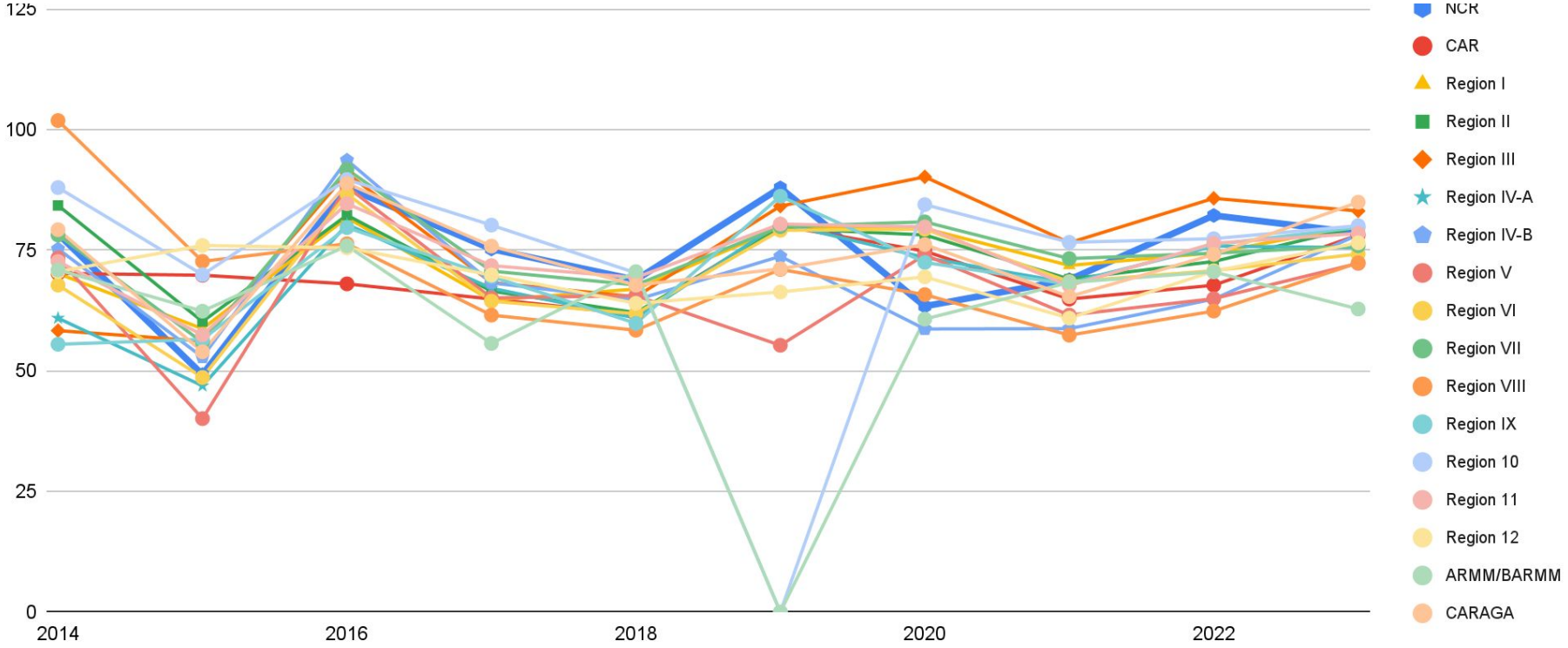
I. Pentavalent vaccine (3-dose primary) in the Philippines (2014 to 2023) [DOH FHSIS]



Key findings: Since 2014, the vaccine coverage have not yet reached the target 95% coverage needed to achieve herd immunity (FHSIS 2022, PPS-PIDSP 2021). The 3-dose primary pentavalent vaccination recorded the lowest rate in 2015 at 55.33%. A minimal decline was observed in 2021 (68.34%), followed by an increase in the subsequent years.

VACCINE COVERAGE *(2 of 5)*

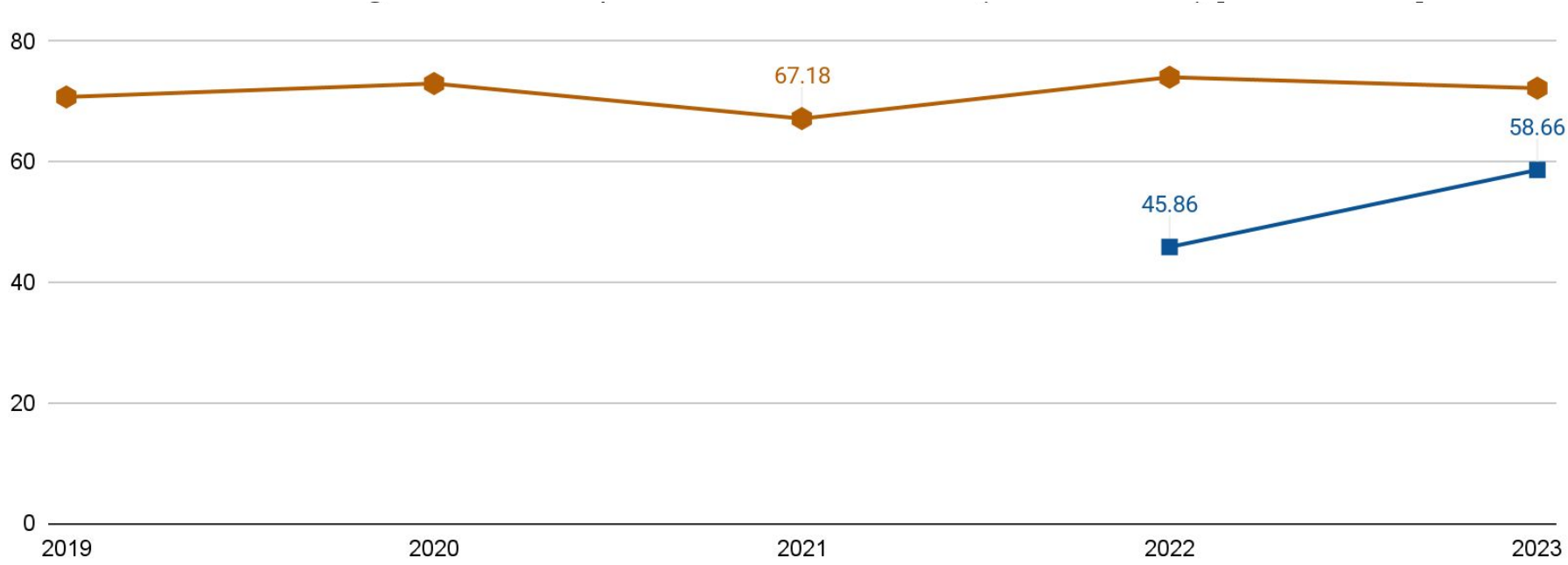
II. Pentavalent vaccine (3-dose primary) by region (2014 to 2023) [DOH FHSIS]



Key findings: Since 2014, all the regions had similar vaccine coverage trends. In 2019, there were no vaccine coverage data available for Region 10 and BARMM.

VACCINE COVERAGE *(3 of 5)*

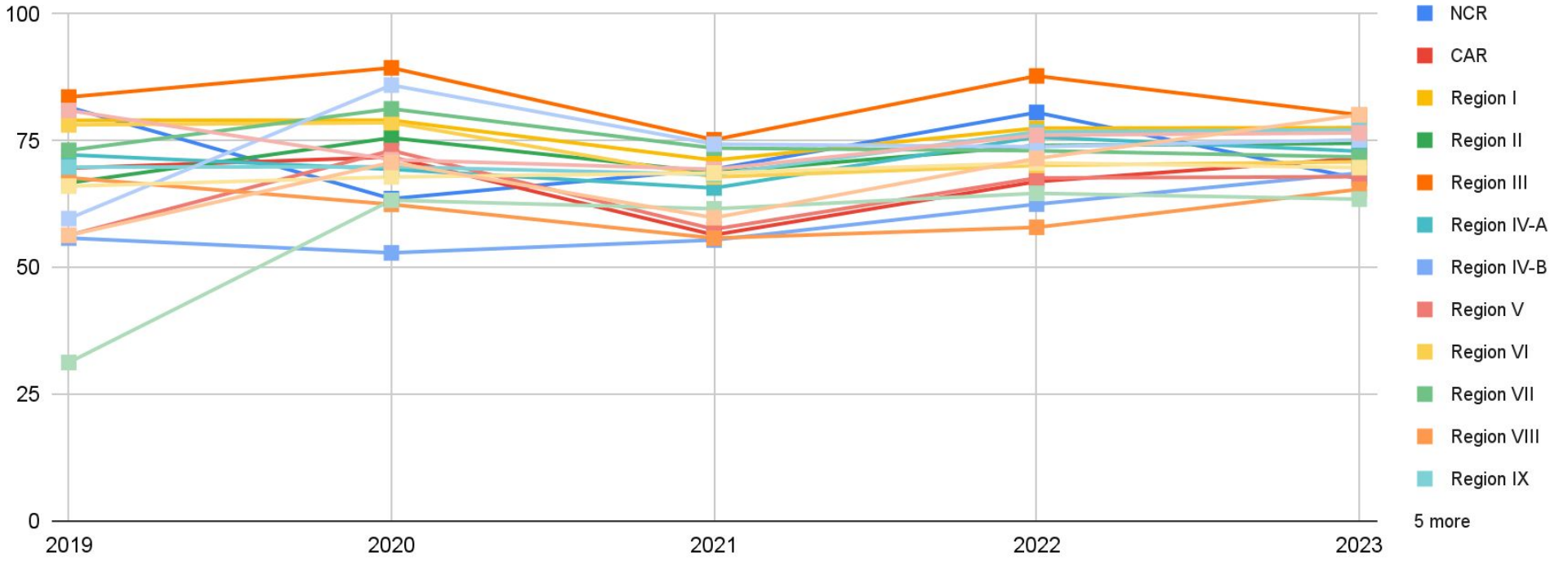
III. IPV (1-dose & 2-dose primary) in the Philippines (2019 to 2023) [DOH FHSIS]



Key findings: The polio vaccine coverage have not yet reached the target 95% coverage for herd immunity (FHSIS 2022, PPS-PIDSP 2021). For 1-dose IPV, similar vaccination coverage rates was observed from 2019 to 2023, with a minimal decrease in 2021 (67.18%). Meanwhile, for two-dose IPV, there is an increase in coverage since its implementation in 2022 (45.86%) to 2023 (58.66%)

VACCINE COVERAGE *(4 of 5)*

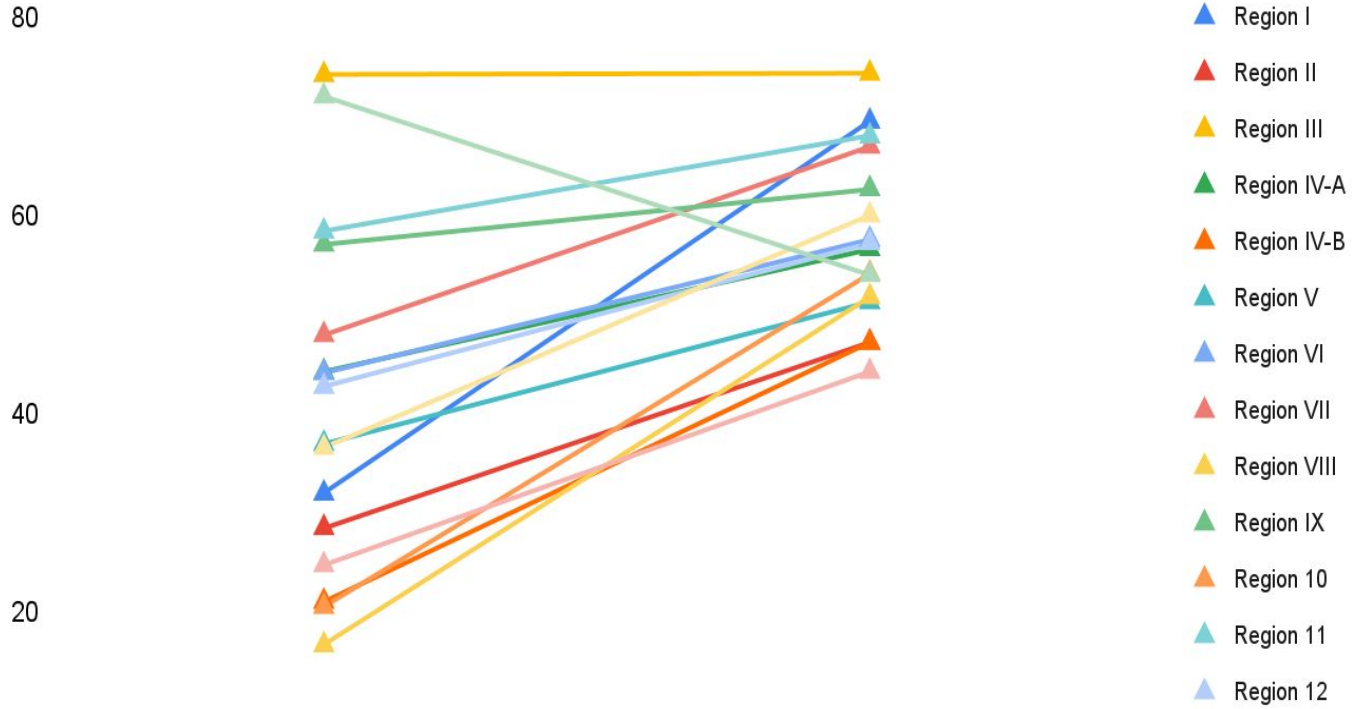
IV. IPV (1-dose primary) by region (2019 to 2023) [DOH FHSIS]



Key findings: Since 2019, the IPV vaccination coverage had similar trends across most regions. Lowest vaccination coverage was observed in 2021, with Region IV-B (55.44%), Region VIII (55.8%), and CAR (56.45%) having the lowest rates.

VACCINE COVERAGE *(5 of 5)*

V. IPV (2-dose primary) by region (2022 to 2023) [DOH FHSIS]



Key findings: Based on the DOH FHSIS, the vaccination with two-dose IPV started in 2022. All of the regions showed an increase in vaccine coverage in 2023 except NCR which reported a decrease from 72.09% to 54.04%.

SUMMARY OF VACCINE COVERAGE

The vaccine coverage for both pentavalent and IPV have not yet reached the target 95% coverage to achieve herd immunity (FHSIS 2022, PPS-PIDSP 2021).

PENTAVALENT VACCINE

- Since 2014, the national coverage data of 3-dose primary pentavalent vaccination recorded the lowest rate in 2015 at 55.33%. A minimal decline was observed in 2021 (68.34%), followed by an increase in the subsequent years
- Since 2014, all the regions had similar vaccine coverage trends. In 2019, there were no vaccine coverage data available for Region 10 and BARMM

INACTIVATED POLIOVIRUS VACCINE (IPV)

- For 1-dose IPV, similar vaccination coverage rates was observed from 2019 to 2023, with a minimal decrease in 2021 (67.18%)
- For two-dose IPV, there is an increase in coverage since its implementation in 2022 (45.86%) to 2023 (58.66%)
- Since 2019, the IPV vaccination coverage had similar trends across most regions. Lowest vaccination coverage was observed in 2021, with Region IV-B (55.44%), Region VIII (55.8%), and CAR (56.45%) having the lowest rates

HTAC Judgment

RQ1: **What is the magnitude and severity of diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *haemophilus influenzae* type B? [1 of 2]**

Diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenzae* type B (HiB) are vaccine-preventable infectious diseases. Globally, the prevalence rate (per 100,000) of these diseases among all ages in 2021 are: 0.01 for diphtheria, 12.54 for pertussis, 0,47 for tetanus and 92.56 for hepatitis B. There are no data for poliovirus and *HiB influenzae* (Global Burden of Disease Study, 2021).

The local burden of these vaccine-preventable infectious diseases are reported in the DOH Field Health Services Information System (FHSIS Annual Report 2014-2023) as follows:

- *Diphtheria*: Most age groups showed a rise in cases between 2017 and 2020, which was followed by a gradual decline in 2020 to 2022. In 2023, the number of cases increased across all age groups, except adults aged 50–64 years old. Among the regions, Region IV-A reported the highest number of cases among all ages in 2023 (189), followed by Region XI (22) and CAR.
- *Pertussis*: From 2017 to 2018, reported cases sharply increased in 1-49 yo, while a gradual increase was observed in individuals <1 and 50 yo and above. Cases began to decline across all age groups with a more significant reduction observed from 2020 onwards. Region IV-A reported the highest number of cases among all ages in 2019 (3,610), 2020 (1,045), 2021 (2,281) and 2022 (675).
- *Tetanus (non-neonatal):* In 2019, all age groups showed an increase in number of cases as compared with the previous years, with children aged 1-4 years having the highest number of cases (195). Region X consistently had the highest number of reported cases among all ages in 2019 (510), 2020 (47) and 2021 (230).
- *Viral hepatitis:* The highest number of cases was reported in 2020, and then cases declined in 2021 and 2022. Most of the age groups saw a slight rise in cases in 2023. Among the regions, Region IV-A reported the highest number of cases among all ages in 2020 (3,061), followed by Region XII (228).

HTAC Judgment

RQ1: **What is the magnitude and severity of diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *haemophilus influenzae* type B? [2 of 2]**

- *Influenza (not specific to h.influenzae type B)*: cases showed an increasing trend across all age groups from 2020 to 2022 followed by a gradual decrease in 2023. In 2022, the highest number of influenza cases among all ages was reported, with Region IV-A (27,664), Region I (24,214), and Region IV-B (6,186) having the highest number of cases. Additionally, Region IV-A consistently had the highest number of cases from 2021 to 2023. DOH FHSIS did not report influenza cases from 2019 and earlier.

These diseases continue to be public health concerns. In the last 5 years, outbreaks such as pertussis in 2024 in some parts of Luzon and Visayas, and polio in 2019-2021 were identified (UNICEF, 2024; International Federation of Red Cross and Red Crescent Societies, 2021). Based on the Global Polio Surveillance 2022-2024, the Philippines remain at medium high risk for polio in 2022. In the following year, the DOH together with UNICEF and WHO, launched the *Chikiting Ligtas 2023* national supplemental immunization campaign against vaccine-preventable diseases including polio (DOH 2023, press release). Meanwhile, pocket of local outbreaks were reported in 2023 for diphtheria and pertussis (DOH DM 2023-0284).

In terms of vaccine coverage from 2014 to 2023, 3-dose primary series of pentavalent vaccine (DTwP-HepB-Hib) recorded the lowest rates in 2015 (55.33%), and the highest in the following year (84.86%). A minimal decline was observed in 2021 (68.34%) most probably because of the COVID-19 pandemic, followed by a gradual increase in the subsequent years. In the same period, all the regions had similar vaccine coverage trends with the national level.

For 1-dose IPV, similar vaccination coverage rates were observed from 2019 to 2023, with a minimal decrease in 2021 (67.18%). Similarly, the rates decreased in 2021 in most regions, with Region IV-B (55.44%), Region VIII (55.8%), and CAR (56.45%) having the lowest rates. Meanwhile, for two-dose IPV, there is an increase in coverage since its implementation in 2022 (45.86%) to 2023 (58.66%). All the regions showed an increase in coverage in 2023, except NCR which reported a decrease from 72.09% to 54.04%. Nonetheless, association between cases and vaccine coverage cannot be established. Lastly, vaccination coverage did not reach the national target of 95% thus not achieving herd immunity (FHSIS 2022, PPS-PIDSP 2021).

C2.I: WHO AND DOH RECOMMENDATIONS

WHO EML AND PREQUALIFIED VACCINES

- **Hexavalent vaccine is not in the EML**. The following related vaccines are in the EML:
  - Diphtheria vaccine
  - Tetanus vaccine
  - Hepatitis B vaccine
  - Diphtheria-tetanus vaccine
  - Pertussis vaccine
  - Poliomyelitis vaccine
  - Haemophilus influenzae type b vaccine

- The following hexavalent vaccine brands are WHO prequalified:
  - **Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenzae type b-Polio (Inactivated)** [DTwP-HepB-Hib-IPV]
  - **DTaP-HBV-IPV-Hib (pre-filled glass syringe)** [DTaP-HepB-Hib-IPV]

WHO RECOMMENDATION - EPI

- The following 13 vaccines (antigen) are recommended by WHO for the Essential Programme on Immunization (EPI) (WHO, n.d.):

Bacillus Calmette-Guérin (BCG)	Measles
Diphtheria	Rubella
Pertussis	pneumococcal disease (PNC)
Tetanus	rotavirus (Rota)
Haemophilus influenzae type B (Hib)	human papillomavirus (HPV)
Hepatitis B (HepB)	COVID-19 (for adults)
Polio	

Hexavalent vaccine (DTaP-HBV-IPV-Hib)

WHO RECOMMENDATION - ROUTINE IMMUNIZATION [1 of 2]

***Recommended Routine Immunizations for Children* (December 2024)**

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose
				1st to 2nd	2nd to 3rd	3rd to 4th	
DTP-containing vaccine: (DTaP or DTwP)		6 weeks (min)	3	4 weeks (min) - 8 weeks	4 weeks (min) - 8 weeks		3 Boosters 12-23 months (DTP-containing vaccine); 4-7 years (Td/ DT containing vaccine)
Haemophilus influenzae type b *(can be monovalent or as part of a combination vaccine)*	Option 1	6 weeks (min) 59 months (max)	3	4 weeks (min) with DTPCV2	4 weeks (min) with DTPCV3		
	Option 2		2-3	8 weeks (min) if only 2 doses 4 weeks (min) if 3 doses	4 weeks (min) if 3 doses	At least 6 months (min) after last dose	
Hepatitis B *(can be monovalent or as part of a combination vaccine)*	Option 1	As soon as possible after birth (<24h)	3	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2		
	Option 2	As soon as possible after birth High risk groups	4	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2		

Hexavalent vaccine (DTaP-HBV-IPV-Hib)

WHO RECOMMENDATION - ROUTINE IMMUNIZATION [2 of 2]

Recommended Routine Immunizations for Children *(December 2024)*

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose
				1st to 2nd	2nd to 3rd	3rd to 4th	
Polio	bOPV + IPV "Preferred schedule" (fractional Salk-IPV permitted)	bOPV 6 weeks IPV 14 weeks	5 (3 bOPV and 2 IPV)	bOPV 4 weeks (min) (e.g. with DTPCV2[1]) IPV ≥ 4 months (min) (e.g. with MCV[2])	bOPV 4 weeks (min) (e.g. with DTPCV3)		
	bOPV+IPV "Early Option" (full dose IPV only)	bOPV 6 weeks IPV 6 weeks	5 (3 bOPV and 2 IPV)	bOPV 4 weeks (min) (e.g. with DTPCV2) IPV 14 weeks (min) (e.g. with DTPCV3)	bOPV 4 weeks (min)		
	IPV / bOPV Sequential	8 weeks (IPV 1st) bOPV (4-8 weeks after 2nd IPV)	4 (2 IPV followed by ≥ 2 bOPV)	IPV (4-8 weeks)	bOPV (4-8 weeks)	bOPV (4-8 weeks)	
	IPV-only	6-8 weeks	3	4-8 weeks	4-8 weeks		IPV booster (6 months after 3rd dose) is needed when 1st dose given at < 8 weeks
	Alternative > 90%) IPV-only (fractional permitted)	≥14 weeks	2	≥ 4 months			

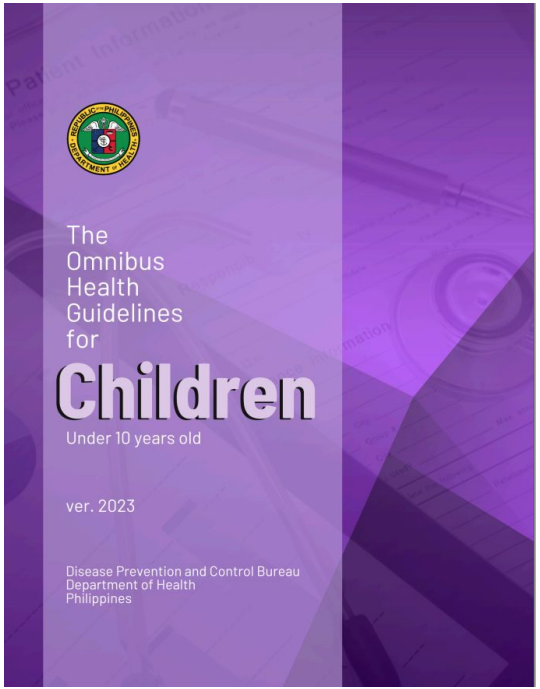
[1]DTP-containing vaccine
[2]Measles-containing vaccine

Hexavalent vaccine (DTaP-HBV-IPV-Hib)

DOH RECOMMENDATION

- In the Omnibus Health Guidelines for Children (2023), **all infants on or before 1 year of age** are recommended to get the following:
  - pentavalent vaccine
  - inactivated polio vaccine (IPV)
  - oral polio vaccine (OPV)

- Additionally, **infants aged 13 to 23 months** are also recommended to get these vaccines during **catch-up immunization** in public health facility or as part of catch-up program



DOH VACCINATION SCHEDULE

Schedule ng pagbibigay ng bakuna para sa mga batang isang taon pababa

Magpabakuna para sa Healthy Pilipinas

Bakuna	Sakit na maiiwasan	AT BIRTH	1ST VISIT 1 1/2 MONTHS	2ND VISIT 2 1/2 MONTHS	3RD VISIT 3 1/2 MONTHS	4TH VISIT 9 MONTHS	5TH VISIT 1 YEAR
BCG Vaccine	Tuberculosis (TB)	✓					
Hepatitis B Vaccine	Hepatitis B	✓					
Pentavalent Vaccine (DPT-Hep B-HIB)	Dipterya, Tetano, Pertussis, Pulmonya, Meningitis, Hepatitis		✓	✓	✓		
Oral Polio Vaccine (OPV)	Polio		✓	✓	✓		
Inactivated Polio Vaccine (IPV)	Polio				✓	✓	
Pneumococcal Conjugate Vaccine (PCV)	Pulmonya, Meningitis		✓	✓	✓		
Measles, Mumps, Rubella Vaccine (MMR)	Tigdas, Beke, German Measles					✓	✓

Mga paalala

Nagsisimula ang pagbabakuna ng bata sa kapanganakan.

Sundin ang schedule ng bakuna at siguruhing makumpleto ang mga ito hanggang sumapit ang kanyang unang kaarawan.

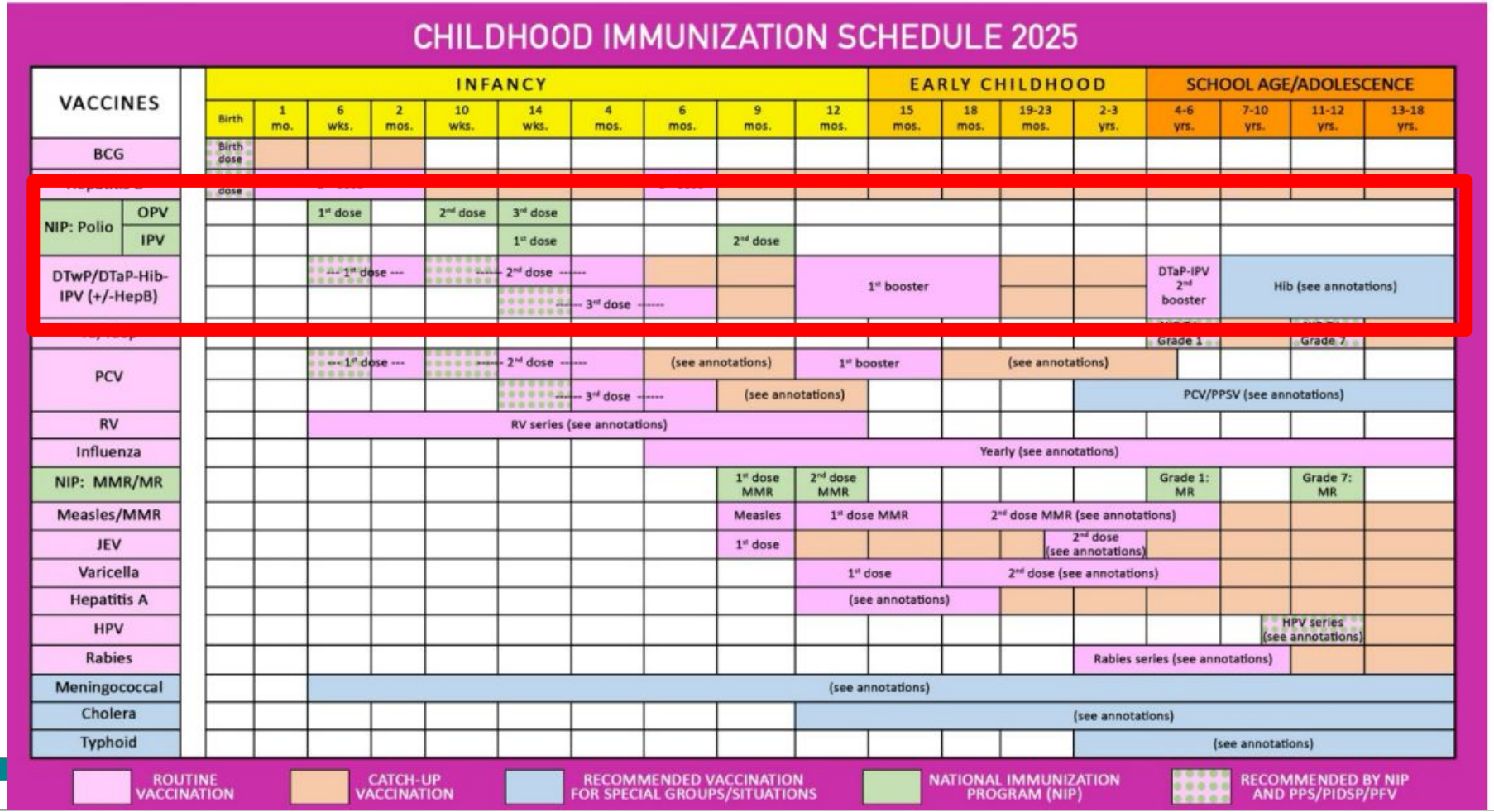
Ingatan ang card na ito. Maaari itong magamit bilang patunay o record ng pagbabakuna ng bata.

Note: The proposed hexavalent vaccine may be given during 1st, 2nd, and 3rd visit as well.

DOH RECOMMENDATION FOR PENTAVALENT AND POLIO VACCINES (OHG, 2023)

Antigen	Minimum age for 1st dose	Recommended age range	Doses needed for primary series	Doses for those who start vaccination late		Minimum interval between doses	
				If ≤ 12 months old	If ≥ 12 months old	1st to 2nd dose	2nd to 3rd dose
Pentavalent	6 weeks	2-23 months	3	3	3	1 month	6 months
IPV	14 weeks	4-23 months	2	2	2	2 months	N/A
OPV	6 weeks	2-23 months	3	3	3	1 month	N/A

PEDIATRIC INFECTIOUS DISEASE SOCIETY OF THE PHILIPPINES (PIDSP, 2025)



C2.II: REVIEW OF SAFETY SURVEILLANCE

Safety Surveillance Scoping

12 implementing countries
(US, UK, Australia, Canada, Singapore, Italy, Malaysia, South Africa, Mexico, Armenia, El Salvador, Paraguay)
were scoped for Hexavalent implementation safety surveillance

4 of 12 countries
with safety surveillance
(US, Australia, Canada*, Italy)
**with safety data but not specific to hexavalent vaccine*

8 of 12 countries
without surveillance data
(UK, Singapore, Malaysia, South Africa, Mexico, Armenia, El Salvador, Paraguay)

Note: To supplement global surveillance data for hexavalent vaccines, we proceeded with approaching 2 companies for locally-available hexavalent brands and both provided their data. For comparison, we also contacted 2 companies for pentavalent which did not respond; and 2 companies for IPV, both providing data.

List of implementing countries scoped (N=12)

High Income Countries (n=6)	Upper Middle Income Countries (n=3)	Lower Middle Income Countries (n=3)
US UK Australia Canada Singapore Italy	Malaysia South Africa Mexico	Armenia El Salvador Paraguay

Summary: Safety Surveillance of scoped implementing Countries (n=12)

	4 with safety surveillance	**8 without surveillance data**
No safety concerns	US HSS Australia DAEN Italy Drug Agency	Singapore MOH Malaysia NPRA UK HSA *South Africa* *Mexico* *Armenia* *El Salvador* *Paraguay*
With safety concerns **Data not specific to penta/hexa vaccine; only a small number of serious adverse events (SAEs) reported across all vaccines (253 out of 2,960 reports)*	Canada MOH	

Note: The surveillance reports specific to hexavalent did not report any safety concerns while the surveillance data with safety concern was not specific to this vaccine. Hence, we collected surveillance data from companies with locally-available brands.

Commonly reported AEs by scoped implementing countries

Country (surveillance population)	Source	Most common AEs reported
US (n=501 reports)	US VAERS	Fever (10.2%) and injection site erythema (5.4%)
Australia (n=15,004 cases)	DAEN (as of 26 Dec 2024)	Pyrexia (9.45%), rash (8.10%), vomiting (5.60%), diarrhea (5.37%), irritability (5.13%)
Italy (n=339 preterm infants)	Post marketing surveillance study	Injection site pain (35.6%), erythema, swelling and induration (25%)
Canada (n=2,960)	CAEFISS	*Data not specific to hexavalent/pentavalent vaccine*
Other countries: *Singapore, Malaysia, UK, South Africa, Mexico, Armenia, El Salvador, Paraguay*	No data*	

**No safety surveillance found*
[1]Data not specific for penta/hexa vaccine

- No safety signal were reported in US, Australia and Italy

Global safety surveillance *[DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)]*

Source	Review (23 February 2000 to 22 October 2017)
Surveillance population	**31,892 spontaneous AE reports worldwide** ● 27.7% (8,838) reports were considered serious *Note: No data specific for Philippines*
Most common adverse events (report rate per 100,000 doses distributed)	Fever (7.74), crying (2.62), injection site erythema (1.87), swelling (1.28)
Countries with Highest Incidences of AE reports	**Italy** (12,386 [38.8%]), **Germany** (5,934 [18.6%]) and **France** (3,629 [11.4%])

**no breakdown of SAEs in the post-marketing surveillance report*

- A review of extensive limb swelling did not reveal any safety concerns.
- An observed-to-expected analysis did not show an increased risk of sudden death after DTPa-HBV-IPV/Hib vaccination, in line with previous observations.

Global safety surveillance *(DTaP-HBV-IPV-Hib [pre-filled glass syringe])*

Source	Review: *(June 2013 to April 2023)*
Surveillance population	**18,320 spontaneous AE reports worldwide** (N= 180,791,895 doses distributed among infants/toddlers) *Note: No data specific for Philippines*
Non serious AEs	**14,958 (8.27 per 100,000 doses)** Frequently reported events: fever, injection site erythema, crying, injection site swelling, rash, irritability, injection site pain, diarrhea, vomiting, and decreased appetite
Serious AEs	**3,362* (1.86 per 100,000 doses)** Frequent reported events: fever, convulsion with or without fever, crying, hypotonic-hyporesponsive episode/hypotonia, and vomiting
Countries with Highest Incidences of AE reports	**Italy** (7,611 reports [41.5%]), **Malaysia** (2,513 reports [13.7%]), **Germany** (1,206 reports [6.6%]), **South Africa** (1,039 reports [5.7%]), and **France** (759 reports [4.1%])

**no breakdown of SAEs in the post-marketing surveillance report*

Local safety surveillance *(DTaP-HBV-IPV-Hib [pre-filled glass syringe + Hib in vial])*

Source	Company submission
Report period	13 December 2019 to 13 March 2024
Setting	Philippines
Adverse events	**Total reports: 31** ● Non-serious - 30 (96.77%) ● Serious case - 1 (3.23%) *"Due to insufficient information (i.e., time to onset, medical history, information on concomitant disease or medication), a causality assessment cannot be provided"*

Local safety surveillance (*DTaP-HBV-IPV-Hib [prefilled glass syringe]*)

Source	Company submission
Report period	2022 to 2024
Setting	Philippines
Adverse events	**Total reports: 7** ● Unsolicited AEs - 5 (71.43%) ○ Off-label use, pyrexia, generalized tonic clonic seizure, rash, expired product administered ● Solicited AEs - 2 (28.57%) ○ pyrexia

Local safety surveillance (IPV)

IPV	Sources of data	AEs reported
Brand A	Company submission	No AEs reported from 2023 to 2024
Brand B	Company submission	No AEs reported since 2011

HTAC Judgment

RQ2: **What are the safety concerns on the use of hexavalent vaccine among implementing countries? *[1 of 2]***

A total of 12 implementing countries (US, UK, Australia, Canada, Singapore, Italy, Malaysia, South Africa, Mexico, Armenia, El Salvador, Paraguay) were scoped regarding safety surveillance reports on the use of hexavalent vaccine (DTaP-HepB-IPV-Hib). Of these, only four countries (US, Australia, Canada, Italy) reported safety surveillance data, three of which (US, Australia, Italy) reported no safety signal. Meanwhile, in Canada, reported data on serious adverse events were not specific to hexavalent vaccine.

For *DTaP-HBV-IPV-Hib (pre-filled glass syringe)*, global safety surveillance data reported a serious AE rate of 1.86 per 100,000 doses, including the following commonly reported events: fever, convulsion with or without fever, crying, hypotonic-hyporesponsive episode/hypotonia, and vomiting. For *DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial),* based on a global surveillance with 31,892 spontaneous AE reports, the most commonly reported AEs are: fever (7.74), crying (2.62), injection site erythema (1.87), swelling (1.28).

HTAC Judgment

RQ2: **What are the safety concerns on the use of hexavalent vaccine among implementing countries? *[2 of 2]***

In terms of local data, company submission showed that *DTaP-HBV-IPV-Hib [prefilled glass syringe]* had 7 reports of AE from 2023 to 2024 including 5 unsolicited AEs: off-label use (n=1), pyrexia (n=1), generalized tonic clonic seizure (n=1), rash (n=1), and administration of expired product (n=1), and 2 solicited AEs: pyrexia (n=2). From December 2019 to March 2024, company submission noted that *DTaP-HBV-IPV-Hib [pre-filled glass syringe + Hib in vial]* had a total of 31 reports, including 30 non-serious cases and 1 serious case with suspected vaccine failure. However, causality assessment cannot be provided due to insufficient information.

On the other hand, there is no available local safety surveillance report for pentavalent vaccines while there are no reported AEs for the two brands of IPV based on company submissions.

C3: COSTING

Overview of Results: Cost of vaccination per vaccinee

Vaccine		Cost per dose	Doses required	Cost per vaccinee per vaccine	TOTAL COST PER VACCINEE*
Hexavalent vaccine	*DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)*	[Redacted, confidential information]	Three-dose	**₱7,720.56**	**₱7,720.56**
	DTaP-HBV-IPV-Hib (prefilled glass syringe)	[Redacted, confidential information]	Three-dose	**₱4,039.20**	**₱4,039.20**
Pentavalent vaccine		₱108.00	Three-dose	**₱364.25**	**₱767.55**
IPV		₱122.57	Two-dose	**₱403.30**	

Overview of Results: Total budget impact

Cost Component Subtotal	Costs (Php)		
	DTaP-HBV-IPV-Hib ***(pre-filled glass syringe + Hib in vial)***	**DTaP-HBV-IPV-Hib** ***(prefilled glass syringe)***	**Pentavalent Vaccine + IPV**
Target Population (<1 year old)	**2.2 million**	**2.2 million**	**2.2 million**
Cost of Vaccines	₱16,256,827,758.60	₱8,887,939,390.20	₱1,327,915,632.58
Vaccine Consumables	₱2,804,739.72	₱2,804,739.72	₱30,346,890.73
Logistics Cost	₱896,170,087.68	₱126,903,080.20	₱347,308,244.13
Service Delivery Cost	₱0.00	₱0.00	₱0.00
TOTAL BUDGET IMPACT	**₱17,155,802,586.00**	**₱9,017,647,210.12**	**₱1,707,570,767.44**

Costing Inputs, Remarks and Assumptions *(1 of 4)*

Costing parameter	Remarks/assumptions			
	DTaP-HBV-IPV-Hib ***(pre-filled glass syringe + Hib in vial)***	**DTaP-HBV-IPV-Hib** ***(prefilled glass syringe)***	**Pentavalent Vaccine + IPV**	
			Pentavalent vaccine	**Inactivated polio vaccine**
Vaccine costs	• 1 dose: 0.5mL per vial: [Redacted, confidential information] • Number of doses per treatment: 3 *(WHO 2024, Product Insert)*	• 1 dose: 0.5mL per vial: [Redacted, confidential information] • Number of doses per treatment: 3 *(WHO 2024)*	• Unit cost [0.5mL per vial (single dose)]: **Php 108.00** *(DPCB, 2025)* • Number of doses per treatment: 3 *(OHG, 2023)*	• Unit cost of 1 dose in [0.5mL per vial (10 doses)]: **Php 122.57** *(DPCB, 2025)* • Number of doses per treatment: 2 *(OHG, 2023)*
	Wastage: 5%			

Costing Inputs, Remarks and Assumptions *(2 of 4)*

<table>
<tr><th rowspan="3">Costing parameter</th><th colspan="3">Remarks/assumptions</th></tr>
<tr><th rowspan="2">DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)</th><th rowspan="2">DTaP-HBV-IPV-Hib (prefilled glass syringe)</th><th colspan="2">Pentavalent Vaccine + IPV</th></tr>
<tr><th>Pentavalent vaccine</th><th>Inactivated polio vaccine</th></tr>
<tr><td>Population</td><td colspan="4">2.2 million
Total population of infants < 1 year old (DOH FHSIS 2025 Projections)</td></tr>
<tr><td rowspan="2">Vaccine consumables cost (includes cost for syringes and safety boxes)</td><td colspan="2">• No cost since syringe is already included</td><td colspan="2">• Syringe
○ Unit cost of syringe: Php 2.06 (DPCB, 2025)
○ Syringe wastage rate: 10%</td></tr>
<tr><td colspan="4">• Safety box
○ Unit cost of safety box: Php 40.07 (DOH, 2024)
○ Safety box wastage rate: 0%</td></tr>
</table>

Costing Inputs, Remarks and Assumptions *(3 of 4)*

<table>
<tr><th rowspan="3">Costing parameter</th><th colspan="3">Remarks/assumptions</th></tr>
<tr><th rowspan="2">DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)</th><th rowspan="2">DTaP-HBV-IPV-Hib (prefilled glass syringe)</th><th colspan="2">Pentavalent Vaccine + IPV</th></tr>
<tr><th>Pentavalent vaccine</th><th>Inactivated polio vaccine</th></tr>
<tr><td rowspan="2">Logistics cost (vaccine consumables)</td><td colspan="4">General assumptions for transportation
• 47.57% of vaccines are transported by land and sea (Luzon areas)
• 52.43% of vaccines are transported by air (Visayas/ Mindanao areas)
• Rate of transport by land and sea is Php 3,400 per cbm
• Average rate of transport by air is Php 189/kg
Safety collector box
• Size: 0.016 cbm per box of safety collector box (ave) containing 25 safety collector boxes
• Weight: 6.45 kg (ave) containing 25 safety collector boxes</td></tr>
<tr><td></td><td></td><td colspan="2">AD Syringe
• Size: 0.089 cbm per box of syringe (ave) containing 2,433 syringe (ave)
• Weight: 12.81kg (ave) containing 2,433 syringe (ave)</td></tr>
</table>

Costing Inputs, Remarks and Assumptions *(4 of 4)*

<table>
<tr><th rowspan="3">Costing parameter</th><th colspan="4">Remarks/assumptions</th></tr>
<tr><th rowspan="2">DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)</th><th rowspan="2">DTaP-HBV-IPV-Hib (prefilled glass syringe)</th><th colspan="2">Pentavalent Vaccine + IPV</th></tr>
<tr><th>Pentavalent vaccine</th><th>IPV</th></tr>
<tr><td>Logistics costs (vaccine)</td><td>Carton dimensions: 5.5x2.4x13.3cm
Box of 1 vial (1 dose)</td><td>Carton dimensions: 7.7 x 3.5 x 4.2 cm
Box of 10 vials (1 dose each)</td><td>Carton dimensions: 17.8 x 9.1 x 4.7 cm
Box of 50 vials (1 dose each)</td><td>Carton dimensions: 5.6 x 13.2 x 13.2 cm
Box of 25 vials (10 doses each)</td></tr>
<tr><td></td><td colspan="4">Transportation
Biothermal packaging dimension: 61.6 x 41.9 x 43.2 cm with 1.00% wastage
47.57% of vaccines are transported by land and sea (Luzon areas)
52.43% of vaccines are transported by air (Visayas/ Mindanao areas)
Rate of transport by land and sea is Php 3,150 per cbm
Average rate of transport by air is Php 636.43/kg
Valuation cost is 0.5% of the total value of vaccine transported by land and sea
Valuation cost is 1% of the total value of vaccine transported by air</td></tr>
<tr><td></td><td colspan="4">Storage
Rate of storage at Php 28.00 per liter per month
Storage of primary vaccines is assumed to last only for 3 days but we assume 1 month to account for staggered delivery.</td></tr>
<tr><td>Service delivery cost</td><td colspan="4">None since for routine implementation</td></tr>
</table>

Costing results: Cost of vaccination per vaccinee

Vaccine	Brand	Cost per dose	Doses required	Cost per vaccinee per vaccine	TOTAL COST PER VACCINEE*
Hexavalent vaccine	*DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)*	[Redacted, confidential information]	Three-dose	**₱7,720.56**	**₱7,720.56**
	DTaP-HBV-IPV-Hib (prefilled glass syringe)	[Redacted, confidential information]	Three-dose	**₱4,058.20**	**₱4,058.20**
Pentavalent vaccine		₱108.00	Three-dose	**₱364.25**	**₱767.55**
IPV		₱122.57	Two-dose	**₱403.30**	

**Source of cost data:*
- *Hexavalent (pre-filled glass syringe + Hib in vial): company submission*
- *Hexavalent (prefilled glass syringe): company submission*
- *Pentavalent: DOH DPCB*
- *Inactivated polio vaccine: DOH DPCB*

vaccine (DTaP-HBV-IPV-Hib)

Costing results: Overall budget impact

Cost Component Subtotal	Costs (Php)		
	DTaP-HBV-IPV-Hib ***(pre-filled glass syringe + Hib in vial)***	**DTaP-HBV-IPV-Hib** ***(prefilled glass syringe)***	**Pentavalent Vaccine + IPV**
Target Population (<1 year old)	**2.2 million**	**2.2 million**	**2.2 million**
Cost of Vaccines	₱16,256,827,758.60	₱8,887,939,390.20	₱1,327,915,632.58
Vaccine Consumables	₱2,804,739.72	₱2,804,739.72	₱30,346,890.73
Logistics Cost	₱896,170,087.68	₱126,903,080.20	₱347,308,244.13
Service Delivery Cost	₱0.00	₱0.00	₱0.00
TOTAL BUDGET IMPACT	**₱ 17.16B** ₱17,155,802,586.00	**₱ 9.02B** ₱9,017,647,210.12	**₱1.71B** ₱1,707,570,767.44

Costing results: Overall budget impact

Cost Component Subtotal	Costs (Php)		
	DTaP-HBV-IPV-Hib *(pre-filled glass syringe + Hib in vial)*	DTaP-HBV-IPV-Hib *(prefilled glass syringe)*	Pentavalent Vaccine + IPV
Target Population (<1 year old)	2.2 million	2.2 million	2.2 million
Cost of Vaccines	₱1(		58
Vaccine Consumables			73
Logistics Cost			13
Service Delivery Cost			00
TOTAL BUDGET IMPACT	**₱ 17.16B** ₱17,155,802,586.00	**₱ 9.02B** ₱9,017,647,210.12	**₱1.71B** ₱1,707,570,767.44
Cost of vaccination per vaccinee	**₱7,720.56**	**₱4,058.18**	**₱767.55**

Key findings: The vaccine strategy with the lowest vaccination cost per vaccinee is pentavalent vaccine + IPV.

The annual budget impact to the government is ₱17.1B for hexavalent (*pre-filled glass syringe + Hib in vial*), ₱9.02B for hexavalent *(prefilled glass syringe)* and ₱1.7B for pentavalent + IPV.

Budget Impact of Vaccine Implementation

Vaccine	Brand	Total cost of vaccine for all target vaccinees for 2025	NIP Budget for 2025	% cost of vaccine from total NIP budget
Hexavalent Vaccine	*DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)*	**₱17.16 B**	**₱5.4 B**	**314.91% Exceeds 2025 NIP Budget**
	DTaP-HBV-IPV-Hib (prefilled glass syringe)	**₱9.02 B**		**165.53% Exceeds 2025 NIP Budget**
Pentavalent Vaccine + IPV		**₱1.71 B**		Estimated to consume **31.31% of the 2025 NIP Budget**

Hexavalent Vaccine (DTaP-HBV-IPV-Hib)

DOST PHILIPPINES

HTAC Judgment

RQ3: **What is the cost implication of adding hexavalent vaccine in the NIP? What is the total cost of vaccination per vaccinee?**

Based on the comparative cost analysis, both brands of hexavalent vaccine (DTaP-HBV-IPV-Hib), *DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)* [Redacted, confidential information] and *DTaP-HBV-IPV-Hib pre-filled glass syringe* [Redacted, confidential information] have **higher vaccination cost per patient** compared to pentavalent vaccine (DTwP-HepB-HiB) + inactivated polio vaccine (IPV) (Php 767.55).

In terms of budget impact, assuming all children less than one year old are to be vaccinated, *DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial)* **will cost Php 17.1 billion** while *DTaP-HBV-IPV-Hib pre-filled glass syringe* will cost **Php 9.02 billion to finance.** Both exceed the 2025 National Immunization Program (NIP) budget of Php 5.4 billion by **314.91% and 165.53%,** respectively. Meanwhile, continuing to implement pentavalent vaccine + IPV will incur **Php 1.7 billion or 31.31% of the total 2025 NIP budget.**

OVERALL JUDGMENT

Summary of results per criterion

RQ	Direction of Judgment
C1: What is the **magnitude and severity** of diphtheria, tetanus, pertussis, poliovirus, hepatitis B, invasive diseases due to influenzae type B?	Significant burden
C2.1 What are the **recommendations and guidelines** of **DOH and WHO** on the use of hexavalent vaccine for children less than 1 year old?	• DTP containing vaccines are recommended for children with minimum age of 6 weeks [PIDSP 2024; WHO Routine Immunization Program (2024)] • Separate formulation of pentavalent vaccine + IPV is recommended in the Omnibus Health Guidelines (2023) • Not listed in the WHO EML
C2.2: What are the **safety concerns** on the use of hexavalent vaccine for children less than 1 year old among implementing countries?	• 4 out of 12 implementing countries scoped have safety surveillance data • **3 of 4 countries have no safety signal** while **1 of 4 has data showing a small number of serious adverse events but is not specific to hexavalent vaccine.**
C3: What is the **cost implication** of adding hexavalent vaccine in the NIP? What is the total cost of vaccination per vaccinee?	• The vaccination cost per vaccinee was lower with using pentavalent vaccine + IPV: **Php 767.55** compared with the two hexavalent vaccine formulation: [Redacted, confidential information] • The annual budget impact to the government are **17.1B (314.91%)** and **9.02B (165.53%)** for DTaP-HBV-IPV-Hib (pre-filled glass syringe + Hib in vial) and DTaP-HBV-IPV-Hib prefilled glass syringe, respectively while **1.7B (31.31%)** for pentavalent vaccine + IPV.

THANK YOU!