Evidence to Recommendations and Proposed Recommendations: Use of Vaxelis among American Indian and Alaska Native Infants

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Haemophilus influenzae type b (Hib) polysaccharide conjugate vaccines remain the primary prevention strategy for Hib disease

- Capsular polysaccharide (PRP) conjugated to carrier proteins
  - Tetanus toxoid (PRP-T)
  - Outer membrane protein of meningococcal serogroup B (PRP-OMP)
- Highly immunogenic via activation of T-cell dependent immunity
  - 95% of infants develop protective antibody levels after a primary series
  - Estimated clinical efficacy 95%–100%
  - Invasive Hib disease is uncommon in children who are fully vaccinated

Current Hib vaccines in the United States

Vaccine Product	Trade Name	Primary series	Booster dose
Monovalent vaccines			
PRP-OMP	PedvaxHIB*	2, 4 months	12–15 months
PRP-T	ActHIB	2, 4, 6 months	12–15 months
PRP-T	Hiberix	2, 4, 6 months	12–15 months
Combination vaccines**			
DTaP-IPV/Hib	Pentacel	2, 4, 6 months	12–15 months
DTaP-IPV-Hib-HepB	Vaxelis	2, 4, 6 months	***

*Recommended vaccine for American Indian/Alaska Native children
**Hib component of Pentacel is PRP-T. Hib component of Vaxelis is PRP-OMP.
***Vaxelis is not recommended for the booster dose. A different Hib-containing vaccine should be administered as a booster at 12–15 months.

PedvaxHIB (PRP-OMP) is preferentially recommended for AI/AN infants

- Vaccination with a 2 dose primary series of a Hib vaccine that contains PRP-OMP (PedvaxHIB) is preferred for AI/AN infants to provide early protection because this vaccine produce a protective antibody response after the first dose
- A booster dose (dose 3) of Hib vaccine is recommended at age 12 through 15 months; for the booster dose, there is no preferred vaccine formulation

Briere EC, et al. Prevention and Control of *Haemophilus influenzae* Type b Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports*. 63(RR01);1-14

Vaxelis (DTaP-IPV-Hib-HepB) does not currently have a preferential recommendation for AI/AN infants

- Post-dose 1 immunogenicity data not previously available
- Lower dose of PRP-OMP than PedvaxHIB

Vaccine Product	Trade Name	PRP	OMP
PRP-OMP	PedvaxHIB	7.5 mcg	125 mcg
DTaP-IPV-Hib-HepB	Vaxelis	3 mcg	50 mcg

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Policy question

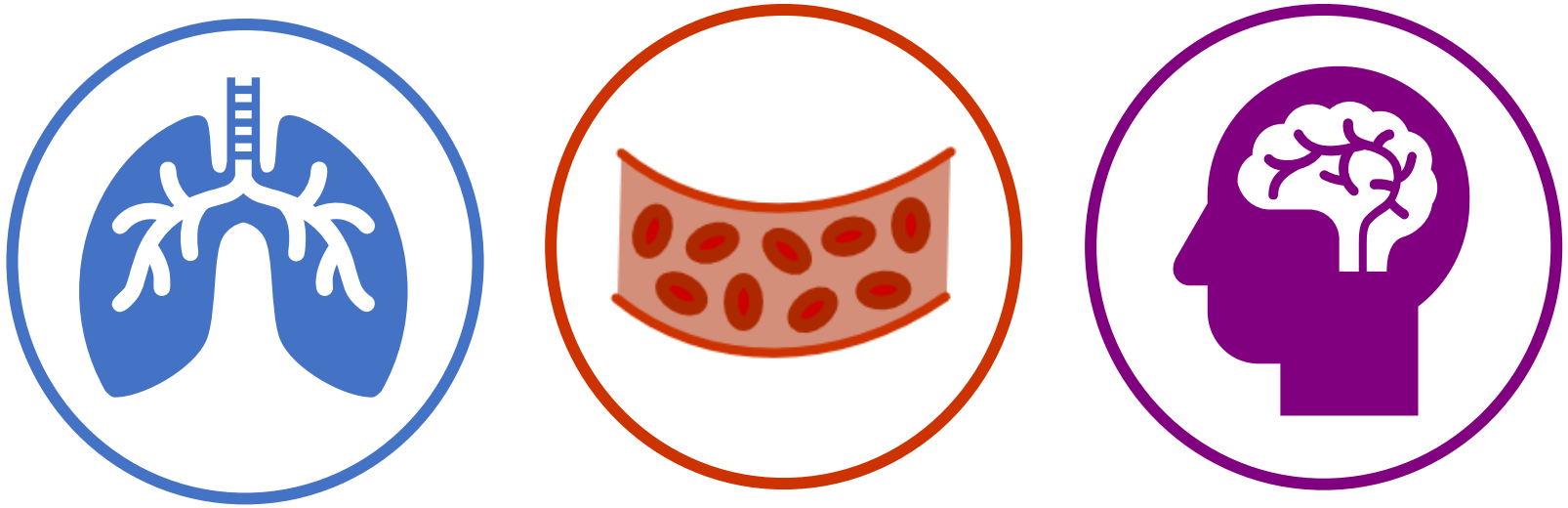
Should DTaP-IPV-Hib-HepB (Vaxelis) be included with PRP-OMP (PedvaxHIB) in the preferential recommendation for American Indian and Alaska Native (AI/AN) infants based on the Hib component?

Public health problem

Is invasive Hib disease among American Indian and Alaska Native infants a problem of public health importance?

Public health problem

- Before the introduction of effective vaccines, Hib was the leading cause of bacterial meningitis and other invasive bacterial disease in the United States, primarily among children aged <5 years
- Most common clinical syndromes of invasive Hib disease in the post-vaccine era



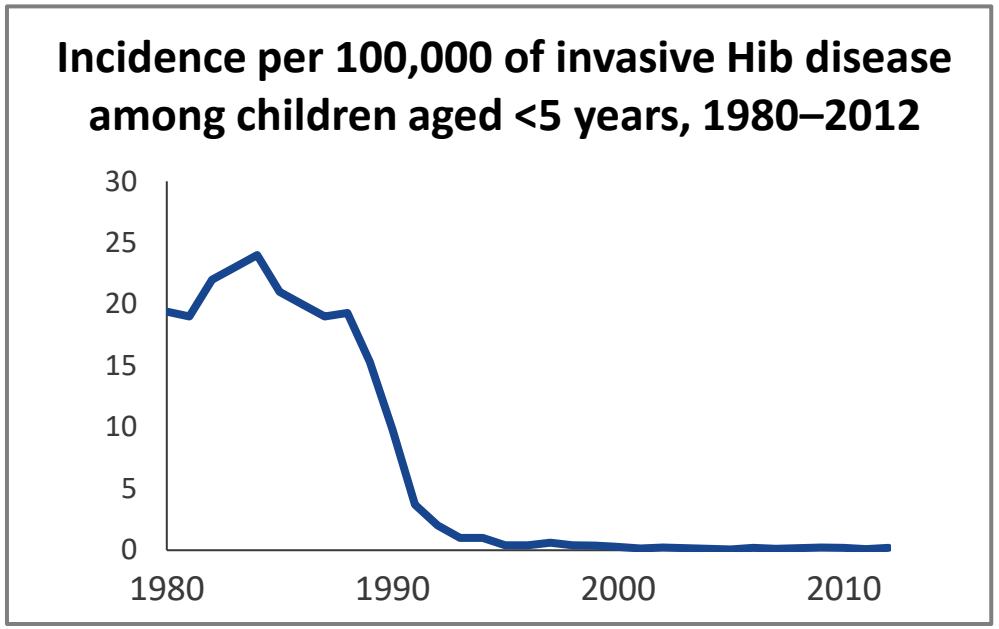
Bacteremic pneumonia

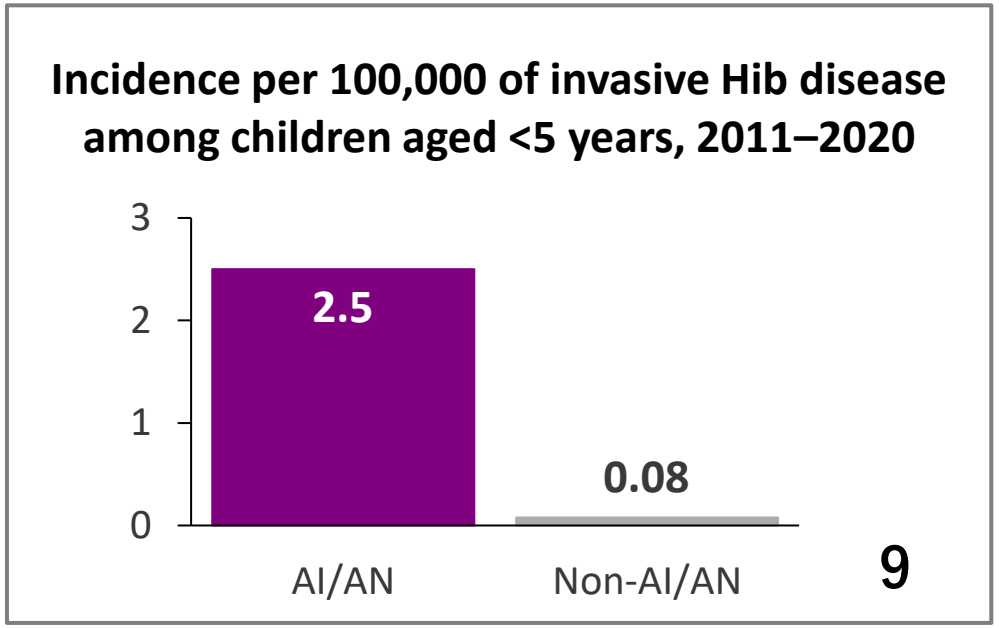
Bacteremia without a focus

Meningitis

Public health problem

- Incidence of invasive Hib disease declined >99% with introduction of Hib vaccines
- American Indian/Alaska Native children aged <5 years have a 31-fold higher incidence of invasive Hib disease than non-Native children





Public health problem: Work Group determination

- Is invasive Hib disease a public health problem among American Indian and Alaska Native populations?

No	Probably no	Probably yes	Yes	Varies	Don't know

Most common 2nd most common

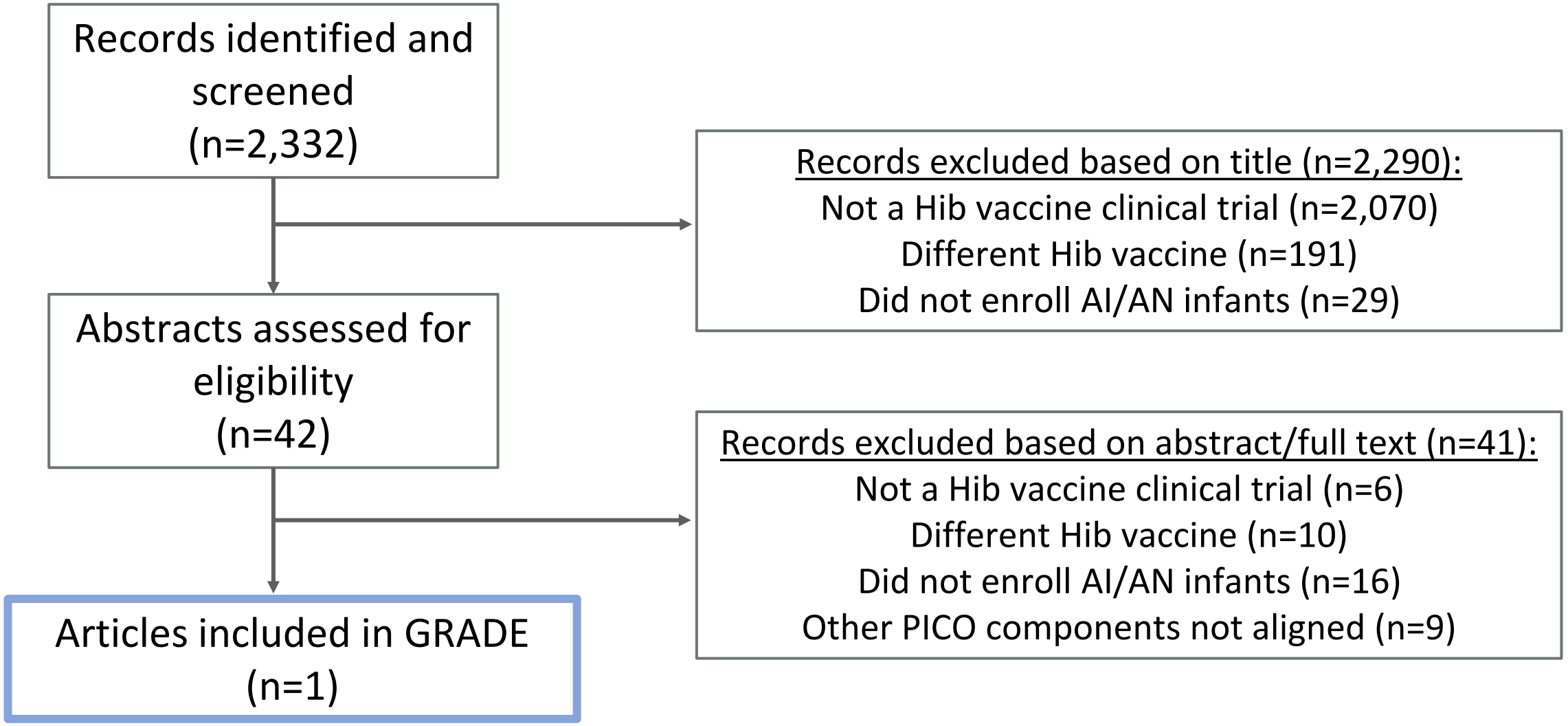
Benefits and harms

- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?
- Do the desirable effects outweigh the undesirable effects?

PICO components

Population	American Indian and Alaska Native infants
Intervention	Vaxelis (DTaP-IPV-Hib-HepB)
Comparison	PedvaxHIB (PRP-OMP)
Outcomes	- Invasive Hib disease - Post-dose 1 immunity - Post-primary series immunity - Serious adverse events

GRADE evidence retrieval



*Search was limited to studies in English from 2014–present based on earliest clinical trials of Vaxelis having been published in 2015. Two reviewers screened titles, abstracts and full-text records, as indicated, to determine whether records should be included.

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GRADE Table 2: Outcomes and Rankings

Outcome	Importance	Included in evidence profile
Invasive Hib disease	Important	No
Post-dose 1 immunity	Critical	Yes
Post-primary series immunity	Important	Yes
Serious adverse events	Critical	Yes

Available evidence

- Immunity and serious adverse events assessed using data from one phase IV, prospective, open-label randomized controlled clinical trial
  - Enrolled healthy infants
    - Born at gestational age ≥35 weeks
    - Aged 42–90 days at the time of first vaccination
    - Identified as AI/AN by parent/legally authorized representative
  - Randomized to Vaxelis vs. PedvaxHIB
    - Vaxelis administered at ages 2, 4, and 6 months
    - PedvaxHIB administered at ages 2 and 4 months
  - Compared antibody levels before vaccination vs. day 30, 120, and 150 post-dose 1
  - Safety monitoring for serious adverse events on day 0, 30, 60, 120, and 150

Post-dose 1 immunity

- Anti-Hib IgG geometric mean concentration (GMC) ratio (Vaxelis: PedvaxHIB) 30 days post-dose 1 met pre-specified non-inferiority criterion
- The proportion of infants with anti-Hib concentration above the putative correlate of short-term protection 30 days post-dose 1 was similar between groups
  - Vaxelis 75.7%
  - PedvaxHIB 71.2%

Primary Outcome: Anti-Hib IgG Geometric Mean Concentration (GMC) 30 Days Post-Dose 1

		PedvaxHIB®	Vaxelis®
Anti-Hib Antibody GMC µg/mL (95% CI)	Observed Data	0.39 (0.31- 0.50)	0.41 (0.33 - 0.52)
	Modeled by cLDA	0.40 (0.31 - 0.50)	0.41 (0.33 - 0.51)

CI: confidence interval; cLDA: constrained longitudinal data analysis

Ratio of GMCs (Vaxelis : PedvaxHib)
1.03 (0.75 - 1.41)

The pre-specified non-inferiority criterion was met based on the lower bound of the 95% confidence interval (CI) around the antibody concentration ratio [Vaxelis / PedvaxHIB] being > 0.67

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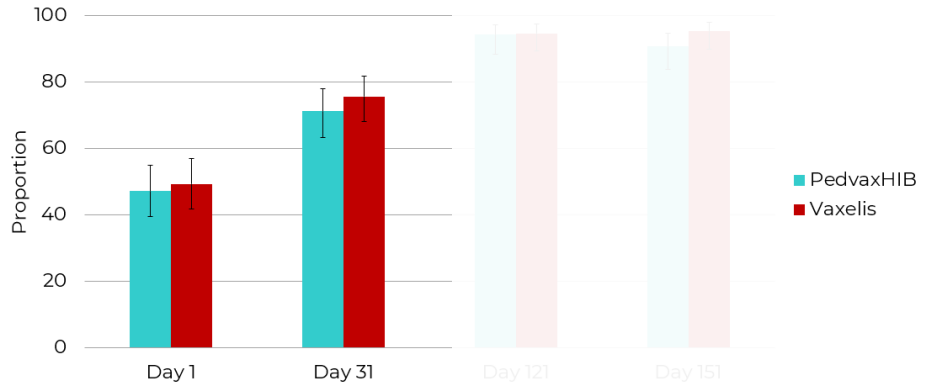
Proportion with Anti-Hib Concentration ≥0.15 µg/mL



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GRADE evidence profile: post-dose 1 immunity

Assessed via proportion with anti-Hib IgG concentration ≥0.15 µg/mL 30 days post-dose 1

Certainty assessment							Summary of findings					Importance
# studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	# patients		Effect		Certainty	
							Vaxelis n/N % (95% CI)	PedvaxHIB n/N % (95% CI)	Relative risk (95% CI)	Absolute risk (95% CI)		
1	RCT	Not serious[a]	Not serious	Not serious[b,c,d]	Serious[e]	None	115/152 (75.7%)	104/146 (71.2%)	1.06 (0.93–1.22)	4,274 more per 100,000 (from 4,986 fewer to 15,671 more)	Moderate	Critical

[a] Similar loss to follow-up for anti-Hib IgG concentration 30 days post-dose 1: Vaxelis: 15/167 (9%), PedvaxHIB: 20/166 (12%), p=0.36. Open-label study design would not affect immune response. Median time of post-dose 1 blood draw was similar between groups: Vaxelis 34 days (IQR 32–37 days) versus PedvaxHIB 34 days (IQR 31–39 days).

[b] Immunity is inferred from proportion with anti-Hib concentration above the putative correlate of short-term protection.

[C] As modeled by constrained longitudinal data analysis, anti-Hib GMC 30 days post-dose 1 for Vaxelis group (0.41; 95% CI: 0.33–0.51) was non-inferior to that of the PedvaxHIB group (0.40; 95% CI: 0.31–0.50). Ratio of GMCs (Vaxelis:PedvaxHIB): 1.03 (95% CI: 0.75–1.41); the pre-specified non-inferiority criterion was met based on the lower bound of the 95% CI being >0.67.

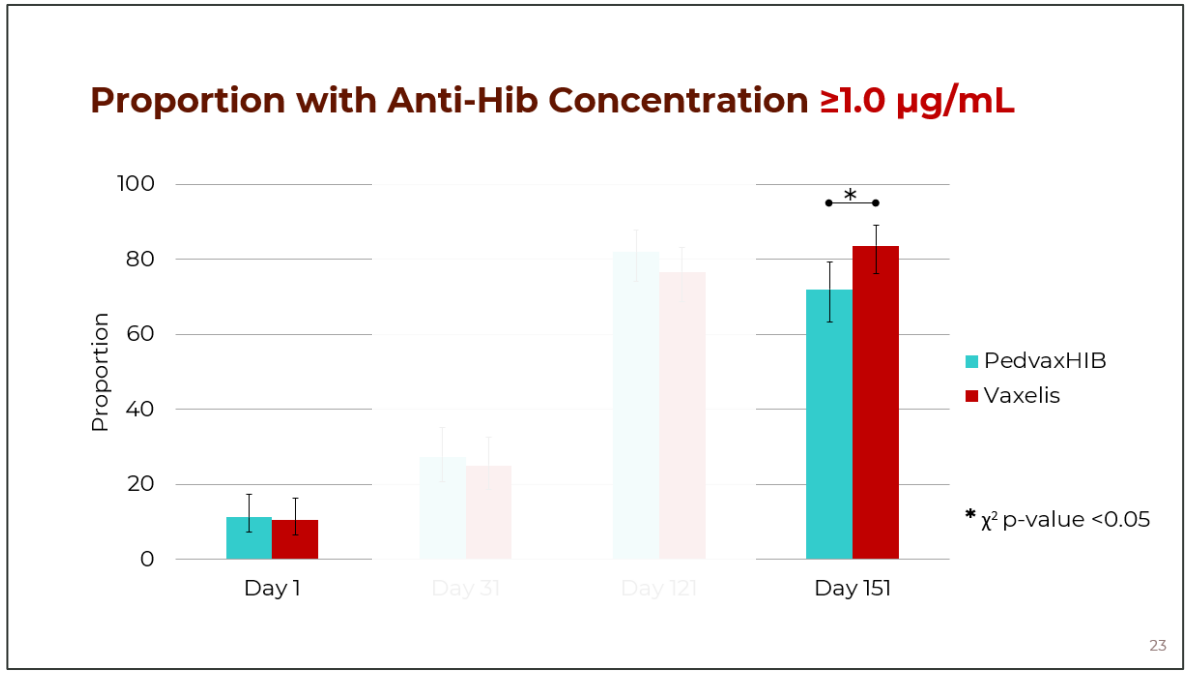
[d] Study was conducted among Navajo Nation and Alaska Native infants and may not be generalizable to other American Indian populations; WG members determined this did not warrant a downgrade.

[e] Downgraded because the absolute effect confidence interval is wide.

Post-primary series immunity

- The proportion of infants with anti-Hib concentration above the putative correlate of long-term protection 150 days post-dose 1 was higher in the Vaxelis group (83.6%) than in the PedvaxHIB group (71.7%, p<0.05)

- Antibody titers were not collected beyond day 150 post-dose 1



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GRADE evidence profile: post-primary series immunity

Assessed via proportion with anti-Hib IgG concentration ≥1.0 µg/mL 150 days post-dose 1

Certainty assessment							Summary of findings					Importance
# studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	# patients		Effect		Certainty	
							Vaxelis n/N % (95% CI)	PedvaxHIB n/N % (95% CI)	Relative risk (95% CI)	Absolute risk (95% CI)		
1	RCT	Not serious[a]	Not serious	Not serious[b,c]	Serious[d]	None	107/128 (83.6%)	84/117 (71.8%)	1.16 (1.02–1.34)	11,487 more per 100,000 (from 1,436 more to 24,410 more)	Moderate	Important

[a] Similar loss to follow-up for anti-Hib IgG concentration 150 days post-dose 1: Vaxelis 39/167 (23%), PedvaxHIB 49/166 (30%), p=0.20. Open-label study design would not affect immune response. Median time of day 150 blood draw was similar between groups: Vaxelis 174 days (IQR 163–187 days) versus PedvaxHIB 180 days (IQR 162–189 days).

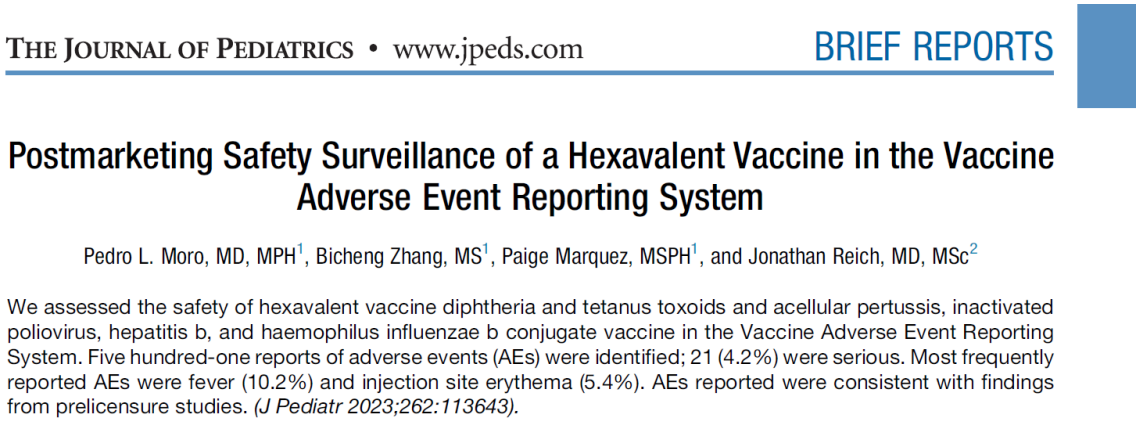
[b] Immunity is inferred from proportion with anti-Hib concentration above the putative correlate of long-term protection.

[c] Study was conducted among Navajo Nation and Alaska Native infants and may not be generalizable to other American Indian populations; WG members determined this did not warrant a downgrade.

[d] Downgraded because the absolute effect confidence interval is wide.

General safety of Vaxelis (DTaP-IPV-Hib-HepB)

- In pre-licensure clinical trials, the safety profile was consistent with that of licensed comparator vaccines except higher rate of fever than with DTaP-IPV/Hib (Pentacel) (47.1%–47.4% vs. 33.2%–34.4%)[1,2]; rates of fever-related medical events were similar between groups
- Post-licensure analysis of Vaccine Adverse Event Reporting System (VAERS) data from June 26, 2019 – June 16, 2023 did not identify new or unexpected safety issues



THE JOURNAL OF PEDIATRICS • www.jpeds.com BRIEF REPORTS

Postmarketing Safety Surveillance of a Hexavalent Vaccine in the Vaccine Adverse Event Reporting System

Pedro L. Moro, MD, MPH[1], Bicheng Zhang, MS[1], Paige Marquez, MSPH[1], and Jonathan Reich, MD, MSc[2]

We assessed the safety of hexavalent vaccine diphtheria and tetanus toxoids and acellular pertussis, inactivated poliovirus, hepatitis b, and haemophilus influenzae b conjugate vaccine in the Vaccine Adverse Event Reporting System. Five hundred-one reports of adverse events (AEs) were identified; 21 (4.2%) were serious. Most frequently reported AEs were fever (10.2%) and injection site erythema (5.4%). AEs reported were consistent with findings from prelicensure studies. *(J Pediatr 2023;262:113643).*

[1]Marshall GS, et al. Immunogenicity, safety and tolerability of a hexavalent vaccine in infants. *Pediatrics* 2015;136:e323–32.

[2]Block SL, et al. Lot-to-lot consistency, safety, tolerability and immunogenicity of an investigational hexavalent vaccine in U.S. infants. *Pediatr Infect Dis J* 2017;36:202–8.

The use of trade names is for identification purposes only and does not imply endorsement by CDC.

GRADE: Serious adverse events among AI/AN infants in the Hibvax Study

- The frequency of SAEs was similar between groups
  - Vaxelis (5%)
  - PedvaxHIB (7%)
- The most common SAE was acute respiratory infection
- No SAEs were deemed related to study participation

Serious Adverse Events (SAEs)

- 25 SAEs were detected during study follow up in 21 individuals.

	PedvaxHIB® N=166	Vaxelis® N=167	Total
SAEs, n	15	10	**25**
Participants, n (%)	12 (7%)	9 (5%)	**21 (6%)**

- No SAEs were associated with study participation.
- The most common SAE was acute respiratory infection (n=21).

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GRADE evidence profile: serious adverse events

Assessed via proportion with SAEs[a]

Certainty assessment							Summary of findings					Importance
# studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	# patients		Effect		Certainty	
							Vaxelis n/N % (95% CI)	PedvaxHIB n/N % (95% CI)	Relative risk (95% CI)	Absolute risk (95% CI)		
1	RCT	Not serious[b]	Not serious	Not serious[c]	Serious[d]	None	9/167 (5.4%) [e]	12/166 (7.2%)[e]	0.75 (0.32–1.72)	1,807 fewer per 100,000 (from 4,916 fewer to 5,205 more)	Moderate	Critical

[a] From the time of the first dose of study vaccine to the end of the last study visit (approximately 5 months).
[b] Similar loss to follow-up through the last study visit: Vaxelis 21/166 (13%) PedvaxHIB 16/167 (10%) p=0.37. Open-label study design may bias reporting of SAEs but WG members determined this did not warrant a downgrade.
[c] Study was conducted among Navajo Nation and Alaska Native infants and may not be generalizable to other American Indian populations; WG members determined this did not warrant a downgrade.
[d] Downgraded because the absolute effect confidence interval is wide.
[e] In the Vaxelis group 10 SAEs occurred among 9 participants. In the PedvaxHIB group, 15 SAEs occurred among 12 participants. The most common SAE was acute respiratory infection 21/25 (84%). No SAEs were deemed related to study participation.

GRADE Summary Table

Type	Outcome	Importance	Design (# studies)	Findings	Evidence type*
Benefits	Invasive Hib disease		n/a	No data available	ND
	Post-dose 1 immunity	Critical	RCT (1)	The proportion participants with anti-Hib concentration ≥0.15 µg/mL* 30 days post-dose 1 was similar between groups	Moderate
	Post-primary series immunity	Important	RCT (1)	The proportion participants with anti-Hib concentration ≥1.0 µg/mL** 150 days post-dose 1 was higher in the Vaxelis group. Antibody titers were not available beyond day 150 post-dose 1.	Moderate
Harms	Serious adverse events	Critical	RCT (1)	The proportion of SAEs was similar between groups; no SAEs were deemed related to study participation	Moderate

*Putative correlate of short-term protection
**Putative correlate of long-term protection

Benefits and harms: Work Group determination

- How substantial are the desirable anticipated effects overall and for each main outcome for which there is a desirable effect?

Minimal	Small	**Moderate**	Large	Varies	Don't know

- How substantial are the undesirable effects overall and for each main outcome for which there is an undesirable effect?

Minimal	Small	Moderate	Large	Varies	Don't know

Most common | 2nd most common | 3rd most common | Majority

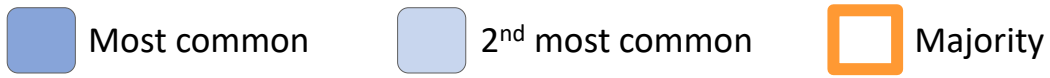
Benefits and harms: Work Group determination

- Do the desirable effects outweigh the undesirable effects?

Favors intervention (Vaxelis only)	Favors comparison (PedvaxHIB only)	**Favors both (Vaxelis & PedvaxHIB)**	Favors neither	Unclear

- What is the overall certainty of evidence for the critical outcomes?

High	**Moderate**	Low	Very low



Values

- Does the target population feel that the desirable effects are large relative to the undesirable effects?
- Is there important uncertainty about or variability in how much people value the main outcome?

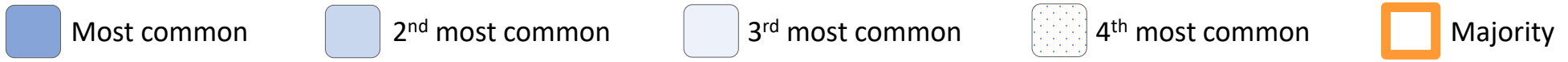
Values

- Limited data were available
- Vaxelis would provide an additional option for AI/AN infants
- In collaboration with CDC' Office of Tribal Affairs and Strategic Alliances (OTASA), NCIRD held a listening session with tribal communities in January 2024
  - 80 attendees, including
    - 9 from tribes or tribal serving organizations
    - 46 from Indian Health Service (IHS)
  - Key questions and concerns raised by participants for WG consideration
    - Will Vaxelis offer the same protection as PedvaxHIB?
    - Need to monitor for possible breakthrough cases
    - Safety and side effects

Values:
Work Group determination

- Does the target population feel the desirable effects are large relative to the undesirable effects?

- Is there important uncertainty about, or variability in, how patients value the outcomes?



Acceptability

Is the intervention acceptable to key stakeholders?

Acceptability

- Limited data were available
- Vaxelis would reduce the number of injections to complete the childhood immunization series for those who receive it and may therefore improve acceptability for parents/guardians and medical providers
- CDC's **General Best Practice Guidance for Immunization** and **American Academy of Pediatrics Red Book** both state a general preference for combination vaccines over separate injections of equivalent component vaccines[1,2]
  - Considerations should include provider assessment, patient preference, and the potential for adverse events.[1]
- Proposed policy option to add Vaxelis retains flexibility for providers to continue using PedvaxHIB

[1]General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
[2]American Academy of Pediatrics. Red Book 2018 Report of the Committee on Infectious Diseases. 31st Edition.

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General best practice guidance for immunization: combination vaccines

Potential advantages	Potential disadvantages
• Improved vaccine coverage rates • Timely catch-up immunizations • Reduced shipping and stocking costs • Reduced costs for extra health care visits necessitated by deferral of vaccination • Facilitation of additional new vaccines into vaccination programs	• Adverse events that might occur more frequently with combination vaccines than with individual components • Confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses • Extra doses of certain antigens in the combination product

[1]General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html

Acceptability: Work Group determination

- Is the intervention acceptable to key stakeholders?
  - Are there key stakeholders that would not accept the distribution of benefits, harms, and costs?
  - Are there key stakeholders that would not accept the costs or undesirable effects in the short term for the desirable effects in the future?

No	Probably no	Probably yes	Yes	Varies	Don't know

Most common | 2nd most common | 3rd most common | Majority

Resource use

- Is the intervention a reasonable and efficient allocation of resources?

Vaxelis protects against 6 infections with fewer injections

Option	2 months	4 months	6 months	12–15 months	Total shots
1	**Vaxelis**	**Vaxelis**	**Vaxelis**	PedvaxHIB DTaP	5
2	PedvaxHIB Pediarix	PedvaxHIB Pediarix	Pediarix	PedvaxHIB DTaP	7
3	PedvaxHIB DTaP IPV HepB	PedvaxHIB DTaP IPV	DTaP IPV HepB	PedvaxHIB DTaP	12

Pediarix is a combination vaccine that protects against diphtheria, tetanus, pertussis, polio, and hepatitis B.
DTaP is a vaccine that protects against diphtheria, tetanus, and pertussis. The 4th dose of DTaP is recommended at age 15–18 months.
IPV is inactivated polio vaccine.

Pediatric/Vaccines for Children (VFC) Vaccine Price List

Vaccine	Trade name	CDC cost/dose	Private sector cost/dose
DTaP-IPV-Hib-HepB	Vaxelis	$100.59	$150.85
PRP-OMP	PedvaxHIB	$16.14	$29.71
DTaP-HepB-IPV	Pediarix	$66.07	$97.97
DTaP	Daptacel	$21.69	$29.31
	Infanrix	$21.66	$28.80
IPV	IPOL	$16.46	$42.64
HepB	Engerix B	$17.38	$28.42
	Recombivax HB	$14.59	$27.12

Pediarix is a combination vaccine that protects against diphtheria, tetanus, pertussis, polio, and hepatitis B.
DTaP is a vaccine that protects against diphtheria, tetanus, and pertussis.
IPV is inactivated polio vaccine.

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Estimated cost of vaccine options that protect against the 6 pathogens in Vaxelis

Option	Vaccines (# doses to complete childhood series)	Total CDC cost (vaccines only*)	Total CDC cost (vaccines + admin**)	Total private sector cost (vaccines only*)	Total private sector cost (vaccines + admin**)
1	Vaxelis (3) PedvaxHIB (1) DTaP (1)	$339.57–339.60	$419.01–419.04	$511.06–511.57	$669.90–670.41
2	Pediarix (3) PedvaxHIB (3) DTaP (1)	$268.29–268.32	$368.45–368.48	$411.84–412.35	$612.12–612.63
3	PedvaxHIB (3) DTaP (4) IPV (3) HepB (2)	$213.62–219.32	$365.58–371.28	$386.49–391.13	$690.37–695.01

*Vaccine cost ranges reflect different costs for DTaP (Daptacel vs. Infanrix) and HepB (Engerix B vs. Recombivax HB).

**Assumptions: private sector administration cost $34.53 for first vaccine based on estimates from a 2014 study, adjusted for inflation.[1] A factor of 0.6 was used to calculate the private sector administration cost of $20.72 for subsequent doses at the same visit based a 2019 study.[2] Public sector administration costs were assumed to be half of private sector costs.[3]

[1]Tsai Y et al. Prev Med Rep. 2019 Jun 7:15:100917. doi: 10.1016/j.pmedr.2019.100917

[2]Tsai Y et al. .Am J Prev Med. 2019 Aug;57(2):180-190. doi: 10.1016/j.amepre.2019.03.011

[3]Tsai Y. Med Care. 2018 Jan; 56(1): 54–61.

Vaccine only costs are higher for option 1 (i.e., using Vaxelis)

Option	Vaccines (# doses to complete childhood series)	Total CDC cost (vaccines only*)	Total CDC cost (vaccines + admin**)	Total private sector cost (vaccines only*)	Total private sector cost (vaccines + admin**)
1	Vaxelis (3) PedvaxHIB (1) DTaP (1)	$339.57–339.60	$419.01–419.04	$511.06–511.57	$669.90–670.41
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[3]Tsai Y. Med Care. 2018 Jan; 56(1): 54–61.

Total costs are similar accounting for administration costs

Option	Vaccines (# doses to complete childhood series)	Total CDC cost (vaccines only*)	Total CDC cost (vaccines + admin**)	Total private sector cost (vaccines only*)	Total private sector cost (vaccines + admin**)
1	Vaxelis (3)	$339.57–339.60	$419.01–419.04	$511.06–511.57	$669.90–670.41
	PedvaxHIB (1)				
	DTaP (1)				
2	Pediarix (3)	$268.29–268.32	$368.45–368.48	$411.84–412.35	$612.12–612.63
	PedvaxHIB (3)				
	DTaP (1)				
3	PedvaxHIB (3)	$213.62–219.32	$365.58–371.28	$386.49–391.13	$690.37–695.01
	DTaP (4)				
	IPV (3)				
	HepB (2)				

*Vaccine cost ranges reflect different costs for DTaP (Daptacel vs. Infanrix) and HepB (Engerix B vs. Recombivax HB).

**Assumptions: private sector administration cost $34.53 for first vaccine based on estimates from a 2014 study, adjusted for inflation.[1] A factor of 0.6 was used to calculate the private sector administration cost of $20.72 for subsequent doses at the same visit based a 2019 study.[2] Public sector administration costs were assumed to be half of private sector costs.[3]

[1]Tsai Y et al. Prev Med Rep. 2019 Jun 7:15:100917. doi: 10.1016/j.pmedr.2019.100917

[2]Tsai Y et al. .Am J Prev Med. 2019 Aug;57(2):180-190. doi: 10.1016/j.amepre.2019.03.011

[3]Tsai Y. Med Care. 2018 Jan; 56(1): 54–61.

Resource use (summary)

- Cost is similar for Vaxelis and other vaccine options that cover the same pathogens, accounting for administration costs
- Resource use has been acceptable for the general U.S. population; equitable to use the same standard for AI/AN children

Resource use: Work Group determination

- Is using Vaxelis among American Indian and Alaska Native infants a reasonable and efficient allocation of resources?

No	Probably no	Probably yes	Yes	Varies	Don't know

Most common | 2nd most common | 3rd most common | Majority

Equity

- What would be the impact on health equity?

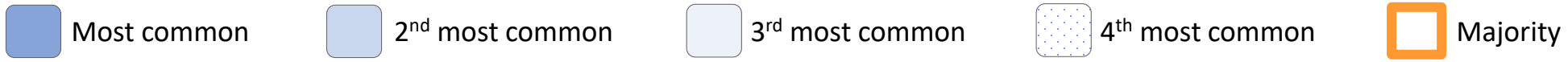
Equity

- Limited data were available
- The option to use a combination vaccine may improve equity by
  - Improving reliability of the vaccine supply
  - Improving Hib vaccination uptake among AI/AN populations, who are disproportionately at risk for invasive Hib disease

Equity: Work Group determination

- What would be the impact of using Vaxelis among American Indian and Alaska Native infants on health equity?

*Would not reduce disparities
**Would greatly reduce disparities



Feasibility

- Is the intervention feasible to implement?

Feasibility

- Widely used in the general U.S. population with >7.4 million doses distributed in the United States (as of Q1 2024)[1]
- Adding Vaxelis to the preferential recommendation for AI/AN infants would
  - Increase flexibility for patients and providers
  - Reduce the number of injections to complete the childhood immunization series for those who receive it
- Neither Vaxelis nor PedvaxHIB require reconstitution
- Shelf life of Vaxelis (4 years) is longer than that of PedvaxHIB (3 years)
- Vaxelis cannot be used for the booster dose; clinics will need to stock additional products
  - Stocking PRP-OMP (PedvaxHIB) for the Hib booster dose would maintain parent/guardian and provider flexibility to choose this for doses 1–3
  - Stocking PRP-T is also an option
    - Vaxelis primary series with a heterologous booster (PRP-T) was shown to produce a robust immune response in a small study[2]
    - Risk of inadvertent administration of PRP-T for doses 1–3 with a less robust immune response following doses 1 and 2

[1]Per the manufacturer
[2]Wilck et al. *Vaccine*. 2021;39(9):1428-1434.
The use of trade names is for identification purposes only and does not imply endorsement by CDC.

Feasibility: Work Group determination

- Is using Vaxelis among American Indian and Alaska Native infants feasible to implement?

No	Probably no	Probably yes	Yes	Varies	Don't know

Most common 2nd most common Majority

Summary

EtR Domain	Question	Work group determination
Public health problem	Is invasive Hib disease among American Indian and Alaska Native children a problem of public health importance?	Yes
Benefits and harms	How substantial are the desirable anticipated effects?	Moderate
	How substantial are the undesirable anticipated effects?	Minimal
	Do the desirable anticipated effects outweigh the undesirable effects?	Favors both (Vaxelis & PedvaxHIB)
	What is the overall certainty of the evidence for the critical outcomes?	Moderate
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably yes or yes
	Is there important variability in how patients value the outcome?	Probably no, probably yes or don't know
Acceptability	Is the intervention acceptable to key stakeholders?	Probably yes
Resource use	Is the intervention a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of the intervention on health equity?	Moderate
Feasibility	Is the intervention feasible to implement?	Yes

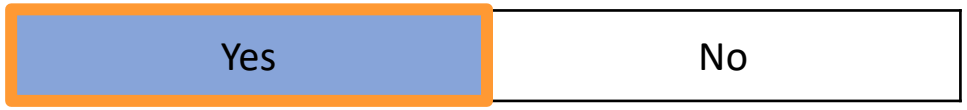
Favorable Uncertain

Balance of Consequences

Undesirable consequences ***clearly outweigh*** desirable consequences in most settings	Undesirable consequences ***probably outweigh*** desirable consequences in most settings	The balance between desirable and undesirable consequences is ***closely balanced or uncertain***	Desirable consequences ***probably outweigh*** undesirable consequences in most settings	Desirable consequences ***clearly outweigh*** undesirable consequences in most settings	There is **insufficient evidence** to determine the balance of consequences

Majority of WG members think desirable consequences probably outweigh undesirable consequences in most settings

Is there sufficient information to move forward with a recommendation?



Most common

2nd most common

Work Group Interpretation:

Should DTaP-IPV-Hib-HepB (Vaxelis) be included with PRP-OMP (PedvaxHIB) in the preferential recommendation for American Indian and Alaska Native infants based on the Hib component?

We do not recommend the intervention

We recommend the intervention

Majority of WG members favored recommending the intervention

Most common

2nd most common

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Draft proposal language

ACIP recommends DTaP-IPV-Hib-HepB (Vaxelis®) should be included with PRP-OMP (PedvaxHIB®) in the preferential recommendation for American Indian and Alaska Native infants based on the *Haemophilus influenzae* type b (Hib) Hib component.

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Thank you!

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U. S. Centers for Disease Control and Prevention.