Factsheet on the Use of Vaxelis™ Combination Vaccine in AI/AN Infants
September 10, 2021

Background: Vaxelis™ is a new hexavalent vaccine containing diphtheria and tetanus toxoids and acellular pertussis (DTaP) adsorbed, inactivated poliovirus (IPV), *Haemophilus influenzae* type b (Hib, PRP-OMP), and hepatitis B (HepB) (recombinant) vaccine. In 2018, the Food and Drug Administration (FDA) licensed Vaxelis™ for use in children aged 6 weeks through 4 years: it is indicated as a 3-dose series for infants at ages 2, 4, and 6 months. The Advisory Committee on Immunization Practices (ACIP) voted to add Vaxelis™ to the Vaccines for Children (VFC) Program in 2019, but the product did not become commercially available in the United States until 2021. Vaxelis™ became available to order through state VFC programs by enrolled VFC-providers in June 2021. PedvaxHIB® is the only Haemophilus influenzae type b (Hib) vaccine that has preferential recommendation for use in American Indian and Alaska Native (AI/AN) children.

Issue: IHS facilities have ordered or are interested in ordering Vaxelis™ but are unsure of the level of protection of the Hib component in AI/AN children.

Interim Recommendation: Until additional data on the immune response after the first dose of Vaxelis™ in AI/AN children is available, PedVaxHIB® is the only vaccine that has an ACIP-preferential recommendation for Hib vaccination in AI/AN children. Although Vaxelis™ is ACIP-approved for use in children under 5 years old, it is not a preferred product for AI/AN children at the present time. Given the potential impact of breakthrough cases of Hib disease in this population and the current ACIP-preferential recommendation for Hib vaccination in AI/AN children, IHS recommends continued use of PedVaxHIB® at this time. Clinical studies evaluating immunogenicity of Vaxelis™ in AI/AN children are currently underway and this recommendation may evolve accordingly.

History: PedvaxHIB® was proven efficacious in clinical trials in the late 1980s that included AI/AN children and was unique among Hib vaccines in that it provided a strong immune response after the first dose (Bulkow, 1993; Santosham et al, 1991). This was important for AI/AN children given that invasive Hib disease occurred in a younger age in Native children compared to non-Native children. From 1991 to 1996, invasive Hib disease decreased by 90% in Alaska Native and non-Native children with Alaska's state-wide use of PedvaxHIB®. During 1996-1997, Alaska switched to a combination vaccine with a different Hib conjugate. This was followed by an increase of invasive Hib disease in Alaska Native children but not in non-Native children. After Alaska returned to the use of PedvaxHIB®, the incidence of invasive Hib disease in Alaska Native children again decreased to low levels. This led to ACIP giving a preferential recommendation for PedvaxHIB® in AI/AN children in 1999.

a. **PRP-OMP Hib Vaccine Preferential Recommendation:** Due to high risk of invasive Hib disease in AI/AN infant populations 6 months old or less, the Indian Health Service and the American Academy of Pediatrics (AAP) recommend polyribosylribitol phosphate-meningococcal outer membrane protein (PRP-OMP) based Hib vaccine. Compared to other Hib vaccines, PRP-OMP (PedvaxHib®) provides the highest antibody levels after the initial dose resulting in better protection for the youngest infants.

b. **Recommendations for Use of Vaxelis**: Vaxelis™ may be given to children from 6 weeks through 4 years of age (prior to the 5th birthday); however, for Hib protection in AI/AN children, ACIP has given a preferential recommendation for use of PedvaxHib® (PRP-OMP) but not for Vaxelis™.

c. **Risks for AI/AN infants**: The amount of Hib component in Vaxelis™ is less than half the dose in PedvaxHIB®. PedvaxHIB® contains 7.5mcg of Hib (PRP-OMP) per dose compared to Vaxelis™, which contains 3mcg of Hib (PRP-OMP) per dose. AI/AN children are currently recommended to receive PedvaxHIB® because it achieves higher antibody titers post-dose 1, at an age when these children have historically been at particularly high risk for invasive Hib disease. When other Hib conjugate vaccines were used, breakthrough cases occurred in Alaska Native children. Clinical trials of Vaxelis™ evaluated 3mcg and 6mcg doses of the Hib PRP-OMP component, but antibody titers post-dose 1 were not assessed. Given the lack of data on the immune response post-dose 1, the ACIP declined to give Vaxelis™ a preferential recommendation for use in AI/AN children. Potentially, considerable risk for AI/AN infants exists when deviations from the preferential recommendations are used. Long-term advantages and protection conferred by Vaxelis™ are not yet clear.

d. **Benefits:** Vaxelis™ is an appealing option because of its simplicity as a combination vaccine. The 2-, 4-, and 6-month doses of PEDIARIX™ (DTap, Hep B, IPV) could be replaced by Vaxelis™. The 2-and 4-month doses of PedvaxHIB® in the AI/AN routine childhood immunization schedule would be obsolete. The use of Vaxelis™ would save patients, nursing, pharmacy, and physicians from administering two separate injections (PEDIARIX ™and PedvaxHIB®) at the scheduled 2- and 4-month timepoints. In addition, this combination vaccine is available in a pre-filled syringe that has several benefits, such as reduced nursing time spent for dose preparation and use of one product for infants under 12 months of age. Changes to combination vaccines and schedules would require education to ensure nursing, pharmacists and providers are aware of this change. The 12–15-month booster of PedvaxHIB® would still be recommended for AI/AN children.

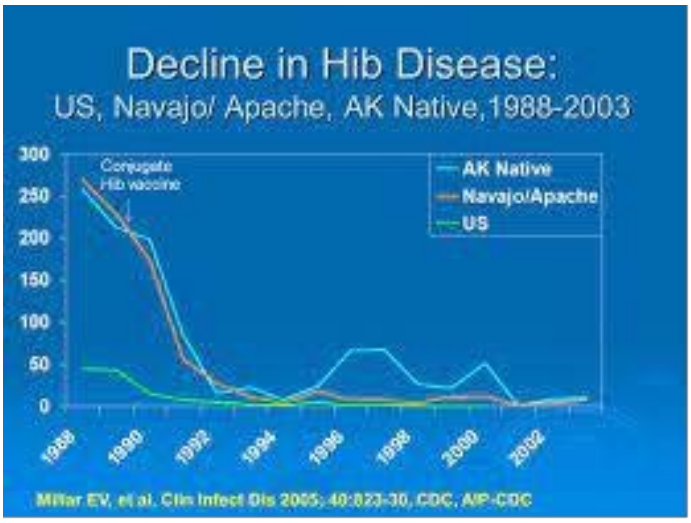

Figure 1. Decline of Hib Disease in the United States compared to Alaska Native and Navajo/Apache infants, 1988-2003.

References:

- Bulkow, L. R., Wainwright, R. B., Letson, G. W., Chang, S. J., & Ward, J. I. (1993). Comparative immunogenicity of four Haemophilus influenzae type b conjugate vaccines in Alaska Native infants. The Pediatric infectious disease journal, 12(6), 484-492.
- Santosham, M., Wolff, M., Reid, R., Hohenboken, M., Bateman, M., Goepp, J., ... & Ahonkhai, V. (1991). The efficacy in Navajo infants of a conjugate vaccine consisting of Haemophilus influenzae type b polysaccharide and Neisseria meningitidis outer-membrane protein complex. New England Journal of Medicine, 324(25), 1767-1772.
- *Morbidity and Mortality Weekly Report* (MMWR), RR-1, May 12, 2014, page 8.
- VFC Resolution for Hib Vaccines. Updated June 26, 2019.
- Package insert for PedvaxHIB®. Revised 2/2020.
- Package insert for Vaxelis™. Revised 9/2020.
- ACIP recommendations for use of Vaxelis™. MMWR, February 7, 2020.
- ACIP 2019 presentation *Haemophilus influenzae* type b in Native American children (cdc.gov)