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To: Health Care Providers
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From: Jeffrey P. Davis, M.D.
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Subject: *Haemophilus influenzae* type B (Hib) Disease Alert and call to increase Hib vaccine coverage in infants and young children

The recent occurrence of five cases of *Haemophilus influenzae* type b (Hib) invasive disease in 2008 among Minnesota children aged <5 years, combined with a shortage of Hib-containing vaccines manufactured by Merck, highlights the need for assuring timely vaccination of Wisconsin infants with Hib containing vaccines and completing the primary series. Thus, we provide the following information to bring you up to date on this important issue.

Introduction: Hib infection can cause bacterial meningitis, bacteremia, pneumonia, and epiglottitis, especially in children under 5 years of age. Before development of Hib conjugate vaccines, Hib was the most common cause of bacterial meningitis in children aged <5 years. Prior to the development of effective Hib vaccines, approximately 20,000 children in the United States annually acquired severe Hib infections, and approximately 4% of all cases were fatal.[1] Since implementation of the Hib conjugate vaccine immunization program in the United States in the early 1990s, the incidence of Hib disease declined from a peak of 41 cases per 100,000 children aged <5 years in 1987 to approximately 0.11 cases per 100,000 in 2007. As with other bacterial diseases in which acquisition of carriage is necessary for development of invasive disease, reductions in asymptomatic carriage and transmission are substantial contributors to the reduction in Hib disease achieved through vaccination programs. This herd immunity provided by high vaccination coverage provides additional protection both for fully vaccinated and undervaccinated persons [CDC MMWR http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e0123a1.htm].

Hib vaccine supply and interim Hib vaccine recommendations: In December 2007, interim guidelines were issued by the Centers for Disease Control and Prevention (CDC) for the use of Hib vaccines following a voluntary recall of certain lots of two conjugate Hib vaccines manufactured by Merck, PedvaxHIB (Hib only) and Comvax (combination Hib/Hepatitis B).[2] The Advisory Committee on Immunization Practices (ACIP) recommended that the vaccine booster dose routinely administered at 12-15 months of age be deferred, except to children in specific high risk groups, as described below; these interim recommendations remain in place.

Providers should track children for whom the booster dose is deferred to facilitate recalling them for vaccination once the supply improves.

Primary series

The primary series consists of 2 doses of the Merck products, PedvaxHIB or Comvax, or 3 doses of ActHIB (Hib only) or Pentacel (combination DTaP/IPV/Hib) vaccines, manufactured by sanofi pasteur. All conjugate Hib vaccines are interchangeable for the primary series (except TriHIBit, which is manufactured by sanofi pasteur, but is licensed only for the booster dose). If it is necessary to change vaccine type, 3 doses of any combination constitute the primary series. **Currently the only Hib vaccines available for healthy children under the interim recommendations are ActHIB and Pentacel, which should be administered at 2, 4 and 6 months of age.**

Unvaccinated children 7 months of age or older may not require a full 3 dose primary series, as the number of doses needed depends upon the child's current age. Please see the Wisconsin Immunization Program webpage at: http://dhs.wisconsin.gov/immunization/inter_hib.htm for further guidance about children who are late in starting the series.

High risk individuals

Children at high risk for invasive Hib disease include those with asplenia, sickle cell disease, human immunodeficiency virus infection and certain other immunodeficiency syndromes and malignant neoplasms. Despite the current non-availability of Merck Hib-containing vaccines, these children should continue to be vaccinated according to the routinely recommended schedule, including the booster dose at 12-15 months of age.[2] Hib conjugate vaccines, including PedvaxHIB, ActHIB (if available), and TriHIBit (if available) may be used for the booster doses for these children during the shortage.

American Indian/Alaska Native children are also at increased risk for Hib disease, particularly in the first 6 months of life. Therefore, CDC recommends that providers continue to vaccinate these children according to the routinely recommended schedule, including the 12-15 month booster dose. CDC recommends that PRP-OMP vaccines (PedvaxHIB and Comvax) are used for these children, as these vaccine formulations offer a more rapid seroconversion to protective antibodies.[2]

Hib invasive disease in Minnesota, 2008: In 2008, the Minnesota Department of Health (MDH) confirmed five cases of *Haemophilus influenzae*, type b invasive disease in children aged 3 years and younger.[3,4] The cases occurred throughout the south central region of the state. Three of the five case individuals were unimmunized, including one infant who died. Minnesota immunization registry data show that coverage for the third dose of Hib vaccines lags significantly behind coverage for the third doses of DTaP and PCV7 vaccines. The five cases of invasive disease occurring in 2008 was the greatest number of cases in children aged <5 years reported in Minnesota since 1992, which suggests a resurgence of invasive Hib disease and the need for increasing vaccinations rates statewide. To date, no other state has reported such a dramatic recent increase in invasive Hib disease. The increase in reported pediatric Hib disease likely is related to an increase in Hib carriage, MDH staff are initiating a Hib carriage study

enrolling approximately 2000 children to examine the extent of Hib carriage and the implications to non-vaccinated and partially vaccinated children in Minnesota.

Hib invasive disease in Wisconsin: During 2006-2008, the Wisconsin Division of Public Health (DPH) received reports of five cases of Hib invasive disease in children aged <5 years (3 cases in 2006, no cases in 2007 and 2 cases in 2008). Four of these cases occurred in unvaccinated children, two cases were fatal. There is no geographic relationship to the cases that were reported in Minnesota during 2008.

For comparison, in Wisconsin among children <5 years old, during 2000-2002, six cases of Hib invasive were reported and at least 3 of those children were unvaccinated. During 2003-2005, 2 cases of Hib invasive disease were reported and both occurred in 2004, one child was not vaccinated.

Hib vaccine-related immunization rates in Wisconsin: The estimated series-complete Hib vaccination coverage among children 19-35 months of age in Wisconsin (2007 National Immunization Survey) is 89.6%. It is essential that children continue to be vaccinated on time and according to the current recommendations to prevent the occurrence of Hib-related disease. Therefore, Wisconsin Immunization Program staff have analyzed statewide Hib vaccination trends in the Wisconsin Immunization Registry (WIR). WIR data indicate that during the calendar year 2008, only 66% of children received their second dose of Hib-containing vaccine by age 5 months in accordance with the recommendations of the ACIP. Thus, many infants and children are unprotected or insufficiently protected against Hib invasive disease.

Vaccine supply: Although the recall and cessation of production of the Merck Hib-containing vaccines (PedvaxHIB and Comvax) in December 2007 has resulted in a nationwide Hib vaccine shortage, supply of the remaining 2 products (ActHIB and Pentacel) manufactured by sanofi pasteur is adequate for **all** infants to complete the 3-dose primary vaccination series. With the introduction of Pentacel in mid-2008, the number of available doses of ActHIB was significantly reduced, including allotments for theVaccines for Children (VFC) programs nationwide, but were replaced with doses of the combination vaccine Pentacel. Therefore, since the majority of Hib doses will be available as Pentacel, providers are strongly encouraged to incorporate this vaccine into their routine schedule to ensure children are protected against Hib infection. Guidance regarding incorporation of Pentacel in the schedule is available from the CDC at http://www.cdc.gov/vaccines/pubs/downloads/pentacel-guidance.pdf. According to recent information, the shortage is anticipated to continue through mid-2009. [5]

The CDC has a limited quantity of PedvaxHIB not affected by the recall in its vaccine stockpile and has made it available to Native American communities for routine immunization including the 12-15 months booster doses. Tribal health clinics can order PedvaxHIB from the Wisconsin Immunization Program by faxing an order on letterhead to the Wisconsin Immunization Program fax number (608) 267-9493. Please note that PedvaxHIB and Comvax vaccines were removed from the vaccine order page on the Wisconsin Immunization Registry.

Summary and reminders: To ensure that children in Wisconsin continue to be adequately protected, the DPH is providing the following reminders to health care providers, local health departments and parent and guardians:

- **Vaccinate infants on time**. It is very important to protect infants from Hib-related disease by timely vaccination with the 3-dose primary series routinely administered at 2, 4 and 6 months of age. Although the ACIP and CDC changed the recommendation for Hib vaccination to defer the booster (4^{th}) dose given at 12-15 months because of a decrease in vaccine supply, providers should continue regular vaccination on schedule for infants under 12 months (all 3 primary series doses received on time). If a child received the first 2 doses of Hib-containing vaccine before age 7 months and presents for dose 3 of the primary series after age 12 months, provide the dose to that child.

Table: Interim recommendations for use of *Haemophilus influenzae* type B vaccine

Vaccine	Age at 1^{st} Dose (Months)	Primary Series[1]
ActHIB[2] HibTITER[3] Pentacel[4]	2-6	3 doses, 8 weeks apart
	7-11	2 doses, 8 weeks apart
	12-59	1 dose
PedvaxHIB[5]	2-6	2 doses, 8 weeks apart
	7-11	2 doses, 8 weeks apart
	12-59	1 dose

1. No booster dose at 12-15 months of age is recommended at this time.
2. ActHIB (PRP-TT) manufactured by sanofi pasteur
3. HibTITER (HbOC) manufactured by Wyeth (Production discontinued as of April 13, 2007).
4. Pentacel (DTaP/IPV/HIB combination) manufactured by sanofi pasteur
5. PedvaxHIB (PRP-OMP) manufactured by Merck

- **Hib vaccine supplies in Wisconsin are adequate**. With the introduction of the Pentacel combination vaccine, Wisconsin's allotment of single antigen ActHIB from CDC was significantly reduced. However, supplies of Pentacel are sufficient to meet the needs of VFC providers. Guidance on scheduling using Pentacel was sent to users of state supplied vaccine in November 2008 and is available from the CDC at: http://www.cdc.gov/vaccines/pubs/downloads/pentacel-guidance.pdf.

- **Continue to use best practices**. Best practices, such as use of reminder/recall systems, have shown to be effective to increase immunization rates. Further information from the CDC on such practices can be found at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00020935.htm

- **Be an advocate for immunization.** There is anecdotal evidence that more parents are questioning the safety of vaccines based on misinformation on websites, in news accounts and from peers. Balanced and accurate sources of information are vital, and reassurances from clinicians, including discussion of what vaccines have accomplished and why they are considered safe and effective, have been shown to be very effective in reducing parents' concerns. [6] Providers and LHDs are encouraged to stress the importance of timely Hib-related vaccination in preventing potentially devastating Hib invasive disease. There are many resources available to provide accurate information to parents, including the following:

Resources:

- CDC: Information on immunization, vaccines and the diseases they prevent. www.cdc.gov/vaccines
- Children's Hospital- Vaccine Education Center: The Center seeks to dispel some of the common misconceptions and misinformation surrounding childhood vaccines. www.chop.edu
- Immunization Action Coalition: Provides childhood, adolescent and adult immunization information and education materials. www.immunize.org
- Immunization Gateway: Links to many expert immunization resources available on the internet. www.immunofacts.com/
- Institute for Vaccine Safety: Information on vaccines currently in the media. www.vaccinesafety.edu;
- National Network for Immunization Information: Information about immunization including a guide to evaluate vaccination on the web. www.immunizationinfo.org/

Resources for providers who provide advice to parents who question vaccines and their use are also available: http://www.cdc.gov/vaccines/pubs/providers-guide-parents-questioning-vacc.htm
For those parents who have previously refused immunizations for their children, it is recommended to periodically assess the parents' willingness to vaccinate their children, including at every well child visit, and to document any refusal to vaccinate.

References:

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4. Centers for Disease Control and Prevention. Invasive *Haemophilus influenzae* Type B Disease in Five Young Children – Minnesota, 2008. MMWR Morb Mortal Wkly Rept 2009;58:1-3. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e0123a1.htm
5. Centers for Disease Control and Prevention. Continued Shortage of *Haemophilus influenzae* Type b (Hib) Conjugate Vaccines and Potential Implications for Hib Surveillance – United States, 2008. MMWR Morb Mortal Wkly Rept 2008;57:1252-1255. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5746a2.htm
6. Kuehn BM. Groups work to boost support for vaccines. JAMA. 2008;300(19):2233-2235