

Interim Guidance for the Use of a Serogroup B Meningococcal Vaccine Under a CDC-Sponsored Expanded Access IND

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Background

- ❑ There is no vaccine for serogroup B meningococcal disease (MenB) licensed in the United States
- ❑ Outbreaks on college campuses highlight the challenge of controlling serogroup B meningococcal disease
- ❑ Vaccination campaigns were conducted at two universities experiencing serogroup B outbreaks in 2013 using a MenB vaccine that is not licensed in the United States under an expanded access IND sponsored by CDC

Expanded Access Investigational New Drug (IND)

- ❑ The U.S. Food and Drug Administration's (FDA) current regulations allow the use of a drug or vaccine that is not approved in the United States to treat serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options

Meningococcal Outbreak Ad Hoc Work Group

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Work Group Terms of Reference

- ❑ Review available data on the recent epidemiology of meningococcal disease and outbreaks
- ❑ Develop guidance for use of MenB vaccines under a CDC-sponsored IND in an outbreak setting
- ❑ Update the current meningococcal disease outbreak guidelines once MenB vaccines are licensed in the United States

Key Issues

- ❑ Delays in getting a vaccination campaign in place under an IND, therefore need to consider options early
- ❑ Reducing confusion about how to define populations in organizations
- ❑ Recognition that waiting for additional cases to occur before acting is difficult for organizations, so need to have clear steps for each case identified
- ❑ Limited evidence MenB vaccines eliminate carriage, providing primary protection to vaccinees is the goal

Current Outbreak Guidelines

- ❑ Included in Appendix B* of 2013 “Prevention and Control of Meningococcal Disease”
- ❑ Outbreak definition: 2-3 cases of the same serogroup in <3 months; attack rate of 10/100,000
 - Based on data from outbreaks of serogroup C prior to routine adolescent meningococcal vaccination
- ❑ Population at risk
 - Organization-based: common affiliations but no close contact (e.g., schools, universities, prisons)
 - Community-based: same area but not close contact or affiliations (e.g. towns, cities, counties)

*Centers for Disease Control and Prevention. Prevention and Control of Meningococcal Disease; Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013;62(No. RR-#2): 1-28.

Purpose of Interim Guidance

- ❑ To identify outbreaks early so that there is time to vaccinate in response to the outbreak
- ❑ To provide guidance for use of MenB vaccine under an expanded access IND sponsored by CDC, not definitive guidelines or recommendations
 - Applies to outbreaks in organizational settings and does not apply to community outbreaks or outbreaks caused by other serogroups

Key Differences Between Interim Guidance and Meningococcal Outbreak Guidelines

- ❑ Divided organizations into two groups based on size instead of requiring calculation of an attack rate
- ❑ Increased the timeframe during which cases may occur from 3 months to 6 months
- ❑ Language around mass chemoprophylaxis revised to allow for some instances where it may be used in conjunction with a vaccination campaign for outbreak response

SUMMARY OF INTERIM GUIDANCE

Objectives

- ❑ To assist decision-makers with determining the need for vaccination with MenB vaccines
- ❑ To clarify the process for obtaining the vaccine
- ❑ To improve timeliness of implementation of a vaccination campaigns

Definitions

- ❑ **Clear definitions are provided in the guidance document for:**
 - Cases that should be included in outbreak case counts (i.e., primary cases vs. secondary and co-primary cases)
 - Organization based outbreaks
 - Population size
 - Vaccination group

Laboratory Testing

- ❑ Serogrouping of clinical specimens should be initiated within 24 hours of identification of *Neisseria meningitidis* from a normally sterile body site whenever possible
 - Laboratories that cannot initiate serogrouping within 72 hours should transfer the isolate or specimen to a laboratory that can perform this testing or to CDC within 24 hours
- ❑ Genotyping data may provide supportive evidence for an outbreak among meningococcal cases
 - Data should be interpreted in the context of the epidemiology

Decision to Vaccinate

- ❑ Decisions to vaccinate should be evaluated on a situational basis in consultation with the local and state health department, and CDC taking into account all circumstances specific to the organization and epidemiology of the outbreak
- ❑ Factors to be taken into consideration:
 - Number of cases
 - Population size of organization
 - Time interval between cases
 - If strains causing cases are identical
 - Feasibility and cost of mass vaccination campaign
 - Vaccine availability
 - If outbreak strain is likely to be covered by a MenB vaccine
 - Public concern (i.e., case-fatality ratio, etc.)

Organizations With Population Size <5,000

❑ 1 case:

- Routine public health practice (serogroup, case investigation, chemoprophylaxis of close contacts)
- Monitor situation closely and save isolate for future molecular genotyping

❑ 2 or more cases in 6 months:

- Same response as after 1 case with the following additions:
 - Send isolates to CDC for molecular genotyping and additional testing
 - If all isolates are identified as serogroup B and likely covered by a MenB vaccine, consult CDC regarding the use of MenB vaccine using a CDC-sponsored expanded access IND

Organizations With Population Size $\geq 5,000$

❑ 1 case:

- Routine public health practice; monitor situation closely and save isolate for future molecular genotyping

❑ 2 cases in 6 months:

- Same response as after 1 case with the following additions:
 - If both isolates are identified as serogroup B, contact CDC to discuss the cases and monitor situation closely; save isolate for future molecular genotyping

❑ 3 or more cases in 6 months:

- ❑ Same response as after 1 case with the following additions:
 - State health department should contact CDC
 - Send isolates to CDC for molecular genotyping and additional testing
 - If all isolates are identified as serogroup B and likely covered by a MenB vaccine, consult CDC regarding the use of MenB vaccine using a CDC-sponsored expanded access IND

Procedures for Obtaining MenB Vaccine

- ❑ CDC will work with state and local health departments and organizations to determine the need for MenB vaccine on a situational basis
- ❑ Organizations that provide MenB vaccine via the FDA's expanded access IND sponsored by CDC are required to identify a local co-investigator on the IND and are required to participate in safety follow-up activities required under the IND

Vaccine Cost and Administration

- ❑ To date, universities implementing a MenB vaccination campaigns have been responsible for funding the cost of the vaccine and its administration
- ❑ Vaccination under CDC's IND has been limited to persons affiliated with the two universities where outbreaks have occurred

Data Reviewed: Mass Chemoprophylaxis for Meningococcal Outbreak Control

❑ Literature review: 1971-present

- Cases where mass chemoprophylaxis was used as outbreak response
- 18 instances included
 - Some with additional control measures

❑ Working Group conclusions:

- Limited data available on use of ciprofloxacin during outbreaks
- Decreases in carriage seen soon after chemoprophylaxis administered, but returned over time and not eliminated
- Unclear impact on preventing additional cases

Antibiotic Chemoprophylaxis

- ❑ Purpose of chemoprophylaxis is to eradicate nasopharyngeal carriage of *N.meningitidis* and thus prevent disease in close contacts of a patient with invasive meningococcal disease
 - Antimicrobial chemoprophylaxis of close contacts is important to prevent secondary cases
- ❑ Mass chemoprophylaxis is not recommended as a stand alone measure to control outbreaks of meningococcal disease
 - May be considered as an interim measure to reduce carriage and transmission in the period before potential protection from vaccination can be achieved

Situations Where Mass Chemoprophylaxis May Be Successful

- ❑ Small or closed populations
- ❑ High antibiotic coverage can be rapidly achieved
- ❑ Limited mixing with outside populations (e.g., jails, residential facilities)

Challenges of Mass Chemoprophylaxis

- ❑ Identifying a smaller logical “at risk” population
- ❑ Ensuring all persons in the target group receive treatment within a short time frame
- ❑ Potential for multiple sources of transmission within a population
- ❑ Prolonged risk for exposure in outbreak setting
- ❑ Cost of drug and administration
- ❑ Drug side effects and idiosyncratic reactions
- ❑ Interactions with frequently used medications such as anti-depressants
- ❑ Emergence of drug-resistant organisms

Implementation of Mass Chemoprophylaxis

- ❑ If mass chemoprophylaxis is undertaken, it should be administered to all targeted persons at the same time (ideally <24 hours)
- ❑ In many outbreak settings, particularly when a small, closed at-risk population cannot be defined, the disadvantages outweigh the possible benefits of mass chemoprophylaxis to prevent further disease
- ❑ If the decision to offer mass chemoprophylaxis prior to implementation of a vaccination campaign is made, communicating the need for vaccination for potential protection for the duration of the outbreak is critical
- ❑ Use of mass chemoprophylaxis should not delay implementation of a vaccination campaign

Other Control Measures

- ❑ Restricting travel to an area with an outbreak, closing schools or universities, or canceling sporting or social events or meetings are generally not recommended as part of outbreak control
 - Interventions are unlikely to alter the course of the outbreak
- ❑ Educating communities, physicians, and other health-care personnel about meningococcal disease to promote early case recognition and early care-seeking behaviors is an important part of managing suspected meningococcal disease outbreaks
 - Education efforts should be initiated as soon as an outbreak is suspected

Next Steps

- ❑ Online publication of interim guidance for the use of a serogroup B meningococcal vaccine under a CDC-sponsored expanded access IND
- ❑ Updates to CDC's comprehensive meningococcal disease outbreak guidelines will be developed once serogroup B meningococcal vaccines are licensed in the United States
- ❑ Identify opportunities to evaluate the impact of using MenB vaccines in outbreak response

Summary

- ❑ **Meningococcal disease is a rare but serious infection**
- ❑ **Outbreaks are rare, but do occur**
 - Timing of additional cases in an outbreak is not easy to predict
 - Will continue to see serogroup B cases, especially in the adolescent age group
 - May be difficult to differentiate between sporadic cases vs. catching an outbreak early
- ❑ **Vaccination is now possible to control serogroup B outbreaks**
 - Implementing vaccination campaign under IND is complex process
- ❑ **Licensure of serogroup B vaccines in the US will be an important step to protect individuals in an outbreak**

Thank you
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