

# Interim Guidance for Control of Serogroup B Meningococcal Disease Outbreaks in Organizational Settings

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## Background

Meningococcal disease is an uncommon but serious infection. Although meningococcal outbreaks comprise only 2% of the 600-1200 annual meningococcal cases in the United States, the onset of an outbreak is unpredictable and the outcomes can be emotionally devastating to affected communities or organizations. A timely public health investigation and outbreak response could prevent additional cases and promptly address public concerns.

Serogroups B, C, and Y are the major causes of meningococcal disease in the United States. Vaccination with the quadrivalent MenACWY conjugate vaccine has been effective in the prevention and control of serogroup C and Y outbreaks. The current meningococcal outbreak guidelines (<http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf>) are based on data from outbreaks of serogroup C disease prior to routine adolescent meningococcal vaccination and the threshold for intervention is based on calculation of an attack rate for cases of the same serogroup over a 3 month period. With high rates of vaccination coverage with the MenACWY vaccine in adolescents and college-age persons, outbreaks of serogroup C and Y disease continue to be rare in these age groups.

Several recent outbreaks of serogroup B meningococcal (MenB) disease on college campuses highlight the challenge of controlling serogroup B disease. From 2008-2010, a prolonged outbreak of serogroup B on a university campus in Ohio led to 13 cases and one death. In 2013, two universities in New Jersey and California experienced serogroup B outbreaks with a combined 13 cases and one death reported. At present, a MenB vaccine has not been licensed by the U.S. Food and Drug Administration (FDA) for use in the United States. However, FDA's 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. The mechanism allowing such use is known as an expanded access Investigational New Drug Application (IND). Vaccination campaigns were conducted at both universities experiencing serogroup B outbreaks in 2013 using a MenB vaccine under the FDA's expanded access program for investigational products with CDC as the sponsor of this IND.

## Rationale

Vaccination with a MenB vaccine not licensed in the United States under the FDA's expanded access program for investigational products with CDC as the sponsor of this IND may have a role in potentially preventing additional cases during a serogroup B outbreak until a licensed MenB vaccine is available. In the interim, the guidance described below for the evaluation and response to serogroup B outbreaks are in part to assist decision-makers to determine the need for vaccination, clarify the process for implementing use of a MenB vaccine under an expanded access IND, and improve timeliness of implementation of a vaccination campaign.

## Objective

The objective of this interim guidance is to provide information for decision-makers about options in an organization-based meningococcal serogroup B outbreak. This guidance is not applicable to community outbreaks or outbreaks caused by other serogroups (e.g., C or Y). Once a MenB vaccine is licensed and available in the United States, the guidelines for control of meningococcal outbreaks caused by all serogroups will be updated.

## Definitions

### Meningococcal cases

For the purposes of this guidance, only primary cases of the same serogroup are to be included in the case count for vaccination decisions. A primary case is defined as one that occurs in the absence of known contact with another case. Secondary cases (cases that occur among close contacts of a primary patient >24 hours after onset of illness of the primary patient) and coprimary cases (two or more cases that occur among a group of close contacts with onset of illness separated by  $\leq 24$  hours) should not be included in case counts for vaccination decisions.

Although secondary and coprimary cases may be included in the overall case count of the outbreak, they should not be included in the case count for vaccination decisions as they likely represent a single transmission event and do not provide evidence of ongoing transmission in the larger population.

### Organization-based outbreaks

In organization-based outbreaks, cases are linked by a common affiliation other than a shared, geographically delineated community. Examples of organizational outbreaks are those that occur in universities, schools, daycare centers, occupational training centers, or correctional facilities. In community-based outbreaks, patients have no common affiliations other than a shared, geographically defined community, such as a neighborhood or town. This guidance will only focus on control of meningococcal disease in organization-based outbreaks.

### Population size

The population size will be defined by the highest level within the organization at which cases occur. For instance, in an outbreak involving elementary school students, the population size is the population of the entire elementary school student body, not just the population of the affected classrooms, and does not include teachers and other staff (unless cases were observed in this group). Likewise, in an outbreak involving inmates at a correctional facility, the population size is the entire population of inmates, not only those in a particular ward of the facility, and not including staff (unless cases were observed in this group). For the purposes of this guidance, the population size for a university outbreak includes only the undergraduate student body, unless cases were observed in graduate or other students, faculty or staff.

### Vaccination group

The vaccination group is those persons determined to be at risk and designated to receive the vaccine during a vaccination campaign. The population determined to be at risk can include either the whole or a subset of the population of an organization, persons within the organization but outside the population determined to be at risk (e.g., those that have underlying medical conditions that place them

at increased risk for meningococcal disease, etc.); therefore the vaccination group may be distinct from the population size.

## Serogroup testing

Serogrouping of clinical specimens or isolates (by slide agglutination and/or real-time PCR) should ideally be initiated within 24 hours of identification of *Neisseria meningitidis*. Laboratories that cannot initiate serogrouping within 72 hours should transfer the specimen or isolate to a laboratory that can perform this testing or to CDC within 24 hours.

## Molecular typing

Isolates from all cases should undergo molecular typing when a suspected outbreak occurs. Molecular typing of *N. meningitidis* isolates by such methods as pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), or whole genome sequencing might provide supportive evidence for an outbreak among meningococcal cases. Molecular typing data should be interpreted in the context of the epidemiology of the cases but not alter the decision to implement a vaccination campaign if it is otherwise indicated; lack of available isolates or lack of identical strains among available isolates should not preclude implementation of a vaccination campaign. Identical molecular typing data on cases with no organizational or geographic affiliation and in whom an outbreak would otherwise not be suspected should not prompt consideration for a vaccination campaign.

## Decision to vaccinate

Many factors should be taken into consideration when determining the need for vaccination. While the number of cases is important, other factors to consider include the population size of the organization, the time interval between cases, whether the strains causing cases are identical, the feasibility and cost of vaccination, vaccine availability, and if the outbreak strain is likely to be covered by the MenB vaccine (if such information is available). The guidance below suggests thresholds for considering vaccination, but decisions to vaccinate should be evaluated on a situational basis in consultation with the local/state health department and CDC taking into account all circumstances specific to the organization and epidemiology of the outbreak.

**Table 1. Organizations with population size <5,000 persons**

<b>1 case</b>	<ul style="list-style-type: none"> <li>• Serogrouping of isolate or clinical specimen performed</li> <li>• If case has serogroup B disease, the state health department should contact CDC (Meningitis and Vaccine Preventable Diseases Branch at 404.639.3158)</li> <li>• Isolate typed or stored for future molecular typing, or sent to CDC, but not discarded</li> <li>• Case investigation</li> <li>• Chemoprophylaxis of close contacts</li> </ul>
<b>2 or more cases in 6 months</b>	<p>Same response as after 1 case with the following additions:</p> <ul style="list-style-type: none"> <li>• If all cases have serogroup B disease, the state health department should contact CDC (Meningitis and Vaccine Preventable Diseases Branch at 404.639.3158)</li> <li>• Send isolates to CDC for molecular typing and testing to predict strain coverage of vaccine</li> <li>• If all cases have serogroup B disease and available information supports use of MenB vaccine, consult CDC regarding the use of MenB vaccine using a CDC-sponsored expanded access IND</li> </ul>

**Table 2. Organizations with population size ≥5,000 persons**

<b>1 case</b>	<ul style="list-style-type: none"> <li>• Serogrouping of isolate or clinical specimen performed</li> <li>• Isolate typed or stored for future molecular typing, or sent to CDC, but not discarded</li> <li>• Case investigation</li> <li>• Chemoprophylaxis of close contacts</li> </ul>
<b>2 cases in 6 months</b>	<p>Same response as after 1 case with the following additions:</p> <ul style="list-style-type: none"> <li>• If both cases have serogroup B disease, the state health department should contact CDC (Meningitis and Vaccine Preventable Diseases Branch at 404.639.3158)</li> <li>• Send isolates to CDC for molecular typing for both cases</li> </ul>
<b>3 or more cases in 6 months</b>	<p>Same response as after 1 case with the following additions:</p> <ul style="list-style-type: none"> <li>• If all cases have serogroup B disease, the state health department should contact CDC (Meningitis and Vaccine Preventable Diseases Branch at 404.639.3158)</li> <li>• Send isolates from additional cases to CDC for molecular typing and testing to predict strain coverage of vaccine</li> <li>• If all cases have serogroup B disease and available information supports use of MenB vaccine, consult CDC regarding the use of MenB vaccine using a CDC-sponsored expanded access IND</li> </ul>

## Procedures for implementation of MenB vaccination via the FDA's expanded access program for investigational products with CDC as the IND sponsor

CDC will work with state and local health departments and organizations on a situational basis to determine the need for MenB vaccine. Organizations that use a MenB vaccine under the FDA's expanded access program for investigational products with CDC as the sponsor of this IND are required to identify a local co-investigator. Both the local co-investigator and the IND sponsor have designated responsibilities for safety follow-up. To date, universities implementing MenB vaccine campaigns have been responsible for funding the cost of the vaccine and its administration. To date, vaccination under CDC's IND has been limited to persons affiliated with the two universities where outbreaks occurred in 2013. Wider vaccination may be considered if warranted.

### Other control measures

The 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. Close contacts include 1) household members, 2) child-care center or preschool contacts, and 3) anyone with unprotected exposure to the patient's respiratory secretions or aerosols, or other exposures indicating close or intimate contact (e.g., kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management) in the 7 days before symptom onset. Additional information on antimicrobial chemoprophylaxis may be found in Appendix A of the 2013 MMWR (<http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf>).

Expanding persons to whom chemoprophylaxis is targeted beyond close contacts of cases (mass chemoprophylaxis) is not recommended as a standalone measure to control outbreaks of meningococcal disease. However, mass chemoprophylaxis may be considered as an interim measure to temporarily reduce meningococcal carriage and transmission in the population in the period before potential protection from vaccination can be achieved. A literature review of outbreaks where mass chemoprophylaxis was used suggests an impact on reducing nasopharyngeal carriage shortly after chemoprophylaxis is administered. There are limited data regarding the use of currently recommended antimicrobials and whether additional cases are prevented by mass chemoprophylaxis. Specific situations where mass chemoprophylaxis is more likely to reduce carriage in the short-term include small or closed populations where high antibiotic coverage can be rapidly achieved and there is limited mixing with outside populations (e.g., jails, residential facilities, etc.). If mass chemoprophylaxis is undertaken, it should be administered to all targeted persons at the same time (ideally <24 hours). Mass chemoprophylaxis should not delay or be used in place of vaccination to provide potential long term protection to the population at risk.

The decision to implement mass chemoprophylaxis in an organization-based serogroup B outbreak should take into account the challenges that may prevent the intervention from successfully controlling an outbreak: identifying an appropriate target group, ensuring that all persons in the target group receive treatment within a short time frame, the potential for multiple sources of transmission within a population, and prolonged risk for exposure in the outbreak setting. Additional complexities of mass chemoprophylaxis include cost of drug and administration, drug side effects including idiosyncratic reactions, interactions with frequently used medications such as anti-depressants, and the emergence of drug-resistant organisms. In many outbreak settings, particularly when a small, closed at-risk population cannot be defined, these disadvantages may 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 period is critical.

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, as these 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 of meningococcal disease is suspected.

\*This guidance has been developed based on a review of published and unpublished literature and expert opinion. More complete meningococcal outbreak guidelines that address use of licensed quadrivalent meningococcal conjugate vaccines (MenACWY) and investigational serogroup B meningococcal vaccines (MenB) for outbreak control are currently being developed.

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