Centers for Disease Control and Prevention

Guidance for the Evaluation and Public Health Management of Suspected Outbreaks of Meningococcal Disease

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Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
CDC	Centers for Disease Control and Prevention
CSF	Cerebrospinal fluid
CSTE	Council of State and Territorial Epidemiologists
FDA	Food and Drug Administration
HIV	Human immunodeficiency virus
IHC	Immunohistochemistry
MenACWY vaccine	Quadrivalent (serogroups ACWY) meningococcal conjugate vaccine
MenB vaccine	Serogroup B meningococcal vaccine
MSM	Men who have sex with men
MLST	Multilocus sequence typing
NNDSS	National Notifiable Diseases Surveillance System
PCR	Polymerase chain reaction
PFGE	Pulsed field gel electrophoresis
SBA	Serum bactericidal antibody assay
WGS	Whole genome sequencing

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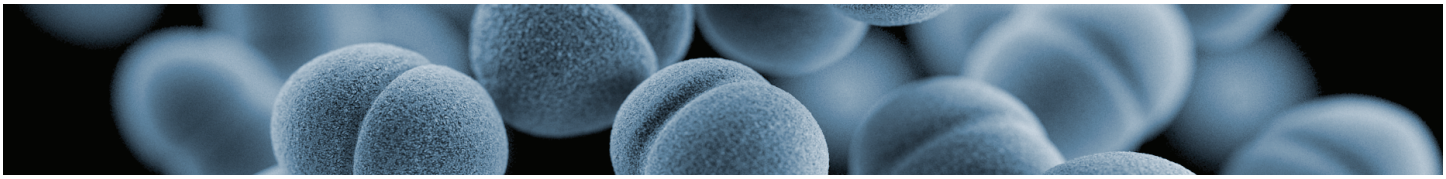

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SUMMARY OF GUIDANCE

Investigation of cases

All cases in a suspected outbreak of meningococcal disease should undergo thorough epidemiologic and laboratory investigation.

- ❒ Neisseria meningitidis is confirmed through culture and/or polymerase chain reaction (PCR) of fluid collected from a normally sterile site. Culture should always be attempted in order to obtain an isolate for molecular typing.
- ❒ Serogrouping should be performed on isolates or specimens from all confirmed cases.
- ❒ Whole genome sequencing (WGS) should be performed on all isolates.

Determination of a meningococcal disease outbreak

- ❒ All cases of meningococcal disease of the same serogroup should be included in the outbreak case count unless molecular typing indicates that the strain from a case is genetically different than the predominant outbreak strain. In outbreaks with well-defined risk groups, probable cases may be included as outbreak-associated even if they are unable to be confirmed or serogrouped.
- ❒ The outbreak threshold for vaccine decision-making should be determined on a case-by-case basis, using the following general guidance:
  - ❍ Organization-based outbreak: 2-3 outbreak-associated cases within an organization during a 3-month period.
  - ❍ Community-based outbreak: Multiple outbreak-associated cases with an incidence of meningococcal disease that is above the expected incidence in a community during a 3-month period.

Vaccination

- ❒ If vaccination is undertaken, vaccine should be selected based on outbreak serogroup:
  - ❍ A, C, W, or Y: quadrivalent meningococcal conjugate (MenACWY) vaccine in persons aged ≥2 months.
  - ❍ B: serogroup B meningococcal (MenB) vaccine in persons aged ≥10 years.
    - MenB-FHbp: 3-dose series (0, 1-2, 6 months)
    - MenB-4C: 2-dose series (0, ≥1 month)
- ❒ For serogroup B outbreaks, the identification of MenB vaccine antigens through WGS of outbreak isolates cannot be used to reliably infer strain coverage at this time; therefore these data should not drive the selection of MenB vaccine product (MenB-FHbp vs. MenB-4C).

Expanded antimicrobial chemoprophylaxis

- ❒ Expanded antimicrobial chemoprophylaxis (administration of antibiotics to a wider circle of individuals than those identified as close contacts of the case-patient) is typically not recommended as a standalone measure, but in some organization-based outbreaks, may be used in conjunction with vaccination or when vaccination is not possible.

Re-evaluation of outbreak status

- ❒ Meningococcal disease risk likely returns to expected levels:
  - ❍ Organization-based outbreak: One year after the last case.
  - ❍ Community-based outbreak: Re-assess one year after the last case to determine whether incidence remains above expected.

1. INTRODUCTION

This report summarizes updated CDC guidance for the evaluation and public health management of suspected outbreaks of meningococcal disease in the United States. Guidance was initially developed in 1997 and subsequently updated following the licensure of the quadrivalent meningococcal conjugate vaccine (MenACWY) and implementation of the routine MenACWY program [1-3]. In 2014, CDC issued interim guidance for the control of serogroup B meningococcal disease outbreaks in organizational settings prior to licensure of serogroup B meningococcal (MenB) vaccines in the United States [4].

This guidance document replaces both the recommendations in Appendix B of the 2013 Advisory Committee on Immunization Practices (ACIP) statement "Prevention and Control of Meningococcal Disease" and the 2014 CDC document "Interim Guidance for Control of Serogroup B Meningococcal Disease Outbreaks in Organizational Settings" [3, 4].

2. BACKGROUND

Since the late 1990s, a sustained decline in the incidence of meningococcal disease has been observed in the United States, decreasing from 1.3 cases per 100,000 population in 1996 to 0.12 cases per 100,000 population in 2015. This decline in incidence began prior to the introduction of MenACWY vaccine in adolescents in 2005 and the licensure of MenB vaccines in 2015. Incidence of serogroups B, C, and Y, the primary disease-causing serogroups in the United States, has declined and incidence of serogroup W has remained stably low.

Information on meningococcal disease cases, including outbreak-associated cases, is collected through the National Notifiable Diseases Surveillance System (NNDSS), though reporting on outbreak-association is likely incomplete. Thus, in 2014, CDC issued requests for this information through the Epidemic Information Exchange (Epi-X), CDC's system for rapid and secure exchange of public health information between CDC and state and local health departments. This call for cases was followed by a standardized questionnaire administered to each state health department, in order to identify and characterize clusters and outbreaks of meningococcal disease from 2009 through 2013. For the purposes of the review, CDC defined a cluster as 2 cases of the same serogroup within 3 months (not including secondary cases) within an organization or an increase in incidence of the same serogroup within a community, with an incidence of at least two times that observed during the same time period in recent years. An outbreak was defined according to the published threshold of ≥ 3 cases of the same serogroup and an attack rate of > 10 cases per 100,000 population during a 3-month period [3]. Of the 3,683 cases reported to NNDSS from 2009 through 2013, 195 (5.3%) primary cases were reported from 41 clusters/outbreaks that met the evaluation criteria.

Among these clusters/outbreaks, 22 were community-based, in which cases had no common affiliation other than a shared geographic space, and 19 were organization-based, in which cases had a common affiliation other than a shared geographic space. Community-based cluster/outbreak-associated cases were predominantly due to serogroup C, whereas organization-based cluster/outbreak-associated cases were predominantly due to serogroup B.

From January 1, 2008, through June 30, 2017, 11 clusters/outbreaks of serogroup B meningococcal disease were reported among university students and close contacts. These clusters/outbreaks ranged in duration from a few days to nearly three years, with a cluster/outbreak size ranging from 2 to 13 cases, and undergraduate population sizes ranging from approximately 4,000 to 35,000 students. MenB vaccines have been used in response to all 8 serogroup B university outbreaks from 2013, when MenB vaccines were first used for outbreak response prior to licensure in the United States, to March 2017.

From January 1, 2010 through June 30, 2017, 5 clusters/outbreaks of serogroup C meningococcal disease were reported among men who have sex with men (MSM) in the United States. These clusters/outbreaks have had duration of up to two and a half years, with 5 to 22 cases reported among MSM. MenACWY vaccination campaigns were implemented in 4 of 5 clusters/outbreaks during this period.

3. OBJECTIVE

The objective of this guidance is to assist state and local health departments in the evaluation and public health management of suspected outbreaks of meningococcal disease in the United States.

4. METHODS

This guidance was developed through a review of published and unpublished data on the epidemiologic and microbiologic features of meningococcal disease outbreaks, immunogenicity and impact of meningococcal vaccines on meningococcal disease and carriage, and use of mass or expanded antimicrobial chemoprophylaxis in outbreak settings, as well as through consultations with subject matter experts.

5. MENINGOCOCCAL DISEASE CASE DEFINITION

According to the 2015 Council of State and Territorial Epidemiologists (CSTE) case definition [5], meningococcal disease cases are classified as suspected, probable, or confirmed (Box 1).

Box 1. 2015 CSTE meningococcal disease case definition.

Case type	Case definition
Suspected	Clinical purpura fulminans in the absence of a positive blood culture; *or* Gram-negative diplococci, not yet identified, isolated from a normally sterile body site (e.g., blood or cerebrospinal fluid (CSF)).
Probable	Detection of *N. meningitidis* antigen in formalin-fixed tissue by immunohistochemistry (IHC) or CSF by latex agglutination.
Confirmed	Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., blood or CSF), using a validated polymerase chain reaction (PCR) assay; *or* Isolation of *N. meningitidis* from a normally sterile body site or purpuric lesions.

6. INVESTIGATION OF SUSPECTED MENINGOCOCCAL DISEASE OUTBREAKS

6.1 Epidemiologic investigation

In addition to soliciting information to identify close contacts of the meningococcal disease patient, health department staff should collect information on each meningococcal disease case to identify epidemiologic linkages with other meningococcal disease patients, organizational affiliations such as university or school attendance, common social networks, or common geographic location. In addition, the sex of sex partners of men aged ≥16 years and behaviors such as illicit drug use, or underlying medical conditions such as human immunodeficiency virus (HIV), should be ascertained from all patients to characterize the population at risk.

6.2 Laboratory investigation

All persons with suspected meningococcal disease should undergo specimen collection from a normally sterile body site as indicated by presenting symptoms (e.g., cerebrospinal fluid [CSF], blood). Gram stain is useful for preliminary identification of likely *N. meningitidis* (Gram negative diplococci). However, it is not a confirmatory test, may be falsely negative or misidentified, and cannot distinguish among meningococcal serogroups. Culture is the preferred confirmatory test given the ability of public health laboratories to subsequently characterize the strain through whole genome sequencing (WGS), and should always be attempted whenever a specimen is obtained. Polymerase chain reaction (PCR) is a sensitive method for identifying *N. meningitidis*, particularly in situations where treatment with antibiotics was initiated prior to specimen collection. PCR should be performed on specimens from any patient with negative culture in whom meningococcal disease is suspected. When culture and PCR are unavailable or are negative despite strong suspicion of meningococcal disease, detection of *N. meningitidis* antigen may also be useful in CSF by latex agglutination or in formalin-fixed tissues by immunohistochemistry (IHC) of fatal cases in whom specimens were not obtained before death.

Once a diagnosis of meningococcal disease is confirmed, identifying the serogroup as quickly as possible is imperative for rapid detection of a suspected outbreak of meningococcal disease and implementation of outbreak response measures with the appropriate meningococcal vaccine. Serogrouping of isolates or clinical specimens (by slide agglutination or real-time PCR) should ideally be initiated within 24 hours of identification of *N. meningitidis*. Laboratories that cannot initiate serogrouping within this time frame should transfer the isolate or specimen to a reference laboratory that can perform this testing, such as

a state public health laboratory or an Association of Public Health Laboratories/CDC Vaccine Preventable Disease Reference Laboratory [6]. State public health laboratories may also send isolates or specimens to CDC's Bacterial Meningitis Laboratory for confirmation and further characterization [7].

Several new commercial multiplex PCR assays capable of simultaneously testing a single specimen for an array of pathogens have become available (e.g., FilmArray® Blood Culture Identification Panel and FilmArray® Meningitis/Encephalitis [ME] Panel from BioFire Diagnostics, Meningitis/Encephalitis Panel by PCR from ARUP Laboratories) [8, 9]. While these assays can rapidly identify *N. meningitidis* species, most do not determine serogroup. Thus, laboratories should continue to perform simultaneous culture and use validated, specific real-time PCR assays capable of detecting and differentiating all six disease-associated serogroups of *N. meningitidis* (A, B, C, W, X, and Y). Otherwise, additional steps need to be taken including performing a reflex culture or at a minimum retaining a clinical specimen for further testing at a public health laboratory [10].

6.2.1 Molecular typing

Molecular typing may provide useful information for determining whether a group of cases represent an outbreak. Isolates from all cases should undergo molecular typing when a suspected outbreak occurs. WGS provides the highest resolution in determining similarity of strains and should be performed on all isolates of confirmed cases. Isolates should be sent to CDC's Bacterial Meningitis Laboratory for WGS in order to facilitate comparison of the isolate against a national/global strain collection and for maintenance of a national strain collection. If WGS is performed elsewhere, sequences and isolates should be shared with CDC. Pulsed-field gel electrophoresis (PFGE), may also be used when WGS is not immediately available, though recent data suggests that it cannot definitively group strains within an outbreak or differentiate strains between outbreaks [11]. Multilocus sequence typing (MLST) may also be useful when only a clinical specimen (e.g., CSF, blood), and not an isolate, is available.

Molecular typing data revealing identical or closely related strains provides supportive evidence to the epidemiologic investigation of a suspected meningococcal disease outbreak. Because not all cases will have an available isolate for WGS, evidence of related strains by WGS is not required to determine that a group of cases represent an outbreak. However, if a case is found to be caused by a strain that is genetically distinct from others occurring as part of an outbreak, this case should not be included in the outbreak case count. Public health action, including vaccination campaigns, should not be delayed while awaiting molecular typing results.

6.3 Enhanced meningococcal disease surveillance during a suspected outbreak

When an outbreak of meningococcal disease is suspected, healthcare providers and laboratories should be alerted and encouraged to remain vigilant for patients with symptoms suggestive of meningococcal disease. In addition, they should be encouraged to ensure that all suspected cases of meningococcal disease have been reported to the local health department and that any subsequent suspected cases are promptly reported. Patients in whom meningococcal disease is suspected but whose laboratory results are negative should still be reported to the local health department to arrange for confirmatory or additional testing at a local or state public health laboratory. Clinical and commercial laboratories should be instructed to send all N. meningitidis isolates recovered from normally sterile body sites, or clinical specimens in the absence of an isolate, to a designated public health laboratory in order to facilitate rapid confirmation, serogrouping, and referral of the isolate or specimen for molecular typing. State health departments are also encouraged to notify CDC once an outbreak of meningococcal disease is suspected, in order to expedite confirmatory testing and/or WGS, as well as to detect and coordinate across outbreaks or outbreak-associated cases occurring in multiple states.

7. ANTIMICROBIAL CHEMOPROPHYLAXIS OF CLOSE CONTACTS

Antimicrobial chemoprophylaxis of close contacts of a patient with meningococcal disease is important to prevent secondary cases, regardless of whether a meningococcal outbreak is suspected. Guidance for antimicrobial chemoprophylaxis of close contacts can be found at bit.ly/meningprophylaxis. In the setting of a suspected meningococcal disease outbreak in which confirmed cases have occurred, it is not necessary to wait for confirmation of N. meningitidis in subsequent cases to initiate chemoprophylaxis of close contacts if meningococcal disease is strongly suspected based on identification of Gram negative diplococci, detection of N. meningitidis antigen from CSF by latex or from formalin-fixed tissue by IHC, or clinical signs such as purpura.

8. DETERMINATION OF A MENINGOCOCCAL DISEASE OUTBREAK

Determining whether a group of cases constitutes an outbreak of meningococcal disease can be challenging, although it is an important measure for public health action.

8.1 Define outbreak-associated cases

All cases of the same serogroup should be included in the outbreak case count unless molecular typing indicates that the strain from a case is genetically different than the predominant outbreak strain (Box 2). In outbreaks with well-defined risk groups, cases classified as probable by the CSTE definition may be included as outbreak-associated even if they are unable to be confirmed or serogrouped.

Box 2. Definition of meningococcal disease outbreak-associated cases

All cases of meningococcal disease of the same serogroup are to be included in the outbreak case count unless molecular typing indicates that the strain from a case is genetically different than the predominant outbreak strain. In outbreaks with well-defined risk groups, probable cases may be included as outbreak-associated even if they are unable to be confirmed or serogrouped.

8.2 Define the population at risk

Outbreaks are defined as either organization- or community-based, depending on the nature of the affiliation among cases (Box 3).

Box 3. Classification of meningococcal disease outbreaks

Outbreak type	Outbreak definition
Organization-based	Cases are linked by a common affiliation other than a shared, geographically defined community. Examples are those that occur in universities, schools, child-care centers, or correctional facilities.
Community-based	Cases have no common affiliations to an organization but are instead linked by a shared, geographically defined community, such as a neighborhood or town. Community outbreaks may include populations with shared characteristics, such as men who have sex with men, as long as no affiliation to a specific organization is identified.

The population at risk is the sub-population within the organization or community that includes most, if not all, of the cases and is the group that would be targeted to receive vaccination if a vaccination campaign were initiated in response to the outbreak. Because meningococcal disease outbreaks can be identified after only 2 to 3 cases have occurred, inferences on the population at risk are often made with incomplete information. Thus, each outbreak should be assessed on a case-by-case basis. The assessment should take into account previous experiences with outbreaks in a particular setting, to best estimate the population at risk, using the epidemiology of the cases and identifying potential common social networks.

8.3 Outbreak thresholds

The purpose of declaring an outbreak is to determine when public health interventions for outbreak response, such as mass vaccination, should be considered. In contrast to previous guidance in which a threshold of 3 cases of the same serogroup with an attack rate of > 10 cases per 100,000 population during a 3-month period was used to define both organization- and community-based outbreaks, the current guidance does not recommend the use of an absolute threshold. However, the following thresholds can be considered as guidance, with considerable flexibility to account for the unique nature of each meningococcal disease outbreak.

For organizations, 2-3 outbreak-associated cases within a 3-month period is considered to be an outbreak (Box 4). In most situations, 2 cases within an organization constitute an outbreak. However, in some situations, such as an outbreak within a large university (e.g., > 20,000 undergraduate students) where no identifiable subgroup at risk within the population can be identified, it may be reasonable to declare an outbreak after 3 cases.

For communities, an outbreak is defined as multiple outbreak-associated cases with an incidence of meningococcal disease that is above the expected incidence in a community during a 3-month period (Box 4). Several strategies may be considered to determine whether incidence is above expected in a community. For instance, incidence during the current 3-month period can be compared with the incidence during a similar time period in previous years, or in the setting of very low or unstable monthly incidence, annual incidence in the 3-5 years prior. If community incidence has historically been very low or zero, comparisons against state or national incidence can be made. Additional supportive evidence of an outbreak should be solicited, such as similarity of the strains by molecular typing and common epidemiologic or social characteristics of cases. Consultation with CDC is encouraged if an outbreak is suspected.

Box 4. Outbreak thresholds

Outbreak type	Outbreak threshold definition
Organization-based	2-3 outbreak-associated cases within an organization during a 3-month period.
Community-based	Multiple outbreak-associated cases with an incidence of meningococcal disease that is above the expected incidence in a community during a 3-month period.

Although an absolute outbreak threshold is no longer used, calculating an outbreak attack rate may still be useful in determining the magnitude of an outbreak and comparing against a historical baseline. An outbreak attack rate per 100,000 population is calculated as follows: [(Number of outbreak-associated meningococcal disease cases during a 3-month period) / (Population at risk)] x 100,000. The epidemiology of the cases should be used to determine the appropriate denominator for attack rate calculations and should include the population of the smallest geographic area that contains the cases and be limited to the sub-populations in which cases were reported (e.g., among certain age-groups or social networks). For some populations, such as MSM, determining the denominator can be very challenging. Results of local or statewide surveys (e.g., proportion of adult male population that is MSM, proportion of population with HIV) along with census data can be helpful in estimating population sizes.

Previous versions of the outbreak guidance do not define the term 'cluster' of meningococcal disease, though this term is used informally by public health officials. In this updated guidance, the term cluster can be used to describe a grouping of cases thought to be epidemiologically related that are still under investigation or that do not meet the definition of an outbreak.

9. VACCINATION

9.1 Decision to vaccinate

Vaccination is the preferred control measure for meningococcal disease outbreaks of all serogroups commonly seen in the United States (B, C, W, and Y). However, 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, ability to define a target group for vaccination, whether ongoing transmission is likely, feasibility of a vaccination campaign, and timing of potential vaccination in relation to cases. In situations where ongoing transmission is unlikely (e.g., cases are limited to household members, roommates, or boyfriend/girlfriend), a vaccination campaign is not necessarily indicated as long as antimicrobial chemoprophylaxis of close contacts is implemented to prevent further transmission.

The guidance above suggests thresholds for considering vaccination, but decisions to vaccinate should be made on a case-by-case basis in consultation with the local/state health department and CDC taking into account all circumstances and epidemiology specific to the outbreak.

9.2 Vaccine choice

Four meningococcal vaccines are licensed and routinely available in the United States (Table 2). Approximately 2 weeks are required following vaccination for the development of protective antibody levels.

Table 2. Meningococcal vaccines licensed and available in the United States, 2017

Formulation	Type	Trade name	Manufacturer	Licensed age group	Serogroups
MenACWY-D	Conjugate	Menactra®	Sanofi Pasteur	9 m–55 y	A, C, W, Y
MenACWY-CRM	Conjugate	Menveo®	GlaxoSmithKline	2 m–55 y	A, C, W, Y
MenB-FHbp	Recombinant	Trumenba®	Pfizer	10–25 y	B
MenB-4C	Recombinant	Bexsero®	GlaxoSmithKline	10–25 y	B

9.2.1 MenACWY vaccination

Outbreaks of meningococcal disease due to serogroups A, C, W, and Y may be controlled using MenACWY in persons aged 2 months and older. ACIP recommends routine MenACWY vaccination for all adolescents aged 11 through 18 years of age and for persons at increased risk for meningococcal disease, including those at risk due to an outbreak of meningococcal disease [3]. Although there are currently no meningococcal vaccines licensed and available in the United States for adults aged ≥ 56 years, ACIP recommends that persons aged ≥ 56 years who are at increased risk for meningococcal disease receive conjugate MenACWY vaccine [12].

ACIP does not state a preference in brand of MenACWY vaccine for outbreak response. Persons who were previously vaccinated with MenACWY may require re-vaccination during a meningococcal disease outbreak depending on the interval since their last dose. For persons who received their last MenACWY dose at age ≥ 7 years, an additional dose should be administered if it has been 5 or more years since their last dose. For persons who received their last MenACWY dose at age < 7 years, an additional dose should be administered if it has been 3 or more years since their last dose [3].

9.2.2 MenB vaccination

ACIP recommends routine use of MenB vaccine for persons aged ≥10 years who are at increased risk for meningococcal disease [13]. In addition, ACIP recommends that adolescents and young adults aged 16 through 23 years may elect to be vaccinated with a MenB vaccine [14].

ACIP recommends MenB vaccines in response to outbreaks of serogroup B meningococcal disease among persons aged ≥ 10 years. Although MenB vaccines are only licensed in the United States for persons aged 10 through 25 years, there are no theoretical differences in safety for persons aged > 25 years; thus, ACIP recommends use of MenB vaccines in persons aged ≥10 years who are at increased risk during meningococcal outbreaks. MenB vaccines are not currently licensed or recommended by ACIP for children aged < 10 years who are at increased risk of meningococcal disease during an outbreak due to serogroup B [13].

MenB-4C is licensed as a 2-dose series, with the doses administered at least one month apart. MenB-FHbp is licensed as either a 2-dose series, with the doses administered 6 months apart, or as a 3-dose series, with doses administered 1-2 and 6 months following the first dose. However, if MenB-FHbp is utilized in response to a serogroup B meningococcal disease outbreak, ACIP recommends the 3-dose series in order to provide earlier protection and maximize the immune response [15]. The same vaccine product should be used for all doses in a series.

Persons who have initiated but not completed a MenB series when they become at increased risk for meningococcal disease during a serogroup B outbreak should complete the series using the same vaccine type at the recommended dosing intervals. For persons who received a single MenB-FHbp dose prior to outbreak exposure, the series should be completed using the recommended schedule for persons at increased risk for meningococcal disease (3-dose series at 0, 1, and 6 months). For persons who received two doses of MenB-FHbp, a third dose should be administered according to the recommended dosing schedule unless the second dose was administered at an interval of ≥6 months after the first dose, in which case no additional doses are needed [16]. For persons who received a single MenB-4C dose prior to outbreak exposure, the series should be completed with a second dose at an interval of ≥1 month since the first dose. If the vaccine type of any previous doses received is not known, the primary series should be restarted using any MenB vaccine.

Persons who previously completed a MenB primary series may require a booster dose during a meningococcal disease outbreak, depending on the interval since their last dose. The same vaccine type administered for the MenB primary series should be used for the booster dose.

In an outbreak setting, persons who previously completed a MenB series should receive a booster dose if it has been at least 1 year since their last dose. However, a booster dose interval of ≥6 months may be considered by public health officials depending on the outbreak circumstances, vaccination strategy, and projected duration of elevated risk. This flexibility may be useful to avoid missed opportunities for vaccination. For example, booster dose coverage may be optimized during a mass vaccination campaign conducted during a limited time period by allowing persons who completed the primary series 6 –11 months before the campaign to be vaccinated. For outbreaks lasting longer than a year, decisions regarding booster vaccination of persons who completed primary vaccination during the outbreak should be made on a case-by-case basis. Of note, whereas an initial booster dose is recommended if it has been at least 1 year since completion of the primary series, seroprotective antibody titers persist for at least 2–3 years following a booster dose. Thus, repeated booster doses are not indicated in most outbreak settings.

The recommendation to use the same vaccine type for the booster dose as was used for the MenB primary series could create additional challenges during outbreak response. Availability of both MenB vaccine types should be ensured for booster dose administration during an outbreak, even if the mass vaccination campaign is conducted using a single MenB vaccine type. If the primary series vaccine type is unknown for a given individual and cannot be quickly determined, an additional MenB vaccine of any type may be administered in order to avoid missed opportunities for booster vaccination during outbreak response-related vaccination campaigns. However, there are no data on efficacy of a single dose of one vaccine type following primary series vaccination with a different vaccine type. Thus, every effort should be made to determine vaccine type of the primary series for each individual. Ensuring the availability of complete immunization records for all individuals in the population at risk is an important part of outbreak preparedness for organization such as universities.

Unlike MenACWY vaccines, which induce an immune response to the meningococcal polysaccharide capsule, MenB vaccines induce an immune response to subcapsular proteins; the presence and expression of these proteins vary by strain. Identification of MenB vaccine antigens (PorA, NadA, NhbA, FHbp) through WGS may be helpful, though the presence of these antigens does not necessarily imply expression or expected coverage by one of the MenB vaccines. Currently, there are limited data to correlate the presence and expression of these subcapsular proteins with a protective immune response as measured by serum bactericidal antibody assay (SBA) [17, 18]. Furthermore, operational challenges can preclude making this available in real-time during an outbreak. Thus, until additional data are available, the identification of vaccine antigens by WGS should not drive the selection of MenB vaccine product (MenB-FHbp or MenB-4C).

10. EXPANDED ANTIMICROBIAL CHEMOPROPHYLAXIS

Expanded antimicrobial chemoprophylaxis involves administering antibiotics to a wider circle of individuals than those identified as close contacts of a case. Because the impact of expanded chemoprophylaxis on the course of an outbreak has not been consistently demonstrated [19], expanded chemoprophylaxis is not usually recommended as a standalone measure to control outbreaks of meningococcal disease. However, it may be considered in some organization-based outbreaks, such as outbreaks involving limited populations or where persons/groups at increased risk can be clearly defined (e.g., jails, child-care centers, residential facilities, smaller primary or secondary schools, or defined social networks within a larger population, such as university fraternity, sorority, or sports team members). Expanded chemoprophylaxis can be used as an interim measure to temporarily reduce meningococcal carriage and transmission before potential protection from vaccination can be achieved, or when a vaccination campaign is indicated but not possible to implement.

If expanded chemoprophylaxis is undertaken, it should be initiated as soon as possible following determination that an outbreak exists. To maximize the potential impact on transmission, chemoprophylaxis should be administered to all targeted persons within the shortest time frame possible (ideally within 24 hours of each other). Expanded chemoprophylaxis should not delay or be used in place of vaccination when vaccination is feasible to provide potential longer term protection to the population at risk.

Antibiotics that are recommended as chemoprophylaxis for N. meningitidis may be considered for expanded chemoprophylaxis (Table 1), though the frequent development of antibiotic resistance following rifampin administration [20] make this antibiotic unsuitable for large-scale use. It may, however, be used in individuals with contraindications to other antibiotic options. Ciprofloxacin, a fluoroquinolone, is the preferred antibiotic for expanded chemoprophylaxis in persons without contraindications due to ease of oral administration as a single dose. Azithromycin is not routinely recommended for chemoprophylaxis due to limited data on effectiveness, but may be considered in the setting of ciprofloxacin resistance. Ceftriaxone, as an intramuscular injection, may not be feasible to rapidly implement on a larger scale, though may be used in pregnant or lactating women or in persons with contraindications to ciprofloxacin.

Potential recipients of ciprofloxacin should be assessed for contraindications or precautions and information should be provided on the potential risks and benefits of this antibiotic [21]. Because of the potential for disabling side effects of the tendons, muscles, joints, nerves, and central nervous system with fluoroquinolone use, the Food and Drug Administration (FDA) conducted a review of the risks and benefits of systemic fluoroquinolones [22]. While this review determined that the risks of fluoroquinolones outweighed the benefits for treatment of three specific conditions (acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, and uncomplicated urinary tract infections), the FDA advised that for some serious bacterial infections, the benefits of fluoroquinolones outweighs the risks, and fluoroquinolones should remain a treatment option in these situations [23, 24]. The serious nature of meningococcal disease and increased risk of meningococcal disease during outbreaks make ciprofloxacin an appropriate antibiotic choice in situations in which expanded chemoprophylaxis is deemed indicated.

The decision to implement expanded chemoprophylaxis should consider the challenges of identifying an appropriate target group, the feasibility of antibiotic administration to all persons in the target group within the shortest time frame possible (ideally within 24 hours of each other) and prolonged risk of exposure due to multiple sources of transmission within a population in an outbreak setting. Additional complexities of expanded chemoprophylaxis include cost of the drug and administration, drug side effects including idiosyncratic reactions, interactions with frequently used medications, and the emergence of drug-resistant organisms. If expanded chemoprophylaxis is offered prior to implementation of a vaccination campaign, it is critical to communicate the need for vaccination and continued reduction of behaviors that may increase risk of meningococcal transmission.

Each meningococcal disease outbreak is unique and public health authorities should carefully weigh the benefits and risks of expanded chemoprophylaxis on a case-by-case basis.

11. OTHER OUTBREAK RESPONSE MEASURES

Generally, CDC does not recommend restricting travel to an area with an outbreak, closing schools or universities, or canceling sporting or social events as part of meningococcal disease 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 care-seeking behaviors and case recognition 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. Information about the signs and symptoms of meningococcal disease is available at http://www.cdc.gov/meningococcal/about/symptoms.html.

12. RE-EVALUATION OF OUTBREAK STATUS

Following declaration of a meningococcal disease outbreak and implementation of public health measures, it is necessary to periodically reassess the status of the outbreak for continued public health decision-making. As meningococcal disease epidemiology is dynamic and unpredictable, with outbreak-associated cases sometimes reported months after the last known case, it is difficult to determine whether an outbreak has ended. Unlike with some pathogens, determination of the end of a meningococcal disease outbreak cannot be based on the passage of 2 incubation periods without a case because of transmission of the organism through asymptomatic carriers. Thus, based on expert opinion, a time frame of one year for reassessment is suggested for organization-based outbreaks. For the purposes of public health decision-making, the risk of meningococcal disease may be considered to have returned to expected levels one year following the last case in an organization-based outbreak. In community-based outbreaks, incidence should be re-assessed one year after the last case to determine whether the incidence remains above expected.

13. REFERENCES

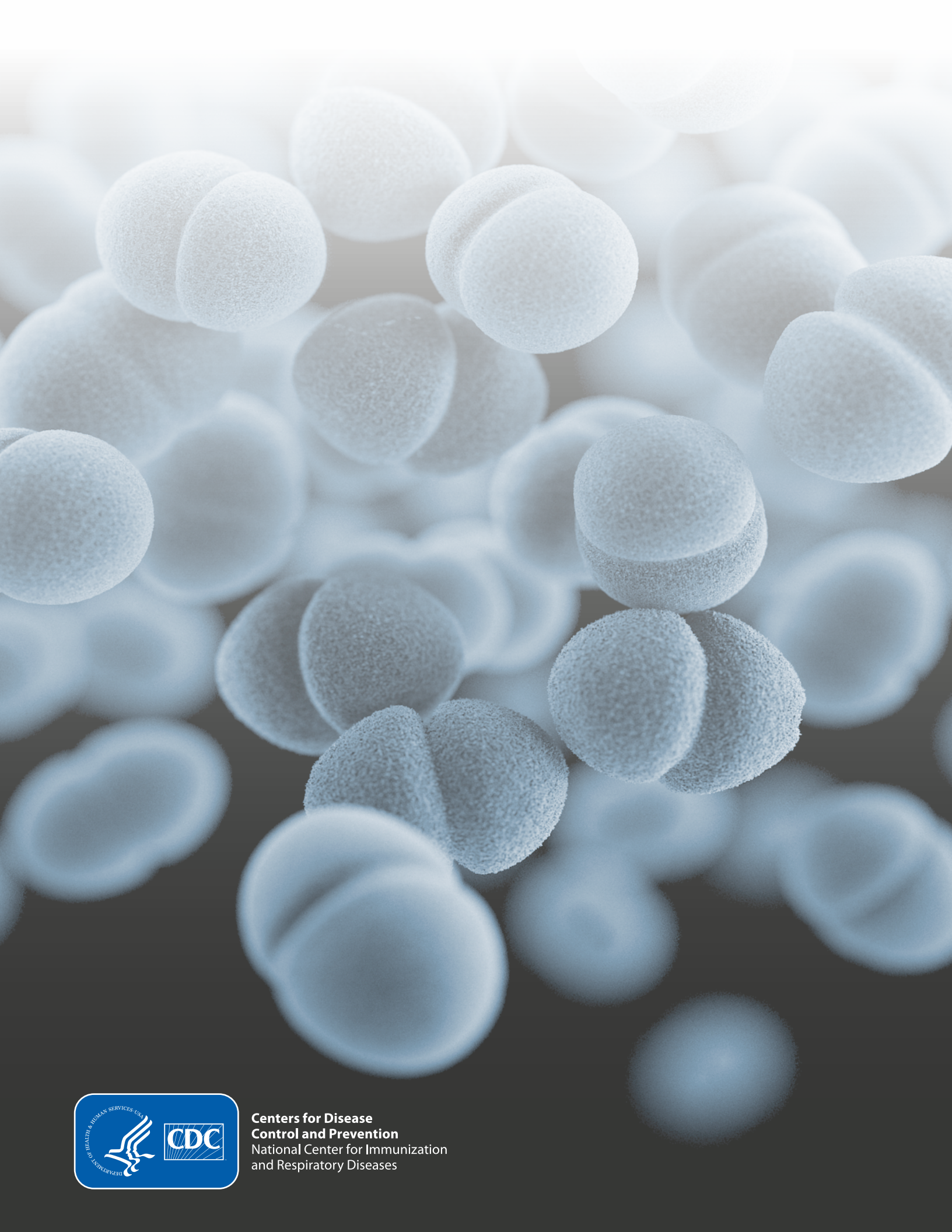
1. Control and prevention of serogroup C meningococcal disease: evaluation and management of suspected outbreaks: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep **1997**; 46(RR-5): 13-21.
2. Bilukha OO, Rosenstein N, National Center for Infectious Diseases CfDC, Prevention. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep **2005**; 54(RR-7): 1-21.
3. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep **2013**; 62(RR-2): 1-28.
4. Center for Disease Control and Prevention. Interim Guidance for Control of Serogroup B Meningococcal Disease Outbreaks in Organizational Settings. Available at: http://www.cdc.gov/meningococcal/downloads/interim-guidance.pdf. Accessed July 29, **2016**.
5. Council of State and Territorial Epidemiologists. Revision of the National Surveillance Case Definition for Meningococcal Disease. Available at: http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/2014PS/14_ID_06upd.pdf. Accessed March 3, 2017.
6. Association of Public Health Laboratories. APHL/CDC Vaccine Preventable Disease Reference Laboratory Project Testing Referral Protocol. Available at: https://www.aphl.org/MRC/Documents/ID_2013July10_VPD-Reference-Laboratory-Testing-Referral-Procedures.pdf. Accessed August 18, 2016.
7. Center for Disease Control and Prevention. Infectious Diseases Laboratories: *Neisseria meningitidis*. Available at: https://www.cdc.gov/laboratory/specimen-submission/detail.html?CDCTestCode=CDC-10220. Accessed May 18, **2017**.
8. ARUP Meningitis/Encephalitis Panel by PCR. Available at: http://ltd.aruplab.com/Tests/Pub/2013305. Accessed May 4, **2017**.
9. Biofire FilmArray® Panels. Available at: http://www.biofiredx.com/products/the-filmarray-panels/. Accessed May 4, **2017**.
10. Center for Disease Control and Prevention. Best Practices for Use of Polymerase Chain Reaction (PCR) for Diagnosing Haemophilus influenzae and Neisseria meningitidis Disease and Public Health Importance of Identifying Serotype/Serogroup. Available at: https://www.cdc.gov/meningococcal/laboratory/pcr-guidance-mening-hflu.html. Accessed May 4, **2017**.
11. Whaley MJ CS, Retchless AC, et. al.,. Molecular characterization of meningococcal outbreak strains in the United States, 2009-2015. International Pathogenic Neisseria Conference. Manchester, UK, **2016**.
12. DS S. Meningococcal Vaccines Session. In: Advisory Committee on Immunization Practices. Atlanta, GA, 2017.
13. Folaranmi T, Rubin L, Martin SW, Patel M, MacNeil JR, Centers for Disease C. Use of Serogroup B Meningococcal Vaccines in Persons Aged >/=10 Years at Increased Risk for Serogroup B Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep 2015; 64(22): 608-12.
14. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of Serogroup B Meningococcal Vaccines in Adolescents and Young Adults: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep **2015**; 64(41): 1171-6.
15. Patton ME SD, Moore K, MacNeil JR,. Updated Recommendations for Use of MenB-FHbp Serogroup B Meningococcal Vaccine — Advisory Committee on Immunization Practices, 2016. MMWR Morbidity and mortality weekly report **2017**; 66: 509-13.
16. Patton ME, Stephens D, Moore K, MacNeil JR. Updated Recommendations for Use of MenB-FHbp Serogroup B Meningococcal Vaccine - Advisory Committee on Immunization Practices, 2016. MMWR Morb Mortal Wkly Rep **2017**; 66(19): 509-13.
17. Basta NE, Mahmoud AA, Wolfson J, et al. Immunogenicity of a Meningococcal B Vaccine during a University Outbreak. N Engl J Med **2016**; 375(3): 220-8.
18. Soeters HM, Dinitz-Sklar J, Kulkarni PA, et al. Serogroup B Meningococcal Disease Vaccine Recommendations at a University, New Jersey, USA, 2016. Emerg Infect Dis **2017**; 23(5): 867-9.
19. McNamara LA MJ, Cohn AC, Stephens DS,. Mass chemoprophylaxis for control of outbreaks of meningococcal disease. In preparation, **2017**.
20. Zalmanovici Trestioreanu A, Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. Cochrane Database Syst Rev **2013**; (10): CD004785.

21. Food and Drug Administration. CIPRO (ciprofloxacin hydrochloride) label. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/019537s085,020780s042lbl.pdf. Accessed May 4, 2017.
22. Trinidad J. Epidemiology of Selected Fluoroquinolone-Associated Adverse Reactions – A Literature Review. Available at: https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM472655.pdf. Accessed March 3, 2017.
23. Food and Drug Administration. FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. Available at: https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm. Accessed May 4, 2017.
24. Food and Drug Administration Center for Drug Evaluation and Research. Summary Minutes of the Joint Meeting of the Antimicrobial Drugs Advisory Committee and the Drug Risk and Safety Management Advisory Comittee. Silver Springs, Maryland, 2015 November 5, 2015.

14. APPENDIX A: SUBJECT MATTER EXPERTS CONSULTED, 2015-2016

Last	First	Organization
Arwady	Allison	Chicago Department of Health
Baker	Carol	Baylor College of Medicine
Black	Stephanie	Chicago Department of Health
Campos-Outcalt	Doug	University of Arizona
Cieslak	Paul	Oregon Department of Health
Even	Susan	Missouri Department of Health
Ferris	Mary	University of California at Santa Barbara
Harriman	Kathleen	California Department of Public Health
Harrison	Lee	University of Pittsburgh
Healy	Mary	Baylor College of Medicine
Herlihy	Rachel	Colorado Department of Health
Johnson	Pete	Princeton University
Kemble	Sarah	Chicago Department of Health
Lee	Lucia	Food and Drug Administration
Luta	Martin	Delaware Department of Health
McKinney	Paul	University of Louisville
Meissner	Cody	Tufts University
Montana	Barbara	New Jersey Department of Health

Last	First	Organization
Moore	Jeffrey	Marshfield Clinic
Offit	Paul	Children's Hospital of Philadelphia
Peter	Georges	Brown University
Rastogi	Anuja	Food and Drug Administration
Rubin	Lorry	Steven and Alexandra Cohen Children's Medical Center of New York
Schaffner	William	Vanderbilt University
Stephens	David	Emory University
Tan	Tina	New Jersey Department of Health
Weiss	Don	New York City Department of Health
Yacovone	Margaret	Department of Defense
Zucker	Jane	New York City Department of Health
Albert	Alison	Centers for Disease Control and Prevention
Blain	Amy	Centers for Disease Control and Prevention
Bowen	Virginia	Centers for Disease Control and Prevention
Briere	Elizabeth	Centers for Disease Control and Prevention
Cohn	Amanda	Centers for Disease Control and Prevention
Duffy	Jonathan	Centers for Disease Control and Prevention
Folaranmi	Temitope	Centers for Disease Control and Prevention
Hadler	Stephen	Centers for Disease Control and Prevention
MacNeil	Jessica	Centers for Disease Control and Prevention
Martin	Stacey	Centers for Disease Control and Prevention
Mayer	Leonard	Centers for Disease Control and Prevention
McNamara	Lucy	Centers for Disease Control and Prevention
Meyer	Sarah	Centers for Disease Control and Prevention
Mootrey	Gina	Centers for Disease Control and Prevention
Ortega-Sanchez	Ismael	Centers for Disease Control and Prevention
Otshudiema	John	Centers for Disease Control and Prevention
Quinn	Conrad	Centers for Disease Control and Prevention
Soeters	Heidi	Centers for Disease Control and Prevention
Wang	Xin	Centers for Disease Control and Prevention



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