Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail. Prepared by Amanda C. Cohn, MD1 Jessica R. MacNeil, MPH1 Thomas A. Clark, MD1 Ismael R. Ortega-Sanchez, PhD2 Elizabeth Z. Briere, MD1 H. Cody Meissner, MD3 Carol J. Baker, MD4 Nancy E. Messonnier, MD1 1Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC 2Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC 3Tufts University School of Medicine, Boston, Massachusetts 4Baylor College of Medicine, Houston, Texas The material in this report originated in the National Center for Immunization and Respiratory Diseases, Anne Schuchat, MD, Director, and the Division of Bacterial Diseases, Rana Hajjeh, MD, Director. Corresponding preparer: Amanda C. Cohn, MD, National Center for Immunizations and Respiratory Diseases, CDC. Telephone: 404-639-6039; E-mail: acohn@cdc.gov. Meningococcal disease describes the spectrum of infections caused by Neisseria meningiditis, including meningitdis, bacteremia, and bacteremic pneumonia. Two quadrivalent meningococcal polysaccharide-protein conjugate vaccines that provide protection against meningococcal serogroups A, C, W, and Y (MenACWY-D [Menactra, manufactured by Sanofi Pasteur, Inc., Swiftwater, Pennsylvania] and MenACWY-CRM [Menveo, manufactured by Novartis Vaccines, Cambridge, Massachusetts]) are licensed in the United States for use among persons aged 2 through 55 years. MenACWY-D also is licensed for use among infants and toddlers aged 9 through 23 months. Quadrivalent meningococcal polysaccharide vaccine (MPSV4 [Menommune, manufactured by sanofi pasteur, Inc., Swiftwater, Pennsylvania]) is the only vaccine licensed for use among persons aged ≥56 years. A bivalent meningococcal polysaccharide protein conjugate vaccine that provides protection against meningococcal serogroups C and Y along with Haemophilus influenzae type b (Hib) (Hib-MenCY-TT [MenHibrix, manufactured by GlaxoSmithKline Biologicals, Rixensart,

Belgium]) is licensed for use in children aged 6 weeks through 18 months. This report compiles and summarizes all recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) regarding prevention and control of meningococcal disease in the United States, specifically the changes in the recommendations published since 2005 (CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2005;54[No. RR-7]). As a comprehensive summary of previously published recommendations, this report does not contain any new recommendations; it is intended for use by clinicians as a resource. ACIP recommends routine vaccination with a quadrivalent meningococcal conjugate vaccine (MenACWY) for adolescents aged 11 or 12 years, with a booster dose at age 16 years. ACIP also recommends routine vaccination for persons at increased risk for meningococcal disease (i.e., persons who have persistent complement component deficiencies, persons who have anatomic or functional asplenia, microbiologists who routinely are exposed to isolates of N. meningitidis, military recruits, and persons who travel to or reside in areas in which meningococcal disease is hyperendemic or epidemic). Guidelines for antimicrobial chemoprophylaxis and for evaluation and management of suspected outbreaks of meningococcal disease also are provided. This report compiles and summarizes all recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) regarding prevention and control of meningococcal disease in the United States, specifically the changes in the recommendations published since 2005 (1), and describes the process undertaken and the rationale used in support of these recommendations. This report is a comprehensive summary of previously published recommendations (Box 1) and does not contain any new recommendations; it is intended for use by clinicians as a resource. Guidelines for antimicrobial chemoprophylaxis (Appendix A) and evaluation and management of suspected outbreaks of meningococcal disease (Appendix B) also are provided. Meningococcal

disease describes the spectrum of infections caused by Neisseria meningitidis, including meningitis, bacteremia, and bacteremic pneumonia. Meningococcal disease develops rapidly, typically among previously healthy children and adolescents, and results in high morbidity and mortality. For unknown reasons, incidence has declined since the peak of disease in the late 1990s, and approximately 800–1,200 cases are reported annually in the United States. This decline began before implementation of routine use of meningococcal vaccines in adolescents and have occurred in all serogroups. Four vaccines are licensed in the United States and provide protection against four (A, C, W, and Y) and two (C and Y) serogroups (Table 1). Vaccines that protect against serogroup B meningococcal disease are not available in the United States. Meningococcal vaccination is recommended for groups at increased risk for disease. These groups include adolescents, persons with certain medical conditions, and persons with increased risk for exposure. Among these risk groups, the number of vaccine doses (i.e., 2- or 4-dose primary series or a single dose with or without a booster dose) and vaccine product are determined by the indication for vaccination and age. In certain situations such as special dosing regimens (i.e., booster dose[s] or serial vaccination and 2-dose primary series for persons aged ≥2 years), off-label use of meningococcal vaccine has been recommended. Special dosing regimens have been recommended on the basis of data from studies of immunologic response to vaccination, postlicensure observational data, and the need for long-term protection in certain risk groups (2–4). ACIP recommendations for meningococcal vaccination have been summarized (Box 2). Details regarding dosing (2- or 4-dose primary series or a single dose with or without a booster dose), contraindications, precautions, and special circumstances (e.g., adolescents infected with human immunodeficiency virus [HIV] and asplenic children) are described elsewhere in this report (see Recommendations for Use of Meningococcal Vaccines). ACIP's Meningococcal Vaccines Work Group* (the Work Group) revised the meningococcal vaccine recommendations on the basis of the most current data on

safety, efficacy, and immunogenicity of meningococcal vaccines. The Work Group comprises a diverse group of health-care providers and public health officials, including professionals from academic medicine (pediatrics, family practice, internal medicine, and infectious disease specialists), federal and state public health professionals, and representatives of provider organizations. Since 2006, the Work Group has held teleconference meetings monthly and has held in-person meetings once or twice a year to discuss recently published studies, review current guidelines, and consider potential revisions to the recommendations. During these meetings, CDC staff members, pharmaceutical manufacturer representatives, and other academic partners delivered presentations on meningococcal disease epidemiology, immunogenicity and safety of meningococcal vaccines, cost effectiveness, programmatic considerations, and vaccine effectiveness studies. The Work Group considers published, peer-reviewed studies as the primary source of data in making recommendations for the prevention and control of meningococcal disease. In addition, unpublished data (e.g., immunogenicity and safety data in age groups outside the licensed indication) that are relevant to issues under discussion also were considered. Randomized, controlled clinical trials for meningococcal vaccines are unable to evaluate clinical efficacy because of the low incidence of meningococcal disease; because efficacy cannot be measured, immunogenicity data are used as a surrogate for efficacy for licensure. In addition, because rare adverse events might not be observed in prelicensure clinical trials because of the limited number of subjects enrolled, postlicensure observational data also were used in the assessment of meningococcal vaccines. Observational data included reports of vaccine failures, a postlicensure case-control study, Vaccine Adverse Events Reporting System (VAERS) data (12), and safety data collected from the Vaccine Safety Datalink (VSD) (13). Data reviewed on the incidence and burden of disease came from the Active Bacterial Core surveillance (ABCs) system and the National Notifiable Diseases Surveillance System (NNDSS) (14). The evidence for the benefits and risks of

meningococcal vaccination in infants and toddlers was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework (GRADE evidence tables for toddler and infant meningococcal vaccine are available at http://www.cdc.gov/vaccines/acip/recs/GRADE/mening-vac-infants.html). Summaries of the data reviewed and Work Group discussions were presented to ACIP before changes were proposed to the recommendations. Proposed changes to meningococcal vaccine recommendations were presented at nine ACIP meetings from October 2007 through October 2012. During these nine meetings, recommendations were approved either as submitted or as amended and approved by ACIP, and ACIP members approved a draft of this report in April 2012. During the review process, CDC modified the statement to update and clarify wording in the report. Meningococcal disease is a bacterial infection caused by N. meningitidis. Meningococcal disease usually presents clinically as one of three syndromes: meningitis (50.2%), bacteremia (37.5%), or bacteremic pneumonia (9.2%) (15). N. meningitidis colonizes mucosal surfaces of the nasopharynx and is transmitted through direct contact with large-droplet respiratory tract secretions from patients or asymptomatic carriers. Nasopharyngeal carriage rates are highest in adolescents and young adults (16,17), who serve as reservoirs for transmission of N. meningitidis. Invasive disease is an infrequent consequence of nasopharyngeal colonization. During 2005–2011, an estimated 800–1,200 cases of meningococcal disease occurred annually in the United States, representing an incidence of 0.3 cases per 100,000 population (CDC, unpublished data, 2012). Incidence has declined annually since a peak of disease in the late 1990s (Figure 1). Even before routine use of a meningococcal conjugate vaccine in adolescents was recommended in 2005, the overall annual incidence of meningococcal disease had decreased 64%, from 1.1 cases per 100,000 population in 1996 to 0.4 cases per 100,000 population in 2005. Since 2005, declines have occurred among all age groups and in all vaccine-containing serogroups. In addition, incidence of disease attributable to serogroup B, a serogroup

not included in the vaccine, declined for reasons that are not known. Although disease incidence is at historic lows, the overall case-fatality ratio remains at 10%–15%, and 11%–19% of survivors have long-term sequelae (e.g., neurologic disability, limb or digit loss, and hearing loss) (15,18,19). Serogroups B, C, and Y are the major causes of meningococcal disease in the United States, each accounting for approximately one third of cases. However, the proportion of cases caused by each serogroup varies by age group. Approximately 60% of disease among children aged 0 through 59 months is caused by serogroup B N. meningitidis, which is not prevented by currently licensed vaccines (Table 1) (15). Serogroups C, Y, or W, which are included in vaccines available in the United States, cause 73% of all cases of meningococcal disease among persons aged ≥11 years (CDC, unpublished data, 2012). In the United States, approximately 98% of cases of meningococcal disease are sporadic; however, outbreaks of meningococcal disease continue to occur (20). During 2010, two serogroup C meningococcal outbreaks were reported to CDC (CDC, unpublished data, 2010); in these two instances, meningococcal conjugate vaccination was recommended for a target age group in the community by local and state health officials as a control measure. These outbreaks ended shortly after vaccination campaigns were implemented, but whether vaccination prevented additional cases from occurring is unknown (21). In 2010, two serogroup B outbreaks also were reported to CDC. Cases associated with all reported outbreaks accounted for 108 (1.5%) of the 7,343 cases reported to CDC during 2005–2011 (CDC, unpublished data, 2012). Incidence of meningococcal disease peaks among persons in three age groups: infants and children aged <5 years, adolescents and young adults aged 16 through 21 years, and adults aged ≥65 years (CDC, unpublished data; Table 2; Figure 2). The highest incidence in the first 5 years of life occurs among infants aged 0 through 5 months; 47% of serogroup C and Y disease among children aged 0 through 59 months occurs before age 6 months. Approximately 60% of disease in the first year of life is caused by

serogroup B. Licensure in 2005 of the first MenACWY vaccine made it possible to address the second peak in disease incidence, which occurs in late adolescence. The third peak in incidence occurs among adults aged ≥65 years; approximately 60% of these cases are caused by serogroup Y, and 43% are characterized by bacteremic pneumonia. The highest case-fatality ratio (23.8%) is observed among adults aged ≥65 years (15). Since 2006, the National Immunization Survey–Teen (22) has assessed vaccination coverage annually among adolescents aged 13 through 17 years. Among this age group, coverage with MenACWY has increased from 10.2% in 2006 to 70.5% in 2011 (22,23); coverage by state in 2011 ranged from 27.6% to 92.1% (23). One method for assessing the impact of MenACWY is to monitor changes in disease incidence caused by vaccine serogroups. During 2005–2009, MenACWY-D was the only meningococcal conjugate vaccine licensed in the United States. Therefore, postlicensure data primarily reflect use of MenACWY-D. During 2009 and 2010, when routine vaccine use was recommended and supply was sufficient, incidence of serogroup C and Y meningococcal disease declined among adolescents aged 11 through 18 years. Incidence did not decline in other age groups, suggesting an impact of vaccination on adolescent disease, but no evidence of herd protection (Table 3). During 2006–2010 (i.e., in the first 5 years after routine use of meningococcal vaccine was recommended), CDC received reports of approximately 30 cases of serogroups C and Y meningococcal disease among persons who had received the vaccine. The case-fatality ratio was similar among persons who had received vaccine compared with those who were unvaccinated (CDC, unpublished data, 2012). To assess vaccine effectiveness among adolescents, CDC carried out a simulation study of breakthrough disease (i.e., cases that occur among vaccine recipients) and a case-control study (24,25). The first estimate of vaccine effectiveness was based on a simulation approach that calculated the expected number of cases in vaccinated persons. The expected number of breakthrough cases was calculated from available vaccine coverage and

disease incidence data, and estimates of expected vaccine effectiveness were based on prelicensure serologic evidence of immune response. When the number of expected cases was compared with the observed number of breakthrough cases, vaccine effectiveness during 2005–2008 was estimated to be 80%–85% (24). Of the 13 reports of breakthrough disease for which data on underlying conditions were available, four persons had underlying conditions or behaviors associated with an increased risk for bacterial infections, including 1) Type 1 diabetes mellitus; 2) current smoking; 3) history of bacterial meningitis and recurrent infections; and 4) aplastic anemia, paroxysmal nocturnal hemoglobinuria, and receipt of eculizumab (which blocks complement protein C5) (24). A case-control study evaluating the vaccine effectiveness of meningococcal conjugate vaccine in adolescents began in January 2006 (25). Because MenACWY-D was the only licensed conjugate vaccine until February 2010, the preliminary results provided in this report are estimates for MenACWY-D only. As of August 29, 2012, a total of 157 case-patients and 180 controls were enrolled in the effectiveness study. The overall estimate of vaccine effectiveness in adolescents vaccinated 0 through 6 years earlier was 69% (95% confidence interval [CI] = 50%–81%). Vaccine effectiveness was 82% (CI = 54%–93%) for adolescents vaccinated <1 year earlier, 80% (CI = 52%–92%) for adolescents vaccinated 1–<2 years earlier, 71% (CI = 34%–87%) for adolescents vaccinated 2–<3 years earlier, and 59% (CI = 5%–83%) for adolescents vaccinated 3–<6 years earlier (25). Although CIs around the point estimates are wide, these results suggest that vaccine effectiveness wanes over time. Risk factors for meningococcal disease can be grouped into organism, host, and environmental factors. Noncapsular strains of N. meningitidis are less virulent than capsular strains. More virulent strains of N. meningitidis can circulate in a population and cause increased incidence of disease or increased mortality (26). Persons who have persistent (i.e., genetic) deficiencies in the common complement pathway (e.g., C3, properdin, Factor D, Factor H, or C5–C9) have up to a 10,000-fold increased risk for meningococcal

disease and can experience recurrent disease (27,28). Although persons with anatomic or functional asplenia also appear to be at increased risk for meningococcal disease, the data are less compelling than data that demonstrate the increased risk for pneumococcal disease in patients with asplenia (29). Antecedent viral infection, household crowding, chronic underlying illness, and both active and passive smoking are associated with increased risk for meningococcal disease (30–36). Early U.S. studies of risk factors for meningococcal disease demonstrated that blacks and persons of low socioeconomic status were at higher risk for meningococcal disease than other persons (37,38); however, race and low socioeconomic status also are considered markers for other risk factors (e.g., smoking and household crowding) (31). As disease incidence has decreased, differences by race also have decreased, and no difference in disease incidence exists now between blacks and whites (15). One study of meningococcal disease among clinical microbiologists who work routinely with N. meningitidis isolates demonstrated an attack rate of 13 cases per 100,000 microbiologists and increased case-fatality ratios. Of the 16 cases identified, 15 occurred in clinical microbiologists who were not using respiratory protection at the time of exposure (39,40). Health-care personnel in general are not identified as a high-risk group unless a person is exposed to respiratory secretions of someone with meningococcal disease. Because the incidence of both meningococcal disease and HIV infection are low in the United States, studies have not established HIV as an independent risk factor for meningococcal infection (32,41). A recent study in the ABCs sites demonstrated that the cumulative average incidence of meningococcal disease among patients aged 25 through 64 years who meet CDC's surveillance case definition for acquired immune deficiency syndrome (AIDS) was 3.5 cases per 100,000 person years (CI = 2.0–5.6), compared with an incidence of 0.3 cases per 100,000 person years (CI = 0.2–0.3) for persons of the same age group in the general population (rate ratio: 12.6; CI = 7.9–20.2) (42). These incidence rates were not adjusted for potential confounding risk

factors such as smoking; however, the incidence of meningococcal disease is higher in persons with AIDS compared with the general adult population. Studies conducted in the 1990s that focused on quantifying the risk for meningococcal disease among college students demonstrated that the overall incidence among college students was similar to or somewhat lower than that observed among persons of approximately the same age in the general population (43). However, in a case-control study involving 50 cases among college students (44), multivariate analysis indicated that first-year college students living in residence halls were at higher risk for meningococcal disease than other students (matched odds ratio [OR]: 3.6; CI = 1.6–8.5). Other studies in the 1990s yielded similar results (45,46). In 2000, before licensure of meningococcal conjugate vaccines, ACIP recommended that first-year college students living in residence halls consider vaccination with the quadrivalent meningococcal polysaccharide vaccine (MPSV4), which was licensed in 1981 (47). Since the 2000 ACIP recommendation, many colleges have required all matriculating students to be vaccinated. Thirty-six states and the District of Columbia have mandates requiring education of college students about meningococcal vaccines or proof of meningococcal vaccination for attendance (a list of these states is available at http://www.immunize.org/laws/menin.asp). When the first meningococcal conjugate vaccine was licensed in 2005, ACIP recommended that all first-year college students living in residence halls be vaccinated with MenACWY-D (1). Four meningococcal vaccines that contain purified capsular polysaccharide(s) alone or that are conjugated to a carrier protein are licensed and available in the United States for the prevention of invasive disease caused by N. meningitidis serogroups A, C, W and Y (Table 1). As stated in the package inserts (Table 1), for the quadrivalent meningococcal polysaccharide vaccine (MPSV4), effectiveness of the vaccine (A and C components) was supported by clinical efficacy data from studies with meningococcal monovalent A and C and bivalent A/C polysaccharide vaccines, and inferred by use of serum

bactericidal antibody assay (SBA) (Y and W components) as an indicator of protection against serogroup-specific meningococcal disease. Effectiveness of the three meningococcal conjugate vaccines, which were licensed after MPSV4, was inferred by comparing SBA measurements of the new vaccine with corresponding antibody responses of the U.S.-licensed meningococcal vaccine representing the standard of care at the time (among persons aged 2 through 55 years) or by achieving a seroresponse at or above a predefined bactericidal antibody titer (among children aged 2 through 23 months). Protection against invasive meningococcal disease is mediated by serum bactericidal antibodies to meningococcal capsular polysaccharides or to protein antigens. Studies have demonstrated that almost all persons who developed invasive serogroup C meningococcal disease had sera that lacked bactericidal activity to the pathogenic meningococcal strain (48,49). In contrast, persons with detectable SBA against a specific strain rarely developed disease. Complement-dependent bactericidal activity can be measured reliably by use of a serum bactericidal antibody assay with a human (hSBA) or baby rabbit (rSBA) complement source. A defined bactericidal antibody titer that is indicative of protection against invasive meningococcal disease is assay-dependent. When sera are tested using a human complement source, SBA titers ≥1:4 are considered protective. Because of greater susceptibility of meningococci to lysis by rabbit complement, antibody titers measured by an rSBA assay are elevated compared with titers generated by an hSBA assay (50–52). Population-based surveillance data from the United Kingdom indicate that following mass vaccination with meningococcal serogroup C conjugate vaccine, bactericidal titers between 1:8 and 1:64, measured by rSBA, can be protective (53). Antibody titers measured by rSBA and hSBA assays are not directly comparable. MPSV4, a quadrivalent (serogroups A, C, Y, and W) meningococcal polysaccharide vaccine (Menomune, manufactured by Sanofi Pasteur, Inc., Swiftwater, Pennsylvania), was licensed in 1981. MPSV4 is approved by FDA for use as a single dose in persons aged ≥2 years. Each dose consists of 50 µg of

each of the four purified capsular polysaccharides from serogroups A, C, W, and Y. MPSV4 is available in single-dose (0.5-mL) and 10-dose (5-mL) vials and is administered as a subcutaneous injection. Further information is provided in the package insert (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM131653.pdf). Conjugation (i.e., covalent coupling) of a meningococcal capsular polysaccharide to a protein carrier that contains T-lymphocyte epitopes changes the nature of the human immune response to the polysaccharide from T-lymphocyte–independent to T-lymphocyte–dependent. Conjugation results in an improved primary response to the polysaccharide antigen, especially in infants, and a stronger anamnestic response (i.e., immunologic memory) at reexposure (54). As of July 2012, two quadrivalent (serogroups A, C, Y, and W) and one bivalent (serogroups C and Y) meningococcal polysaccharide-protein conjugate vaccines have been licensed by FDA: MenACWY-D (Menactra, manufactured by sanofi pasteur, Inc., Swiftwater, Pennsylvania), MenACWY-CRM (Menveo, manufactured by Novartis Vaccines, Cambridge, Massachusetts), and Hib-MenCY-TT (MenHibrix, manufactured by GlaxoSmithKline Biologicals, Rixensart, Belgium). MenACWY-D was licensed by FDA in January 2005. MenACWY-D is approved by FDA as a single dose for persons aged 2 through 55 years and as a 2-dose series in children aged 9 through 23 months. A single 0.5-mL dose of MenACWY-D contains 4 µg each of capsular polysaccharide from serogroups A, C, Y, and W conjugated to approximately 48 µg of diphtheria toxoid. MenACWY-D is available in single-dose vials and is administered as an intramuscular injection. More information is provided in the package insert (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM131170.pdf). MenACWY-D often will be administered concomitantly with other vaccines (e.g., with typhoid vaccines in international travelers or with other routinely recommended vaccinations in adolescents and young children). As stated in the

package insert (Table 1), concomitant administration of MenACWY-D and typhoid vaccines (Typhoid Vi Polysaccharide Vaccine, manufactured by Sanofi Pasteur, Inc., Swiftwater, Pennsylvania) was evaluated in persons aged 18 through 55 years, and concomitant administration of MenACWY-D and Td (Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use; manufactured by Sanofi Pasteur, Inc., Swiftwater, Pennsylvania) vaccine was evaluated in persons aged 11 through 17 years. Concomitant administration of typhoid vaccine and MenACWY-D did not affect the immunogenicity of either vaccine. The proportion of participants with a fourfold or greater increase in rSBA titer to meningococcal serogroups C, Y, and W was higher when MenACWY-D was administered with Td (86%–96%) than when MenACWY-D was administered 1 month following administration of Td (65%–91%). Antitetanus and antidiphtheria antibody responses were similar in both study groups. Affect on immunogenicity varied by vaccine administerd concomitantly. Concomitant administration of MMRV (measles, mumps, rubella, and varicella combination vaccine) and the fourth dose of PCV7 (7-valent pneumococcal conjugate vaccine) and a second MenACWY-D dose was evaluated in children aged 12 months who had received the first MenACWY-D dose at age 9 months. Lower geometric mean concentrations (GMCs) of IgG antibodies to some pneumococcal serotypes were observed compared with corresponding IgG GMCs when PCV7 was administered alone. The noninferiority criteria (twofold differences in IgG GMC) for the prespecified pneumococcal endpoints were not met for PCV7 serotypes 4, 6B, and 18C (10). However, the IgG antibody responses and opsonophagocytic responses to the seven pneumococcal vaccine serotypes were still robust. No interference with immune responses to antigens contained in MMRV was observed. Details about these studies are provided in the package insert. MenACWY-CRM was licensed by FDA in February 2010. MenACWY-CRM is approved by FDA as a single dose for persons aged 2 through 55 years. A single 0.5-mL dose of vaccine contains 10 µg of capsular polysaccharide from serogroup A and 5 µg of

capsular polysaccharide from serogroups C, Y, and W conjugated to approximately 33–64 µg of CRM197, a naturally occurring, nontoxic form of diphtheria toxin from Corynebacterium diphtheriae. MenACWY-CRM must be prepared by reconstituting the lyophilized serogroup A conjugate with the liquid serogroups C, W, and Y conjugate components. More information is provided in the package insert (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM201349.pdf). MenACWY-CRM is likely to be administered concomitantly with tetanus and diphtheria toxoids and acellular pertussis vaccine absorbed (Tdap) because both vaccines are routinely recommended for adolescents. Concomitant use of MenACWY-CRM and Tdap was evaluated in an open-label, randomized, controlled study conducted among adolescents aged 11 through 18 years. Antibody responses to pertussis antigens were lower when MenACWY-CRM and Tdap were administered concomitantly than when MenACWY-CRM was administered 1 month following Tdap: antipertussis toxin GMCs were 51 versus 63 EIA Units (EU)/mL, antifilamentous hemagglutinin GMCs were 342 versus 511 EU/mL, and antipertactin GMCs were 819 versus 1,197 EU/mL, respectively. Because no serologic correlates of protection for pertussis have been established, the clinical implications of the lower pertussis antigen responses are unknown. Immune responses to MenACWY-CRM and to diphtheria and tetanus toxoid antigens in Tdap were similar. Details about this study are provided in the package insert (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM201349.pdf). Hib-MenCY-TT was licensed by FDA in June 2012. Hib-MenCY-TT is approved by FDA as a 4-dose series for children aged 6 weeks through 18 months. Hib-MenCY-TT is supplied as a sterile, lyophilized powder that is reconstituted at the time of use with the accompanying saline diluent for intramuscular injection. A single 0.5mL dose of vaccine contains 5 µg of capsular polysaccharide from serogroups C conjugated to approximately 5 µg of tetanus toxoid, 5 µg of capsular polysaccharide

from serogroup Y conjugated to approximately 6.5 µg of tetanus toxoid, and 2.5 µg of Haemophilus influenzae type b capsular polysaccharide conjugated to approximately 6.25 µg of tetanus toxoid. More information is provided in the package insert (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM308577.pdf). Concomitant administration with routinely recommended vaccines is anticipated. Hib-MenCY-TT was co-administered with DTaP-HepB-IPV and 7-valent pneumococcal conjugate vaccine (PCV7) at ages 2, 4, and 6 months, and with measles-mumps-rubella, varicella, and PCV7 vaccines at age 12–15 months. In clinical trials, no decreased immunogenicity of coadministered vaccines was observed (55,56). A randomized, controlled, multicenter study evaluated the percentage of subjects with hSBA titers ≥1:8 at 2 months after the second dose was administered at age 4 months. In the group vaccinated with Hib-MenCY-TT, 94% and 83% of subjects achieved hSBA antibody titers ≥1:8 for meningococcal serogroups C and Y, respectively, after dose 2 (57). Rates of local and systemic adverse events observed after administration of Hib-MenCY-TT were comparable to rates observed after administration of Hib-TT. Thus, Hib-MenCY-TT was found to be safe and immunogenic for both Hib and meningococcal serogroups C and Y. The immunogenicity and clinical efficacy of serogroups A and C meningococcal polysaccharide vaccines are well- established. The serogroup A polysaccharide induces antibody response among children as young as age 3 months, although a response comparable with that occurring in adults is not achieved until age 4 to 5 years; the serogroup C component is poorly immunogenic among recipients aged <24 months (58–60). The serogroups A and C vaccines have demonstrated estimated clinical efficacies of ≥85% among school-aged children and adults during outbreaks (61–64). Although clinical protection has not been documented, vaccination with Y and W polysaccharides induces production of bactericidal antibodies (65–67). The antibody responses to each of the four polysaccharides in the quadrivalent vaccine are

serogroup specific and independent (i.e., there is no cross-protection). Reduced clinical efficacy has not been demonstrated among persons who have received multiple doses of polysaccharide vaccine. However, serologic studies have indicated that multiple doses of serogroup A and C polysaccharide vaccine can cause immunologic hyporesponsiveness (i.e., a reduced antibody response after subsequent doses with the same polysaccharide antigen) to group A (68,69) and C polysaccharide (70,71). Hyporesponsiveness to serogroups C and A polysaccharides can be overcome partially by vaccination with serogroup C or A conjugate vaccine (72). An advantage of vaccines in which proteins are conjugated to polysaccharide antigens is their ability to elicit immunologic memory. Meningococcal conjugate vaccines prime the immune system, and immunologic memory persists even in the absence of detectable bactericidal antibodies. However, while vaccine-induced immunologic memory might be protective against infection with other disease-causing encapsulated bacteria, the presence of detectable circulating antibody appears to be important for protection against N. meningitidis. In most cases, meningococcal infection progresses rapidly, with fulminant disease occurring within 1–4 days after invasion of normally sterile body sites. Studies of antibody response kinetics following boosting with serogroup C meningococcal vaccines in the United Kingdom have demonstrated that up to 10 days might be required to achieve protective rSBA titers ≥1:8 in healthy young adults (73). If antibody is not present in sufficient quantity before colonization, this delay in antibody synthesis might not be rapid enough to protect against infection with N. meningitidis. Analyses of breakthrough disease among previously vaccinated persons in the United Kingdom identified evidence of immunologic priming but low SBA activity at the time of disease onset. Although infected persons demonstrated a boost response to N. meningitidis and bactericidal antibody levels increased, the response was not rapid enough to prevent disease (74). Therefore, circulating bactericidal antibody at the time of exposure appears to be critical for protection against meningococcal disease. Meningococcal

vaccination coverage has increased in the United States, but no evidence of herd protection has been demonstrated (75). However, herd protection has been an important component associated with long-term protection with use of serogroup C meningococcal vaccine in the United Kingdom and other countries. Evidence of herd protection after the MenC vaccine program was implemented in the United Kingdom, where catch-up campaigns led rapidly to high coverage in all persons aged 2 months through 22 years, included reduction in nasopharyngeal carriage of serogroup C N. meningitidis and reduction of serogroup C disease in unvaccinated age groups (infants too young to be vaccinated and adults aged ≥25 years) (76,77). One year after introduction of MenC vaccine in the United Kingdom, serogroup C carriage was reduced 66% among students aged 15 through 17 years (78). Attack rates among unvaccinated children aged <1 year in the United Kingdom also declined 67% in the 4 years following vaccine introduction. During 1998–2009, the incidence of serogroup C disease in the United Kingdom in persons aged >25 years decreased from 0.55 per 100,000 persons to 0.02 per 100,000 persons, and the total number of cases in infants aged <3 months decreased from 13 in 1998 to one in 2009 (79). The vaccination program in the United Kingdom effectively eliminated a single highly virulent clone that had high expression of the polysaccharide capsule (80). Variability of strains, different vaccines, and different target populations likely account for the differences in vaccine impact observed to date in the United States compared with the United Kingdom. Longitudinal vaccine effectiveness studies as well as evaluation of persistence of antibody after vaccination with MenACWY vaccines are critical to monitoring duration of protection. Persistence of detectable bactericidal antibodies 3 years after a single vaccination (administered at age 11 through 18 years) and antibody responses consistent with immunologic boosting have been observed in adolescent MenACWY-D recipients. Lower bactericidal antibody titers to each of the four serogroups were observed 3 to 5 years postvaccination relative to bactericidal antibody responses observed 1 month after a

single MenACWY dose (81,82). For serogroup C, geometric mean antibody titers (GMTs) declined by as much as 90% over 3 years. The proportion of adolescents vaccinated at age 11 years with MenACWY-D determined to have protective antibodies 3 years later was 71%–95% (81). Antibody persistence following MenACWY-CRM vaccination also has been described. Among persons vaccinated with a single dose of MenACWY-CRM at age 11 through 18 years, approximately 65% maintained hSBA ≥1:8 for serogroups C and Y at 21 months and 36 months postvaccination (83,84). These serologic data have been summarized (Table 4); the data are consistent with results of studies discussed previously in this report that suggest waning vaccine effectiveness. Other serologic studies conducted among infants and young children demonstrate a similar decline in hSBA titers. The proportion of children aged 2 years with hSBA titers ≥1:4 6 months following a single vaccination with MenACWY-D was approximately 50% for serogroups C, Y, and W-135 (85,86). In another study, approximately 60 infants were vaccinated at age 9 months and at age 12 or 15 months, and hSBA titers were measured approximately 3 years after the second dose. Fewer than half of the study subjects had maintained an hSBA titer ≥1:8 for any of the meningococcal serogroups (ACIP, unpublished data, 2011). Among infants who received a 4-dose series of Hib-MenCY-TT, 83% and 70% of subjects had persistence of bactericidal antibody for serogroups C and Y, respectively, 5 years after the fourth dose (87). In three separate studies, bactericidal antibody responses after a booster dose of MenACWY-D were evaluated in adolescents 3 years after receiving a MenACWY-D primary dose (administered at age 11 through 18 years), in children 5 years after receiving a MenACWY-D primary dose (administered at age 2 through 10 years) and after a booster dose of MenACWY-CRM in adolescents 3 years after a MenACWY-CRM primary dose (administered at age 11 through 18 years) (ACIP, unpublished data, 2009), At both 3 and 5 years after the first MenACWY conjugate vaccine dose, revaccination with the same MenACWY conjugate vaccine elicited substantially higher GMTs compared with the titers elicited after a

single primary dose. In the MenACWY-D booster studies, when rSBA was used as a measure of immune response, a dose administered 5 years after the first dose (administered at age 2 through 10 years) elicited a GMT for serogroup C of 23,613 compared with 9,045 among meningococcal vaccine-naïve subjects aged 7 through 15 years who had received a single primary dose (ACIP, unpublished data, 2010). In all of the studies, local and systemic reactions following a booster dose of either MenACWY conjugate vaccine were comparable with reactions in persons receiving a primary dose of the same vaccine. The duration of protection after a booster dose in adolescents, when administered at ages 16 through 18 years, is not known, but expert members of the Work Group expect protection to last through at least age 21 years. A booster dose of MenACWY-D in children initially vaccinated with MenACWY-D at age 9 months and then at age 12 or 15 months was evaluated 3 years after the second administered dose. Following booster immunization, at least 98% of children achieved an hSBA titer ≥1:8 to each of the serogroups. ACIP evaluated the data available and decided to recommend a booster dose of MenACWY for persons who remained at increased risk for meningococcal disease and for adolescents at age 16 years. Limited data suggest that different conjugate vaccine products can be used interchangeably. The safety and immunogenicity of MenACWY-CRM vaccination have been evaluated in adolescents 3 years after they received a single dose of MenACWY-CRM or MenACWY-D administered at age 11 through 18 years (88). Following revaccination with MenACWY-CRM, ≥99% of persons previously immunized with MenACWY-CRM or MenACWY-D had hSBA titers ≥1:8. The solicited adverse event rates (including injection-site reactions) reported after revaccination were similar to the rates reported after primary immunization (88). No data exist on the use of MenACWY-D following primary vaccination with MenACWY-CRM. Asplenic persons are at increased risk for invasive infection caused by many encapsulated bacteria, including N. meningitidis. Moreover, the mortality rate is 40%–70% among these persons when they become infected with N. meningitidis.

Asplenic persons achieve significantly lower geometric mean rSBA titers than healthy persons after vaccination with a meningococcal C conjugate vaccine, with 20% not achieving rSBA titers ≥1:8. This proportion was reduced to 7% when a second dose of vaccine was administered to nonresponders 2 months later (2), suggesting that a 2-dose primary series might be effective in achieving higher circulating antibody levels and persistence of bactericidal antibodies. The complement pathway is important in prevention of meningococcal disease, and N. meningitidis is the primary bacterial pathogen affecting persons with inherited late component complement or properidin deficiency. Although persons with late-component complement deficiency are able to mount an overall antibody response equal to or greater than complement-sufficient persons after vaccination with MPSV4, antibody titers wane more rapidly in persons with complement component deficiency, and higher antibody levels are needed for other clearance mechanisms, such as opsonization to function (27,28). Although persons with HIV infection are not at as high a risk for meningococcal disease as persons with persistent complement component deficiency or asplenia, reduced antibody responses following meningococcal vaccination have been reported in persons with HIV infection (3,4). Two studies have investigated the response rates to MenACWY-D among HIV-infected adolescents and children (3,4). Among HIV-infected adolescents and young adults vaccinated with a single dose at age 11 through 24 years, response rates to vaccination measured by rSBA titers ≥1:128 were 86%, 55%, 73%, and 72% for serogroups A, C, Y, and W, respectively. Response rates were significantly lower among patients with a CD4+ T-lymphocyte percentage of <15% ($p = 0.003$) or viral loads >10,000 copies/mL ($p = 0.005$) (4). Surveillance for adverse events following receipt of meningococcal conjugate vaccines has been performed primarily by two systems in the United States, VAERS and VSD. VAERS is a national passive surveillance system operated jointly by CDC and FDA that receives reports of adverse events following vaccination from health-care personnel, manufacturers,

vaccine recipients, and others. The VAERS reporting form collects information about vaccine recipient demographics, vaccines administered, recipient medical history, and signs and symptoms of adverse events. VAERS can generate, but not test, vaccine safety hypotheses and is subject to several limitations, including reporting biases and inconsistent data quality (12.) Passive surveillance data from VAERS should be interpreted with caution. The VSD project is a collaborative effort between CDC and 10 managed care organizations. The VSD project allows for planned vaccination safety studies as wells as timely investigations of hypotheses that arise from review of medical literature, reports to VAERS, changes in immunization schedules, or introduction of new vaccines (13). From licensure of MenACWY-D in January 14, 2005, through September 30, 2011, VAERS received 8,592 reports involving receipt of MenACWY-D in the United States; 89.0% reports involved persons aged 11 through 19 years. MenACWY-D was administered alone in 22.5% of case reports. The median time from vaccination to onset of an adverse event was 1 day. Males accounted for 40.6% of the reported events. The most frequently reported adverse events were fever 16.8%, headache 16.0%, injection site erythema 14.6%, and dizziness 13.4%. Syncope previously has been identified as an adverse event following any vaccination, with a higher proportion of syncope events reported to VAERS having occurred in adolescents compared with other age groups (89). Syncope was reported in 10.0% of reports involving MenACWY-D. Among all MenACWY-D reports, 563 (6.6%) were coded as serious (i.e., resulted in death, life-threatening illness, hospitalization, prolongation of hospitalization, or permanent disability). Among those reports coded as serious, the most frequent adverse events reported included headache (37.5%), fever (32.5%), vomiting (23.6%), and nausea (22.2%). Cases of Guillain-Barré Syndrome (GBS) were recorded in 86 (15.3%) reports coded as serious, although the diagnosis has not been validated by medical records for all reports. A total of 24 (0.3%) deaths were reported, each of which was documented by autopsy report or other medical records and

occurred in persons aged 10 through 23 years. Among the 24 reports of death, 11 (45.8%) indicated that the cause of death was meningococcal infection (nine with a serogroup included in the vaccine and two with a nonvaccine serogroup). Among the other 13 (54.2%) reports of death, which occurred from the day of vaccination to 127 days following vaccination, stated causes of death were cardiac (five), neurologic (two), infectious (two), behavioral (i.e., suicide) (two), rheumatologic (one), and unexplained (one). There was no pattern among these reports. Except for the finding of GBS, which was further evaluated and is discussed below, no signals were identified in VAERS after MenACWY-D vaccination. During February 19, 2010–September 30, 2011, VAERS received 284 reports of adverse events following receipt of MenACWY-CRM in the United States. Approximately three fourths (78.9%) of the reported events concerned persons aged 11 through 19 years. Males were the subject of 44.0% of reports; 45.4% of reports involved other vaccines administered at the same time, and 4.2% of reports were coded as serious. One death was reported, with the cause of death stated as unexplained. The median time from vaccination to adverse event onset was 0 days (the day of vaccination). The most common adverse event reported was injection-site erythema (19.7%) followed by injection-site swelling (13.7%). Syncope was reported in 8.8% of reports. No cases of GBS were reported. Administration errors (e.g., wrong diluent used or subcutaneous injection) without adverse events were described in 15.5% of reports involving MenACWY-CRM. In 2005, shortly after licensure of MenACWY-D, several cases of Guillain-Barré Syndrome (GBS) were reported to VAERS (90,91). Symptom onset clustered approximately 14 days after vaccination with MenACWY-D. No deaths were reported, and most persons recovered fully. ACIP reviewed the data at the time and determined that the potential small increased risk for GBS post-MenACWY-D vaccination was outweighed by the protection that the vaccine offers against meningococcal disease (92). However, because the risk for recurrence of GBS after meningococcal vaccination was unknown, FDA considered previous history of

GBS a contraindication for use of this vaccine (93). A large retrospective cohort study of adolescents aged 11 through 21 years that was conducted during 2005–2008 included approximately 1.4 million persons vaccinated with MenACWY-D (94). In an analysis that took into account the missing data, estimates of the attributable risk for GBS ranged from zero to 1.5 additional cases of GBS per 1 million vaccines within the 6-week period following vaccination (http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM131170.pdf). VSD conducts near-real time surveillance for adverse events and tests vaccine safety hypotheses (13). The system collects medical care and vaccination information on approximately 9 million members. VSD uses Rapid Cycle Analysis to monitor vaccine safety in near real-time. Each week, the number of outcomes in vaccinated persons is compared with the expected number of outcomes in the comparison group using maximized sequential probability ratio testing (95). No cases of GBS were identified within 1–42 days following 889,684 vaccine doses of MenACWY-D administered during January 2005–March 2010 (ACIP, unpublished data, 2010). In June 2010, after reviewing the two safety studies, ACIP voted to remove the precaution for persons with a history of GBS because the benefits of meningococcal vaccination outweigh the risk for recurrent GBS in these persons. A history of GBS continues to be listed as a precaution in the package inserts for MenACWY-D (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM131170.pdf) and MenACWY-CRM (available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM201349.pdf). Since the June 2010 ACIP meeting, no specific concerns have been raised about the risk for GBS in persons who both have a history of this condition and have been vaccinated with meningococcal conjugate vaccine (96). During January 1, 2005–June 30, 2010, a total of 80 reports were submitted to VAERS regarding pregnant women or infants born to women who received MenACWY-D during pregnancy. The

majority (57.5%) of women were vaccinated in the first trimester (0 through 13 weeks of gestation). Thirty-three (41.3%) reports indicated no adverse events, and the reason for submitting the report to VAERS was vaccine exposure during pregnancy (pregnancy category C)†. No maternal deaths were reported. The most common pregnancy-specific adverse event was spontaneous abortion (12 cases; 15%) and the most common nonpregnancy specific adverse event was nausea, with or without vomiting (four cases; 5%). One case of a congenital anomaly (aqueductal stenosis with severe ventriculomegaly in a newborn) was reported. However, no concerning patterns of adverse events after MenACWY-D in pregnancy were identified. Two postlicensure studies have evaluated use of Tdap when administered simultaneously or sequentially with MenACWY (97,98). In a clinical trial to evaluate administration of one Tdap product (Boostrix, GSK) and MenACWY-D, immune responses to the meningococcal serogroups and to pertussis, diphtheria, and tetanus were similar regardless of whether the two vaccines were administered simultaneously or separated by 30 days. There were no differences in the safety evaluation in either of the groups. In a postlicensure surveillance study using VSD data, the risk for medically attended adverse events was low (0–2.6 per 10,000 vaccinations) and similar regardless of whether persons received Tdap and MenACWY simultaneously or sequentially (98). As part of the evaluation of the adolescent vaccination program, a cost-effectiveness analysis was performed to compare the cost-effectiveness of the following three vaccination strategies: 1) a single dose at age 11 years, 2) a single dose at age 15 years, and 3) a dose at age 11 years with a booster dose at age 16 years (ACIP, unpublished data, 2010). The economic costs and benefits of these meningococcal vaccination strategies in adolescents were assessed from a societal perspective (99,100). A multivariable analysis was performed with a Monte Carlo simulation in which multiple parameters were varied simultaneously over specified probability distributions. These parameters included disease incidence (46%–120% of the 10-year average), case-fatality ratio (34%–131% of the 10-year

average), rates of long-term sequelae, acute meningococcal disease costs (i.e., inpatient care, parents' work loss, public health response, and premature mortality costs), lifetime direct and indirect costs of meningococcal disease sequelae (i.e., long-term special education and reduced productivity), and cost of vaccine and vaccine administration (range: $64–$114). Vaccination coverage (37%–90%) and initial vaccine efficacy (39%–99%) also were varied for evaluation purposes. The vaccine was assumed to be 93% effective in the first year, and then waning immunity was modeled as a linear decline over the next 9 years unless a booster dose was administered. The vaccine effectiveness of the second dose was assumed to be higher with a slower rate of waning immunity. The results of the cost-effectiveness analysis indicate that a 2-dose series at ages 11 years and 16 years has a similar cost-effectiveness compared with moving the single dose to age 15 years or maintaining the single dose at 11 years. However, the number of cases and deaths prevented is substantially higher with the 2-dose strategy (Table 5). Meningococcal disease can cause severe and devastating illness. Disease incidence is low and has decreased since the late 1990s before widespread vaccination of adolescents with MenACWY. Meningococcal disease occurs in all age groups, with an overall incidence in 2011 of 0.2 cases per 100,000 population. The burden of disease is highest among infants aged <1 year (2.6 cases per 100,000 persons), young adults aged 16 through 21 years (0.4 cases per 100,000 persons), and persons aged ≥65 years (0.3 cases per 100,000 persons) (CDC, unpublished data, 2012). Among infants, disease incidence peaks within the first 6 months of life, and most cases in this age group are caused by serogroup B (see Future Meningococcal Vaccines, Areas for Research, and Public Education). Rates of nasopharyngeal carriage are highest in adolescents and young adults (16,17), and adolescents are likely the main source of transmission of the organism to persons in other age groups. The vaccines licensed currently are recommended routinely for adolescents and other persons at increased risk for meningococcal disease. After licensure of the first

MenACWY vaccine in 2005, the initial supply of vaccine was not sufficient to vaccinate all adolescents. ACIP prioritized vaccination for persons aged 11 or 12 years, persons entering high school, and first-year college students living in residence halls. Two years later, in 2007, after reviewing information on the adequacy of vaccine supply, ACIP expanded its recommendation for routine 1-dose vaccination at the earliest opportunity for all adolescents aged 11 through 18 years. At the time, some experts predicted that the vaccine would be effective for up to 10 years, providing protection through the period of highest risk in late adolescence and early adulthood. Since the 2005 ACIP recommendations, additional data have led to improved understanding of meningococcal conjugate vaccines, including new data on duration of vaccine-induced immunity. Antibody persistence studies indicate that circulating antibody declines 3 to 5 years after a single dose of MenACWY. In addition, results from a vaccine effectiveness study demonstrate waning effectiveness, and many adolescents are not protected 5 years after vaccination. ACIP concluded that a single dose of meningococcal conjugate vaccine administered at age 11 or 12 years is unlikely to protect most adolescents through the period of increased risk at ages 16 through 21 years. On the basis of this information, in 2010, ACIP considered two options to optimize protection through late adolescence into early adulthood: 1) moving the single recommended dose to age 15 years or 2) retaining the recommended dose at ages 11 or 12 years and adding a booster dose at age 16 years. The benefits of the booster dose and a desire to continue to protect younger adolescents prompted the recommendation for a routine booster dose at age 16 years (7). In 2010, ACIP revised the recommendations for dosing regimens (e.g., primary series and booster doses) for persons who have functional or anatomic asplenia, who have persistent complement component deficiencies, or who have HIV infection and are otherwise recommended to be vaccinated. For these immunosuppressed persons, a 2-dose primary series was recommended instead of a single dose (7). For persons with persistent complement

component deficiency, a 2-dose primary series will help achieve the high levels of SBA needed to confer protection in the absence of effective opsonization. For persons with asplenia or HIV, a 2-dose primary series will increase the likelihood of a sufficient primary immune response. Booster doses after primary vaccination are important for persons with prolonged increased risk (persons with asplenia, persons with complement component deficiencies, and microbiologists) to ensure high levels of SBA are maintained over time. In 2011 and 2012, ACIP voted to recommend meningococcal vaccination for children aged 2 through 23 months who are at increased risk for disease. ACIP does not recommend routine vaccination of children aged ≤10 years. The number of infants and young children who are or will be at increased risk for meningococcal disease is limited. ACIP reviewed the burden of meningococcal disease among infants and children aged ≤10 years. In the United States, during 1993–2011, average annual rates of meningococcal disease were higher among children aged ≤59 months. However, approximately 60% of disease among children aged ≤59 months is caused by serogroup B N. meningitidis which is not prevented by Hib-MenCY-TT or MenACWY-D. In addition, the highest incidence in the first 5 years of life occurs in infants aged 0 through 6 months, many of whom are too young to have received the minimum 2 or 3 doses of vaccine that likely are needed to provide protection. Of the 205 cases of meningococcal disease in children aged <59 months that occur annually, it is estimated that a universal infant meningococcal vaccination program would prevent 40–50 cases (approximately 25% of cases in this age group) (CDC, unpublished data, 2012). The epidemiology of meningococcal disease is dynamic, and rates of disease could increase in the future requiring a reassessment of immunization strategy.

ACIP recommends routine administration of a MenACWY vaccine for all persons aged 11 through 18 years (Table 6). A single dose of vaccine should be administered at age 11 or 12 years, and a booster dose should be administered at age 16 years. Adolescents who receive their first dose at age 13 through 15 years should receive a

booster dose at age 16 through18 years. The minimum interval between doses of MenACWY is 8 weeks. Adolescents who receive a first dose after their 16th birthday do not need a booster dose unless they become at increased risk for meningococcal disease. Persons aged 19 through 21 years are not recommended routinely to receive MenACWY. MenACWY may be administered up to age 21 years as catch-up vaccination for those who have not received a dose after their 16th birthday. Health-care personnel should use every opportunity to provide the booster dose when indicated, regardless of the vaccine brand used for the previous dose or doses. Persons at increased risk for meningococcal disease also are recommended for routine meningococcal vaccination (Tables 6 and 7). Vaccine product, number of doses, and booster dose recommendations are based on age and risk factor and are described below in detail for each risk group. In general: MenACWY or Hib-MenCYTT is recommended for use in control of outbreaks caused by vaccine-preventable serogroups (A, C, Y, and W-135) of N. meningitidis (Appendix B). An outbreak is defined by the occurrence of at least three confirmed or probable primary cases of meningococcal disease caused by the same serogroup in ≤3 months, with a resulting primary attack rate of ≥10 cases per 100,000 population. For calculation of this threshold, population-based rates are used rather than age-specific attack rates. MenACWY is preferred if the population targeted for vaccination includes age groups for which MenACWY is licensed (i.e., 9 months through 55 years). Detailed recommendations on evaluation and management of suspected outbreaks of meningococcal disease are provided (Appendix B). Routine vaccination against meningococcal disease is not recommended for children aged 2 months through 10 years. Hib-MenCY-TT is licensed as a 4-dose primary series for children aged 6 weeks through 18 months. Hib-MenCY-TT can be administered in any infant for routine vaccination against Hib and will offer some protection against serogroups C and Y meningococcal disease; 4 doses of Hib-MenCY-TT fulfill the primary series and booster dose Hib immunization recommendations. If the reason for use of Hib-MenCY-TT

vaccine is to achieve protection against serogroups C and Y, it should be used for all 4 doses of Hib vaccine. Infants and children who received Hib-MenCY-TT and are travelling to areas with high endemic rates of meningococcal disease such as the "meningitis belt" are not protected against serogroups A and W-135 and should receive a quadrivalent meningococcal conjugate vaccine licensed for children aged ≥9 months before travel. MenACWY-D is licensed as a 2-dose primary series for children aged 9 through 23 months and as a single dose for children ages 2 through 10 years. MenACWY-CRM is licensed as a single dose for children aged 2 through 10 years. Children who receive Hib-MenCY-TT, MenACWY, or both Hib-MenCY-TT and MenACWY before their 10th birthday should receive the routinely recommended doses at age 11 or 12 years and at age 16 years. MenACWY-D, MenACWY-CRM, and Hib-MenCY-TT vaccines are administered intramuscularly, and MPSV4 is administered subcutaneously. Individual doses of all vaccines are 0.5 mL. In persons aged 2 through 55 years, MenACWY and MPSV4 vaccines can be administered concomitantly with other vaccines, but at a different anatomic site, if feasible. Because of limited data suggesting immunologic blunting of the meningococcal vaccine, MenACWY-D should be administered to children aged 2 through 6 years either before, at the same time, or more than 6 months after receipt of DTaP. If MenACWY-D is administered inadvertently in the 6 months after receipt of DTaP, the dose does not need to be repeated. MenACWY-CRM may be administered at any time in relation to DTaP administration. If a child is traveling to a high-risk area or is part of a community outbreak, waiting to administer MenACWY-D following receipt of DTaP is not recommended, even if there may be blunting. There is no evidence of immunologic blunting between Tdap and MenACWY when either MenACWY-D or MenACWY-CRM is administered following administration of Tdap. In children aged 2 through 18 months, Hib-MenCY-TT can be administered concomitantly with other vaccines, but at a different anatomic site, if feasible. In children aged 9 through 23 months, MenACWY-D can be administered with

other vaccines concomitantly in healthy children at different anatomic sites, if feasible. Children with asplenia should not receive MenACWY-D concomitantly with PCV13; if MenACWY-D is used in persons with asplenia, it should be administered at least 4 weeks after completion of all PCV13 doses. All health-care personnel administering vaccinations should be aware of the potential for syncope after vaccination, especially among adolescents, and should take appropriate measures to prevent potential injuries. If syncope occurs, the vaccine recipient should be observed until symptoms resolve. Providers should strongly consider observing patients for 15 minutes after they are vaccinated (97). Vaccination with MenACWY, MPSV4, or Hib-MenCY-TT is contraindicated among persons known to have a severe allergic reaction to any component of the vaccine, including diphtheria or tetanus toxoid. ACIP does not consider a history of GBS to be a contraindication or precaution for meningococcal vaccination. Recommended vaccinations can be administered to persons with minor acute illness (e.g., diarrhea or mild upper-respiratory tract infection with or without low grade fever). Vaccination should be deferred for persons with moderate or severe acute illness until the person's condition improves (101). Because MenACWY, MPSV4, and Hib-MenCY-TT are inactivated vaccines, they can be administered to persons who are immunosuppressed as a result of disease or medications; however, response to the vaccine might be less than optimal. To date, no randomized, controlled clinical trials have been conducted primarily to evaluate use of MPSV4 or MenACWY vaccines in pregnant or lactating women. VAERS reports of exposure to MPSV4 during pregnancy have not identified adverse effects among either pregnant women or newborns of women vaccinated during pregnancy. From VAERS reports available for women found to be pregnant at the time of MenACWY-D vaccination, no major safety concerns associated with vaccination have been identified in the mother or fetus. Pregnancy should not preclude vaccination with MenACWY or MPSV4, if indicated. Women of childbearing age who become aware that they were pregnant at the time of MenACWY

vaccination should contact their health-care provider or the vaccine manufacturer so that their experience might be captured in the manufacturer's registry of vaccination during pregnancy. Any adverse event following receipt of MenACWY, MPSV4 or Hib-MenCY-TT vaccine should be reported to VAERS at telephone 1-800-822-7967 or at http://vaers.hhs.gov/index. MenACWY vaccines were licensed on the basis of data regarding safety and short-term immunogenicity. However, immunogenicity data alone are insufficient to predict vaccine effectiveness and herd immunity effect, which depends largely on the ability of vaccine to alter transmission patterns. Multiple changes to the recommendations have been made since 2005 (Box 1); the effect of these changes needs to be monitored over time for their effectiveness and impact on disease to be assessed. Because serogroup B capsular polysaccharide is poorly immunogenic in humans, vaccine development for serogroup B N. meningitidis has focused on common proteins, including the outer membrane vessicles (OMV) of specific epidemic strains. Efficacy of OMV vaccines has been demonstrated among older children and adults but not among infants and young children, in whom rates of disease are highest (102–105). In addition, the variability in OMV strains causing endemic disease will likely limit their usefulness in the United States (106,107). Two vaccines developed to prevent serogroup B vaccine are in late-stage clinical development in the United States. A multicomponent serogroup B meningococcal vaccine (4CMenB), approved for use in Europe by the European Medicines Agency in January 2013, was developed by sequencing the meningococcal B genome and testing surface antigens for their ability to elicit an immunogenic response. Three novel antigens identified, factor-H binding protein (fHbp), Neisserial adhesion A (NadA), and Neisseria heparin binding antigen (NHBA), were combined with OMV from the New Zealand epidemic strain NZ98/254 (108). The second vaccine, bivalent recombinant lipoprotein 2086 vaccine, contains two families of the same protein, fHbp, as 4CMenB (109). When these vaccines are licensed, vaccines to prevent all five serogroups that cause most meningococcal

disease worldwide will be available for the first time. However, extensive research is needed to understand better how to conduct optimal implementation of noncapsular based meningococcal vaccines. Although the signs and symptoms of meningococcal disease are frequently nonspecific, increasing awareness for meningococcal disease can result in earlier medical care-seeking behavior and improved clinical outcomes. In addition, educating adolescents and their parents about the benefits of receiving MenACWY is key to preventing a substantial number of cases of meningococcal disease. Finally, educating policy makers and the general public about the benefits of receiving MenACWY vaccine might improve vaccination coverage rates and substantially decrease the burden of meningococcal disease in the United States. *A list of the Work Group appears on Page 28. †FDA classification categories available at http://chemm.nlm.nih.gov/pregnancycategories.htm ACIP Membership List As of June 2012 Chair: Carol Baker, MD, Baylor College of Medicine, Houston, Texas. Executive Secretary: Larry Pickering, MD, National Center for Immunization and Respiratory Diseases, CDC, Atlanta, Georgia. Members: Nancy Bennett, MD, University of Rochester School of Medicine and Dentistry, Rochester, New York; Joseph Bocchini, MD, Louisiana State University Health Sciences Center, Shreveport, Louisiana; Douglas Campos-Outcalt, MD, University of Arizona College of Medicine, Phoenix, Arizona; Tamera Coyne-Beasley, MD, University of North Carolina, Chapel Hill, North Carolina; Jeffrey Duchin, MD, University of Washington, Seattle, Washington; Kristen Ehresmann, MPH, Minnesota Department of Health, St. Paul, Minnesota; Renée Jenkins, MD, Howard University School of Medicine, District of Columbia; Wendy Keitel, MD, Baylor College of Medicine, Houston, Texas; Michael Marcy, MD, UCLA Center for Vaccine Research, Torrance, California; Cody Meissner, MD, Tufts Medical Center, Boston, Massachusetts; Sara Rosenbaum, JD, Georgetown University, District of Columbia; Mark Sawyer, MD, University of California at San Diego, California; Jonathan Temte, MD, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; Marietta Vázquez,

MD, Yale University School of Medicine, New Haven, Connecticut. Ex Officio Members: Geoffrey S. Evans, MD, Health Resources and Services Administration, Rockville, Maryland; Jesse Geibe, MD, Department of Defense, CDC, Atlanta, Georgia; Bruce Gellin, MD, National Vaccine Program Office, District of Columba; Richard Gorman, MD, National Institutes of Health, Bethesda, Maryland; Amy Groom, MPH, Indian Health Service, Albuquerque, New Mexico; Mary Beth Hance, Centers for Medicare and Medicaid Services, Baltimore, Maryland; Linda Kinsinger, MD, Department of Veterans Affairs, Durham, North Carolina; Wellington Sun, MD, Food and Drug Administration, Bethesda, Maryland. Liaison Representatives: American Academy of Family Physicians, Jamie Loehr, MD, Ithaca, New York; American Academy of Pediatrics, Michael Brady, MD, Columbus, Ohio, David Kimberlin, MD, Birmingham, Alabama; American Academy of Physician Assistants, Marie-Michèle Léger, MPH, Alexandria, Virgina; American College Health Association, James C. Turner, MD, Charlottesville, Virginia; American College of Obstetricians and Gynecologists, Laura Riley, MD, Boston, Massachusetts; American College of Physicians, Gregory Poland, MD, Rochester, Minnesota; American Geriatrics Society, Kenneth Schmader, MD, Durham, North Carolina; America's Health Insurance Plans, Mark Netoskie, MD, Houston, Texas; American Medical Association, Litjen Tan, PhD, Chicago, Illinois; American Nurses Association, Katie Brewer, MSN, Silver Springs, Maryland; American Osteopathic Association, Stanley Grogg, DO, Tulsa, Oklahoma; American Pharmacists Association, Stephan L. Foster, PharmD, Memphis, Tennessee; Association of Immunization Managers, Kelly Moore, MD, Nashville, Tennessee; Association for Prevention Teaching and Research, W. Paul McKinney, MD, Louisville, Kentucky; Association of State and Territorial Health Officials, José Montero, MD, Concord, New Hampshire; Biotechnology Industry Organization, Clement Lewin, PhD, Cambridge, Massachusetts; Canadian National Advisory Committee on Immunization, Bryna Warshawsky, MDCM, Ontario, Canada; Council of State and Territorial Epidemiologists, Christine Hahn, MD, Boise, Idaho; Department of Health,

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Meningococcal Vaccines Work Group Chair: Lorry Rubin, MD, Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, New York. Members: Carol Baker, MD, Baylor College of Medicine, Houston, Texas; Michael Brady, MD, Ohio State University, Columbus, Ohio; Douglas Campos-Outcalt, MD, University of Arizona College of Medicine, Phoenix, Arizona; Richard Clover, MD, University of Louisville School of Public Health, Lousiville, Kentucky; Kristen Ehresmann, MPH, Minnesota Department of Health, St. Paul, Minnesota; Lucia Lee, MD, Food and Drug Administration, Rockville, Maryland; Martin Luta, MD, Delaware Division of Public Health, Dover, Delaware; Michael Marcy, MD, UCLA Center for Vaccine Research, Torrence, California; W. Paul McKinney, MD, Association for Prevention Teaching and Research, Louisville, Kentucky; Cody Meissner, MD, Tufts University School of Medicine, Boston, Massachusetts; Amy Middleman, MD, Society for Adolescent Health and Medicine, Houston, Texas; Karen O'Brien, MD, US Army Training and Doctrine Command, Fort Monroe, Virginia; Paul Offit, MD, Children's Hospital of Philadelphia,

Philadelphia, Pennsylvania; Georges Peter, MD, Rhode Island Hospital, Providence, Rhode Island; William Schaffner, MD, National Foundation for Infectious Diseases, Nashville, Tennessee; David Stephens, MD, Emory University School of Medicine, Atlanta, Georgia; James C. Turner, MD, American College Health Association, Charlottesville, Virginia; Marietta Vázquez, MD, Yale University School of Medicine, New Haven, Connecticut. Contributors: William Atkinson, MD; Elizabeth Briere, MD; Thomas Clark, MD; Jonathan Duffy, MD; Jessica MacNeil, MPH; Nancy E. Messonnier, MD; Ismael R. Ortega-Sanchez, PhD; Shannon Stokley, MPH, CDC, Atlanta, Georgia. Secretariat (CDC): Amanda C. Cohn, MD, CDC, Atlanta, Georgia. BOX 1. Timeline of meningococcal conjugate vaccine ACIP recommendations, 2005 — 2012 2005: Licensure of and first recommendation for routine vaccination of adolescents with MenACWY-D.* 2006: Because of limited vaccine supply, vaccination was first limited to cohorts of children entering high school and entering college and persons aged 11–55 years at increased risk for meningococcal disease.† 2007: After vaccine supply became sufficient, ACIP recommended vaccination for all adolescents aged 11–18 years.§ ACIP recommended vaccination of children aged 2–10 years at increased risk for meningococcal disease.¶ 2009: ACIP recommended booster dose for persons who remain at increased risk for meningococcal disease, administered every 5 years except for children who received their previous dose prior to their seventh birthday; these children should receive a booster dose 3 years after their previous dose.** 2010: The Food and Drug Administration licensed a second vaccine product, MenACWY-CRM.†† ACIP added a booster dose at age 16 years and recommended a 2-dose primary series for all persons with asplenia, persistent complement component deficiency, and for persons with human immunodeficiency virus infection.§§ 2011: ACIP recommended a 2-dose primary series for children aged 9–23 months at increased risk for meningococcal disease.¶¶ 2012: ACIP recommended a 4-dose primary series of Hib-MenCY-TT for children aged 2–18 months at increased risk for meningococcal disease.*** *Source: CDC

Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54(No. RR-7). † Source: CDC. Notice to readers: limited supply of meningococcal conjugate vaccine, recommendation to defer vaccination of persons aged 11–12 years. MMWR 2006:55;567–8. § Source: CDC. Revised recommendations of the Advisory Committee on Immunization Practices to vaccinate all persons aged 11–18 years with meningococcal conjugate vaccine. MMWR 2007;56:794–5. ¶ Source: CDC. Recommendation from the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MCV4) in children aged 2–10 years at increased risk for invasive meningococcal disease. MMWR 2007;56:1265–6. ** Source: CDC. Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for revaccination of persons at prolonged increased risk for meningococcal disease. MMWR 2009;58:1042–3. †† Source: CDC. Licensure of a meningococcal conjugate vaccine (Menveo) and guidance for use—Advisory Committee on Immunization Practices (ACIP), 2010. MMWR 2010;59:273. §§ Source: CDC. Updated recommendations for use of meningococcal conjugate vaccines—Advisory Committee on Immunization Practices (ACIP), 2010. MMWR 2011;60:72–6. ¶¶ Source: CDC. Recommendation of the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MenACWY-D) among children aged 9 through 23 months at increased risk for invasive meningococcal disease. MMWR 2011;60:1391–2. ***Source: CDC. Infant meningococcal vaccination: Advisory Committee on Immunization Practices (ACIP) recommendations and rationale. MMWR 2013;62:52–4. TABLE 1. Licensed meningococcal vaccines — United States, 1981–2012 Formulation Type Trade name Manufacturer Licensed (yr) Age group Dose(s) Serogroups MPSV4* Polysaccharide Menomune Sanofi Pasteur 1981 ≥2 yrs Single dose A, C, W, and Y MenACWY-D† Conjugate Menactra Sanofi Pasteur 2005 11–55 yrs Single dose A, C, W, and Y MenACWY-D† Conjugate Menactra Sanofi Pasteur 2007 2–10 yrs

Single dose A, C, W, and Y MenACWY-D† Conjugate Menactra Sanofi Pasteur 2011 9–23 mos 2-dose series A, C, W, and Y MenACWY-CRM§ Conjugate Menveo Novartis 2010 11–55 yrs Single dose A, C, W, and Y MenACWY-CRM§ Conjugate Menveo Novartis 2011 2–10 yrs Single dose A, C, W, and Y Hib-MenCY-TT¶ Conjugate MenHibrix GlaxoSmithKline 2012 6 wks–18 mos 4-dose series C and Y *Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM308370.pdf. †Package insert available at http://www.fda.gov/downloads/BiologicBloodVaccines/Vaccines/ApprovedProducts/UCM131170.pdf. §Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM201349.pdf. ¶Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM308577.pdf. BOX 2. Meningococcal vaccination recommendations — Advistory Committee on Immunization Practices, 2013 ACIP recommends meningococcal vaccination for the following groups: FIGURE 1. Rate* of meningococcal disease, by year — United States, 1970–2011† Source: CDC, Unpublished data, National Notifiable Diseases Surveillance System (NNDSS) for 1970–1996 and Active Bacterial Core surveillance (ABCs) system for 1997–2011. * Per 100,000 population. †ABCs cases from 1997–2011 estimated to the U.S. population. In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and might not be representative. Alternate Text: This figure shows the rate per 100,000 population of meningococcal disease in the United States during 1970-2011 by year, using data from the National Notifiable Diseases Surveillance System for 1970-1996 and from the Active Bacterial Core surveillance system for 1997-2011. Incidence has declined annually since a peak of disease in the late 1990s. TABLE 2. Average annual estimated number and rate* of cases of meningococcal disease, by age group and serogroup — United States,

2002–2011† Age group Serogroup B Serogroup C Serogroup Y Other§ Total No. (Rate) No. (Rate) No. (Rate) No. (Rate) No. (Rate) < 1 yr 117 (2.8) 14 (0.3) 38 (0.9) 8 (0.2) 177 (4.3) 0–5 mos 74 (3.6) 5 (0.3) 23 (1.1) 6 (0.3) 108 (5.3) 6–11 mos 43 (2.1) 9 (0.4) 15 (0.7) 2 (0.1) 69 (3.4) 1 yr 28 (0.7) 9 (0.2) 2 (0.1) 3 (0.1) 42 (1.0) 2–4 yrs 38 (0.3) 16 (0.1) 8 (0.1) 7 (0.1) 69 (0.6) 5–10 yrs 31 (0.1) 16 (0.1) 12 (0) 3 (0) 62 (0.3) 11–18 yrs 28 (0.1) 43 (0.1) 43 (0.1) 10 (0) 124 (0.4) 19–21 yrs 26 (0.2) 23 (0.2) 16 (0.1) 3 (0) 68 (0.5) 22–24 yrs 21 (0.2) 22 (0.2) 7 (0.1) 1 (0) 51 (0.4) 25–64 yrs 93 (0.1) 129 (0.1) 125 (0.1) 21 (0) 368 (0.2) ≥65 yrs 20 (0.1) 33 (0.1) 114 (0.3) 19 (0.1) 186 (0.5) Total 402 (0.1) 305 (0.1) 365 (0.1) 76 (0) 1,146 (0.4) Source: CDC, Unpublished data, Active Bacterial Core surveillance (ABCs) system, 2002–2011. *Per 100,000 population. †ABCs cases from 2002–2011 estimated to the U.S. population with 18% correction for underreporting. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System and might not be representative. §Includes serogroup W135, nongroupable, and other serogroups. FIGURE 2. Rate* of meningococcal disease, by age group — United States, 2002–2011† Source: Unpublished data, Active Bacterial Core surveillance (ABCs) system. *Per 100,000 population. †ABCs cases from 2002–2011 estimated to the U.S. population with 18% correction for nonculture-confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System and might not be representative. Alternate Text: This figure shows the rate per 100,000 population of meningococcal disease in the United States during 2002-2011 by age group, using data from the Active Bacterial Core surveillance system. Incidence of meningococcal disease peaks among persons in three age groups: infants and children aged <5 years, adolescents and young adults aged 16 through 21 years, and adults aged ≥65 years. TABLE 3. Rate* of meningococcal disease, by age group and serogroup — United States, 1998–2011† Years Serogroup C, Y, W Serogroup B <1 yr 11–19 yrs ≥20 yrs <1 yr 11–19 yrs ≥20 yrs Rate (CI) Rate (CI) Rate (CI) Rate (CI)

Rate (CI) Rate (CI) 1998–1999 5.86 (4.24–7.90) 1.13 (0.90–1.41) 0.47 (0.41–0.54) 3.32 (2.21–4.86) 0.22 (0.13–0.36) 0.14 (0.11–0.19) 2000–2001 2.32 (1.45–3.55) 0.71 (0.54–0.91) 0.38 (0.33–0.44) 4.30 (3.02–5.95) 0.27 (0.17–0.41) 0.13 (0.10–0.17) 2002–2003 2.06 (1.23–3.26) 0.55 (0.40–0.73) 0.25 (0.21–0.30) 4.30 (3.06–5.90) 0.20 (0.12–0.32) 0.11 (0.09–0.15) 2004–2005 0.77 (0.33–1.55) 0.27 (0.17–0.39) 0.17 (0.14–0.21) 3.10 (2.10–4.42) 0.11 (0.06–0.20) 0.07 (0.05–0.09) 2006–2007 1.20 (0.61–2.11) 0.31 (0.21–0.45) 0.23 (0.19–0.28) 2.11 (1.32–3.22) 0.05 (0.02–0.12) 0.06 (0.04–0.09) 2008–2009 0.93 (0.48–1.69) 0.15 (0.08–0.26) 0.23 (0.19–0.27) 2.92 (1.99–4.18) 0.10 (0.04–0.18) 0.07 (0.05–0.10) 2010–2011 1.37 (0.74–2.33) 0.05 (0.02–0.12) 0.14 (0.11–0.18) 1.33 (0.72–2.29) 0.00 (0.00–0.05) 0.03 (0.02–0.05) Abbreviation: CI = 95% confidence interval. Source: CDC, Unpublished data, Active Bacterial Core surveillance (ABCs) system, 1998–2011. *Per 100,000 population. †ABCs cases from 1998–2011 estimated to the U.S. population with 18% correction for nonculture-confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System and might not be representative. TABLE 4. Summary of serogroup C bactericidal antibody persistence as determined by serum bactericidal antibody assay (SBA) 2–5 years after vaccination with meningococcal vaccines — United States, 2006–2010 Age group at vaccination (yrs) Yrs post- vaccination Serogroup C SBA Vaccine Vaccine recepients No. % with protective antibody levels 11–18* 2 % hSBA ≥1:8 Menveo 273 62 Menactra 185 58 11–18† 3 % rSBA ≥1:128 Menactra 71 75 MPSV4 72 60 2–10† 5 % rSBA ≥1:128 Menactra 161 55 MPSV4 207 42 11–18† 5 % rSBA ≥1:128 Menactra 50 56 MPSV4 68 62 11–17§ 5 % hSBA ≥1:8 Menveo 50 72 MPSV4 50 62 Abbreviations: hSBA = SBA using human complement; rSBA = SBA using baby rabbit complement; MPSV4 = quadrivalent meningococcal polysaccharide vaccine. *Source: Gill C, Baxter R, Anemona A, Ciavarro G, Dull P. Persistence of immune responses after a single dose of Novartis meningococcal serogroup A, C, W-135 and Y CRM-197 conjugate vaccine

(Menveo) or Menactra among healthy adolescents. Human Vaccines 2010;6:881–7. †Source: Advisory Committee on Immunization Practices, unpublished data, 2009. §Source: Jacobson RM, Jackson LA, Reisinger K, Izu A, Odrljin T, Dull T. Antibody persistence and response to a booster dose of a quadrivalent conjugate vaccine for meningococcal disease in adolescents. Pediatr Infect Dis J [Epublished ahead of print]. DOI: 10.1097/INF.0b013e318279ac38. TABLE 5. Summary of cost-effectiveness analyses of different strategies for adolescent vaccination — United States Dosage Cases averted Deaths averted QALY saved Cost per QALY saved ($) No. (Range) No. (Range) No. (Range) No. (Range) 1 dose at 11 yrs 94 (43–165) 11 (5–20) 736 (330–1,130) 256,000 (84,000–650,000) 1 dose at 15 yrs 115 (51–205) 14 (6–25) 850 (390–1,380) 219,000 (63,000–600,000) 1 dose at 11 yrs with booster dose at 16 yrs 184 (92–308) 22 (11–40) 1,442 (610– 2,130) 212,000 (67,000–535,000) Abbreviation: QALY = quality-adjusted life years. Source: Unpublished data with updated estimates, Advisory Committee on Immunization Practices (ACIP) meeting, October 2010. Methods described in Shepard CW, Ortega-Sanchez IR, Scott RD 2nd, Rosenstein NE. Cost-effectiveness of conjugate meningococcal vaccination strategies in the United States. Pediatrics 2005;115:1220–32. TABLE 6. Recommended meningococcal vaccines for use in children and adults — Advisory Committee on Immunization Practices (ACIP), United States, 2012 Age group Vaccine Status 2 mos–10 yrs MenACWY-D (Menactra, Sanofi)* Not routinely recommended; see Table 7 for persons at increased risk MenACWY-CRM (Menveo, Novartis)† Not routinely recommended; see Table 7 for persons at increased risk HibMenCY-TT (MenHibrix, GSK)§ Not routinely recommended; see Table 7 for persons at increased risk 11–21 yrs MenACWY-D or MenACWY-CRM Primary: Booster: 22–55 yrs MenACWY-D or MenACWY-CRM Not routinely recommended; see Table 7 for persons at increased risk ≥56 yrs MPSV4, MenACWY-D, or MenACWY-CRM Not routinely recommended; see Table 7 for persons at increased risk Source: Adapted from American Academy of Pediatrics. Meningococcal infections.

In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red book: 2012 report of the Committee on Infectious Diseases. 29th ed. Elk Grove, IL: American Academy of Pediatrics; 2012:500–9. *Licensed only for persons aged 9 months–55 years. †Licensed only for persons aged 2–55 years. Under investigation for use at ages 2, 4, 6, and 12–15 months. §Licensed only for children aged 6 weeks–18 months. TABLE 7. Recommended immunization schedule and intervals for persons at increased risk for meningococcal disease — Advisory Committee on Immunization Practices (ACIP), United States, 2012* Age group Subgroup Primary vaccination Booster dose† 2–18 mos with high-risk conditions§ Children who: 4 doses of Hib-MenCY-TT (MenHibrix), at 2, 4, 6, and 12–15 months Person remains at increased risk and completed the primary dose or series at age: 9–23 mos with high-risk conditions¶ Children who: 2 doses of MenACWY-D (Menactra), 12 weeks apart** 2–55 yrs with high-risk conditions and not vaccinated previously Persons who: 2 doses of MenACWY, 8–12 weeks apart†† Persons who: 1 dose of MenACWY†† Source: Adapted from American Academy of Pediatrics. Meningococcal infections. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red book: 2012 report of the Committee on Infectious Diseases. 29th ed. Elk Grove, IL: American Academy of Pediatrics; 2012: 500–9. *Includes persons who have persistent complement deficiencies (e.g., C5–C9, properdin, factor H, or factor D), and anatomic or functional asplenia; travelers to or residents of countries in which meningococcal disease is hyperendemic or epidemic; and persons who are part of a community outbreak of a vaccine-preventable serogroup. †If the person remains at increased risk for meningococcal disease. §Infants and children who received Hib-MenCY-TT and are travelling to areas with high endemic rates of meningococcal disease such as the African "meningitis belt" are not protected against serogroups A and W-135 and should receive a quadrivalent meningococcal vaccination licensed for children aged ≥9 months prior to travel. ¶Because of high risk for invasive pneumococcal disease, children with functional or anatomic asplenia should not be immunized with MenACWY-D (Menactra)

before age 2 years to avoid interference with the immune response to the pneumococcal conjugate vaccine (PCV) series. **If an infant is receiving the vaccine prior to travel, 2 doses may be administered as early as 8 weeks apart. ††If MenACWY-D is used, it should be administered at least 4 weeks after completion of all PCV doses. Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services. References to non-CDC sites on the Internet are provided as a service to MMWR readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of pages found at these sites. URL addresses listed in MMWR were current as of the date of publication. All MMWR HTML versions of articles are electronic conversions from typeset documents. This conversion might result in character translation or format errors in the HTML version. Users are referred to the electronic PDF version (http://www.cdc.gov/mmwr) and/or the original MMWR paper copy for printable versions of official text, figures, and tables. An original paper copy of this issue can be obtained from the Superintendent of Documents, U.S.

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