Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

MEMORANDUM

To:	Scott Proestel, MD Director, Division of Epidemiology (DE), Office of Biostatistics and Epidemiology (OBE), Center for Biologics Evaluation and Research (CBER)
Through:	Craig Zinderman, MD, MPH Associate Director for Product Safety, DE, OBE, CBER
From:	Bethany Baer, MD Medical Officer, DE, OBE, CBER
Subject:	Menveo Pediatric Safety and Utilization Review for the Pediatric Advisory Committee (PAC)
Sponsor:	GlaxoSmithKline Biologicals S.A. (formerly Novartis Vaccines and Diagnostics, Inc.)
Product:	Menveo (Meningococcal [Groups A, C, Y, and W-135] Oligosaccharide Diphtheria CRM197 Conjugate Vaccine)
STN:	125300/502
Indication:	For active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135. Menveo is approved for use in persons 2 months through 55 years of age.
Meeting Date:	Pediatric Advisory Committee Meeting, Sep. 14, 2016

1. INTRODUCTION

1.1 Product Description

Menveo is a meningococcal oligosaccharide diphtheria CRM_{197} conjugate vaccine indicated for active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135. Menveo is approved for use in persons 2 months through 55 years of age.

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) currently recommends routine vaccination with a quadrivalent meningococcal conjugate vaccine for all adolescents, with a primary dose in early adolescence and a booster dose at 16 years of age.[1] The ACIP also recommends a meningococcal conjugate vaccine series for persons 2 months through 55 years of age at increased risk for meningococcal disease.[2,3,4] Persons considered to be at increased risk for meningococcal disease vary by age group and include those who have persistent complement deficiencies, have functional or anatomic asplenia, have HIV (if another indication for vaccination exists), are first-year college students aged ≤21 years living in residential housing, travel to or are residents of countries where meningococcal disease is hyperendemic or epidemic, are at risk during a community outbreak attributable to a vaccine serogroup, or are microbiologists routinely exposed to isolates of *Neisseria meningitidis.*

1.2 Regulatory History

Menveo was approved by the FDA on February 19, 2010, for active immunization of individuals 11 through 55 years of age. On January 28, 2011, the FDA approved an expansion of the approved use to include children 2 through 10 years of age. The age range was further expanded on Aug. 1, 2013, to include use in children 2 months through 23 months of age.

2. OBJECTIVE

The objective of this memorandum for the Pediatric Advisory Committee (PAC) is to present a comprehensive review of the postmarketing pediatric safety covering a period including 18 months following the approval of an expanded age range in accordance with Section 505B (i) (1) of the Food and Drug Cosmetic Act [21 U.S.C. §355c]. The trigger for this pediatric postmarketing safety review is the Aug. 1, 2013, approval for the expanded use of Menveo to include children 2-23 months of age. This review will cover the time period of August 1, 2013 – Dec. 31, 2015.

An abbreviated presentation of this review to the PAC is planned for this product as it does not meet the criteria that would necessitate a full oral presentation or a justified abbreviated presentation. Specifically, no new safety signals were identified. During the review period, there were no reports of pediatric deaths that were attributed to Menveo. There was one pediatric death reported in the review period, but it was not attributed to Menveo due to documentation of an alternate cause of death and based on FDA medical/epidemiological review of the case. The product does not have a requirement for a post-marketing safety study or Risk Evaluation and

Mitigation Strategy (REMS), and there have been no label changes regarding safety. Although the PAC presentation is abbreviated, the analysis of the safety data is comprehensive, and this memorandum documents FDA's complete evaluation, including review of adverse event reports in passive surveillance data, periodic safety reports from the manufacturer, data mining, and a review of the published literature.

3. MATERIALS REVIEWED

3.1 Vaccine Adverse Events Reporting System (VAERS)
VAERS reports for Menveo for vaccination dates Aug. 1, 2013 – Dec. 31, 2015

3.2 Manufacturer's Submissions

- Menveo US package insert, dated Aug. 2013
- Letter regarding dose distribution data, dated July 14, 2016
- Risk Management Plan, dated Dec. 2012
- Study V59_34OB final study report. Phase IV safety surveillance study in 11-21 year olds, dated June 18, 2015
- Study V59_54OB final study report. Phase IV safety surveillance study in 2-10 year olds, dated Nov. 24, 2015
- Erratum to Observational Study Report V59_54OB, dated Mar. 30, 2016
- Study V59_74OB protocol. Phase IV safety surveillance study in 2-23 month olds, dated May 19, 2014
- Study V59_04TB interim report for VAMPSS pregnancy study, dated Oct. 15, 2012
- V59_72OB protocol for a postmarketing pregnancy registry, dated Sep. 12, 2013 and Sep. 1, 2014

3.3 FDA Documents

- Menveo Supplement Approval Letter, dated Aug. 1, 2013
- Menveo Pediatric Advisory Committee Review for May 7, 2012 meeting
- Menveo review of pharmacovigilance plan as part of Supplement 226, dated June 13, 2013
- Menveo Study V59_34OB final study report review, dated Nov. 4, 2015
- Menveo Study V59_54OB final study report review, dated Mar. 3, 2016
- Menveo pregnancy study interim report and proposed protocol for replacement pregnancy registry review, dated Nov. 12, 2013

3.4 Publications (see Literature Search in section 8 and endnotes)

4. LABEL CHANGES IN REVIEW PERIOD

There were no label changes related to safety concerns for Menveo during the review period.

5. PRODUCT UTILIZATION DATA

The manufacturer estimates that during the PAC review period of Aug. 2013 - Dec. 2015, there were 3.9 million doses of Menveo distributed in the US and 24.5 million doses distributed globally. During the historic period of Mar. 2010 - Jul. 2013, there were 4.3 million doses distributed in the US and 9.9 million doses distributed globally. Data are not available for pediatric-specific utilization.

6. PHARMACOVIGILANCE PLAN AND POSTMARKETING STUDIES

6.1 Pharmacovigilance Plan

There were no important identified risks for Menveo from pre-licensure clinical trials or from postmarketing safety monitoring. Important potential risks include Guillain-Barré syndrome, acute disseminated encephalomyelitis, Kawasaki disease, anaphylactic reactions, and vaccine failure. These outcomes are each included as outcomes of interest in at least one of the postmarketing commitment studies, either directly or through inclusion as an event requiring hospitalization. Additional important potential risks in the pharmacovigilance plan were severe injection site reactions and severe systemic reactions which are addressed in the Adverse Reaction section of the package insert. The pharmacovigilance plan states that the areas of important missing information are: safety during pregnancy and lactation, use in subjects with altered immunocompetence, and use in patients with bleeding disorders. The package insert contains statements that safety and effectiveness have not been established in pregnant women or evaluated in immunocompromised persons. Additionally, there is a pregnancy registry to gain information on use during pregnancy.

6.2 Postmarketing Commitment (PMC) in Adolescents

This study was a phase IV self-controlled case-series study in 48,899 subjects vaccinated with Menveo between 11-21 years of age. There were 26 pre-specified events of interest that included certain neurological, autoimmune, vascular, musculoskeletal, and hematological disorders. These events of interest were selected based on conditions found in this age group in other vaccine safety studies. Chart review to confirm diagnosis and event onset timing was conducted for certain pre-specified events and for events that had an elevated relative incidence (RI) in the risk window versus the control window using automated health care billing data. Following the chart review, Bell's palsy was the single event of interest that had a statistically significant adjusted increased RI. The RI was 2.9 (95% confidence interval: 1.1-7.5) in the 1-84 days following vaccination compared to a subsequent nine month control period. In the subset of cases where the patient received both Menveo and a concomitant vaccine, the RI for Bell's palsy was 5.0 (95% CI: 1.4-17.8). Of note, facial paresis is included in the Adverse Reactions section of the package insert. There were no other events of interest with an increased relative incidence found in this study, but many of the less common events of interest did not have a sufficient number of cases to meet the study's pre-specified power requirement for the self-controlled case-series analysis.

6.3 Postmarketing Commitment in Children 2-10 Years of Age

This descriptive, observational phase IV safety study included subjects aged 2-10 years old who received Menveo as part of their regular health care. The study was continued for 3 years in a health maintenance organization and included 327 subjects. Because there was not an ACIP recommendation for routine use of a meningococcal conjugate vaccine in this age group, the study had a limited sample size. The study included 26 pre-specified events of interest occurring in the 1 year after vaccination. Like the adolescent PMC, the events of interest for this study included certain neurological, autoimmune, vascular, musculoskeletal, and hematological disorders that were selected based on conditions found in this age group in other vaccine safety studies. There was only 1 chart-confirmed pre-specified event of interest (new-onset asthma) that occurred during the observation period of the study. Additionally, the serious medically-attended events did not show any trend in types of events or temporal clustering following the vaccination. While the data from this study was limited due to sample size, there were no new safety concerns identified.

6.4 Postmarketing Commitment in Children 2-23 Months of Age

This ongoing descriptive safety surveillance study of the use of Menveo in children 2 months through 23 months of age was outlined in the Aug. 1, 2013, approval letter for expansion of Menveo use to this age group. The endpoints of interest include all medical events that require emergency room visits or hospitalizations within the 6 months following vaccination with Menveo. If there is no ACIP recommendation for routine use of a meningococcal conjugate vaccine in this age group, then the study will be complete after 3 years of observation (November 2017). If there is an ACIP recommendation for routine use in this age group, then the study will continue and will include 20,000 children or last 1 year, whichever occurs last.

6.5 Pregnancy Safety Postmarketing Commitment

Following initial approval in 2010, a study to collect safety data on the use of Menveo during pregnancy was started using the Vaccines and Medications in Pregnancy Surveillance System (VAMPSS). An interim report on this study in 2013 showed that the study was not feasible due to limited enrollment of patients and will not be completed. Instead, a pregnancy registry was initiated and will include 100 exposed patients over a 3 year period. This study is to be completed in August 2018.

7. ADVERSE EVENT REVIEW

7.1 Methods

The Vaccine Adverse Event Reporting System (VAERS) was queried for adverse event reports following use of Menveo between Aug. 1, 2013, and Dec. 31, 2015. Spontaneous surveillance systems such as VAERS are subject to many limitations, including underreporting, variable report quality and accuracy, inadequate data regarding the numbers of doses administered, and lack of direct and unbiased comparison groups.

7.2 Results

The results of the VAERS search of adverse event reports for Menveo during the review period are listed in Table 1 below. Table 1: VAERS Reports for Menveo (Aug. 1, 2013 through Dec. 31, 2015)

	Serious Non-Fatal (includes OMIC)*		Deaths		Non-serious		Total	
Age	US	Non-US	US	Non-US	US	Non-US	US	Non-US
<2 years	0	3	0	0	17	0	17	3
2-<18 years	127	22	1	0	1244	0	1372	22
≥18 years	39	9	0	0	381	0	420	9
Unknown	18	24	0	0	121	0	139	24
Total	184	58	1	0	1763	0	1948	58

*Serious adverse events (including Otherwise Medically Important Conditions (OMIC)) are defined in 21CFR600.80

7.2.1 Deaths

There was a single report of a death following Menveo. A 16-year-old female with a history of asthma was diagnosed with a pontine glioma 5 months after receiving Menveo, Havrix, and Gardasil and three months after receiving Fluvirin. She died (b) (6) months following the brain tumor diagnosis.

7.2.2 Non-fatal serious reports

During the reporting period, there were 127 non-fatal serious reports in patients <18 years of age in the US. Of these, 11 reports were duplicates. The principal adverse events in the 116 unique cases are summarized in Table 2 below.

Table 2. Serious VAERS US Reports for Menveo (Aug. 1, 2013-Dec. 31, 2015; <18 years of age)

Principal Adverse Event*	n=116
Skin disorders	
Injection site reaction or cellulitis	27 (includes 1 with abscess)
Erythema multiforme	2
Rash (non-allergic)	1
Nervous system disorders	
Presyncope/Syncope	36 (includes 4 with convulsive syncope)
Seizure	7 (includes 1 with pre-existing seizure disorder)
Postural Orthostatic Tachycardia Syndrome	2
Bell's palsy	3 (includes 1 with concurrent ear infection and 1 with polyneuritis)
Facial numbness with tooth abscess	1
Polio-like syndrome	1
Headache, weakness	1

Principal Adverse Event*	n=116
Immunologic disorders	
Allergic/hypersensitivity reaction	22 (includes 4 with anaphylactoid reactions)
Other immunologic disorders (each diagnosis with a single case)	3
Psychiatric disorders	
Suicidal ideation	2
Other psychiatric disorders (each diagnosis with a single case)	3
Neoplasms	
Osteosarcoma	1
Respiratory disorders	
Pneumonia, sepsis	1
Gastrointestinal disorders	
Appendicitis	1
Vomiting with dehydration or with fever	2

*Based on review of the reported signs, symptoms, and diagnoses, the most important clinical entity was determined to be the principal adverse event.

There were 3 serious reports in the newly approved age group of 2-23 months. All of these reports were from outside of the US (and involved several concomitant vaccines that are not approved in the US). Two of the reports appear to refer to the same patient and event, resulting in two cases total in this age group. The first case was a 6-month-old female who had two episodes of a febrile "convulsive syndrome" several hours after vaccination with Rotateq, Quinvaxem, Opvero, and Menveo. She was found to have pansinusitis and right otomastoiditis, and she improved with antibiotics without further convulsive symptoms. The second case was an 11-month-old female who received Menveo, Varilrix, MMR II, Avaxim, and Prevenar 13. On the day of vaccination, she had an episode of vomiting, cyanosis in the limbs, hypotonia, and fever. She had a second episode of cyanosis in the limbs, hypotonia, and fever 3 days later. No diagnosis was provided in the report, but it was stated that the patient had recovered.

7.2.3 Non-serious reports

During the reporting period, there were 1763 non-serious reports with 1261 of those involving patients <18 years old. Table 3 below lists the 10 most frequently reported MedDRA preferred terms (PTs) for these reports. Of note, these PTs are not mutually exclusive; a single report can include multiple PTs.

Table 3. Ten most frequently reported PTs for non-serious VAERS reports (Aug. 1, 2013-Dec. 31, 2015; <18 years of age)

MedDRA PT	No. of Reports	Label
No adverse event (*see text below)	322	N/A
Injection site erythema	225	Labeled
Injections site swelling	180	Labeled
Erythema	154	Labeled
Incorrect product storage	116	N/A (not an AE)

MedDRA PT	No. of Reports	Label
Injection site warmth	109	Labeled ("inflammation")
Injection site pain	98	Labeled
Dizziness	75	Labeled
Skin Warm	74	Labeled ("inflammation")
Incorrect storage of drug	64	N/A (not an AE)

The non-serious adverse events are consistent with those seen in the pre-licensure studies and are included in the package insert. *The PT of no adverse event often accompanies a report of an event related to the vaccination (e.g., a vaccine storage or administration error) that was not associated with a clinical adverse event even though it resulted in a VAERS report. The PTs related to incorrect product storage refer to storage and handling errors such as temperature deviations when refrigerating the vaccine.

7.2.4 Historical VAERS comparison

The PAC review presented on May 7, 2012, reviewed the first 23 months of licensure for Menveo during which time the product was approved for active immunization of individuals 11 through 55 years of age and then expanded to use in 2 through 10 year olds. The most common serious and non-serious PTs for that period were similar to those presented in Table 2 and 3 for this PAC review period. While the number of cases was lower during the period immediately following licensure, the most common serious PTs were syncope, injection site reaction/cellulitis, and fever. Similarly, there continues to be the largest number of serious AE reports associated with injection site reaction/cellulitis and syncope in the current PAC review period. The most common PTs for clinical adverse events in non-serious reports for <18 year olds in the current review period are consistent with the non-serious PTs seen in 2012 with injection site symptoms (pain, warmth, erythema, swelling) continuing to be the most commonly reported adverse events.

7.3 Data mining

Data mining was performed to evaluate whether any reported events following the use of Menveo were disproportionally reported compared to other vaccines in the VAERS database. The background database contains VAERS reports since 1990. Disproportionality alerts do not, by themselves, demonstrate causal associations; rather, they may serve as a signal for further investigation. A query of Empirica Signals Management with the US VAERS Vac Name run with a data lock date of Sep. 22, 2015, identified four PTs with a disproportional reporting alert for Menveo (EB05>2; the EB05 refers to the lower bound of the 90% confidence interval around the Empiric Bayes Geometric Mean). Of note, these PTs are not mutually exclusive; a single report can include multiple PTs. The four PTs were:

- *Incorrect product formulation administered* (EB05=16.9): Many of these cases involved administration errors in which only one of the two Menveo components was given to the patients due to a failure to reconstitute the lyophilized MenA component with the liquid MenCWY component. Almost all of the cases involved no adverse event.
- *Wrong technique in drug usage process* (EB05=11.6): Cases with this PT were reviewed and the majority involved only one vial of the two component vaccine being given. This PT was often associated with the PT for "no adverse event."

- *Immunisation* (EB05=2.17): These cases were reviewed and all refer to repeat immunization following an administration error which resulted in receipt of an incomplete dose of Menveo.
- *No adverse event* (EB05=2.07): These cases were reviewed and many of them refer to an administration or product storage error that resulted in a VAERS report but not in a clinical adverse event for the recipient.

7.4 Administration errors related to the two vial presentation

Menveo is supplied as two vials that must be combined prior to intramuscular injection. The MenA component is lyophilized and is to be reconstituted with the liquid MenCYW-135 component immediately before administration. As seen in the data mining results, there have been reports of administration errors associated with improper reconstitution of the vaccine. The CDC and FDA recently published an article in Morbidity and Mortality Weekly Report analyzing the reports of administration errors seen with Menveo. [5] This MMWR article identified VAERS reports associated with patients receiving only one component of the two component vaccine from March 2010 to Sep. 2015. As noted in the MMWR publication, 85% of the VAERS reports in their analysis did not involve an adverse event associated with the administration error. While relatively infrequent compared to the total usage of Menveo vaccine, reports of reconstitution errors have been and continue to be consistently submitted to both the sponsor and VAERS. Instructions for reconstitution are included in the package insert in the highlights section under the "Dosage and Administration" and "Dosage Forms and Strengths" sections. There are three diagrams illustrating the proper preparation of the vaccine under "Reconstitution Instructions" in the Full Prescribing Information. Additionally, each of the two vials is labeled with the message "NOT TO BE USED ALONE" and instructions on reconstitution. The sponsor has implemented additional educational resources to reinforce the proper reconstitution methods with health care providers, including a "leave behind" reconstitution flashcard for healthcare providers and vaccine administrators, a video of the reconstitution process, and the availability of elastitags that customers can use to bind the two component vials together. (b) (5)

7.5 Periodic Adverse Event Report (PAER)

The manufacturer's postmarket periodic safety reports for Menveo covering the surveillance period were reviewed. The adverse events reported in the periodic safety reports were consistent with those seen in VAERS. No additional safety issues were identified.

8. Literature Review

A search of the US National Library of Medicine's PubMed.gov database on 5/16/2016 for peer-reviewed literature published between Aug. 1, 2013, and Dec. 31, 2015, with the search term "Menveo" and "safety" retrieved 100 articles. The titles and abstracts of these articles were reviewed and those with the most relevant safety information are listed below. No new safety issues for Menveo were identified in these articles.

Article	Safety Conclusion
Nolan TM, Nissen MD, Naz A, et al. Immunogenicity and safety of a CRM-conjugated meningococcal ACWY vaccine administered concomitantly with routine vaccines starting at 2 months of age. Hum Vaccin Immunother. 2014 Feb;10(2):280-9.	This study of Menveo administered with routine infant vaccines starting at 2 months of age concluded that Menveo was well tolerated and immunogenic in this age group.
Abdelnour A, Silas PE, Lamas MR, et al. Safety of a quadrivalent meningococcal serogroups A, C, W and Y conjugate vaccine (MenACWY-CRM) administered with routine infant vaccinations: results of an open-label, randomized, phase 3b controlled study in healthy infants. Vaccine. 2014 Feb 12;32(8):965-72.	This phase IIIb, open-label study evaluated the safety of Menveo given with routine infant vaccinations. There were 7744 subjects and 1898 of them were in the detailed safety arm. The rates of solicited adverse events and SAEs were similar in the Menveo + routine vaccines group versus the routine vaccines alone group.
Baxter R, Reisinger K, Block SL, et al. Antibody persistence and booster response of a quadrivalent meningococcal conjugate vaccine in adolescents. J Pediatr. 2014 Jun;164(6):1409-15.e4.	This article describes a phase III study of Menveo given as a booster dose to 730 adolescents 3 years after primary vaccination with either Menveo or Menactra. The booster dose was found to be immunogenic and well tolerated.
Huang LM, Chiu NC, Yeh SJ, et al., Immunogenicity and safety of a single dose of a CRM-conjugated meningococcal ACWY vaccine in children and adolescents aged 2-18 years in Taiwan: Results of an open label study. Vaccine. 2014 Sep 8;32(40):5177-84.	This article described a phase III, open-label study of a single injection of Menveo in 34 subjects in Taiwan aged 2-18 years of age. The authors concluded that the single dose of Menveo had a robust immune response and an acceptable safety profile in these subjects.
Tregnaghi M, Lopez P, Stamboulian D, et al., Immunogenicity and safety of a quadrivalent meningococcal polysaccharide CRM conjugate vaccine in infants and toddlers. Int J Infect Dis. 2014 Sep;26:22-30.	This article described a phase III study of Menveo given as part of routine vaccines starting at 2 months of age. The authors concluded that the vaccination in infants and toddlers was immunogenic and well tolerated.
Ilyina N, Kharit S, Namazova-Baranova L, et al. Safety and immunogenicity of meningococcal ACWY CRM197-conjugate vaccine in children, adolescents, and adults in Russia. Hum Vaccin Immunother. 2014;10(8):2471-81.	This is a phase III, open-label study on Menveo given to 197 subjects in Russia aged 2 years and above. The authors concluded the vaccine was immunogenic and had an acceptable safety profile.
Lee HJ, Chung MH, Kim WJ, et al. Immunogenicity and safety of a novel quadrivalent meningococcal conjugate vaccine (MenACWY-CRM) in healthy Korean adolescents and adults. Int J Infect Dis. 2014 Nov;28:204-10.	This phase III study evaluated the immunogenicity and safety of Menveo teenagers and adults in Korea. There were no serious adverse events, deaths, or premature withdrawals reported during the study. The authors concluded that the vaccine was well tolerated.
Read RC, Baxter D, Chadwick DR, et al. Effect of a quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. Lancet. 2014 Dec 13;384(9960):2123-31.	This study evaluated possible herd immunity through carriage rates following vaccination with either Menveo or 4CMenB (serogroup B). Menveo was found to be well-tolerated without new safety concerns. In the study, Menveo had lower rates of local pain and myalgia than 4CMenB did.
Block SL, Christensen S, Verma B, et al. Antibody persistence 5 years after vaccination at 2 to 10 years of age with Quadrivalent MenACWY-CRM conjugate vaccine, and responses to a booster vaccination. Vaccine. 2015 Apr 27;33(18):2175-82.	This extension study conducted in 2013 included children vaccinated previously or naïve to Menveo who then received a booster or primary dose. The authors stated that there were no safety concerns raised during the study.
Lalwani S, Agarkhedkar S, Gogtay N, et al. Safety and immunogenicity of an investigational	This article describes the phase 3, open-label study of the immunogenicity and safety of Menveo in healthy Indian

Article	Safety Conclusion
meningococcal ACWY conjugate vaccine (MenACWY-CRM) in healthy Indian subjects aged 2 to 75 years. Int J Infect Dis. 2015 Sep;38:36-42.	subjects conducted for licensure in India. There were 180 subjects in the study and adverse events were collected for 29 days post-vaccination. The authors concluded that Menveo was well tolerated in the study.

9. CONCLUSION

This postmarketing pediatric safety review of passive surveillance adverse event reports, periodic safety reports, and the published literature for Menveo does not indicate any new safety concerns. This PAC review was initiated due to the expansion of use to include children 2-23 months old, and there were very few adverse event reports submitted for this age group. For all of the pediatric age groups, most adverse event reports were non-serious and were consistent with the known safety profile of Menveo. However, there have been reports of administration errors related to failure to follow the reconstitution instructions. In addition to the instructions on reconstituting the vaccine provided in the product labelling, the sponsor has implemented methods to educate health care providers on the reconstitution of Menveo and continues to evaluate this issue. A completed postmarketing commitment study found an increased relative incidence of Bell's palsy, which is a subset of the labeled event of facial paresis. There were no new safety concerns found in the PMC studies.

10. RECOMMENDATIONS

FDA recommends continued routine safety monitoring of Menveo. The results of the postmarketing study in 2-23 month olds and the pregnancy registry will be reviewed.

[1] CDC. Prevention and control of meningococcal disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013:62 (2):1-32.

[2] CDC. Infant meningococcal vaccination: Advisory Committee on Immunization Practices (ACIP) recommendations and rational. MMWR 2013:62:52-4.

[3] CDC. Recommended Immunization Schedule for Persons Age 0 Through 18 Years, United States, 2016. Accessed on May 6, 2016 at http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

[4] CDC. Use of MenACWY-CRM Vaccine in children Aged 2 Through 23 Months at Increased Risk for Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices, 2013. MMWR 2014:63 (24):527-530.

[5] Su JR, Miller ER, Duffy J, Baer BM, Cano MV. Notes from the Field: Administration Error Involving a Meningococcal Conjugate Vaccine – United States, March 1, 2010-September 22, 2015. MMWR Morb Mortal Wkly Rep. 2016 Feb 19;65(6):161-2.