MINUTES OF THE PEDIATRIC ADVISORY COMMITTEE

The public meeting was convened 8:00 a.m. to 4:25 p.m. on September 14, 2016

Members Present (Voting)	**Temporary Voting Members (Voting Consultants)**
Mary Cataletto, MD Avital Cnaan, PhD Melody Cunningham, MD Robert Dracker, MD, MHA, MBA, CPI Peter Havens, MD, MS Sarah Hoehn, MD, MBe Mark Hudak, MD *(Chair)* Bridgette Jones, MD Christy Turer, MD, MHS Kelly Wade, MD, PhD, MSCE Michael G. White, MD, PhD (presiding Chair for Sustiva)	Premchand Anne, MD, MPH Jeffrey Campbell, MD, MS Gwenyth Fischer, MD Marc Moon, MD Wael Sayej, MD Tor Shwayder, MD Kenneth E. Towbin, MD (by phone for the Sustiva review only)
Non-Voting Members Bridgette Jones, MD	**Designated Federal Official (DFO)** Marieann Brill, MBA, RAC, MT (ASCP)

U.S. Food and Drug Administration (FDA) Participants

Office of Pediatric Therapeutics Robert "Skip" Nelson, MD, PhD Judith Cope, MD, MPH LCDR Kenneth Quinto, MD, MPH **CDER DPMH** John Alexander, MD, MPH Miriam Dinatale, DO Ethan Hausman, MD Mona Khurana, MD LCDR Erica Radden, MD Amy Taylor, MD, MHA Carolyn Yancey, MD **CDER OSE**: Allen Brinker, MD CAPT Corrinne Kulick, PharmD TL Travis Ready, PharmD Paula Gish, RPh Patty Greene, PharmD Lisa Harinstein, PharmD, BCPS LCDR Dipti Kalra, RPh Joann Lee, PharmD Robert Levin, MD Karen Long, PharmD	Kusum Mistry, PharmD Saharat Patanavanich, PharmD, BCACP Anhtu Nguyen, RPh Tracy Pham, PharmD Peter Waldron, MD Ron Wassel, PharmD **CDER Divison** Alla Bazini, MD Yodit Belew, MD Leah Crisafi, MD Marjorie Dannis, MD Patricia Dinndorf, MD Norman Hershkowitz, MD, PhD Leonard Kapcala, MD Anil Rajpal, MD Peter Starke, MD Ergun Velidedeoglu, MD Prabha Viswanathan, MD	**CBER** Bethany Baer, MD CAPT Craig Zinderman, MD, MPH **CDRH** Vasum Peiris, MD, MPH, FAAP, FACC, FASE George Aggrey, MD, MPH Colin Anderson-Smits, MPH Ryan Foringer, BS Kellie Kelm, PhD Steven Kurtzman, MD John Laschinger, MD Courtney Lias, PhD Chin-Hsin K. (Jenny) Liu, RN, BSN, MSN Shirin Marfatia, PhD Lauren Min, MPH Catherine Ricketts, RN, BSN Priya Venkataraman-Rao, MD Jacqueline Wieneke, MD Rebecca Ward, MPH

Welcome and Introductory Remarks

- Marieann Brill, Designated Federal Official, Pediatric Advisory Committee, Office of Pediatric Therapeutics, Office of Special Medical Programs, FDA
- Mark Hudak, MD, Chair of the Pediatric Advisory

Presentation: Risk-based Assessment Review Procedure - LCDR Kenneth Quinto, MD, MPH

This presentation provided a brief review of the FDA risk-based assessment of the pediatric post-marketing safety and utilization reviews. It also provided an overview on how the general public can access the web-posted reviews and submit comments to the docket.

Open Public Hearing

An opening statement was read by the Marieann Brill, DFO.
Craig Butler, the National Executive Director of the Cooley's Anemia Foundation read a statement.

Presentations

Center for Biologics Evaluation and Research (CBER): Abbreviated Review of Adverse Event Presentations

MENVEO (Meningococcal [Groups A, C, Y, and W-135] Oligosaccharide Diphtheria CRM197 Conjugate Vaccine) Abbreviated Presentation: Judith Cope MD, MPH

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance**.**

IXIARO (Japanese Encephalitis Vaccine, Inactivated, Adsorbed)
Abbreviated Presentation: Judith Cope MD, MPH

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance.

Center for Drug Evaluation and Research (CDER): Standard Review of Adverse Event Presentations

Sustiva (efavirenz) – Carolyn Yancey, MD

The Safety Review concluded that FDA is considering adding the term catatonia to labeling, and recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 14; No - 0; Recused - 1) with the FDA proposal to considering adding the term catatonia to labeling.
- The Committee voted against (Yes - 5; No - 9; Abstain - 1; Recused - 1) the FDA to return with drug levels and genetic variations in the labeling.
- The Committee (Yes - 14; No - 0; Recused - 1) with the FDA proposal to continue post-marketing safety surveillance.

The Committee discussed the role of therapeutic drug levels, the risks to rapid metabolizers, how genomic testing would be useful, and the importance of adding this information to the label. The Committee welcomed a future discussion and review of these general issues.

Topamax (topiramate) - Mona Khurana, MD

The Safety Review concluded that no new pediatric safety signals were identified. FDA plans to monitor for anorexia nervosa, bulimia nervosa, and acute hepatic failure in all patient populations. FDA will review the PREA PMR once it is submitted and recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance.

Asacol/Asacol HD and Delzicol (mesalamine) - LCDR Erica Radden, MD

The safety review identified benign intracranial hypertension as a safety signal, but imaging was insufficient to distinguish the events from cerebral venous thrombosis. The PAC disagreed. The safety review identified nephrogenic diabetes insipidus as a drug related safety signal. FDA recommends (1) no change to product labeling for any mesalamine product regarding benign intracranial hypertension; (2) adding nephrogenic diabetes insipidus to the list of adverse reactions that have been reported in the post-marketing section of product labeling for mesalamine products; and (3) continued post-marketing safety surveillance.

- The Committee voted against (Yes - 0; No - 15) the FDA recommendation to not change the label regarding benign intracranial hypertension. They requested that FDA further review this possible association.
- The committee concurred (Yes - 15; No - 0) with the FDA recommendation to add nephrogenic diabetes insipidus to the list of adverse reactions that have been reported in the post-marketing section of product labeling for mesalamine products.

Kepivance (palifermin) - LCDR Erica Radden, MD

The safety review concluded that the cases were related to patient's underlying medical conditions, confounded by concomitant medications, or had limited information to assess causality. No new safety signals were identified, however, the review highlights the risks of Kepivance off-label use for pulmonary indications and such practice is discouraged unless further study shows a positive risk benefit profile. The FDA recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance.

Presentation: Update on Exjade (deferasirox) - Peter Waldron, MD

Exjade was presented to the PAC in September 2015 and the PAC requested that FDA review any data regarding safety of continued medication with Exjade (deferasirox) to children who have fever and report back to the PAC. This presentation provided updated information on FDA's ongoing evaluation of acute illness events and adverse effects of kidney and liver injury. A final report is expected in March 2017 which will include a discussion of possible label changes.

Presentation: Pregnancy and Lactation Labeling Rule (PLLR) - Miriam Dinatale, DO

This presentation provided an introduction, history, and overview of the PLLR which went into effect on June 30, 2015.

Bloxiverz (neostigmine methylsufate) - Amy Taylor, MD, MHS

The review noted five reports of pulmonary edema after administration of neostigmine. All cases could be considered confounded by potential airway management difficulties that can occur in patients with advanced airway support. The FDA recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue ongoing monitoring.

Doryx (doxycycline hyclate) – Amy Taylor, MD, MHS
The review concluded that no new safety signals were identified. The FDA recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance.

Xolair (omalizumab) – Amy Taylor, MD, MHS

The review concluded that no new safety signals were identified. The FDA recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0) with the FDA proposal to continue post-marketing safety surveillance.

Karbinal ER (cabinoxamine maleate) – Ethan Hausman, MD
The review concluded that no new safety signals were identified. The FDA recommends continued post-marketing safety surveillance.

- The Committee concurred (Yes - 15; No - 0; Recused - 1) with the FDA proposal to continue post-marketing safety surveillance.

Center for Devices and Radiological Health (CDRH): Annual Post-Market HDE Reviews:

Berlin Heart EXCOR® Pediatric Ventricular Assist Device (VAD) – Rebecca Ward, MPH

The annual review of the ADN, published literature, and MDRs did not identify any new or unexpected risks for the pediatric population, and the benefit/risk profile of the Berlin Heart EXCOR® Pediatric VAD for its Indication for Use continues to support the HDE for which the exemption was granted.

- The Committee concurred (Yes - 14; No - 0; Recused - 1) with the FDA proposal to continue surveillance and report the annual distribution number, literature review, MDR review to the PAC in 2017.

Contegra Pulmonary Valved Conduit - George Aggrey, MD, MPH

The annual review of the ADN, published literature, and MDRs did not identify any new or unexpected risks for the pediatric population, and the benefit/risk profile of the Contegra Pulmonary Valved Conduit for its Indication for Use continues to support the HDE for which the exemption was granted.

- The Committee concurred (Yes - 14; No - 0; Absent - 1) with the FDA proposal to continue surveillance and report the annual distribution number, literature review, MDR review to the PAC in 2017.

Pleximmune - Kellie Kelm, PhD

The annual review of the ADN, published literature, and MDRs did not identify any new or unexpected risks for the pediatric population, and the benefit/risk profile of the Pleximmune for its Indication for Use continues to support the HDE for which the exemption was granted.

- The Committee concurred (Yes - 14; No - 0; Absent - 1) with the FDA proposal to continue surveillance and report the annual distribution number, literature review, MDR review to the PAC in 2017.

Enterra™ Therapy System - Catherine Ricketts, RN, BSN
The annual review of the ADN, published literature, and MDRs did not identify any new or unexpected risks for the pediatric population, and the benefit/risk profile of the Enterra™ Therapy System for its Indication for Use continues to support the HDE for which the exemption was granted.

- The Committee concurred (Yes - 13; No - 0; Recused - 1; Absent - 1) with the FDA proposal to continue surveillance and report the annual distribution number, literature review, MDR review to the PAC in 2017.

Elana Surgical Kit (HUD) -Colin Anderson-Smits, MPH

The review concluded that there was no reported use, no sales, and literature review. The post approval study will continue with reported sales and use.

- The Committee concurred (Yes - 13; No - 0; Absent - 2) with the FDA proposal to continue surveillance and report the annual distribution number, literature review, MDR review to the PAC in 2017.

Adjournment
Mark Hudak, MD, Chair