

MINUTES OF THE PEDIATRIC ADVISORY COMMITTEE (PAC)

The public meeting was convened 8:30 a.m. to 12:45 p.m. on September 12, 2017

<p><u>Members Present (Voting)</u> Kelly Wade, MD, PhD (Acting Chair) David Callahan, MD Mary Cataletto, MD, FAAP Melody Cunningham, MD Robert Dracker, MD, MHA, MBA, CPI Peter Havens, MD, MS Sarah Hoehn, MD, MBe, FAAP Bridgette Jones, MD Wael Sayej, MD Christy Turer, MD, MHS, FAAP, FTOS Michael G. White, MD, PhD, FACC, FAAP</p>	<p><u>Temporary Voting Members (Voting Consultants)</u> Jeffrey Campbell, MD, MS Amy Celento, BS Gwentyth Fischer, MD James McGough, MD Kathleen Neville, MD, MS, FAAP, FCCP</p>
<p><u>Non-Voting Members</u> Bridgette Jones, MD Ronald Portman, MD</p>	<p><u>Designated Federal Official (DFO)</u> Marieann Brill, MBA, RAC, MT (ASCP)</p>

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

<p>Office of Pediatric Therapeutics Judith Cope, MD, MPH Robert “Skip” Nelson, MD, PhD Ann McMahan, MD, MS LCDR Kenneth Quinto, MD, MPH</p> <p>CDER DPMH John Alexander, MD, MPH Ethan Hausman, MD Yeruk (Lily) Mulugeta, MD Carolyn Yancey, MD</p>	<p>CDER OSE: Vicky Chan, PharmD, MD Robert Levin, MD Karen Long, PharmD Shekhar H. Mehta, PharmD, MS LT Ofir Noah Nevo, PharmD, BCPP LT Travis Ready, PharmD</p> <p>CDER Division Teresa, Buracchio, MD Natalie Getzoff, MD Marc Stone, MD</p>	<p>CDRH George Aggrey, MD, MPH Chin-Hsin K. (Jenny) Liu, RN, BSN, MSN Courtney Lias, PhD Lauren Min, MPH Vasum Peiris, MD, MPH, FAAP, FACC, FASE Catherine Ricketts, RN, BSN Dora Vega, MD, PhD Priya Venkataraman-Rao, MD</p>
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Welcome and Introductory Remarks

- Marieann Brill, Designated Federal Official (DFO), Pediatric Advisory Committee, Office of Pediatric Therapeutics, Office of Special Medical Programs, US Food and Drug Administration (FDA)
- Kelly Wade, MD, PhD, Acting Chair of the Pediatric Advisory Committee

Office of Pediatric Therapeutics: Presentation: State of the PAC – Robert “Skip” Nelson, MD, PhD

This presentation summarized the past and ongoing process for mandated pediatric post-market safety reviews to the PAC, starting with abbreviated reviews and transitioning to web-posting for CDER and CBER products. A proposal of web-posting for annual device reviews that do not have new safety concerns was also presented, and will be implemented in Spring 2018.

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Open Public Hearing

An opening statement was read by the Marieann Brill, DFO. One presentation was given by Mr. Jack Mitchell, Director of Health Policy, from the National Center for Health Research (NCHR) related to the topic of Abilify.

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

Abilify (aripiprazole) – Carolyn Yancey, MD

FDA did not identify any new safety signals, and recommended to continue ongoing post-marketing safety monitoring. The PAC discussed the limitations of adverse event data collected in regards to rates of suicidality, serious metabolic disorders, and weight gain. One PAC member noted that some pediatric patients with autism may not be able to communicate about suicidal ideation.

- The Committee concurred with the FDA plan to continue ongoing post-marketing safety monitoring. (Yes - 12; No - 2; Abstained - 0)

Keppra and Keppra XR – Lily Mulugeta, MD

FDA did not identify any new safety signals, and plans to monitor for cardiovascular adverse events, rhabdomyolysis, and encephalopathy in all patient populations. FDA recommended to continue ongoing post-marketing safety monitoring.

- The Committee concurred with the FDA plan to continue ongoing post-marketing safety monitoring. (Yes - 14; No - 0; Abstained - 0).

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

Contegra Pulmonary Valved Conduit – Dora Vega, MD, PhD

The annual review of the Medical Device Reports (MDRs) identified a case of conduit replacement for unclear reason(s). The FDA believes that currently there is insufficient information to determine if this was a case of tracheal compression due to the device and has requested additional information from the manufacturer. FDA recommended to continue device surveillance and to report again to the PAC in 2018.

- The Committee concurred with the FDA plan to continue device surveillance and report to the PAC in 2018. (Yes - 14; No - 0; Abstained - 0)

Enterra™ Therapy System – Dora Vega, MD, PhD

The annual review did not identify any new or unexpected risks for the pediatric population. FDA recommended to continue device surveillance and to report again to the PAC in 2018.

- The Committee concurred with the FDA plan to continue device surveillance and report to the PAC in 2018. (Yes - 14; No - 0; Abstained - 0)

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Elana Surgical Kit Humanitarian Use Device (HUD) – Dora Vega, MD, PhD

FDA reported that there was no reported use, sales, or new publications in the last year. The post approval study has been put on hold due to non-use in the United States, and would resume if there are any reported sales and use. FDA recommended to continue device surveillance and to report again to the PAC in 2018.

- The Committee concurred with the FDA plan to continue device surveillance and report to the PAC in 2018. (Yes - 14; No - 0; Abstained - 0)

Pleximmune – Courtney Lias, PhD

FDA did not identify any new or unexpected safety concerns for the pediatric population. FDA recommended to continue device surveillance and to report again to the PAC in 2018.

- The Committee concurred with the FDA plan to continue device surveillance and report to the PAC in 2018. (Yes - 14; No - 0; Abstained - 0)

Berlin Heart EXCOR – Vasum Peiris, MD, MPH

In June 2017, the Berlin Heart EXCOR was approved following a Premarket Approval (PMA) application, and no longer is a pediatric HDE. Annual safety reviews for the PAC are no longer required.

Office of Pediatric Therapeutics: Presentation - Kidnet Trajectory: Where have we been? Where should we go? – Ann McMahon, MD, MS

This presentation provided updated information on postmarket studies using Kidnet, a network of pediatric hospitals coordinated by FDA. Data from pediatric intensive care units (ICUs) was reviewed for adverse events in two studies, one with octreotide and proton pump inhibitors and another with the use of fentanyl and azithromycin. A third study evaluated renal adverse effects of intravenous acyclovir in neonates.

Committee Discussion: The committee discussed the use of electronic medical record (EMR) systems and expanded databases to collect information from a larger cohort of pediatric hospitals. One member of the PAC noted that other important pediatric safety issues such as contraceptive use and bone health might be elucidated with a larger database. Another alternative would be to explore some of the adverse events noted in the the PAC safety reviews, such as Abilify and cerebrovascular accidents. It was noted, however, that the Kidnet network was insufficiently powered to explore these questions adequately.

Adjournment

Kelly Wade, MD, PhD, Acting Chair

FINAL APPROVAL:

_____/s/
Marieann R. Brill, MBA, RAC, MT(ASCP)
Designated Federal Officer, PAC

_____/s/
Kelly Wade, MD, PhD
Acting Chair, PAC