MINUTES OF THE PEDIATRIC ADVISORY COMMITTEE (PAC) ADVISORY COMMITTEE
The public meeting was convened from 10:00 am - 3:00 pm EDT, September 17, 2021

Members Present (voting)	**Temporary Voting Members**
Kelly Wade, MD, PhD, MSCE (*Chair*) Angela Czaha, MD, MSc Robert Dracker, MD, MBA, MPH, FACC Randall Flick, MD, MPH Peter Havens, MD, MS Sarah Hoehn, MD, MBe, FAAP Richard Holubkov, PhD Bridgette Jones, MD, MS Roberto Ortiz-Aguayo, MD, MMM Wael Sayej, MD **Patient Family Representative** Gianna McMillan, DBe **Consumer Representative** Randi Oster, MBA	Gwenyth Fischer, MD Jeffrey Lukish, MD, FACS, FAAP Jennifer Plumb, MD, MPH **Non-Voting Members** **Industry Representative** Ronald Portman, MD, FAAP **Designated Federal Officer (DFO)** Marieann Brill, MBA, RAC, MT(ASCP)

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

Office of Pediatric Therapeutics	**Center for Devices and Radiological Health (CDRH)**
Dionna Green, MD, FCP **CDER Division of Pediatric and Maternal Health** Ethan D. Hausman, MD	Vasum Peiris, MD, MPH, FAAP, FACC, FASE Shani Haugen, PhD Lauren Min, PhD Jian Connell, DNP, MSN, CPN

Welcome and Introductory Remarks

- Kelly Wade, Chair, Pediatric Advisory Committee opened the meeting. Dr Wade directed those participating in the meeting and the audience to the FDA press contact, April Grant, Press Officer, OC/OEA/OMA. Her email (april.grant@fda.hhs.gov) and her telephone number (202-657-8179) were provided. Dr. Wade also directed the industry and press to the PAC email inbox.
- Marieann Brill, Designated Federal Officer (DFO), read the required disclosures and conflict of interest statement.
- Dionna Green, MD, FCP, Acting Director of the Office of Pediatric Therapeutics, gave the opening remarks.
    - Dr. Green announced the general topics for discussion for the September 17, 2021 PAC Meeting.
    - Personnel announcements
        - Welcome to the new PAC members: Dr. Angela Czaja, Dr. Robert Dracker, and Dr. Bridgette Jones.

        - Celebrating the career and retirement of Dr. Suzie McCune, MD, former Director of the Office of Pediatric Therapeutics.
    - Web-Posted Reviews: CDER = 12; CBER = 7; CDRH = 9
    - New PREA noncompliance letters since the September 2020 PAC Meeting: CDER = 21; CBER = 0

CDRH - Annual Update of Post-Market Humanitarian Device Exemption (HDE) Review

"Flourish™ Pediatric Esophageal Atresia Device: H150003" – presented by Lauren Min, PhD; and Jian Connell, DNP, MSN, CPN

- Lauren Min, PhD, Epidemiologist provided an overview of the Humanitarian Device Exemption Program (HDE); described esophageal atresia and current standard of care treatment; discussed the device, the HDE approval, and indications for use. Dr. Min discussed the post-approval study (PAS) requirement to collect data on 20 patients for a 2 year follow-up and described post-approval data collected outside of PAS. She described a systematic literature review and summarized the post-approval data collected thus far. Anastomosis rate is higher in pre-approval than post-approval; there is incomplete stricture data in 9 patients from this reporting period.

- Jian Connell, DNP, MSN, CPN, Consumer Safety Officer/Senior MDR Analyst described the strengths and limitations of the Medical Device Reporting (MDR) System used to monitor device performance (passive surveillance). She stated 7 MDR reports were received related to the FLOURISH™ Pediatric Esophageal Atresia Device during this reporting period, which included perforations, anastomosis failure, device placement failure (insufficient magnet strength), stenosis, and tracheal-esophageal fistula. She discussed four of the seven MDRs, which were new adverse events of perforations, tracheal-esophageal fistula, and insufficient magnet strength, as well as mitigation strategies including labeling changes. The root cause in some cases was identified as improper use of the device and in other cases could not be identified.

- CDRH Conclusions: The HDE was approved with sufficient but circumscribed data that demonstrated an appropriate benefit/risk profile consistent with the evidentiary standards for safety and probable benefit.Data collected in the current reporting period show an evolving benefit/risk profile with limited data in non-PAS patients. Probable benefit outweighs risk when used as indicated. FDA recommends additional labeling changes with continued surveillance ofthe annual distribution number, PAS results, MDRs, and literature.

Sponsor presentation

"Flourish™ Pediatric Esophageal Atresia Device" – presented by Ted Heise, PhD, RAC; Mario Zaritzky, MD; and Bethany Slater, MD, MBA

- Ted Heise, PhD, RAC, VP Regulatory and Clinical Services described the device benefits: avoid surgical intervention and avoid dissection of esophageal pouches. Dr.

Heise also discussed devices placed to date; considerations for magnet forces: high pressure associated with increased risk of perforations and anastomotic leaks and magnet force higher with greater gaps; reported that some physicians modified device placement and maintenance, leading to adverse events. He also reviewed the labeling changes and provided an update on the PAS which was modified to collection of real-world data (pragmatic study design); sponsor on target to complete data collection on 20 patients for final study report due in 2023.

- Mario Zaritzky, MD, Radiologist, University of Chicago Medicine Comer Children's Hospital partnered with Cook Medical, showed film of family of infant with successful anastomosis. A video on surgical intervention was included in the presentation by Ted Heise as well as live presentation by Mario Zaritzky.

- Bethany Slater, MD, MBA, Surgeon, University of Chicago Medicine Comer Children's Hospital described the complications associated with a surgical repair. Dr. Slater presented live during the presentation.

Open Public Hearing

- There were no speakers for the open public hearing session.

Committee Discussion

- The PAC Chair provided a summary of the discussion including 1) EA/TEF is a serious disease, 2) PAC strongly encourages the Sponsor to enroll patients in PAS to get comprehensive data, 3) patient selection is important as is comparison of like patients, 4) historical controls may be useful comparators, and 5) physician training on device operation is important.

Voting Questions

Question 1: Recurrent improper use of device was observed in the new serious adverse events. Also, the attractive force of the magnet increases as the distance is reduced. Does the committee agree that additional warnings about improper device use, including excess user manipulations of the device, and explanation of the magnet behavior would address and mitigate the risk of perforations or TEFs?

Vote Results: **Yes – 13** **No – 0** **Abstain - 1**

Committee Discussion: The majority of PAC members who voted "Yes," felt that this labeling recommendation was necessary but not sufficient to address the risks; they wanted to include language for pediatric surgeons who would be using the device. One PAC member suggested changing "would" mitigate to "may" mitigate. Although one PAC member agreed with the comments of the other PAC members, she abstained from voting because she felt the warnings listed were incomplete.

Please see the transcript for details of the Committee's discussion

Question 2: There are multiple clinical factors that can impact the effectiveness of the anastomosis. Does the committee agree that physicians should be given additional information regarding the clinical variables to better identify suitable candidates for treatment with the Flourish device?

Vote Results: Yes -14 No – 0 Abstain – 0

Committee Discussion: The PAC members reiterated the importance of robust data collection and reporting.

Please see the transcript for details of the Committee's discussion

Question 3: The FDA will report on the following to the PAC in 2022:

- Annual distribution number
- PAS follow-up results
- MDR review
- Literature review

Does the Committee agree with the FDA's plan for continued surveillance of the Flourish device?

Vote Results: Yes – 14 No – 0 Abstain – 0

Adjournment

- Kelly Wade, Chair, PAC

The summary minutes for the September 17, 2017 meeting of the Pediatric Advisory Committee (PAC) were approved on November 8, 2021

I certify that I attended the September 17, 2021 meeting of the meeting of the Pediatric Advisory Committee (PAC) and that these minutes accurately reflect what transpired.

/s/	**/s/**
Marieann Brill, MBA, RAC, MT (ASCP)	Kelly Wade, MD, PhD, MSCE
Designated Federal Officer, PAC	Chair, PAC