MINUTES OF THE PEDIATRIC ADVISORY COMMITTEE
The public meeting was convened 8:30 a.m. to 11:30 a.m. on March 7, 2017

Members Present (Voting)	Temporary Voting Members (Voting Consultants)
Mary Cataletto, MD Avital Cnaan, PhD Erin Moore, BS (*Family-Patient Rep.)* Wael Sayaj, MD Christy Turer, MD, MHS Kelly Wade, MD, PhD, MSCE Michael G. White, MD, PhD	Premchand Anne, MD, MPH David Callahan, MD Frederick Kaskel, MD, PhD Priya Kishnani, MD (phone) Michael Peck, MD ScD (phone only for Epicel) Athena Zuppa, MD, MSCE
Non-Voting Members	Designated Federal Official (DFO)
Mark Hudak, MD *(Chair)* Bridgette Jones, MD (*PHO Rep.)* Ronald Portman, MD (*Industry Rep.)*	Marieann Brill, MBA, RAC, MT (ASCP)

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

Office of Pediatric Therapeutics	**CBER**	**CDRH**
Robert "Skip" Nelson, MD, PhD Judith Cope, MD, MPH LCDR Kenneth Quinto, MD, MPH	CDR Craig Zinderman, MD, MPH Meghna Alimchandani, MD Bethany Baer, MD LCDR Wambui Chege, MD Carolyn Yong, PhD Yao-Yao Zhu, MD	Vasum Peiris, MD, MPH George Aggrey, MD, MPH Kelly Bauer, RN, BSN John Laschinger, MD Timothy Marjenin, BS Andrew Miller, MS Courtney Millin,PhD Nasrin Mirsaidi, MSN, RN Ann Myers, MS, RN Catherine Ricketts, BSN, RN Douglas Silverstein, MD

Welcome and Introductory Remarks

- Marieann Brill, MBA, RAC, MT (ASCP), Designated Federal Official, Pediatric Advisory Committee, Office of Pediatric Therapeutics, Office of Special Medical Programs, FDA
- Mark Hudak, MD, Chair of the Pediatric Advisory Committee
- Robert "Skip" Nelson, MD, PhD, Office of Pediatric Therapeutics, Office of Special Medical Programs, FDA

Open Public Hearing
An opening statement was read by the Marieann Brill, DFO.
There were no public presentations and the session was closed.

Center for Biologics Evaluation and Research (CBER) Abbreviated Presentations

Novoeight® (turotocog alfa) Antihemophilic Factor (Recombinant), LCDR Kenneth Quinto MD, MPH

The Safety and Utilization Review does not indicate any new safety concerns for Novoeight.

FDA recommends continued surveillance and will report the following to the PAC in 2018.

- The Committee concurred with the FDA proposal to continue surveillance and report back to the PAC in 2018. (Yes – 11, Abstain - 1).

RIXIBUS [Coagulation Factor IX (Recombinant)], - LCDR Kenneth Quinto MD, MPH

The Safety and Drug Utilization Review does not indicate any new safety concerns for Rixubis.

FDA recommends continued surveillance and will report the following to the PAC in 2018.

- The Committee concurred with the FDA proposal to continue surveillance and report back to the PAC in 2018. (Yes - 11; Abstain - 1).

Initial CBER Pediatric HDE Review

Epicel® (cultured epidermal autografts) HDE, - Meghna Alimchandani, MD and Nasrin Mirsaidi, MSN, RN

Epicel is indicated for use in adult and pediatric patients who have deep dermal or full thickness burns comprising a total body surface area (TBSA) of ≥ 30%. FDA did not identify any new safety signals during this comprehensive safety review and concluded that the Humanitarian Device Exemption (HDE) for this device remains appropriate for the adult and pediatric population for which it was granted. The recent Epicel label revision included the risk of squamous cell carcinoma. The adverse events reported in children and adults are relatively constant over time and consistent with comorbidities in severe burn injury. FDA did not identify any new safety signals.

FDA recommends continued surveillance and will report the following to the PAC in 2018: Annual Distribution Number (ADN), literature review, and Medical Device Reports (MDRs) review.

- The Committee concurred with the FDA proposal to continue surveillance and report back to the PAC in 2018. (Yes - 13; No - 0)

Center for Devices and Radiological Health (CDRH)

Annual Update of Post-Market HDE Reviews:

Medtronic Activa® Neurostimulator for Dystonia Treatment - Andrew Miller, MS

The FDA Review reported that 58 MDRs with 43 unique events associated with the use of Activa neurostimulator in pediatric patients. Infection and a return or worsening of dystonia symptoms (loss of therapeutic effect) were the most frequently reported pediatric patient problems. The most frequently reported device problems were battery/charging issues and impedance issues. No MDRs associated with pediatric stroke or cognitive changes were reported. No new device or patient problems were identified. The review of the published literature found no new safety events detected since the last PAC. The findings of this review are consistent with the conclusions from the systematic review conducted for the previous PAC meetings.

FDA recommends continued surveillance and will report the following to the PAC in 2018: Annual Distribution Number (ADN), literature review, and MDR review.

- The Committee concurred with the FDA proposal to continue surveillance and report to the PAC in 2018 (Yes - 12; No - 0).

Impella® RP System – George Aggrey, MD, MPH

FDA concluded that there were no pediatric patients reported in the MDRs, and that the thrombosis, hemolysis, bleeding and positioning issues are addressed in the Indications for Use (IFU) and are known complications of this type of device. FDA found no other safety concerns at this time.

FDA recommends continued surveillance and will report the following to the PAC in 2018: Annual Distribution Number (ADN), literature review, and MDR review.

- The Committee concurred with the FDA proposal to continue surveillance and report to the PAC in 2018 (Yes - 12; No - 0).

Liposorber® LA-15 System, - Douglas Silverstein, MD

FDA reported that as of January, 2017, 8 pediatric patients had received a full course (9 weeks, 12 treatments) of therapy for focal segmental glomerulosclerosis (FSGS) with the Liposorber® LA-15 system. Of the 8 patients who finished a complete course of therapy, 6 have 3-6 month follow-up data: 3 exhibited either a complete or partial remission, with reduction in urine protein/creatinine and all showed stabilization or improvement in GFR. While some adverse events were not insignificant, none were thought to be device-related, but rather consistent with those observed in the underlying disease or with associated devices (catheter).

Summary - FDA believes that the device labeling could potentially be enhanced related to issues of anemia with multiple LDL-A treatments and risk for hypovolemia and hemodynamic changes in patients who receive LDL-A therapy and another extracorporeal therapy (e.g., hemodialysis) on the same day. FDA will discuss these issues with the sponsor.

FDA recommends continued surveillance and will report the following to the PAC in 2018: Annual Distribution Number (ADN), literature review, and MDR review.

- The Committee concurred with the FDA proposal to continue surveillance and report to the PAC in 2018 (Yes - 12; No - 0).

Committee Discussion: Committee members raised issues regarding (1) adiposity/obesity (not just weight) and its influence on FSGS, (2) extravascular fluid volume in nephrotic syndrome/FSGS patients and its influence on accurate weight/lean body mass assessment, (3) nutritional status and its influence on lean muscle mass, which influences creatinine metabolism and value of serum creatinine (SCr) on estimated glomerular filtration rate (eGFR), and (4) the influence of shifts in total body fluid volume (intravascular and extravascular) during Liposorber therapy on hemodynamic status. The committee also discussed possible labeling changes with anemia, hypotension/hemodynamic changes and lipid profiles.

Adjournment:
Mark Hudak, MD, Chair

FINAL APPROVAL:

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

/s/
Mark Hudak, MD
Chairperson, PAC