FOOD AND DRUG ADMINISTRATION (FDA)
Office of the Commissioner (OC)
MINUTES OF THE PEDIATRIC ADVISORY COMMITTEE (PAC)
The public meeting was convened on September 18, 2024

Designated Federal Officer (DFO)
Shivana Srivastava, RN, MS, PMP

PAC Members Present (voting)
Gwenyth Fischer, MD *(Chair)*
David Callahan, MD
Angela Czaja, MD, MSc, PhD
Douglas Diekema, MD, MPH
Charleta Guillory, MD, MPH
Richard Holubkov, PhD
Bridgette Jones, MD, MS
Steven Krug, MD
Roberto Ortiz-Aguayo, MD, MMM
Michael White, MD, PhD

Patient Family Representative (voting)

Gianna McMillan, DBe

Consumer Representative (voting)

Randi Oster, MBA

Pediatric Health Organization Representative (non-voting)
Jennifer Goldman, MD, MS

Industry Representative (non-voting)
Robert Nelson, MD, PhD

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

Office of Pediatric Therapeutics

Dionna Green, MD, FCP

Director

Mohammed Mohamoud, PharmD, MPH

Senior Clinical Analyst

Center for Drug Evaluation and Research (CDER)

Ivone Kim, MD

Senior Medical Officer

Center for Devices and Radiological Health (CDRH)

Vasum Peiris, MD, MPH, FAAP, FACC, FASE

Associate Director and Chief Medical Officer for Pediatrics and Special Populations

Director – Program for Pediatrics and Special Populations

Center for Biologics Evaluation and Research (CBER)

Craig Zinderman, MD, MPH

Associate Director for Medical Policy

Call to Order and Introduction of the Committee

Gwenyth Fischer, MD

- Dr. Gwenyth Fischer, Chairperson, commenced the Pediatric Advisory Committee (PAC) meeting. Dr Fischer directed those participating in the meeting and the audience to the FDA press contact, April Grant and reviewed information about how to access closed captioning. Dr. Fischer officially called the meeting to order and stated that no new safety signals were identified by the FDA for the products being reviewed at this meeting. She explained that the scope of the meeting will be focused on post-marketing safety only and all discussion and clarifying questions should focus on these post-marketing safety reviews for the specific CDER, CDRH and CBER products reviewed. Dr. Fischer also emphasized the general rules of order for the meeting and introduced the PAC Representatives and conducted the PAC member meeting attendee roll call.

Introduction of FDA Representatives

Shivana Srivastava, RN, MS, PMP Designated Federal Officer

- Shivana Srivastava, Designated Federal Officer (DFO), facilitated the introductions of FDA Representatives present at the meeting.

Conflict of Interest Statement

Shivana Srivastava, RN, MS, PMP Designated Federal Officer

- Shivana Srivastava read the conflict-of-interest statement.

FDA Opening Remarks

Dionna Green, MD, FCP

- Dr. Dionna Green, Director of the Office of Pediatric Therapeutics, gave the opening remarks. Dr. Green welcomed and thanked the PAC for reviewing today's meeting materials and thanked FDA staff that contributed to the content, meeting logistics and technical support for this meeting. Dr. Green provided an update and overview of Pediatric Research Equity Act (PREA) noncompliance letters to sponsors noting that since the September 2023 PAC meeting, no new letters were issued by CBER and 24 new letters were issued by CDER. Dr. Green gave an overview of the meeting agenda, shared the voting question that will be applied to all votes ("FDA recommends continuing routine, ongoing postmarket safety monitoring of each of the [CDER/CDRH/CBER] products under discussion. Does the Pediatric Advisory Committee concur?") and explained the meaning for a "yes," "no," "abstain," "recused" vote. Dr. Green issued a reminder that FDA's safety surveillance reviews did not identify any new pediatric safety concerns.

FDA Background Presentation: Postmarket pediatric-focused safety reviews for the PAC

Mohamed Mohamoud, PharmD, MPH

- Dr. Mohamed Mohamoud's presentation summarized the legislation that governs the PAC's work and illustrated changes that have been implemented over time in how postmarket pediatric-focused safety reviews are presented to the PAC. He began by describing the seminal legislation that created the PAC and established the PAC's role in postmarket pediatric safety monitoring (the Best Pharmaceuticals for Children Act (BPCA) of 2002) and subsequent legislation that expanded the

scope, including PREA in 2003, and the Pediatric Medical Device Safety and Improvement Act (PMDSIA) in 2007.

- Dr. Mohamoud summarized the data sources FDA uses to identify the adverse events that are presented in the pediatric-focused postmarket safety reviews including passive surveillance data (FAERS, VAERS and MAUDE databases), periodic safety reports from manufacturers, summaries of any relevant post-approval studies, and summaries of relevant peer-reviewed literature. Dr. Mohamoud described the increasing number of pediatric labeling changes for drugs and biologics over time and described the various approaches FDA has used to streamline pediatric-focused postmarket safety reviews to address the increased volume, including how FDA presents the reviews to the PAC. He summarized how FDA began web-posting safety reviews for "low safety risk" products in 2016, with the goal of optimizing use of FDA and PAC resources. A product could be deemed a "low safety risk" if the review met prespecified criteria. Web-posting these low safety risk products offered the potential to decrease the backlog of CDER products awaiting PAC review, led to more safety reviews completed in a shorter amount of time and allowed for the PAC to spend more time discussing products that were not designated "low safety risk."
- Dr. Mohamoud described the definition of the phrase, "routine ongoing postmarket safety monitoring" for the PAC, noting that it means the product will return to the ongoing surveillance process that FDA does on a regular basis to detect possible safety signals. It also means that FDA safety evaluators will continue to review, assess and analyze incoming safety reports that FDA receives from sponsors, consumers and health care providers.
- Finally, Dr. Mohamoud described FDA's future plans for the PAC and the postmarket pediatric-focused safety review process, noting that FDA will engage the PAC in "low safety risk" drug, device and biologic product reviews during PAC meetings to provide an open forum for discussion and obtain any recommendations. FDA will also continue to present reviews with new safety concerns to the PAC for discussion and to obtain advice and recommendations. FDA will continue to engage the PAC in other advisory committee activities and explore alternative ways to optimize FDA's approach to conducting pediatric-focused postmarket safety reviews.

Open Public Hearing

Gwenyth Fischer, MD

- There were no Open Public Hearing Speakers at this meeting.

Center for Drug Evaluation and Research (CDER)

Listing of products and clarifying questions

Ivone Kim, MD

- Dr. Kim read the listing of products evaluated in the post-marketing pediatric-focused safety reviews conducted by CDER and answered clarifying questions from the PAC members. The majority of questions were not about safety concerns for individual products, but rather more general questions about CDER's approach to conducting postmarket pediatric-focused safety reviews.

Committee Discussion and Vote

Voting Question: FDA recommends continuing routine, ongoing postmarket safety monitoring of each of the CDER products under discussion. Does the Pediatric Advisory Committee concur?

The results of the vote are displayed in the table below. Following the vote, each PAC member had the opportunity to comment on their vote.

CDER Voting Results

	David Callahan	Angela Czaja	Douglas Diekema	Charleta Guillory	Richard Holubkov	Bridgette Jones	Steven Krug	Gianna McMillan	Roberto Ortiz-Aguayo	Randi Oster	Michael White
AZSTARYS (serdexmethylphenidate/dexmethylphenidate)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CAFCIT (caffeine citrate)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
CHANTIX (varenicline)	Recused	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	No	Yes
CIMDUO, TEMIXYS (lamivudine/tenofovir disoproxil fumarate)	Recused	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	No	Yes
CLEOCIN HYDROCHLORIDE, CLEOCIN PHOSPHATE, CLEOCIN PHOSPHATE IN DEXTROSE 5% IN PLASTIC CONTAINER, CLINDAMYCIN PHOSPHATE IN 0.9% SODIUM CHLORIDE (clindamycin hydrochloride, clindamycin phosphate)	Recused	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	No	Yes
DYANAVEL XR (amphetamine)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
EVEKEO ODT (amphetamine)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
GATTEX (teduglutide)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
GILENYA and TASCENSO ODT (fingolimod)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
JANUVIA, JANUMET and JANUMET XR (Sitagliptin, sitagliptin/metformin, and sitagliptin/metformin extended release)	Yes	Yes	Yes	Yes	Yes	Recused	Yes	Yes	Yes	No	Yes
KAPSPARGO SPRINKLE (metoprolol succinate extended release)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
LITHIUM (lithium carbonate, lithium oral solution)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
LOTEMAX (loteprednol etabonate)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
LUMASON (sulfur hexafluoride lipid-type A microspheres)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
MAVYRET (glecaprevir/pibrentasvir)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
MIRCERA (methoxy polyethylene glycol-epoetin beta)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
MULTRYS, TRALEMENT, ZINC SULFATE, SELENIOUS ACID (trace elements)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
MYDAYIS (mixed salts of a single-entity amphetamine)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
NATROBA (spinosad)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
PRADAXA (dabigatran mixed salts of a single-entity)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
QELBREE (viloxazine extended release)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
RIOMET ER (metformin hydrochloride extended-release)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TEFLARO (ceftaroline fosamil)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
TIROSINT-SOL (levothyroxine sodium)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
TYBOST (cobicistat)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
ULTRAVATE and LEXETTE (halobetasol propionate)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
VEKLURY (remdesivir)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
VYVANSE (lisdexamfetamine dimesylate)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
XACIATO (clindamycin phosphate)	Yes	Yes	Yes	Yes	Yes	Recused	Yes	Yes	Yes	No	Yes
XEGLYZE (abametapir)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
XELSTRYM (dextroamphetamine)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
YERVOY (ipilimumab)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes

Center for Devices and Radiological Health

Listing of products and Clarifying Questions
Vasum Peiris MD, MPH, FAAP, FACC, FASE

- Dr. Peiris read the listing of products evaluated in the post-marketing pediatric-focused safety reviews conducted by CDRH and answered clarifying questions from the PAC members. There were questions about the risk of electric shock with the ENTERRA THERAPY SYSTEM and general questions about two products that will no longer be monitored, FLOURISH and PULSERIDER.

Committee Discussion and Vote

Voting Question: FDA recommends continuing routine, ongoing postmarket safety monitoring of each of the CDRH products under discussion. Does the Pediatric Advisory Committee concur?

The results of the vote are displayed in the table below. Following the vote, each PAC member had the opportunity to comment on their vote.

CDRH Voting Results

	David Callahan	Angela Czaja	Douglas Diekema	Charleta Guillory	Richard Holubkov	Bridgette Jones	Steven Krug	Gianna McMillan	Roberto Ortiz-Aguayo	Randi Oster	Michael White
CONTEGRA PULMONARY VALVED CONDUIT	Yes	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	Yes	Yes
ENTERRA THERAPY SYSTEM	Yes	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	No	Yes
FLOURISH PEDIATRIC ESOPHAGEAL ATRESIA DEVICE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
PLEXIMMUNE IN-VITRO DIAGNOSTIC TEST	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
PULSERIDER ANEURYSM NECK RECONSTRUCTION DEVICE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
SONALLEVE MR-HIFU	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Center for Biologics Evaluation and Research

Listing of products and Clarifying Questions
Craig Zinderman, MD, MPH

- Dr. Zinderman read the listing of products evaluated in the post-marketing pediatric-focused safety reviews conducted by CBER and answered clarifying questions from the PAC members. There were questions about the methodology of CBER's safety ascertainment system and about the injection volume of CUTAQUIG.

Committee Discussion and Vote

Voting Question: FDA recommends continuing routine, ongoing postmarket safety monitoring of each of the CBER products under discussion. Does the Pediatric Advisory Committee concur?

The results of the vote are displayed in the table below. Following the vote, each PAC member had the opportunity to comment on their vote.

CBER Voting Results

	David Callahan	Angela Czaja	Douglas Diekema	Charleta Guillory	Richard Holubkov	Bridgette Jones	Steven Krug	Gianna McMillan	Roberto Ortiz-Aguayo	Randi Oster	Michael White
AGRIFLU (influenza virus vaccine)	Recused	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CUTAQUIG (immune globulin subcutaneous (human)-hipp, 16.5%)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
XYNTHA (antihemophilic factor (recombinant), plasma/albumin free)	Recused	Yes	Yes	Yes	Recused	Yes	Yes	Yes	Yes	Yes	Yes

ADJOURNMENT **Gwenyth Fischer, MD**
Chairperson, PAC

The summary minutes for the September 18, 2024 meeting of the Pediatric Advisory Committee (PAC) were approved on November 6, 2024

I certify that I attended the September 18, 2024 meeting of the meeting of the Pediatric Advisory Committee (PAC) and that these minutes accurately reflect what transpired.

_____**/s/**_____
Shivana Srivastava, RN, MS, PMP
Designated Federal Officer, PAC

_____**/s/**_____
Gwenyth Fischer, MD
PAC Chairperson