



**Final Summary Minutes of the Pediatric Subcommittee of the Oncologic Drugs Advisory  
Committee Meeting  
June 20, 2018**

The Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (pedsODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on June 20, 2018 at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the briefing materials from the FDA. The meeting was called to order by Alberto S. Pappo, MD (Chairperson). The conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 65 people in attendance. There were two Open Public Hearing (OPH) speakers for Topic 2. There were no OPH speakers for Topics 1 and 3.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

**Agenda:** The particular matter for this meeting was to review and discuss a list of molecular targets for which evidence and/or biologic rationale exist to determine their potential relevance to the growth or progression of one or more pediatric cancers and a list of those targets deemed unlikely to be associated with the growth or progression of pediatric tumors for which requirement for early pediatric evaluation would be waived. These lists are expected to fulfill the statutory obligation of the Food and Drug Administration Reauthorization Act (FDARA) and provide some guidance to industry in planning for initial Pediatric Study Plan submissions for new drug and/or biologic products in development for cancer in accordance with the amended provisions of the Pediatric Research Equity Act. The committee also reviewed and discussed considerations other than scientific relevance which the FDA will include in decision making with respect to the need and timing of pediatric evaluation of specific new drug and biologic products. The committee also discussed possible criteria and mechanisms for the prioritization by sponsors and the clinical investigator community of select targeted new agents for pediatric evaluation especially in the setting of multiple same in class agents. Preliminary discussion on approaches to coordination and collaboration for pediatric clinical investigations of new agents that might be pursued to efficiently accommodate international regulatory requirements and global pediatric product development. The OPH sessions were: Topic 1: Target List, Topic 2: FDARA Implementation and Topic 3: Mechanisms to assure efficiency and to enhance global coordination through international collaboration.

**Attendance:**

**ODAC Members Present (Voting):** Alberto S. Pappo, MD (pedsODAC Chairperson);  
Courtney J. Preusse, MA (Consumer Representative)

**ODAC Members Not Present (Voting):** Harold J. Burstein, MD, PhD; Susan Halabi, PhD;  
Philip C. Hoffman, MD; Heidi D. Klepin, MD, MS; Grzegorz S. Nowakowski, MD; Vassiliki

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A. Papadimitrakopoulou, MD; Gregory J. Riely, MD, PhD; Brian I. Rini, MD, FACP; Bruce J. Roth, MD; Alice T. Shaw, MD, PhD; Thomas S. Uldrick, MD, MS

**ODAC Member Present (Non-Voting):** Phuong Khanh (P.K.) Morrow, MD, FACP

**Temporary Members (Voting):** Steven G. DuBois, MD; Ira Dunkel, MD; Julia Glade Bender, MD; Katherine Janeway, MD, MMSc; E. Anders Kolb, MD; Theodore W. Laetsch, MD; Donna M. Ludwinski (Patient Representative); Tobey J. MacDonald, MD; Rajen Mody, MD, MS; Kathleen Neville, MD, MS, MBA, FAAP, FCCP; Elizabeth A. Raetz, MD; Nita Seibel, MD; Malcom A. Smith IV, MD, PhD; Brenda J. Weigel, MD, MSc

**Speaker (Non-Voting):** Lia Gore, MD (Participation in Topic 2)

**FDA Participants (Non-Voting):** Amy Barone, MD; Diana Bradford, MD; Sandra J. Casak, MD; Gregory Reaman, MD

**Designated Federal Officer (Non-Voting):** Lauren D. Tesh, PharmD, BCPS

**Open Public Hearing Speakers:** Topic 2: Nancy Goodman (Kids V Cancer); Jonathan Agin, Esq. (Max Cures Foundation); None for Topics 1 and 3

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*The agenda was as follows:*

Call to Order and Introduction of Subcommittee	<b>Alberto S. Pappo, MD</b> Chairperson, pedsODAC
Conflict of Interest Statement	<b>Lauren Tesh, PharmD, BCPS</b> Designated Federal Officer, ODAC

**Topic 1: Target List**

Implementing FDARA 2017 Provisions: Facilitating Precision Cancer Medicine for Children	<b>Gregory H. Reaman, MD</b> Associate Director Oncology Sciences Office of Hematology and Oncology Products (OHOP) Office of New Drugs (OND), CDER, FDA Associate Director for Pediatric Oncology Oncology Center of Excellence, FDA
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Clarifying Questions

**OPEN PUBLIC HEARING**

Charge to the Subcommittee

Questions to the Subcommittee/Subcommittee Discussion

**BREAK**

**Topic 2: FDARA Implementation**

**SPEAKER PRESENTATION**

Scientific and Logistical Considerations in Applying “The List”

**Lia Gore, MD**

Professor of Pediatrics, Medical Oncology, and Hematology  
University of Colorado Anschutz Medical Campus  
Chief, Pediatric Hematology/Oncology/Bone Marrow Transplant  
The Ergen Family Endowed Chair in Pediatric Oncology  
Children's Hospital Colorado, Center for Cancer and Blood Disorders

Clarifying Questions

**GUEST SPEAKER PRESENTATIONS**

Implications of the 2017 FDA Reauthorization Act on Pediatric Cancer Drug Development: An Industry Perspective

**Lisa Bollinger, MD**

Vice President, Regulatory Affairs  
Amgen, Inc

Clarifying Questions

Investigator Perspectives on New Agent Prioritization and Challenges with Multiple Same in Class Agents

**Elizabeth Fox, MD**

Professor of Pediatrics, the Perelman School of Medicine at the University of Pennsylvania  
Head, Developmental Therapeutics in Oncology, Children's Hospital of Philadelphia

Clarifying Questions

**LUNCH**

**GUEST SPEAKER PRESENTATIONS (CONT.)**

Industry Perspective on Prioritization of Pediatric Relevant Targets and Molecules

**Hubert N. Caron, MD, PhD**

Principle Medical Director  
Pediatric Oncology Drug Development Group  
Hoffmann-La Roche Ltd.

Clarifying Questions

**OPEN PUBLIC HEARING**

Charge to the Subcommittee

Questions to the Subcommittee /Subcommittee Discussion

**BREAK**

**Topic 3: Mechanisms to Assure Efficiency and to Enhance Global Coordination Through International Collaboration**

**GUEST SPEAKER PRESENTATIONS**

Recommendations for International Collaborations and Coordination	<b>Gilles Vassal, MD, PhD</b> Head, Clinical and Translational Research Division Gustave Roussy
Addressing Challenges to Global Coordination	<b>Christina Bucci-Rechtweg, MD</b> Head, Pediatric & Maternal Health Policy Global Regulatory Affairs Novartis Pharmaceuticals
Clarifying Questions	

**OPEN PUBLIC HEARING**

Charge to the Subcommittee	
Questions to the Subcommittee /Subcommittee Discussion	
Closing Comments	<b>Gregory Reaman, MD</b>

**ADJOURNMENT**

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***Questions to the Committee:***

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**Topic 1: Target List**

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1. **DISCUSSION:** Title V of the FDA Reauthorization Act (FDARA) 2017 assigns FDA to establish, publish and regularly update a list of molecular targets considered on the basis of data the FDA determines to be adequate to be substantially relevant to the growth or progression of pediatric cancers. New drug products directed at these targets may trigger the requirement for pediatric investigations [21 USC 355c(m)(1)(A)]. As well, a list of targets considered “not relevant” [21 USC 355c(m)91)(B)] has been developed. Comment on the process utilized to construct the list, the classification of molecular targets, the factors utilized to designate a target as relevant or non-relevant and indicate your concurrence with the lists as currently presented.

*Committee Discussion:* The subcommittee members commented that the list as currently developed should be as fluid and inclusive as possible. By having a more inclusive list, the subcommittee noted it could serve as a guide for early pediatric drug development. Targets should be able to be added or removed from the list and waiver list based on sufficient scientific rationale or recommendations from the subcommittee or other sources determined appropriate by the FDA such as a public docket where

*industry, academic investigators or patients and advocates could comment or public workshops. Members of the subcommittee noted that several targets should be added to the list including PTEN, tumor mutational burden, VEGF, VEGFR and DNA damage response modifiers. There is currently no process to prioritize the targets on the lists or combinations of products that should be on the list, but the subcommittee noted it should be informed by priorities of patients and investigators. Please see the transcript for details of the subcommittee discussion.*

2. **DISCUSSION:** Please comment on the process proposed for formally updating the lists at semi-annual public workshops, the methods for nominating potential future candidate targets, and the required transparency in multi-stakeholder discussions to determine relevance. Comment on additional measures to assure timely discussion of emerging science and its clinical translation which has the potential to expedite drug development to improve the care and outcome of children with cancer.

**Committee Discussion:** *The subcommittee suggested adding RET fusions, RET point mutations, KIT mutations, CCND123, CCNE1, STAG2, and histone1H13D onto the list. One subcommittee member expressed that the proposed public docket is a good idea but questioned how the information is going to be vetted and impact changes to the list. The subcommittee suggested that FDA can summarize suggestions posted in the public docket and utilize the Pediatric ODAC meetings or public workshops as a forum to publicly examine these suggestions. To ensure transparency and timely discussion of emerging science, the list can be formally updated at the Pediatric ODAC meetings or public workshops since it is not expected that targets will change frequently. Please see the transcript for details of the subcommittee discussion.*

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## Topic 2: FDARA Implementation

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1. **DISCUSSION:** Please comment on the proposed additional considerations for which the FDA might engage with industry, clinical investigators, and advocates when making decisions regarding the requirement for pediatric studies of new drug and biologic products based on molecular mechanism of action and their timing.

**Committee Discussion:** *The subcommittee discussed how industry sponsors can communicate with FDA and study investigators regarding the level of evidence needed to move an agent forward into early phase clinical trials. Public transparency from the sponsors was encouraged since the FDA is not able to share confidential information. The subcommittee recommended that the FDA should not grant pediatric study waivers solely because of low disease prevalence for certain targets. It was also suggested that age distribution and the clinical outcomes of the disease should also be considered for target and agent prioritization. The subcommittee also encouraged sponsors to consider other aspects of clinical trials such as bioinformatics, molecular and companion diagnostics, and novel assays to support screenings for clinical trials to know in advance if a drug is likely to benefit the patient. Please see the transcript for details of the subcommittee discussion.*

**Topic 3: Mechanisms to Assure Efficiency and to Enhance Global Coordination Through International Collaboration**

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1. **DISCUSSION:** Please comment on process development aimed at enhancing international collaboration between clinical trial networks to facilitate global cancer drug development for children in light of currently non-aligned regulatory requirements.

*Committee Discussion:* The subcommittee mentioned that they can provide advice and recommendations regarding prioritizing targets on the list and it is recommended that the FDA hold workshops more than twice a year, if necessary, with international involvement. The subcommittee also noted that the lists of targets that aren't relevant should be twofold: those that are not biologically applicable for pediatrics, an example being prostate cancer targets and those targets in which previous studies have shown to not be active in pediatrics. The subcommittee again noted the need for transparency between sponsors and investigators and the community so that development is not being slowed due to multiple sponsors investigating agents with the same mechanism of action and competing for the same patients. Instead, there should be more open investigator/industry networks to facilitate an exposed process that is mutually beneficial to all parties involved. It was noted again that workshops could be held with investigators, sponsors and the public. Please see the transcript for details of the subcommittee discussion.

2. **DISCUSSION:** Please discuss transparent mechanisms for industry, advocates, and the academic investigator community to communicate and provide input to the FDA for purposes of eliminating unnecessary duplication of clinical trials in rare pediatric cancer populations of same in class agents.

*Committee Discussion:* The subcommittee clarified with FDA on how sponsor companies receive guidance for conducting clinical trials from the FDA and EMA, then suggested methods for both organizations to collaborate. The subcommittee recommended to hold workshops with sponsors, FDA, and EMA. It was discussed that there is need for strategies in which sponsors can conduct international trials and integrate study databases to avoid duplicating datasets for different FDA and EMA requirements. It was also mentioned that collaboration among investigators in both the US and internationally, including countries outside of Europe, is important to conduct one study with multiple sites to maximize patient utilization. Industry sponsored trials would likely be best to achieve this. Please see the transcript for details of the subcommittee discussion.

The meeting on June 20, 2018 was adjourned at approximately 4:10 p.m.