PART FOUR

Advancing International Pediatric Clinical Research

Facilitating Pediatric Medicines Development: Models of Global Cooperation

Part 1: 29 November 2022, 9:00-11:30 am ET

Part 2: 30 November 2022, 9:00-11:00 am ET

This series is supported by the FDA Scientific Conference Grant Program.

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Disclaimer

PART FOUR

- The opinions expressed today are those of the speakers and are not intended to represent the position of Brigham and Women's Hospital, Harvard University, or any other organization, government, or entity.
- The MRCT Center is supported by voluntary contributions from foundations, corporations, international organizations, academic institutions and government entities (see www.MRCTCenter.org) and well as by grants.
- We are committed to autonomy in our research and to transparency in our relationships. The MRCT Center—and its directors—retain responsibility and final control of the content of any products, results and deliverables.
- I have no personal financial conflicts of interests to disclose.
- This webinar will be recorded and will be posted publicly on our YouTube channel.

The MRCT Center

PART FOUR

Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

Promoting Global Clinical Research in Children

PART FOUR

Where we started & why this is important:

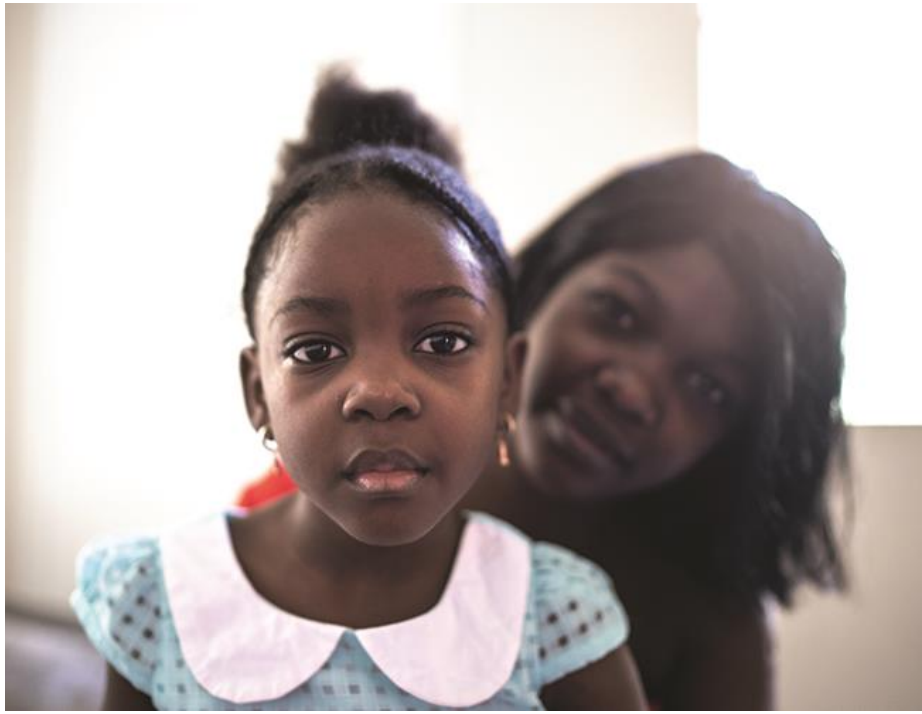
- Children **deserve access** to safe and effective medicines
- Children **historically excluded** from or underrepresented in research
- **Pediatric population widely dispersed** so clinical trials must be conducted in multiple jurisdictions
- **Persistent ethical issues:** while governing ethical principles may be generally agreed upon, differences in interpretation and application of principles exist
- Differing or nonexistent pediatric **regulations**
- Challenges in **trial initiation and conduct**
- The **pediatric patient and family voice** is not routinely solicited nor included in research life-cycle**.**
- **Children are not routinely offered a seat at the table.**

Project Objectives

PART FOUR

Broadly, sought to identify and propose solutions to regulatory, ethical, and operational challenges

- Current global landscape of pediatric research governance, focusing on legislative, regulatory, and guidance gaps and inconsistencies
- Identify current initiatives to improve pediatric research globally
- Identify challenges related to decision making by and on behalf of children
- Address benefit and risk considerations that create barriers and inefficiencies in transnational research with children.
- Identify meaningful ways to engage patients/families/ community members
- Diverse leadership (Academia, EMA, Industry, participant advocates)
- 80+ members from all stakeholder groups with geographic diversity



Webinar Series:
Advancing International Pediatric Clinical Research

PART FOUR

- An offshoot of the MRCT Center's *Promoting Global Clinical Research in Children* project
- Funded in part through an FDA scientific conference grant award
- 5 virtual webinars

1. Informing the future from COVID-19 lessons learned: October 2021
2. Time to Listen—Hearing from young people in clinical research: February 2022
3. Assent and Consent in the Field: Culture, Context, and Respect: June 2022
4. **Facilitating Pediatrics Medicines Development: Models of Global Cooperation:** 29 & 30 Nov 2022
5. Winter 2023: MRCT Center Pediatrics Project Launch

Please see "Bio Book" for extended introductions to the speakers and panelists

And we are pleased to share…..

PART FOUR

Prioritizing Young People's Voices in Clinical Research

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

iCAN

International Children's Advisory Network

Today's Agenda

PART FOUR

- Brief Presentations of 4 existing models of pediatric regulatory approval:
  - Pediatric Regulatory Cluster: Dr. Donna Snyder (US FDA)
  - Parallel Scientific Advice: Dr. Tahira Khan (AbbVie)
  - ACCELERATE Multi-Stakeholder Discussion Forum: Dr. Gilles Vassal (ACCELERATE)
  - Reliance Model: Dr. Marie Valentin (WHO)

- Panel Discussion: *Strengths and Opportunities of Existing Models of Global Cooperation*

The Pediatric Regulatory Cluster

Donna Snyder
U.S. Food and Drug Administration

Global Collaboration and the Pediatric Cluster

Donna Snyder, MD, MBE
Office of Pediatric Therapeutics (OPT)
Office of Clinical Policy and Programs (OCPP)
Office of Commissioner (OC)
Food and Drug Administration (FDA)

Disclaimer

- The views expressed in this presentation do not necessarily represent the policies of the Food and Drug Administration (FDA) or the Department of Health and Human Services (HHS)
- The speaker has no relevant personal, professional or financial relationship(s) with respect to this presentation

Objectives of Today's Talk

- Provide an overview of US and EU (European Union) regulatory requirements as they apply to global drug development in pediatrics, including some similarities and differences
- Describe the history of the Pediatric Cluster
- Review the processes and procedures of the Pediatric Cluster
- Provide an overview of the Pediatric Cluster output since inception
- Summary

Historical Milestones and Legislation in Pediatrics

1902
National Institutes of Health enacts the Biologics Control Act following the death of 22 children from tainted anti-toxins

1938
FD&C Act: enacted after the deaths of over 100 people, many of whom were children, following use of the Elixir Sulfanilamide; all marketed drugs must be safe for use as directed

1962
The FD&C Act amended: Drugs not tested in children should not be used in children

Following the thalidomide tragedies in Europe, the Kefauver–Harris amendments to the FD&C Act requiring that all approved drugs demonstrate both safety and effectiveness

1974
AAP Committee on Drugs issues guidelines for evaluating drugs for pediatric use

1979
FDA requires sponsors to conduct pediatric clinical trials before including pediatric information in the labeling

1990
Institute of Medicine holds workshop regarding the lack of labeling for pediatric drugs

1992
Agency proposed pediatric labeling and extrapolation

1994
Pediatric Plan to encourage voluntary development of pediatric data

1997
The pediatric exclusivity provision, FDAMA: provides 6-month market exclusivity incentive to sponsors who, in response to a FDA pediatric written request, conduct pediatric studies for drugs with potential use in children

1998
Pediatric Rule (mandatory): newly approved products are required to include pediatric assessments if the drug is likely to be used in a "substantial number of pediatric patients" (50,000) or if it may provide a "meaningful therapeutic benefit" unless requirement is waived or deferred

2002
FDAMA reauthorized as the BPCA 2002. Maintains the 6-month market exclusivity added to the remaining patent life of the active moiety. Biological products are not eligible

Pediatric Rule declared invalid by the Federal Court for the District of Columbia. The court determined that the rule exceeded the FDA's existing statutory authority

2003
PREA reinstates the FDA's 1998 pediatric rule. Requires each new drug or biological product application contain data adequate to assess the safety and effectiveness of the drug for its claimed adult indication and to support safe and effective dosing formulations for each pediatric subgroup. Products with orphan designation are exempted

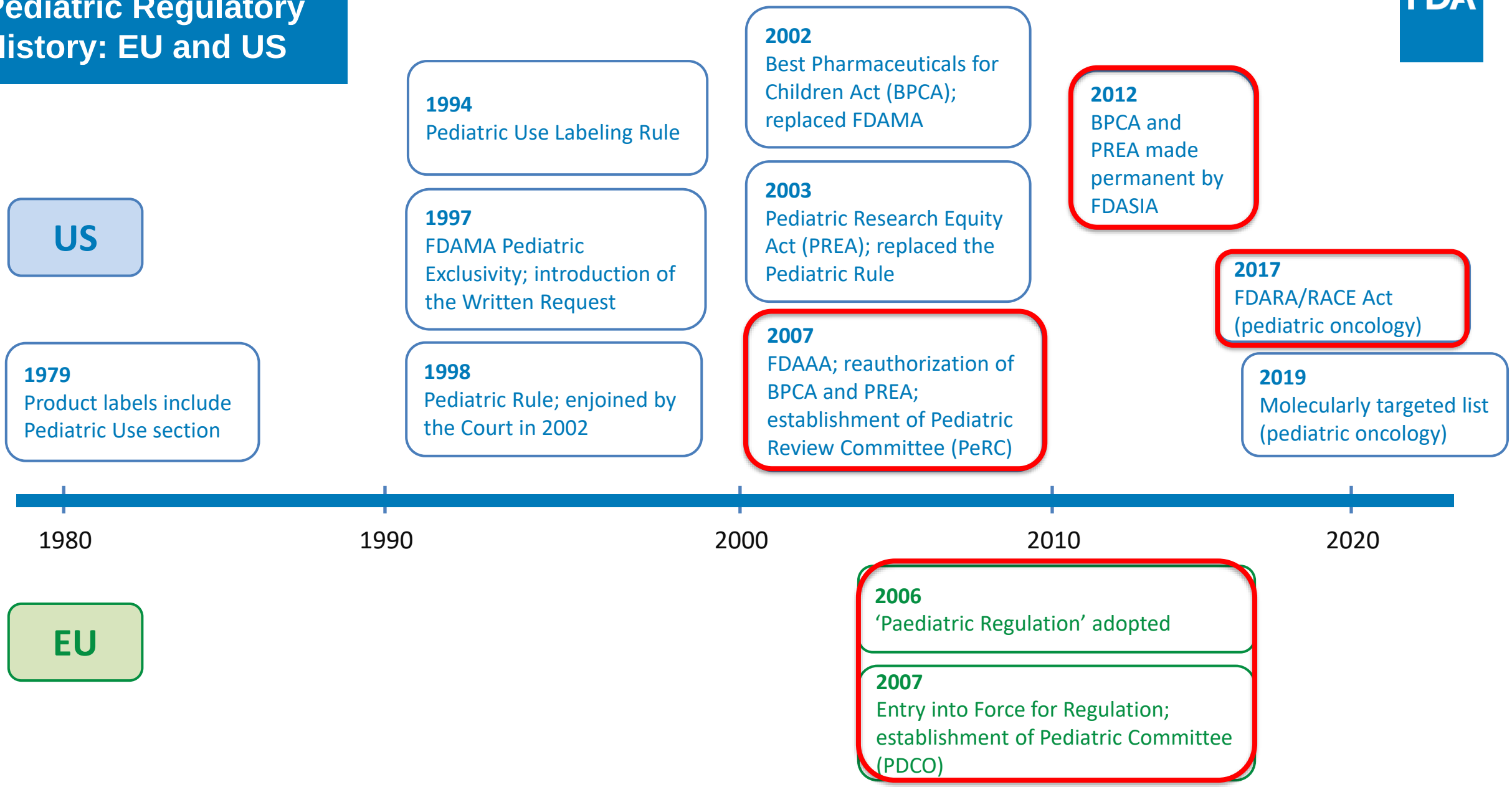
2007
Reauthorization of BPCA & PREA for 5 years under the FDAAA: Pediatric Review Committee (PeRC) formed for consults on pediatric plans/assessments and reviews all requests for deferrals, waivers, and pediatric plans. Studies submitted will result in pediatric labeling information

2012
FDASIA legislation BPCA and PREA are permanent

2017
FDARA implemented for oncology products

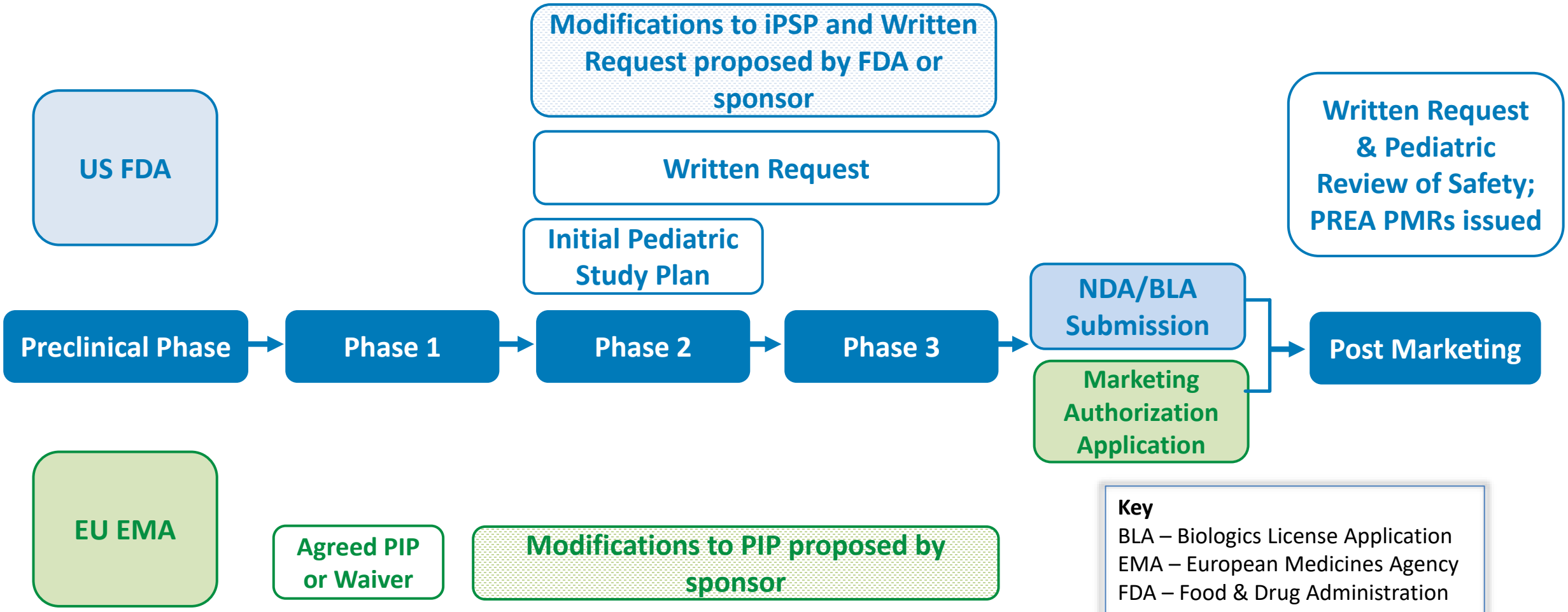
2019
Molecular Target list posted publicly in August

Pediatric Regulatory History: EU and US



Source: adapted from Mette Due Theilade Thomsen, 2019

Regulatory Process for New Drug Development – US and EU



Key
BLA – Biologics License Application
EMA – European Medicines Agency
FDA – Food & Drug Administration
iPSP – initial Pediatric Study Plan
NDA – New Drug Application
PIP – Pediatric Investigation Plan

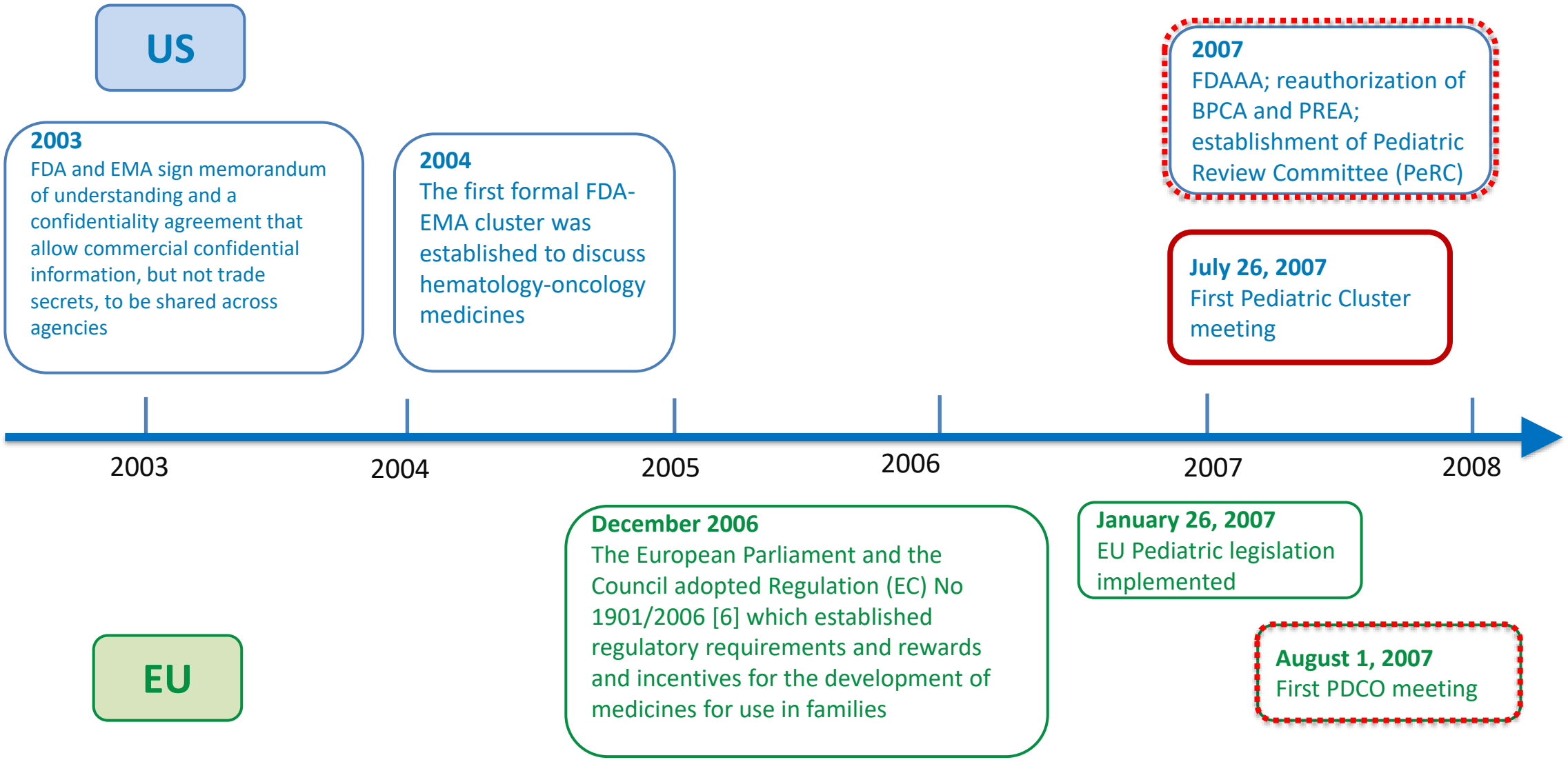
Source: Adapted from: https://www.ema.europa.eu/en/documents/presentation/presentation-paediatric-investigation-plan-assessment-procedure_en.pdf

Global Priorities in Pediatric Drug Development

"FDA and EMA are committed to ongoing harmonization of scientific issues and convergence of approaches through the work of the Pediatric Cluster with a view toward a more global approach to the effective and efficient development of medicines for pediatric patients."

Source: Penkov D, Tomasi P, Eichler I, Murphy D, Yao LP, Temeck J. Pediatric Medicine Development: An Overview and Comparison of Regulatory Processes in the European Union and United States. Therapeutic Innovation and Regulatory Science. 2017;51:360-371

History of the Pediatric Cluster



Objectives of the Pediatric Cluster

- **Facilitate regular exchange of information** related to scientific and ethical issues on pediatric product development submitted according to EU/US legislation to avoid exposing children to unnecessary or duplicative trials
- **Aim at global pediatric development** in line with the pediatric legislation and regulations in the EU and US
- **Understand the scientific rationale** when differences in opinion exist
- **Discuss post-marketing pediatric requirements** and issues, including risk management and plans for long term safety monitoring
- To **discuss general topics** of regulatory and scientific interest to the participating agencies
- **Inform the participants** of planned scientific meetings or workshops related to pediatric matters with the possibility of attending the meetings

Source: Terms of Reference for the Pediatric Medicinal products cluster June 2007, updated August 2018

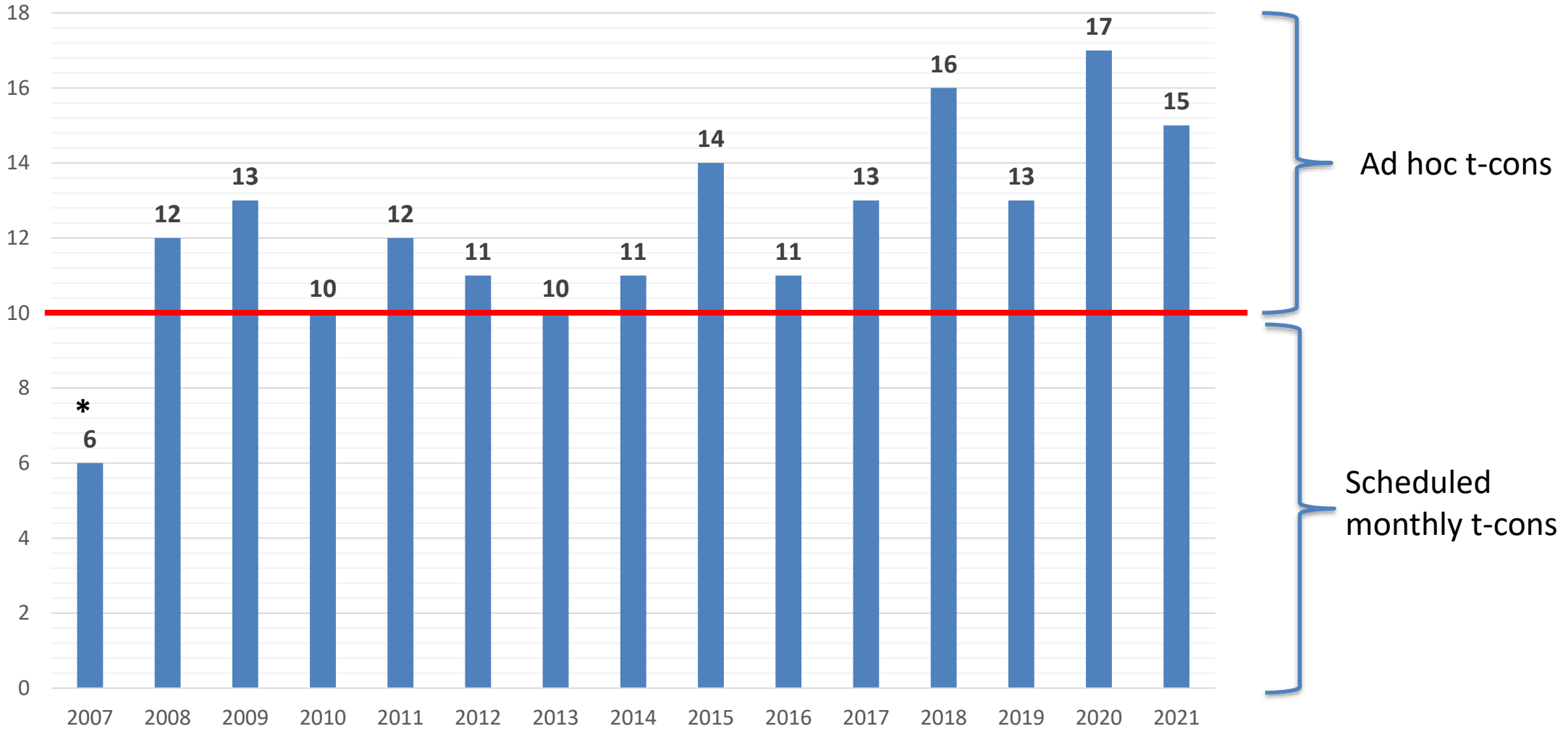
Participation in Pediatric Cluster by Agency

- FDA and EMA: since August 2007
- Japan's Pharmaceuticals and Medical Device Agency (PMDA) joined as observers in November 2009
- Health Canada (HC) joined as observers in September 2010
- Active participation by PMDA and HC since October 2012
- Australia's Therapeutic Goods Administration (TGA) joined as observers in February 2014
- Active participation by TGA since 2016

Pediatric Cluster: July 2007 – October 2022

- Established in 2007 as monthly informal teleconferences
- 194 t-cons: 663 products, 198 general topics
- Most frequently discussed product issues through 2021:
  - Scope of pediatric development
  - Safety
  - Types of clinical studies
  - Study design
  - Study population
- High rate of convergence, historically ~70%
  - Convergence is when FDA and EMA agree, or a similar approach/view is expected on a specific clinical trial issue discussed at the Pediatric Cluster

Number of Pediatric Cluster Teleconferences 2007- 2021



*Partial year since the Pediatric Cluster was established in July 2007

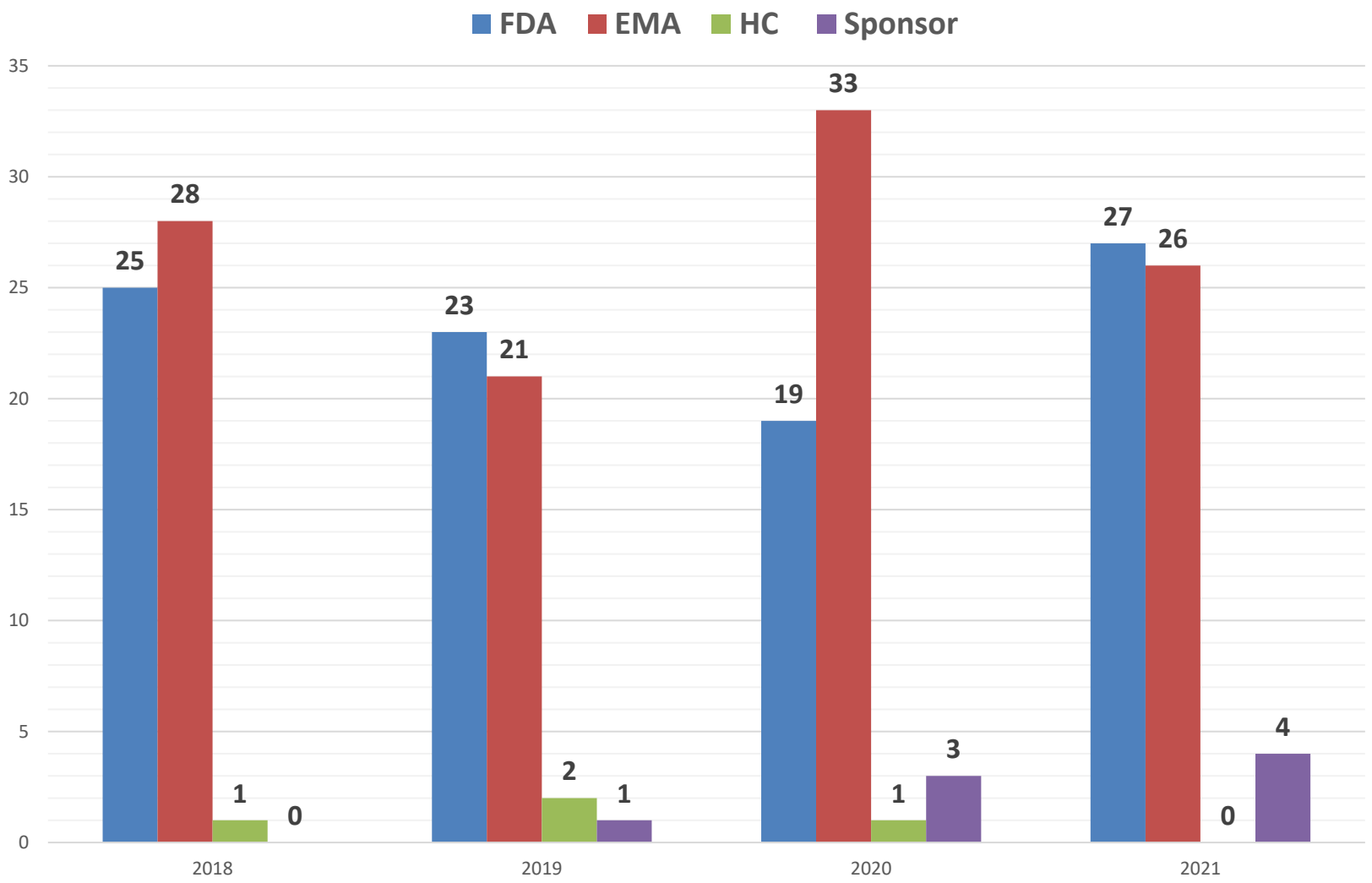
Examples of Areas of Discordance

- Clinical trial endpoints
- Interpretation of significance of non-clinical data
- Ability to extrapolate and the use of bridging biomarkers
- Potential need for juvenile toxicology studies
- Differences in clinical standard of care

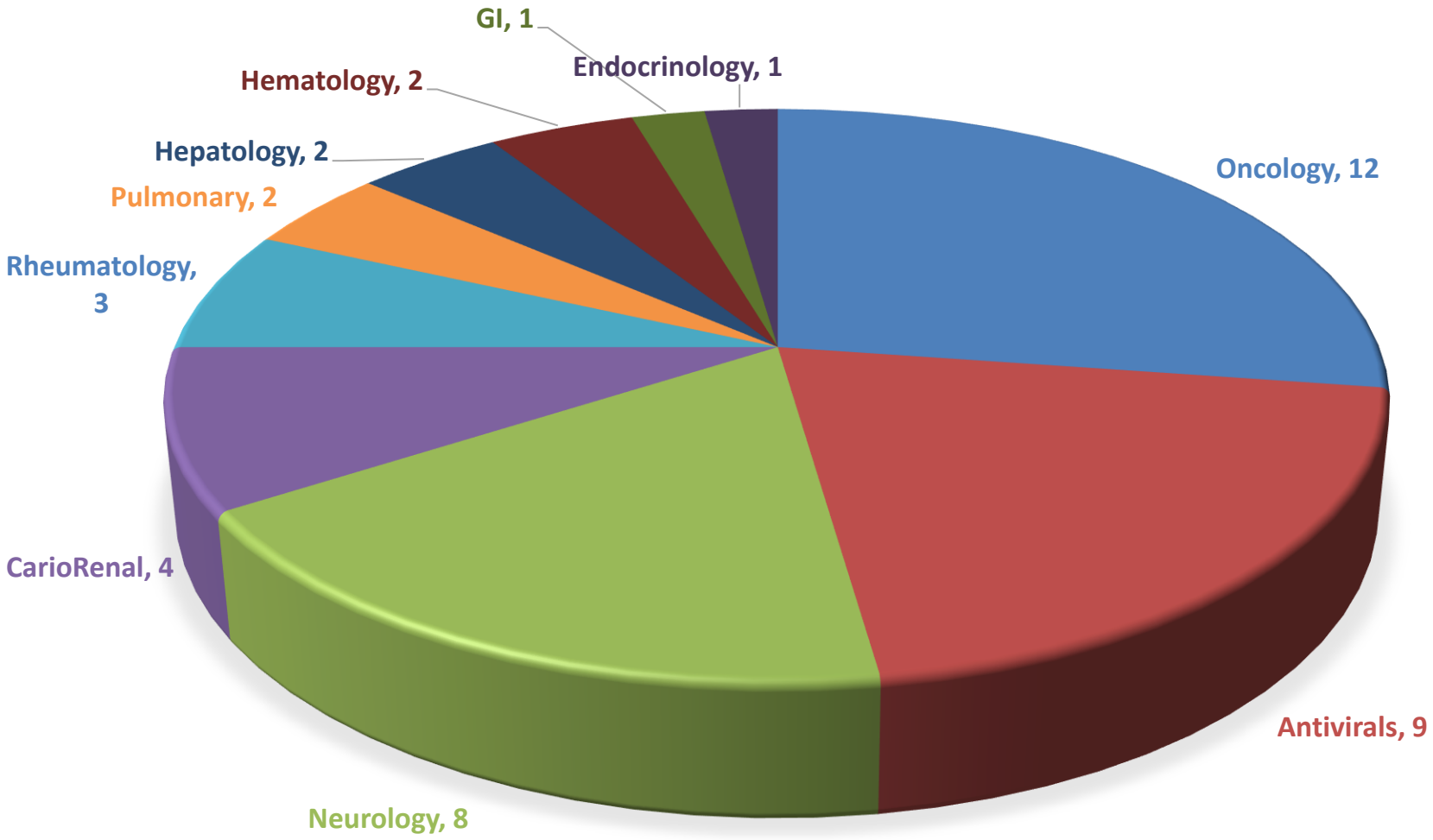
Process by Which Topics are Added to the Agenda

- Topics often suggested at Pediatric Review Committee meetings
- Anyone from any of the participating agencies can request topic
  - Sponsors may request that their product be discussed at the Pediatric Cluster; ultimately it is at the discretion of the Agencies to decide if a discussion at the Pediatric Cluster would be helpful
  - For FDA, the request should be sent to the relevant review division, not OPT
- Topics can be general or for a specific product

Who Proposed Topics for the Pediatric Cluster 2018-2021?



Therapeutic Areas Discussed in 2021



Pediatric Cluster External Communications

The Pediatric Cluster and its external communications are managed by OPT

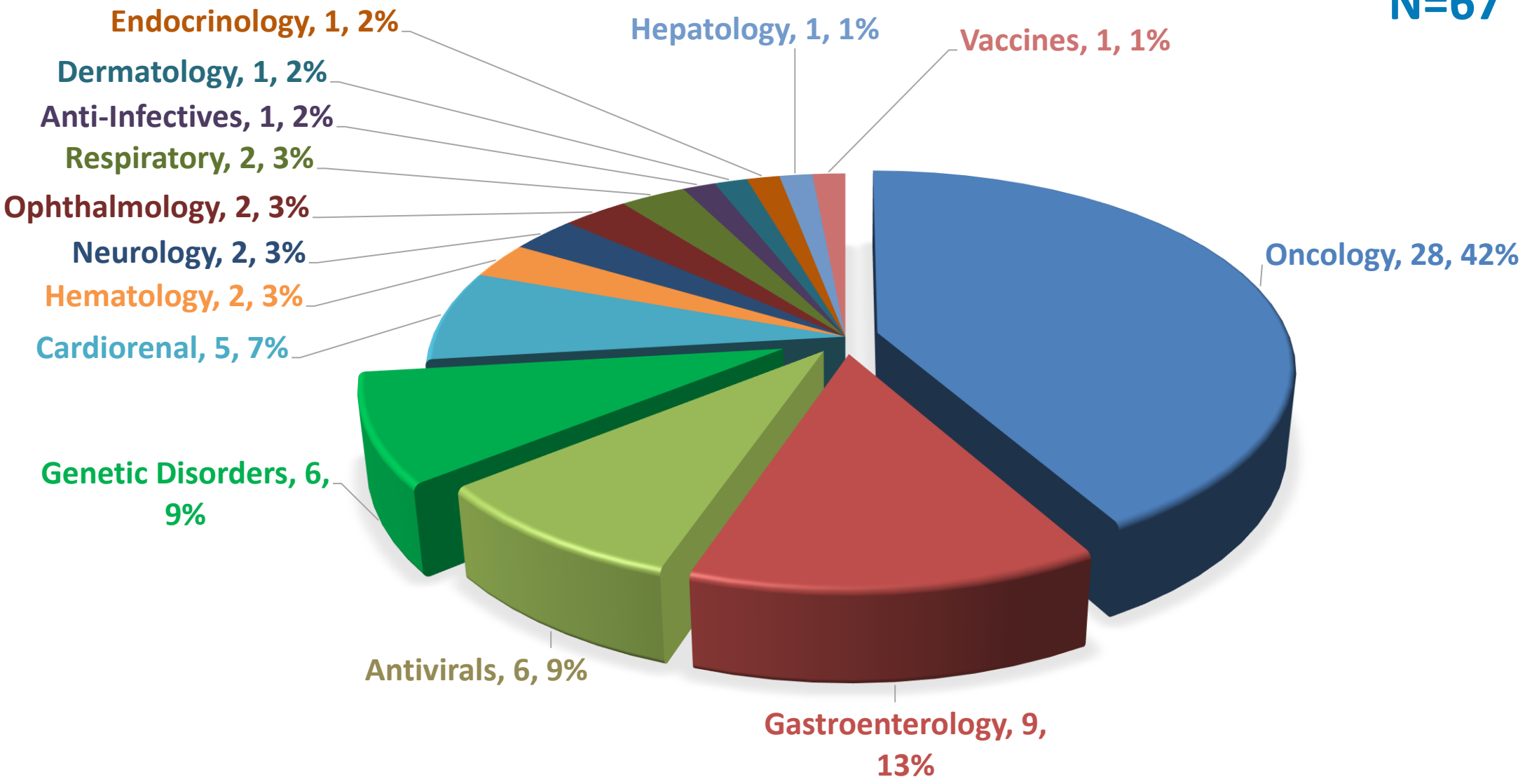
- Common Commentary – started in 2012
  - Informal comments are NOT binding or formal regulatory advice
- Action items from Pediatric Cluster shared with Sponsors if appropriate – started in 2018
  - High level comments to inform sponsors that their product was discussed and the agreed action
- Process for conveying action items to the sponsor
  - If the procedure is still ongoing at EMA, EMA will incorporate the action into the Summary Report to inform the sponsor
  - If the PIP is already agreed or is in clock stop, OPT will inform the sponsor
- Joint scientific documents and workshops - examples
  - Joint guidance - Gaucher disease
  - EMA/FDA/Health Canada joint workshop addressing unmet needs of children with pulmonary arterial hypertension.

Common Commentary Process

- Purpose of a Common Commentary is to provide informal non-binding comments to sponsors:
  - Simultaneous pediatric development plans are submitted to EMA and FDA
  - Pediatric development plans are currently under review
  - The product is discussed at the Pediatric Cluster
- Product-specific Common Commentary considered:
  - Serious or life-threatening disease particularly for those with few or no therapeutic options (e.g., oncology product)
  - Non-life-threatening disease but major issue, such as trial design, endpoint, safety or dosing
- General-topic Common Commentaries considered when the agencies determine that sharing information on the approach to studying a disease or condition will be helpful to sponsors
- FDA and EMA discuss if a Common Commentary is appropriate during the Pediatric Cluster teleconference
  - Document is cleared by both agencies before being sent to the sponsor
  - General common commentaries may be posted on the respective agencies' websites

Common Commentaries by Therapeutic Area 2012 – Oct 2022

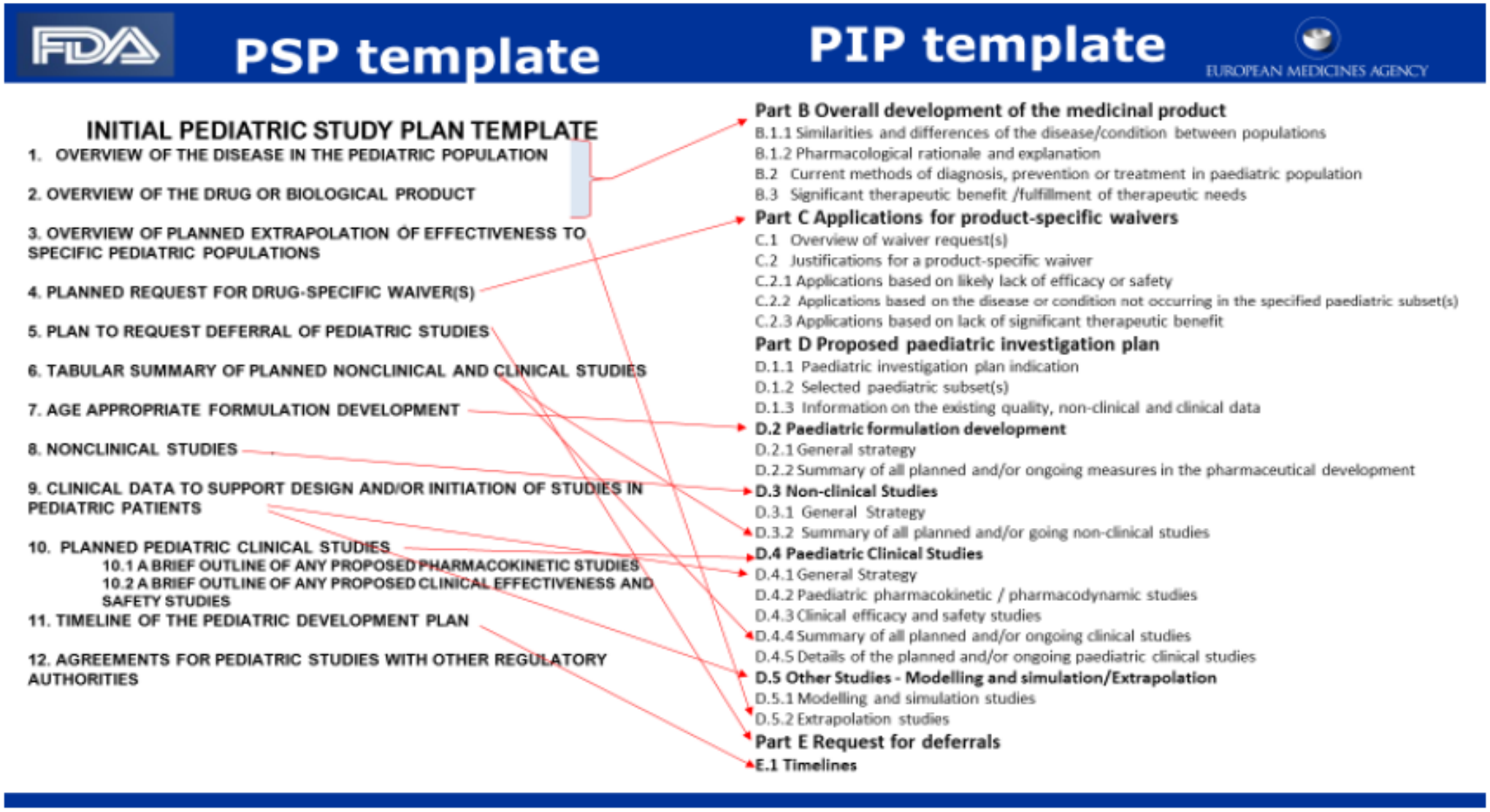
N=67



Public Common Commentaries

- FDA / EMA Common Commentary on Submitting an initial Pediatric Study Plan (iPSP) and Paediatric Investigation Plan (PIP) for the Prevention and Treatment of COVID-19
- Common issues requested for discussion by the respective agency (EMA/PDCO and FDA) concerning pediatric oncology development plans (Paediatric Investigation Plans [PIPs] and initial Pediatric Study Plans [iPSPs])
- Gaucher Disease Common Commentary- a collaborative approach from EMA and FDA

COVID-19 Common Commentary



The International Team in the Office of Pediatric Therapeutics

Donna Snyder, MD, MBE: team leader for Ethics and International team

donna.snyder@fda.hhs.gov

Sarah Zaidi, MD: medical officer liaison for the Pediatric Cluster

sarah.zaidi@fda.hhs.gov

Gerald 'GT' Wharton, MS: project manager for the Pediatric Cluster

gerold.wharton@fda.hhs.gov

Suzanne Malli, RN: liaison for PMDA (Japan) workshop and consultative support for the Pediatric Cluster

suzanne.malli@fda.hhs.gov

Summary

- The goal of the Pediatric Cluster is to promote a global approach to pediatric development plans with harmonization of scientific issues and convergence of approaches when possible
- FDA and EMA may issue a Common Commentary or provide action items from Pediatric Cluster discussions to sponsors, when appropriate
- Sponsors can request to have their products discussed at the Pediatric Cluster and can request a Common Commentary
  - For FDA, contact the appropriate review division
- COVID-19 Common Commentary illustrates how iPSP and PIP submissions may be aligned to meet the regulatory requirements of the FDA and EMA

U.S. FOOD & DRUG ADMINISTRATION

Thank you!


FDA
U.S. FOOD & DRUG
ADMINISTRATION

Parallel Scientific Advice

Tahira Khan
AbbVie

Parallel Scientific Advice

Tahira Khan

Director, Oncology Early Development and Pediatric Strategy

Regulatory Affairs, Abbvie

30 November 2022

Disclaimer

The views and opinions expressed in this presentation are those of the presenter and should not be attributed to Abbvie

Parallel Scientific Advice

Outline

1. Background
2. Procedure
3. Outcome
4. Benefits
5. A Hypothetical Case Study

Note: material presented in some of these slides is based upon published FDA and EMA guidance documents (references are provided)

Parallel Scientific Advice: Background

Objective: to enable **EMA and FDA** assessors and **Sponsors to exchange their views on scientific issues** during the development phase of new medicinal products

Best candidates for PSA include:

- **Important medicines** for which guidelines do not exist or for which guidelines differ significantly
- Products with **unique or significant issues** that could impede further development e.g. **clinical safety, animal toxicology, or unique manufacturing concerns**

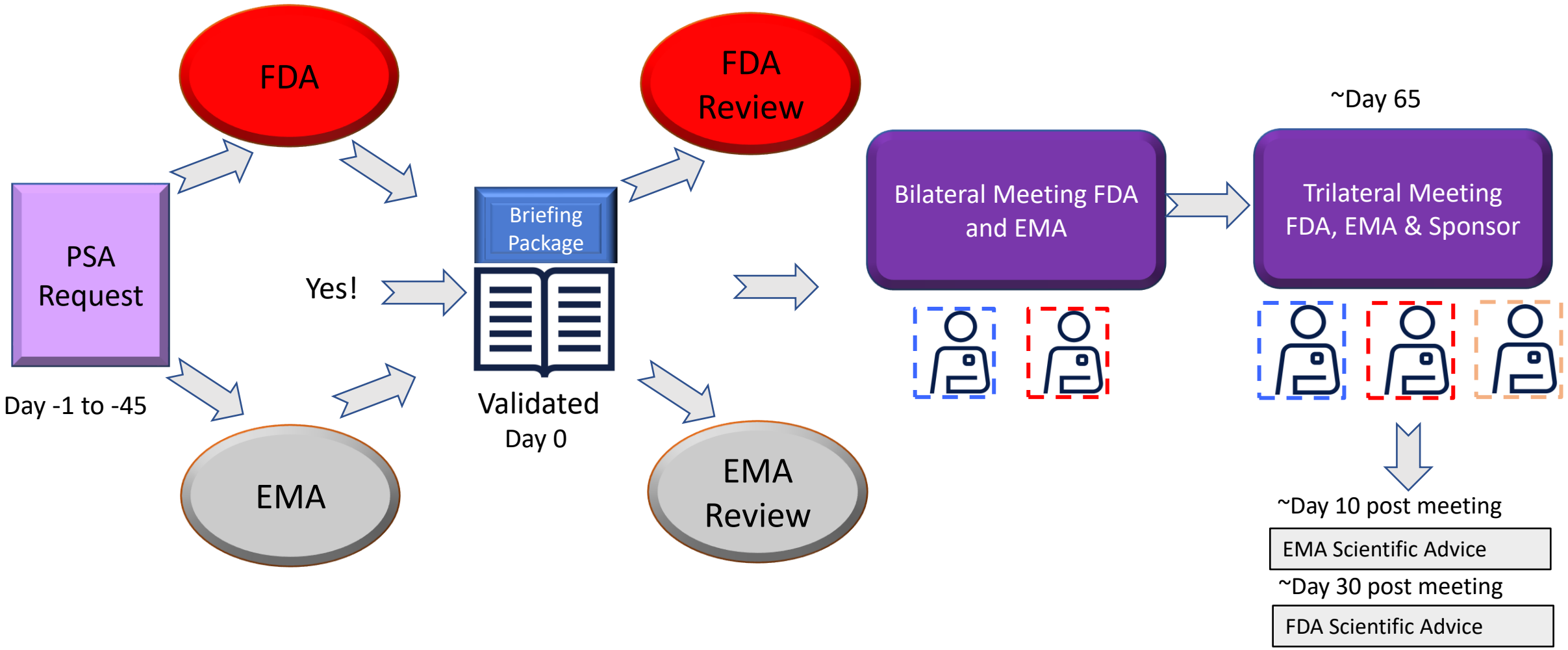
Reference: PSA "General Principles", July 2021

Parallel Scientific Advice: Procedure

- Voluntary and usually initiated at the Sponsor's request
- May also be initiated by either Agency in cooperation with the Sponsor
- Should focus primarily on specific questions or issues involving the development of the product for further scientific input from both FDA and EMA
- Addresses one set of questions by the sponsor; it is not a series of consultations
- Meetings are conducted under the provision of the confidentiality arrangement between the FDA and EMA and with the Sponsor's authorization
- If request is denied by one or both Agencies, independent Scientific Advice may be sought by Sponsor or experts from one agency may be invited by the other for discussions (consultative advice)

Reference: PSA "General Principles", July 2021

Parallel Scientific Advice: Procedure



Published PSA Timeline follows SAWP meeting timelines: ~75-90 days from validated briefing book to final advice
Predictable timeline once the briefing package is validated; pre-submission meeting with EMA may be requested

Parallel Scientific Advice: Outcome

Sponsor receives **independent advice from FDA and EMA** on the questions posed during the PSA

FDA and EMA will **aim to provide responses that are convergent**. However, Sponsors **may not receive the same recommendations from the two Agencies**

Reference: PSA "General Principles", July 2021

Parallel Scientific Advice: Benefits

Concurrent FDA and EMA scientific advice through a **single meeting** mechanism

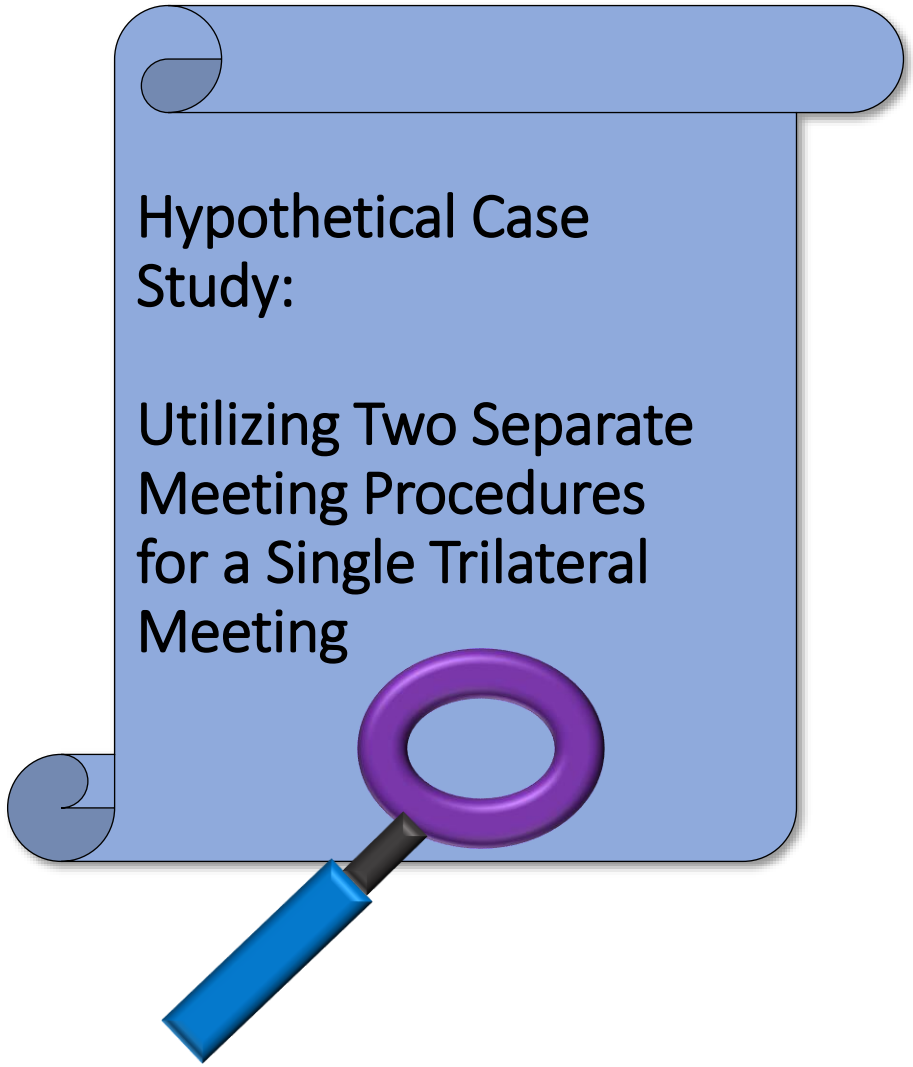
Clearer and deeper understanding of FDA and EMA regulatory and scientific perspectives on the development program, and, if divergent, the reasons for divergence

Provides FDA and EMA with an opportunity **to identify Sponsor's concerns** in implementing regulatory advice, if divergent between the Agencies

Optimizes global medicinal development, avoids unnecessary duplication of work/testing

May identify hurdles in global development of new medicines in unmet disease settings **to inform policy development and potential regulatory changes**

Reference: PSA "General Principles", July 2021



- **Objective: *Qualification* of a *novel study design*** and associated regulatory processes for pediatric medicinal development with joint input from EMA and FDA
- **Issue:** *Joint* FDA and EMA *Qualification* procedure does not exist for "novel study designs"; joint applications accepted for qualification of biomarkers and clinical outcome assessments
- **Solution:**
  - Proceed with **EMA Qualification procedure**
  - Utilize the **PSA procedure to invite FDA** to discuss the issues raised with EMA
  - Submit the same briefing package to both FDA and EMA
  - **Joint FDA and EMA discussion** followed by **a trilateral meeting** with Sponsor
- **Outcome:** better understanding of the scientific and regulatory issues related to proposed study design and feasibility of implementing the study globally

References

- https://www.fda.gov/media/105211/download (July 2021)
  - General principles ema-fda parallel scientific advice (human medicinal products)
- https://www.fda.gov/drugs/news-events-human-drugs/fda-ema-parallel-scientific-advice-psa-program-03162022 (March 16, 2022)
  - Parallel Scientific Advice 101
  - 5-Year Program Review and “Myth-busting” the PSA Timeline
  - FDA/EMA Parallel Scientific Advice (PSA) - Two case studies
  - Considering a PSA Request? Summary and Best Practices
- https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en.pdf

ACCELERATE Pediatric Strategy Forum

Gilles Vassal
Gustave Roussy
Comprehensive Cancer Center

ACCELERATE Pediatric Strategy Forums

Gilles Vassal, MD, PhD

Gustave Roussy Comprehensive Cancer Center

MRCT Webinar November 29, 2022

Disclosure

Pr Gilles Vassal, MD, PhD

Advice on pediatric oncology drug development to:
Astra-Zeneca, Bayer, BMS, Hutchinson-Medi Pharma, Pyramid, Lilly, Novartis, Pfizer, Roche/Genentech

Do not accept personal remuneration.

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Childhood cancers

- More than 400,000 new cases worldwide, annually
- In Low and Middle Income Countries
  - 15% - 45% cure rate
  - Challenge : access to standard effective treatments
- In High Income Countries
  - 80% disease free at 5 years with major differences across malignancies
  - 2/3 survivors with long term toxicity
  - Leading cause of death from disease beyond 1 year of age (6,000 deaths in Europe)

World Health Organization

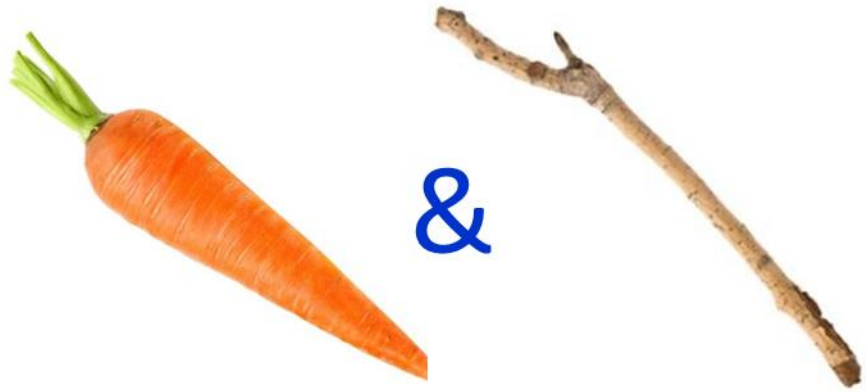
Global Childhood Cancer Initiative

Save 1 million children's lives from cancer by 2030

Cure More, Cure Better and Tackle inequalities

ANDREW McDONOUGH B+ FOUNDATION

A regulatory environment For better medicines for children



Obligations, incentives, rewards

Not delivering well for childhood cancers

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

2002

BPCA

stands for

Best Pharmaceuticals for Children Act

2003

PREA

stands for

Pediatric Research Equity Act

2017

RACE for Children Act

2006

Paediatric Regulation (EC) N°1901/2006

Ongoing process for revision as part of EU Pharmaceutical Strategy

ANDREW McDONOUGH B+ FOUNDATION

The issue - The ALK inhibition story

10 YEARS

1994 ⋯⋯▸ 2011 ⋯⋯▸ 2012 ⋯⋯▸ JAN 14, 2021

Discovery

ALK+

Lung cancer

ALCL*

IMT**

Neuroblastoma

In adults
In children and adults
In children

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Marketing authorisation

FDA U.S. FOOD & DRUG ADMINISTRATION

European Commission

Crizotinib in ALK+ Lung cancer

PREA
stands for
Pediatric Research Equity Act

Paediatric Regulation (EC) N°1901/2006

Waivered pediatric development

(lung cancer does not occur in children)

Academic pediatric development

More than 200 patients

Marketing authorization

FDA U.S. FOOD & DRUG ADMINISTRATION

Crizotinib in ALCL

SEPT 15, 2022

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Crizotinib in ALCL and IMT

*anaplastic lymphoma kinase gene
** inflammatory myofibroblasic tumor

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

An international multistakeholder organization to

Improve and accelerate new drug development for children and adolescents with cancer

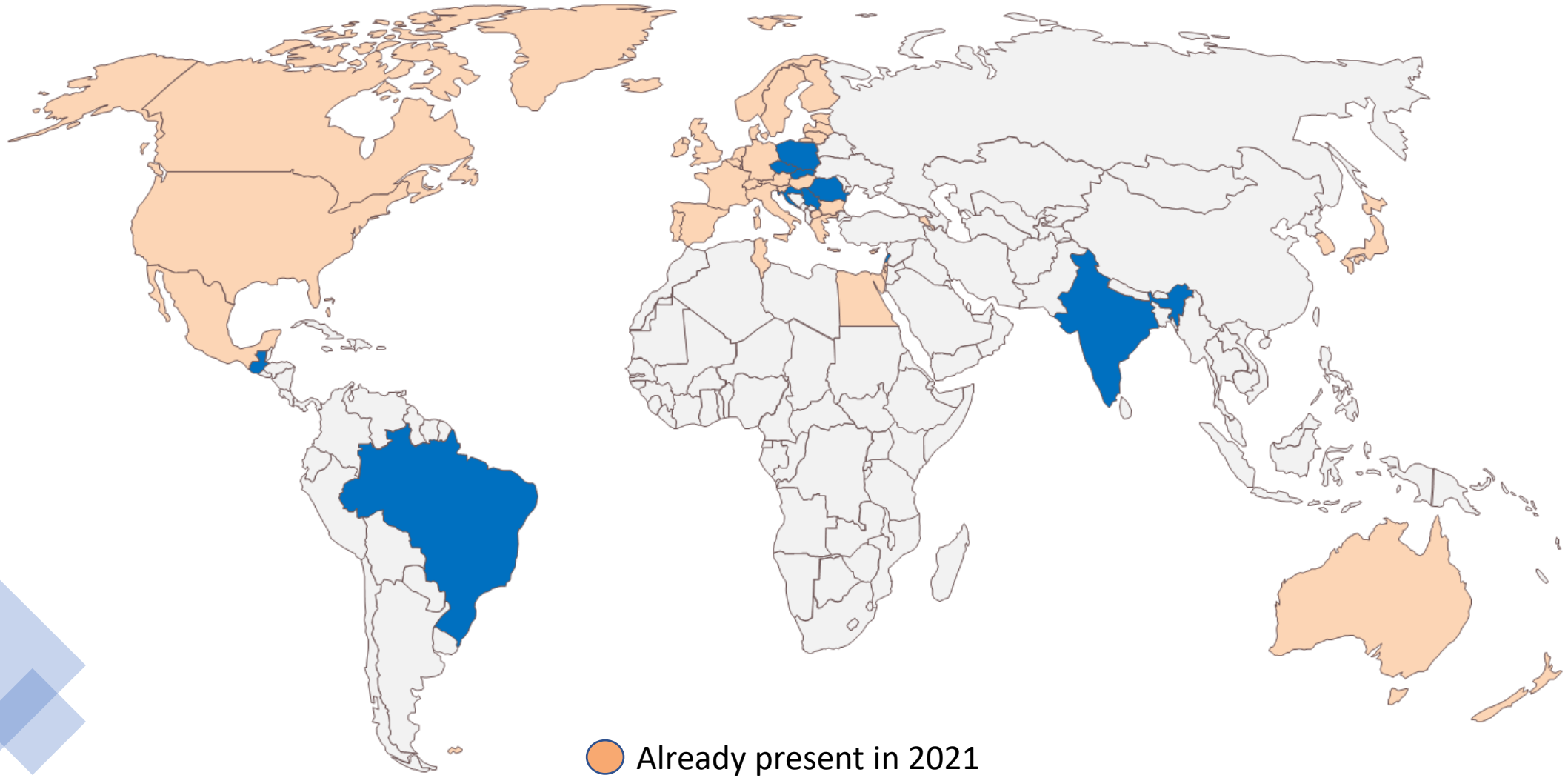
A patient centric organisation to solve problems

Created in 2015

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

International participation



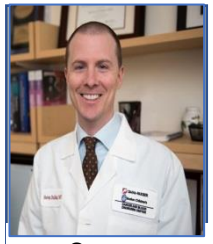
Already present in 2021
New entries

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

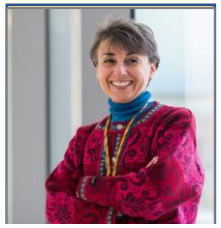
Steering Committee Members

Academia


Steven DuBois


Pam Kearns


Lynley Marshall


Lia Gore

Industry


Elly Barry


Hubert Caron


Heather Wasserstrom


Darshan Wariabharaj

Patients Advocacy


Leona Knox


Patricia Blanc


Susan Weiner


Nicole Scobie

Regulators


Sara Galluzzo


Dominik Karres


Gregory Reaman


Alberto Pappo

In tuitu personae


Jeffrey Skolnik


Raphael Rousseau


Peter Adamson

SIOP Europe CEO


Samira Essiaf

ITCC President / ACCELERATE Chair


Gilles Vassal

PSF Oversight Committee Chair/Senior Advisor


Andy Pearson

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

A patient centric organisation to solve problems

And shape the international landscape of pediatric oncology drug development

Principles

- Identify together a problem (annual conference)
- Understand the issue in an open multistakeholder dialog
  No blame ! No shame!
- Generate data
- Find solutions
- Implement solutions

ANDREW McDONOUGH B+ FOUNDATION

Multistakeholder working group on new development strategy to solve the ALK issue


Andy Pearson


Nicole Scobie

2016

European Journal of Cancer 62 (2016) 1–8

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

ELSEVIER

Current Perspective

Implementation of mechanism of action biology-driven early drug development for children with cancer

Andrew D.J. Pearson [a,*,1], Ralf Herold [b], Raphaël Rousseau [c], Chris Copland [d], Brigid Bradley-Garelik [e], Debbie Binner [f], Renaud Capdeville [g], Hubert Caron [h,i], Jacqueline Carleer [j], Louis Chesler [k], Birgit Geoerger [l], Pamela Kearns [m], Lynley Marshall [n], Stefan M. Pfister [o], Gudrun Schleiermacher [p], Jeffrey Skolnik [q], Cesare Spadoni [r], Jaroslav Sterba [s,t], Hendrick van den Berg [b], Martina Uttenreuther-Fischer [u], Olaf Witt [v], Koen Norga [w], Gilles Vassal [x] on behalf of Members of Working Group 1 of the Paediatric Platform of ACCELERATE[2]

Authors From Academia, Advocavy, Industry and Regulatory bodies

Request for Mechanism of action biology-driven early drug development

- Aggregated database of paediatric biological tumour drug targets √
- Joint academic–pharmaceutical industry pre-clinical platform to analyse the activity of new drugs = ITCC-P4 and PIVOT √
- ➢ Paediatric Strategy Forums to facilitate prioritisation √
- Molecular profiling of paediatric tumours at diagnosis and relapse √
- Suppression of article 11b of the European Paediatric Regulation

ACCELERATE-EMA-FDA Paediatric Strategy Forum

- **Goal –**
  To ***share*** information between **all** stakeholders,
  to ***evaluate*** science,
  to ***inform*** paediatric drug development strategies and *subsequent* decisions
  a multi-stakeholder meeting with open dialog in a pre-competitive setting, on a malignancy or class of compounds
- Improve the selection *and prioritisation* of innovative drugs being evaluated for children and adolescents cancer, this will be driven by science and meet patients' unmet needs

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

FDA U.S. FOOD & DRUG ADMINISTRATION

Paediatric Strategy Forums
Continually evolving

Lancet Oncol 2022, 23:1354

2017

PSF - 1
ALK inhibition

PSF - 2
Mature B-cell lymphoma

2018

PSF - 3
CheckPoint Inhibitors

2019

PSF - 4
Acute Myeloid Leukemia

PSF Prioritisation
Acute Myeloid Leukemia

2020

PSF - 5
Epigenetic modifiers

PSF Prioritisation
BET inhibitors

2021

PSF - 6
Second ALK inhibition

PSF - 7
CAR T cells

PSF - 8
TKI in Sarcomas

2022

PSF - 9
MAPK inhibitors

PSF -10
DNA Damaging agents

2023

PSF - 11
PI3K/AKT/mTOR Pathway

PSF - 12
CDK 4, 6 & 9 inhibitors

PSF - 13
Topic To be decided

Overall more than 200 assets discussed by 1000 participants.

ANDREW McDONOUGH B+ FOUNDATION

PUBLICATION of PEDIATRIC STRATEGY FORUMS and PRIORITISATION MEETING

N°2 Mature B cell Lymphoma

European Journal of Cancer 110 (2019) 74–85

Available online at www.sciencedirect.com

ELSEVIER

Original Research

ACCELERATE and European Medicine Agency Paediatric Strategy Forum for medicinal product development for mature B-cell malignancies in children

Andrew D.J. Pearson [a,*,1], Nicole Scobie [b], Koenraad Norga [c], Franca Ligas [d], Davy Chiodin [e], Amos Burke [f], Veronique Minard-Colin [g], Peter Adamson [h], Lynley V. Marshall [i,am], Arun Balakumaran [j,2], Bouchra Benettaib [k], Pankaj Bhargava [l], Catherine M. Bollard [m], Ellen Bolotin [n], Simon Bomken [o], Jochen Buechner [p], Birgit Burkhardt [q], Hubert Caron [r], Christopher Copland [s], Pierre Demolis [t], Anton Egorov [u], Mahdi Farhan [v], Gerhard Zugmaier [w], Thomas Gross [x], Danielle Horton-Taylor [y], Wolfram Klapper [z], Giovanni Lesa [d], Robert Marcus [aa], Rodney R. Miles [ab], Kerri Nottage [ac], Lida Pacaud [ad], Rosanna Ricafort [ae], Martin Schrappe [af], Jaroslav Sterba [ag], Remus Vezan [ah], Susan Weiner [ai], Su Young Kim [aj], Gregory Reaman [ak], Gilles Vassal [al]

N°3 Check Point Inhibitors

European Journal of Cancer 127 (2020) 52–66

Available online at www.sciencedirect.com

ELSEVIER journal homepage: www.ejcancer.com

Original Research

ACCELERATE and European Medicines Agency Paediatric Strategy Forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients

Andrew D.J. Pearson [a,*], Claudia Rossig [b], Giovanni Lesa [c], Scott J. Diede [d], Susan Weiner [e], John Anderson [f], Juliet Gray [g], Birgit Geoerger [h], Veronique Minard-Colin [h], Lynley V. Marshall [i], Malcolm Smith [j], Paul Sondel [k], Marcis Bajars [l], Claudia Baldazzi [m], Elly Barry [n], Sam Blackman [a], Patricia Blanc [o], Renaud Capdeville [p], Hubert Caron [q], Peter D. Cole [r], Jorge Camarero Jiménez [s], Pierre Demolis [t], Martha Donoghue [u], Mabrouck Elgadi [v], Thomas Gajewski [w], Sara Galluzzo [x], Robert Ilaria Jr [y], Alessandro Jenkner [z], Dominik Karres [c], Mark Kieran [aa], Franca Ligas [c], Israel Lowy [ab], Michael Meyers [ac], Corina Oprea [ad], Vijay G.R. Peddareddigari [ae], Jaroslav Sterba [af], Paul K. Stockman [ag], Peter Suenaert [ah], Uri Tabori [ai], Cornelis van Tilburg [aj], Todd Yancey [ak], Brenda Weigel [al], Koenraad Norga [am], Gregory Reaman [u], Gilles Vassal [h]

N°4 Acute Myeloid Leukemia

European Journal of Cancer 136 (2020) 116–129

Available online at www.sciencedirect.com

ScienceDirect

Original Research

Paediatric Strategy Forum for medicinal product development for acute myeloid leukaemia in children and adolescents☆
ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration

Andrew. D.J. Pearson [a,*,1], C.Michel Zwaan [b,c,1], E.Anders Kolb [d,1], Dominik Karres [e], Julie Guillot [f], Su Young Kim [g], Lynley Marshall [h], Sarah K. Tasian [i], Malcolm Smith [j], Todd Cooper [k], Peter C. Adamson [l], Elly Barry [m], Bouchra Benettaib [n], Florence Binlich [o], Anne Borgman [p], Erica Brivio [b,c], Renaud Capdeville [q], David Delgado [r], Douglas V. Faller [s], Linda Fogelstrand [t], Paula Goodman Fraenkel [u], Henrik Hasle [v], Delphine Heenen [w], Gertjan Kaspers [b,c], Mark Kieran [x], Jan-Henning Klusmann [y], Giovanni Lesa [e], Franca Ligas [e], Silvia Mappa [z], Hesham Mohamed [aa], Andrew Moore [ab], Joan Morris [ac], Kerri Nottage [ad], Dirk Reinhardt [ae], Nicole Scobie [af,ag], Stephen Simko [ah], Thomas Winkler [ai], Koen Norga [aj], Gregory Reaman [ak], Gilles Vassal [a,al]

N°5 Epigenetic Modifiers

European Journal of Cancer 139 (2020) 135–148

Available online at www.sciencedirect.com

ELSEVIER

Review

Paediatric Strategy Forum for medicinal product development of epigenetic modifiers for children ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration

Andrew DJ. Pearson [a,*,1], Kimberly Stegmaier [b,1], Franck Bourdeaut [c,1], Gregory Reaman [d], Delphine Heenen [e], Michael L. Meyers [f], Scott A. Armstrong [b], Patrick Brown [g], Daniel De Carvalho [h], Nada Jabado [i], Lynley Marshall [j], Miguel Rivera [k], Malcolm Smith [l], Peter C. Adamson [m], Amy Barone [d], Christian Baumann [n], Samuel Blackman [o], Vickie Buenger [p], Martha Donoghue [d], Aundrietta D. Duncan [q], Elizabeth Fox [r], Brian Gadbaw [s], Maureen Hattersley [t], Peter Ho [u], Ira Jacobs [v], Michael J. Kelly [w], Mark Kieran [x], Giovanni Lesa [y], Franca Ligas [y], Donna Ludwinski [z], Joe McDonough [aa], Zariana Nikolova [ab], Koen Norga [ac], Adrian Senderowicz [ad], Tilmann Taube [ae], Susan Weiner [af], Dominik Karres [y], Gilles Vassal [ag]

N°6 ALK inhibitors

European Journal of Cancer 157 (2021) 198–213

ELSEVIER journal homepage: www.ejcancer.com

Review

Second Paediatric Strategy Forum for anaplastic lymphoma kinase (ALK) inhibition in paediatric malignancies
ACCELERATE in collaboration with the European Medicines Agency with the participation of the Food and Drug Administration

Andrew D.J. Pearson [a,*], Elly Barry [b], Yael P. Mossé [c], Franca Ligas [d], Nick Bird [e], Teresa de Rojas [a], Zachary F. Zimmerman [f], Keith Wilner [g], Willi Woessmann [h], Susan Weiner [i], Brenda Weigel [j], Rajkumar Venkatramani [k], Dominique Valteau [l], Toby Trahair [m], Malcolm Smith [n], Sonia Singh [o], Giovanni Selvaggi [p], Nicole Scobie [q], Gudrun Schleiermacher [r], Nicholas Richardson [o], Julie Park [s], Karsten Nysom [t], Koen Norga [u], Margret Merino [o], Joe McDonough [v], Yousif Matloub [w], Lynley V. Marshall [x], Eric Lowe [y], Giovanni Lesa [d], Meredith Irwin [z], Dominik Karres [d], Amar Gajjar [aa], François Doz [r], Elizabeth Fox [aa], Steven G. DuBois [ab], Martha Donoghue [o], Michela Casanova [ac], Hubert Caron [ad], Vickie Buenger [ae], Diana Bradford [o], Patricia Blanc [af], Amy Barone [o], Gregory Reaman [o], Gilles Vassal [a,l]

N°7 CART-cells

European Journal of Cancer 160 (2022) 112–133

Available online at www.sciencedirect.com

ELSEVIER

Review

Paediatric Strategy Forum for medicinal product development of chimeric antigen receptor T-cells in children and adolescents with cancer
ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration[2]

Andrew DJ. Pearson [a,*,1], Claudia Rossig [b,1], Crystal Mackall [c,1], Nirali N. Shah [d,1], Andre Baruchel [e,1], Gregory Reaman [f], Rosanna Ricafort [g], Delphine Heenen [h], Abraham Bassan [i], Michael Berntgen [j], Nick Bird [k], Eric Bleickardt [l], Najat Bouchkouj [f], Peter Bross [f], Carrie Brownstein [m], Sarah Beaussant Cohen [n], Teresa de Rojas [a], Lori Ehrlich [f], Elizabeth Fox [o], Stephen Gottschalk [o], Linda Hanssens [p], Douglas S. Hawkins [q], Ivan D. Horak [r], Danielle H. Taylor [s], Courtney Johnson [f], Dominik Karres [t], Franca Ligas [t], Donna Ludwinski [u], Maksim Mamonkin [v], Lynley Marshall [w], Behzad K. Masouleh [x], Yousif Matloub [y], Shannon Maude [z], Joe McDonough [aa], Veronique Minard-Colin [ab], Koen Norga [ac], Karsten Nysom [ad], Alberto Pappo [o], Laura Pearce [ae], Rob Pieters [af], Martin Pule [ag], Alfonso Quintás-Cardama [ah], Nick Richardson [f], Martina Schüßler-Lenz [ai,as], Nicole Scobie [aj], Martina A. Sersch [ak], Malcolm A. Smith [al], Jaroslav Sterba [am], Sarah K. Tasian [z], Brenda Weigel [an], Susan L. Weiner [ao], Christian Michel Zwaan [af,ap,ar], Giovanni Lesa [t], Gilles Vassal [a,aq]

Prioritising BET inhibitors

European Journal of Cancer 146 (2021) 115–124

Available online at www.sciencedirect.com

ScienceDirect

Review

Bromodomain and extra-terminal inhibitors—A consensus prioritisation after the Paediatric Strategy Forum for medicinal product development of epigenetic modifiers in children—ACCELERATE

Andrew DJ. Pearson [a,*], Steven G. DuBois [b], Vickie Buenger [c], Mark Kieran [d], Kimberly Stegmaier [b], Pratiti Bandopadhayay [b], Kelly Bennett [e], Franck Bourdeaut [f], Patrick A. Brown [g], Louis Chesler [h], Jessica Clymer [b], Elizabeth Fox [i], Christopher A. French [j], Eva Germovsek [k], Francis J. Giles [l], Julia G. Bender [m], Maureen M. Hattersley [n], Donna Ludwinski [o,p], Katarina Luptakova [q], John Maris [r], Joe McDonough [s], Zariana Nikolova [t], Malcolm Smith [u], Athanasios C. Tsiatis [v], Rajeev Vibhakar [w], Susan Weiner [x], Joanna S. Yi [y], Fred Zheng [z], Gilles Vassal [a,aa]

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act

Guidance for Industry

December 2019

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Can a Multistakeholder Prioritization Structure Support Regulatory Decision Making? A Review of Pediatric Oncology Strategy Forums Reflecting on Challenges and Opportunities of this Concept

Dominik Karres[1,*], Giovanni Lesa[1], Franca Ligas[1], Pia Annunen[2,3], Maaike van Dartel[3,4], Pierre Demolis[5,6], Sara Galluzzo[3,7], Ralf Herold[8], Olga Kholmanskikh van Crickingen[9], Violeta Stoyanova-Beninska[3,10] and Koen Norga[3,11,12,13]

CPT, 108, 3, 553, 2020

Unmet therapeutic needs

i) develop innovative treatments for patients remaining incurable

ii) reduce high acute toxicity of current therapy

Conclusion

- Successful de-escalation at low risk in front line therapy can only be undertaken with an effective salvage regimen
- **Priority = developing treatment for relapse**
  - Very small number of patients = global strategy
  - Combination approach rather than monotherapy

GLONHL*

Consensus of clinicians on priorities

- Antibody drug conjugates
- CAR-T cells
- T-cell Engagers

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Paediatric Strategy Forum: Mature B cell malignancies in children
13 & 14 November 2017

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Impact of the Forum

Time Period	Number of Products	PIP	Full-Waivers
B-cell products			
July 2007 – November 2017	27	15/27 (56%)	12/27 (44%)
December 2017 – June 2021	36	9/36 (25%)	27/36 (75%)

Prioritisation + Medically and Scientifically justified Waivers

* International academic platform trial

Multistakeholder cooperation to facilitate prioritization: a pilot experience beyond oncology

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

2021

Multi-stakeholder Meeting on Paediatric Inflammatory Bowel Disease

In press in Journal of Crohn's and Colitis

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

2022

Multistakeholder Meeting on Pediatric Atopic Dermatitis

ACCELERATE 360°

mutistakeholder working groups

Nathalie Gaspar & Chris Copland

Fostering Age Inclusive Research

FAIR FOR AYA

ACCELERATE

Elly Barry & PamKearns

Fit For Filing

The Critical Role of Academic Clinical Trials in Pediatric Cancer Drug Approvals: Design, Conduct, and Fit for Purpose Data for Positive Regulatory Decisions

Bram De Wilde, MD[1,2]; Elly Barry, MD[3]; Elizabeth Fox, MD[4]; Dominik Karres, MD[5]; Mark Kieran, MD[3]; John Manlay, BA[6]; Donna Ludwinski, BSChE[7]; Gregory Reaman, MD[8]; and Pamela Kearns, MBChB, PhD[9]

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Daniele Horton & Mark Kieran

Long Term Follow Up

Received: 2 February 2021 | Revised: 5 March 2021 | Accepted: 18 March 2021
DOI: 10.1002/pbc.29047

Pediatric Blood & Cancer | aspho | WILEY

COMMENTARY

A global approach to long-term follow-up of targeted and immune-based therapy in childhood and adolescence

Mark W. Kieran[1,2] | Hubert Caron[3] | Jeanette Falck Winther[4,5] | Tara O. Henderson[8] | Riccardo Haupt[7,9] | Lars Hjorth[7,10] | Melissa M. Hudson[11] | Leontien C.M. Kremer[6,7] | Helena J. van der Pal[6,7] | Andrew D.J. Pearson[12] | Leonardo Pereira[13] | Gregory Reaman[14] | Roderick Skinner[7,15] | Gilles Vassal[12,16] | Susan L. Weiner[17] | Danielle Horton Taylor[1,12,18] | for the ACCELERATE Long-Term Follow-Up Working Group[1]

Leona Knox, Nicole Scobie & Greg Reaman

International Collaboration

RESEARCH ARTICLE

Cancer Medicine | WILEY

Intercontinental collaboration in clinical trials for children and adolescents with cancer—A systematic review by ACCELERATE

Teresa de Rojas[1] | Andrew J. Pearson[1] | Nicole Scobie[2] | Leona Knox[3] | Darshan Wariabharaj[4] | Pamela Kearns[5] | Gilles Vassal[1,6] | Gregory Reaman[7]

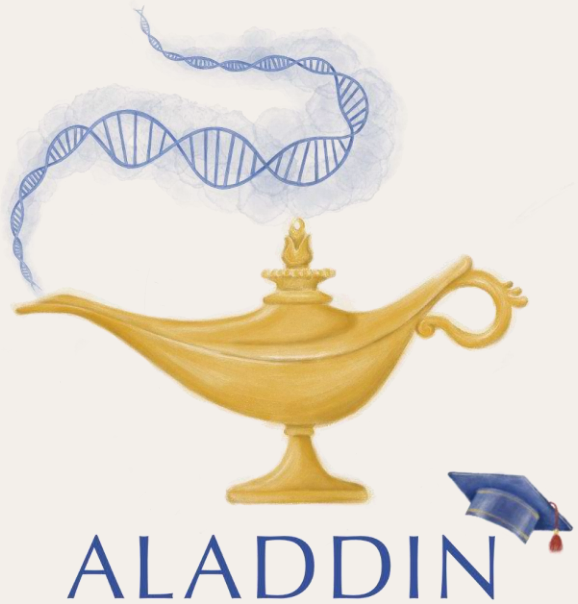
ACCELERATE

ANDREW McDONOUGH B+ FOUNDATION®

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

ALADDIN

Multi-stakeholder Education Alliance to Accelerate Drug Development for Children and Adolescents with Cancer



This project has received funding from the European Union's Erasmus+ programme under Grant Agreement No 101056190. Call: ERASMUS-EDU-2021-PI-ALL-INNO

European Commission

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Key success factors for accelerating the development of innovative therapies for children and adolescents with cancer

- Science-driven and patient-centered developments to address unmet needs
- Introduce use of real word data and deep learning of multiomics data
- Multistakeholder collaboration and engagement in a favorable an incentivizing regulatory environment to facilitate prioritisation
- Equal access to innovative and essential medicines for all children and adolescents 24/7
- A necessary global endeavour with international academic collaboration
- WORK TOGETHER : feasible and efficient

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Thanks

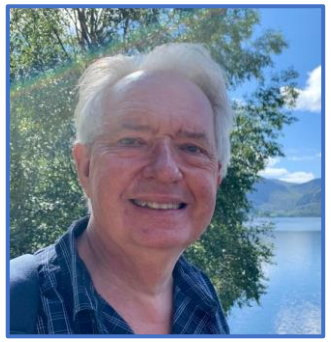
ANDREW McDONOUGH
B+
FOUNDATION®

ANDREW McDONOUGH
B+
FOUNDATION®

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

The Team

Prof. Gilles Vassal, MD, PhD
ITCC President / ACCELERATE Chair



Prof. Andy DJ Pearson, MD
Forums Committee Chair

Teresa de Rojas, MD, PhD
Scientific Coordinator

Andrea Demadonna (MA)
Operations Coordinator

Beatriz Martinez (SPA)
Communication and Marketing Coordinator

Jessica Rigoldi (MA)
Project Manager

Samira Essiaf
CEO

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

11th ACCELERATE PAEDIATRIC ONCOLOGY ANNUAL CONFERENCE

9–10 FEBRUARY 2023
BRUSSELS

@ACCELERATE_cure

Supported by

FOUNDATION

ANDREW McDONOUGH B+ FOUNDATION

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

OUR NAME IS OUR MISSION!

www.accelerate-platform.org

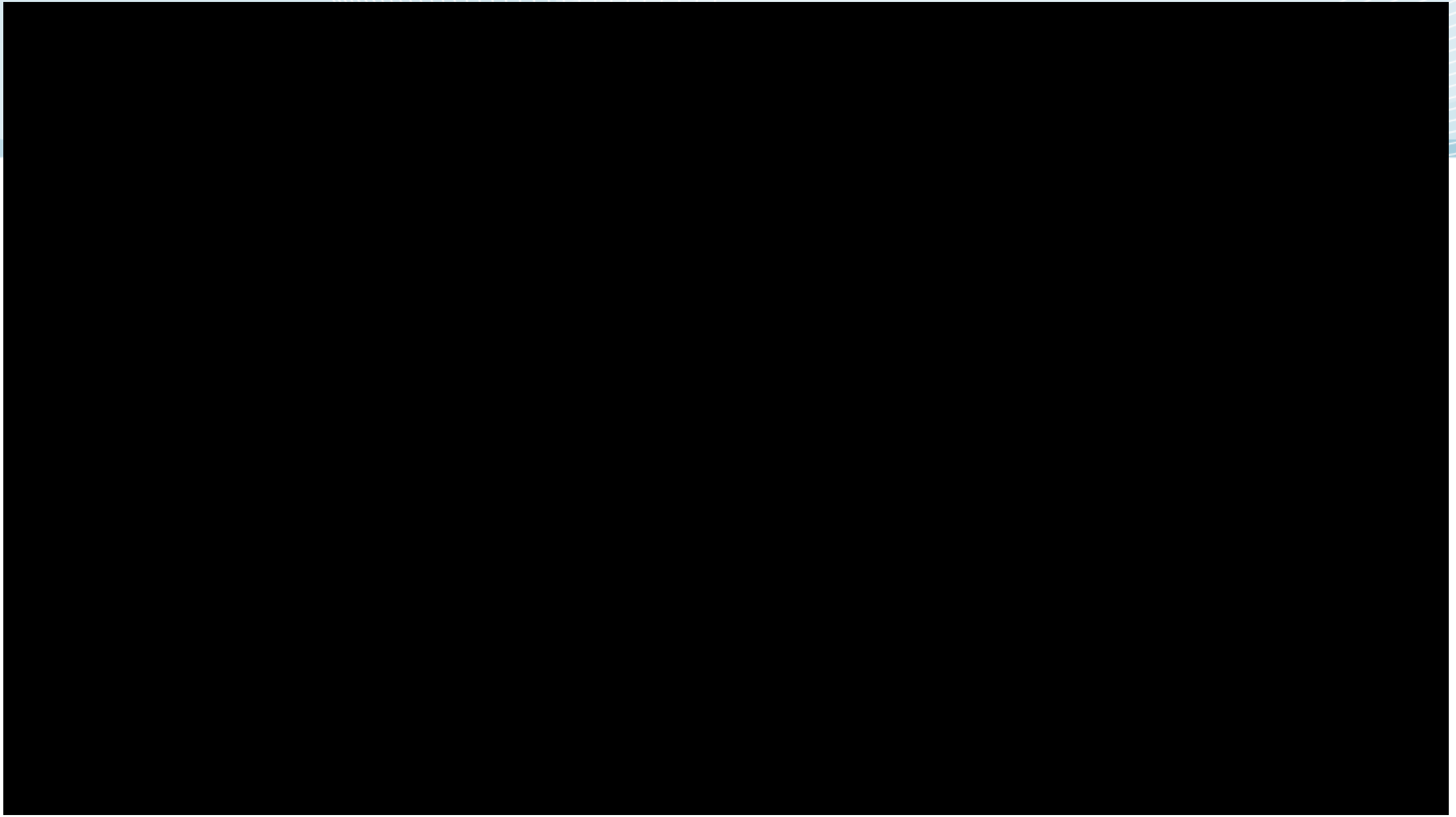
contact@accelerate-platform.org

Join on Twitter

@ACCELERATE_cure

Reliance Models

Marie Valentin
World Health Organization



PART FOUR

Panel Discussion: Strengths and Opportunities of Existing Models of Global Cooperation

PART FOUR

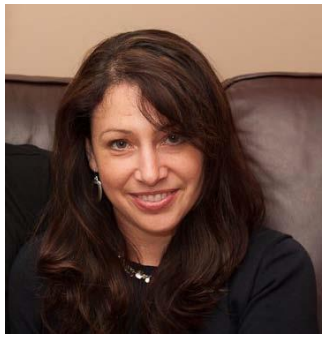
Dominik Karres
European Medicines Agency

Donna Snyder
U.S. Food and Drug Administration

Tahira Khan
AbbVie

Gilles Vassal
Gustave Roussy Comprehensive Cancer Center

Marie Valentin
World Health Organization



Elly Barry
Day One Bio

Gregory Reaman
National Cancer Institute

Franca Ligas
European Medicines Agency

Looking Ahead: Today's Wrap Up & Part 2 Agenda

- Reflections on today

- 30 November 2022, 9-11 am ET
  - Presentation: *Moving Towards Greater Global Cooperation for Pediatric Medicines Development*
  - Panel: Actions Towards Improving Existing Processes and Looking to the Future
  - Wrap up/moving ahead

Thank You!

PART FOUR

Please follow the MRCT Center:

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD