EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Facilitating engagement with the FDA to allow shaping paediatric development programmes

1st industry stakeholder platform on research and development support (EMA, London)

Presented by Irmgard Eichler on 25 April 2017
Senior Scientific Officer EMA Paediatric Medicines Office

Overview

Experience with the EMA-FDA paediatric cluster

Common commentary

How to facilitate discussions with EMA and FDA to shape paediatric development programmes

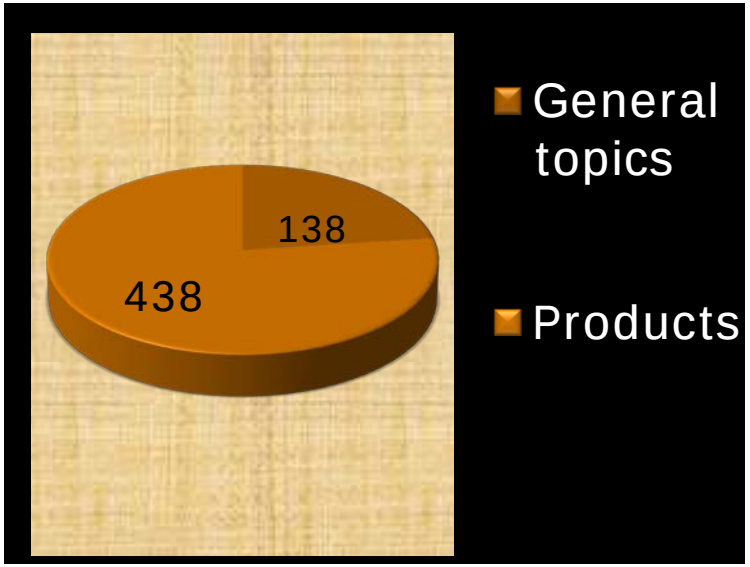
Experience with paediatric cluster

EUROPEAN MEDICINES AGENCY

How do regulators address global development in paediatric medicines?

Topics discussed 08/2007- 03/2017

Paediatric Cluster N=576



- We talk to each other frequently
- EMA/FDA **Paediatric Cluster**
- Monthly 2-3 hour teleconferences to discuss products/general issues
- More than one approach may be possible, but unnecessary studies are to be avoided
- Understand rationale when scientific approaches differ
- Aim for harmonization to the extent possible

Experience with paediatric cluster

EUROPEAN MEDICINES AGENCY

Topics discussed at paediatric cluster T-conferences

Product specific discussions:

Waiver
Quality, Non-clinical
Paediatric overall development
Adult study results - Paediatric study results
Indication
Population , Age groups
Study design, Sample size
Dose, Endpoints
Safety
Extrapolation
Timelines
Long-term follow-up

General discussions:

Endpoints
Extrapolation
Meetings/workshops
Joint publications
Regulatory action

Differences EU / USA

(EU Paediatric Regulation / BPCA-PREA-FDASIA)

	US BPCA	US PREA	EU
Development	Optional	Mandatory	Mandatory *(optional for off-patent)*
Instrument	Written Request	Paediatric Study Plan	Paediatric Investigation Plan
Waiver	N/A	3 grounds	3 grounds
Timing	anytime adequate information available	End of phase 2	> End of phase 1
Reward	6-month exclusivity	-	Main: 6-month SPC extension (patent)
Orphan products	Included	Excluded	Included
Decision	FDA	FDA	EMA (not EC) Opinion: Paed. Committee
Scope of paed. development	not limited to adult indication	= adult indication	Derived from adult indication
Scientific advice	Normally in global fee	Normally in global fee	Free for paediatrics

Differences / similarities EU / USA

EUROPEAN MEDICINES AGENCY

Review

DIA DEVELOP INNOVATE ADVANCE

Therapeutic Innovation
& Regulatory Science
1-12
© The Author(s) 2017
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/2168479017696265
tirs.sagepub.com

Pediatric Medicine Development: An Overview and Comparison of Regulatory Processes in the European Union and United States

Dobromir Penkov, MD[1], Paolo Tomasi, MD[1], Irmgard Eichler, MD[1], Dianne Murphy, MD[2], Lynne P. Yao, MD[2], and Jean Temeck, MD[2]

Abstract

Pediatric legislation in the US and the EU is driving pediatric product development on an international scale. To facilitate harmonization and global development of pediatric medicines, it is important to understand the legislative requirements that must be met along with incentives that exist in the US and the EU to include pediatric patients in therapeutic clinical trials. Although there are many similarities, differences exist. This review is an effort to enhance understanding of the pediatric legislation in both regions. It is intended as an overview to supplement the region-specific legislation and guidance documents that are available on the websites of the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Despite differences, the goal of the legislation in both the EU and the US is to incentivize and require timely, ethical, and sound scientific development of pharmaceutical products for the pediatric population and to provide information for their safe and effective use.

EU - US strategic meeting on the future of paediatric medicine 09/2016

- Representatives from the EC, EMA, FDA
- Discussion focused on how to harmonize and further streamline global paediatric product development
- Envisioned goal for the next few years: Aim for a convergent and harmonised paediatric development programme for each medicine

through

- Early proactive collaboration
- Joint outreach programmes to identify high priority needs and to facilitate related research and development
- Collaboration with all stakeholders to bring experts, researchers and industry together
- Organisation of joint initiatives to bring stakeholders together
- Paediatric Cluster to serve as key forum for continued discussion and resolution of scientific issues among regulators

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/12/WC500218004.pdf

Common commentary

- Tool to inform sponsors of products discussed at Paed Cluster
- Issue(s) for discussion identified (e.g. study design, timing)
- One or more discussions of the issues may be needed
- Discussion points, identifying similarities and/or differences in FDA's and EMA's approach, are summarized and approved by FDA and EMA
- Approved 1-2 page common commentary document sent to sponsor for information
- Comments sent are NOT binding on either Agency (i.e. they do NOT constitute regulatory advice)- but hopefully helpful

Common commentaries

Between October 2012- February 2017: N=25

- 10 Oncology
- 9 GI
- 2 Cardiology
- 1 Neurology
- 1 Inborn error metabolism
- 1 Dermatology
- 1 Antimicrobial

FDA/EMA common commentary: Impact on paed cancer drug development

G. Reaman, R. Herold et al; Pediatric Blood & Cancer, 2016

- 36 month period evaluated:
- 46 scientific discussions of 26 distinct oncology products:
- Focus on
  - toxicity; non-clinical data vs. adult patient experience and suggested monitoring plans, eligible patient populations and planned indication, study design
- CCs issued for 8 oncology products

- Global collaborative studies recommended in many cases
- All Common Commentaries directly influenced decisions PIPs, PSPs, and WRs
- Initial CC resulted in parallel scientific advice in some cases

How to facilitate discussions with EMA and FDA to shape paediatric development programmes

- Possibility to pilot an interaction with EMA and FDA on paediatric development programmes to further support global alignment
- Using the paediatric cluster T-conferences as platform
- Output as non-binding common commentary providing recommendations for streamlined PIP/PSP/PPSP addressing children's needs and regulatory requirements
- In case needed, option for trilateral discussions with the applicant and both agencies at the same time (not routinely)

Would this approach be considered helpful by developers?

Thank you for your attention

Any questions

Back-up slides

SP template

Similar!

PIP template

EUROPEAN MEDICINES AGENCY

Contains Nonbinding Recommendations

Draft — Not for Implementation

APPENDIX 2:
INITIAL PEDIATRIC STUDY PLAN TEMPLATE[37]

1. OVERVIEW OF THE DISEASE IN THE PEDIATRIC POPULATION (1-5 pages)
2. OVERVIEW OF THE DRUG OR BIOLOGICAL PRODUCT (1-5 pages)
3. OVERVIEW OF PLANNED EXTRAPOLATION TO SPECIFIC PEDIATRIC POPULATIONS (1-5 pages) *
4. REQUEST FOR DRUG-SPECIFIC WAIVER(S) (1-3 pages)
5. SUMMARY OF PLANNED NONCLINICAL AND CLINICAL STUDIES
6. PEDIATRIC FORMULATION DEVELOPMENT (1-3 pages)
7. NONCLINICAL STUDIES (1-5 pages)
8. CLINICAL DATA TO SUPPORT DESIGN AND/OR INITIATION OF STUDIES IN PEDIATRIC PATIENTS (1-5 pages)
9. PLANNED PEDIATRIC CLINICAL STUDIES
   - 9.1 Pediatric Pharmacokinetic Studies (1-10 pages)
   - 9.2 Clinical Effectiveness and Safety Studies (1-10 pages)
10. TIMELINE OF THE PEDIATRIC DEVELOPMENT PLAN (1-2 pages)
11. PLAN TO REQUEST DEFERRAL OF PEDIATRIC STUDIES (1-2 pages)
12. AGREEMENTS FOR OTHER PEDIATRIC STUDIES (1-5 pages)

(EMA PIP)

[37] This template is also available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM338453.pdf.

Table of contents