European Federation of Pharmaceutical Industries and Associations

Paediatric Clinical Research: Overcoming challenges and hurdles to foster innovation with Enpr-EMA

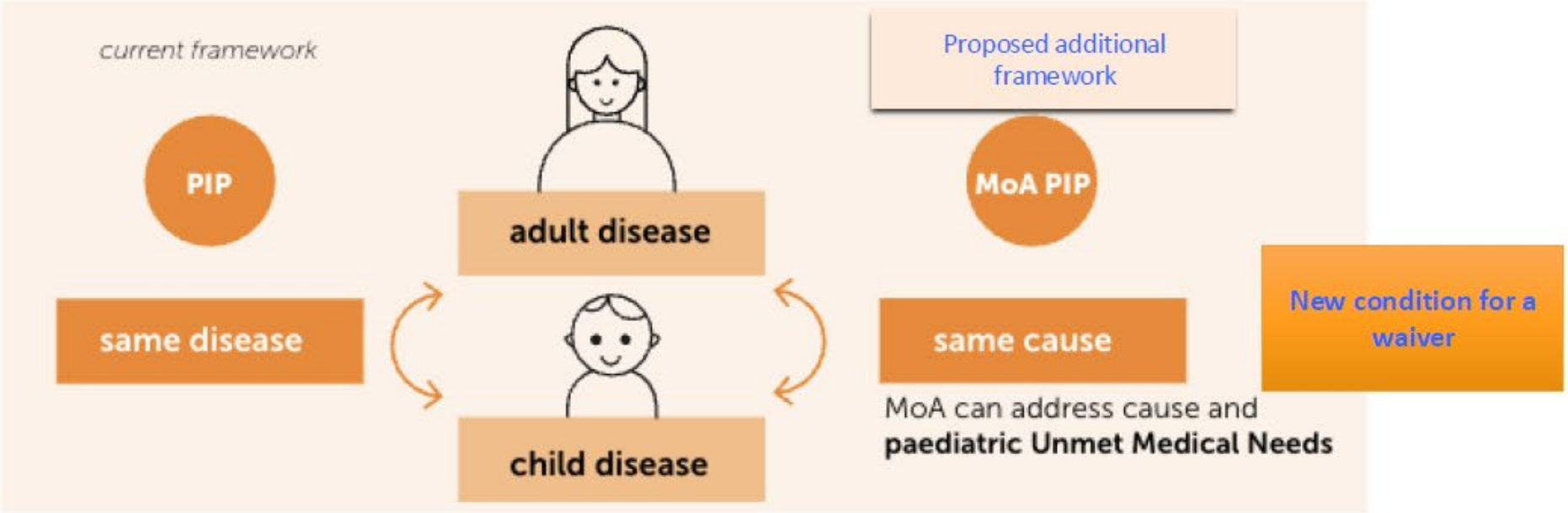
Paediatric drug development based on mechanism of action – Industry perspective

Dr Angeliki Siapkara

Senior Regulatory Affairs director, Global Paediatric oncology strategist

AstraZeneca

From an adult-centric to a child-centric approach: Mechanism of Action PIP



- Applicable to all therapeutic areas

Mechanism of action PIP

Summary of position (exact text to be determined as variability between EC and EP/council) :

To better address paediatric-only diseases, it has been proposed (in Art.75 of the Regulation) to restrict the granting of waivers where the intended condition for adults does not occur in children (or where the product is not expected to represent a significant therapeutic benefit for paediatric patients).

In such cases, the developer would be required to conduct a **PIP based on the mechanism of action of a product** which could have an impact on a different disease in children, **if and when there is scientific evidence to support this**.

Definitions

MoA is often used synonymously with “molecular target,” although some investigators reserve this term to describe the drug's action at a higher level of biological complexity, referring to a cell signalling system or processes that are impacted by the drug through its interaction with a specific molecular target. Thus MoA can encompass various pathways on which the drug has an impact.

In the US, oncology MOA-based iPSPs have been in place since the implementation of the RACE for Children Act (August 2020)

- If a molecularly targeted pediatric cancer investigation is warranted, it should provide clinically meaningful study data, “using appropriate formulations, regarding dosing, safety and preliminary efficacy to inform potential pediatric labeling.”*
- FDA to establish a Relevant Molecular Target List and Non-Relevant Molecular Target Leading to Waiver List to help guide industry

*FDARA Title V Sec 504 (a)(3)(A) or FD&C Act Sec. 505B (a)(3)(A)

Mechanism of action PIP

Where can EnprEMA and the paediatric networks assist ?

- **Further advances are needed in the knowledge of paediatric disease's biology to address potential benefit of MOA -**
  - How could "scientific evidence" with regards to "definitions of a condition" be made consistent and transparent for EMA/PDCO and industry to rely on?
  - Are lists of conditions and/or relevant and non relevant MOAs possible to be developed for paediatric diseases outside oncology ?
- **It is likely to be moving into CTs in paediatric diseases without prior adult data for the relevant compound in that disease which may create increased uncertainty -**
  - In such scenario, how can we safely initiate paediatric trials that can identify a paediatric potential benefit?
  - What would investigators, ethics committees and parents need to be assured of, to be part of such CTs?
- **When the uncertainty is too high, waiver should still be granted -**
  - How can robust scientific data be generated to support the clinical development of the compound in a paediatric indication?
- **In some areas of paediatric diseases, there is already competition for limited population numbers -**
  - Can there be a strong steer on where the unmet needs exist ?
  - How can development of multiple assets within the same MOA be prioritised?
  - How can we ensure enrolment of children in only those clinical trials that will deliver real benefit for this population?
- **The European ecosystem must collaborate and engage for success -**
  - Can there be platforms of multi-stakeholder collaborations per therapeutic area/disease to work on delivering scientific knowledge and regulatory predictability for drug development?

Mechanism of action PIP

EFPIA position

Need to appropriately frame the new requirements (in the law and more detailed guidelines).

We need a robust framework underpinned by science to ensure that this new obligation will lead to scientifically and clinically meaningful, doable R&D that is most effective and productive for the children who take part in the trials, and most beneficial for the wider paediatric patient population awaiting treatment.

At the same time this research should not place undue burden on innovators and developers to conduct multiple, unlimited numbers of studies or trials.

It is essential that the framework allows developers to focus efforts where the highest paediatric unmet medical need exists and for which the most robust, supportive underlying science is available.

efpia

European Federation of Pharmaceutical Industries and Associations

Thank you





EFPIA Brussels Office
Leopold Plaza Building * **51** Rue Montoyer
B-1000 Brussels * Belgium
Tel: + 32 (0)2 626 25 55
www.efpia.eu * info@efpia.eu