R&D Pharmaceutical Industry Perspective on Specifications for Pediatric Medicines

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About IFPMA

- IFPMA is a non-profit, non-governmental organization founded in 1968, representing 25 research-based pharmaceutical companies and 46 national and regional associations.

- IFPMA advocates policies that encourage discovery of and access to life-saving and life-enhancing new medicines to improve the health of patients everywhere.

- IFPMA has consultative status with the United Nations and its specialist agencies, including World Health Organization (WHO) and United Nations Children's Fund (UNICEF).

- The IFPMA Pediatric Task Force (PTF) was established in 2008 to actively partner with the WHO and other interested parties, to help improve the availability of treatments appropriately adapted to meet the needs of children especially for conditions/diseases prevalent in developing countries.
Industry is facing challenges in the R&D pediatric pharmaceutical products and in facilitating on access to these products. These include:

- development of age-appropriate formulations
- use of suitable excipients
- performing suitable clinical trials
- legal and ethical considerations in obtaining pediatric R&D data
- cost-effective manufacturing
- fulfilling regulatory requirements
- adequate logistics / supply chain in developing countries
- absence of stimuli for R&D and market uptake

IFPMA PTF has formulated the following key messages to communicate its viewpoints and demonstrate its contributions to the solution.
IFPMA strongly encourages early collaboration among all stakeholders (e.g., regulators, practitioners, patients, academia, industry and international organizations) to develop safe and efficient pediatric medicines, and to ensure timely global access.

IFPMA PTF Priority Focus on

• Contribution to Standards Development
• Knowledge Transfer on Dosage Forms
• Pharmacokinetic Data
• Regulatory Road Blocks
Early collaboration: IFPMA PTF activities

- Supporting WHO in implementation of existing evidence-based standards for pediatric clinical trials in developing countries (2010 World Pharma workshop - July 18, 2010 - Copenhagen).

- Participating in WHO consultative working groups, who are developing guidelines on pediatric formulations.

- Facilitating the identification of unpublished PK data, if existing, by sharing WHO requests for specific products with industry representatives and sharing best practices in PK assessment, including use of modeling / simulation with IUPHAR* and WHO.

- Sharing regulatory experience and tackle roadblocks with WHO and collaborates to this end with the Pediatric Medicines Regulators’ Network (PmRN).

* International Union of Basic and Clinical Pharmacology
2. Stimulating R&D

- IFPMA members recognize the need for international donors and governments to introduce more incentives to stimulate R&D for pediatric medicines.

Gathering evidence to make the case for researching, developing and manufacturing medicines for the developing world. This includes epidemiological studies, disease burden and demand forecast. (e.g. Accelerated Development and Introduction of Priority New Vaccines (ADIP))

Innovative financing mechanisms
- Transferable priority review voucher
- Expanding existing mechanisms
- Advance Market Commitments
- Research incentives (e.g. R&D tax credits, research grants, lower regulatory fees, fast track approval).

Public-Private Section Partnerships (PPPs) including Product Development Partnerships (PDPs) (e.g. Medicines for Malaria Venture (MMV), Malaria Vaccine Initiative, TB Alliance…)}
Examples of our industry’s long-term partnership programs:

- Pediatric Formulations for ARVs
- PEPFAR Partnership for Pediatric AIDS Treatment
- Viiv Healthcare Collaborative Research Program for Resource-Poor Settings
- Sanofi-Aventis - Impact Malaria
- Medicines for Malaria Venture (MMV)
- Novartis R&D for Malaria

Source: The IFPMA Developing World Health Partnerships Directory
www.ifpma.org/Healthpartnerships
3. Same Universal Quality Standards

- IFPMA members emphasize that medicines for children in developing countries should meet the **same universal quality standards as for the developed world**, thereby ensuring safety and efficacy of the drug treatment.

- Practically, this is ensured by:
  - Supporting the **WHO Prequalification Program**
  - **Knowledge transfer** on international policies supporting the use of high quality standards (e.g. WHO policy on Quality Assurance and Quality Control)
  - Supporting **regulatory capacity across emerging countries** to increase availability of medicines (e.g. ICH Global Cooperation Group; African Medicine Regulatory Harmonization Initiative; Pan-Asia Regulatory Conference)
4. Scientific Approach

- IFPMA members pursue a **scientific approach** to arrive for each specific treatment case at conclusions regarding the
  - route of drug delivery,
  - pharmaceutical form,
  - dosage strengths,
  - use of excipients,
  - administration devices,
  - packaging,
  - stability and interaction with food,
  - supply chain…

“Extensive and pervasive inappropriate use of medicines has been documented in developing countries, some relating to the health care systems and some relating to cultural beliefs, traditions, and practices”

5. Benefit / risk

- IFPMA members aim to deliver pediatric products with optimal balance between
  - efficacy/ease of use
  - patient safety
  - patient access
  - public health benefit and individual risk
  - scientific possibilities and cost-effectiveness

- Despite some general principles, the preferred pediatric formulation may vary case to case, depending on the
  - specific disease to be treated
  - selected drug substance
  - specific caregiver
  - age of the child
  - peripheral or indirect scientific evidence…
6. Flexibility

- Our industry will look for specific scientific formulations to provide flexibility in dosing and administration, e.g. dispersible tablets or mini-tablets, whenever possible.

- Moreover, our industry can only support a reasonable range of dosages and package sizes without compromising patient access at acceptable cost.
IFPMA members understand that, especially in resource-constrained settings, where pediatric formulations may not be available, children may benefit from industry verification of extemporaneous formulations as an approach to mitigate risk.

IFPMA PTF was consulted by WHO on development of pediatric dosage forms including (i) use of safe excipients and (ii) preparation of extemporaneous formulations.

PTF experts will be available to share further information and/or advise on matters related to pediatric drug development and manufacturing (e.g. extemporaneous preparation).
Industry recognizes the importance of selecting excipients based on good scientific rationale and in consideration of available safety data.

- Excipients may lead to adverse events in children that are not experienced in adults, or not seen to the same extent.
- The acceptability of a particular excipient will depend on the context of its use with regard to the pediatric age range, acute versus chronic use, and clinical risk/benefit.
- Where data are particularly limited, it is important that potentially useful excipients are not unnecessarily and prematurely categorized as unsuitable for pediatric use.
IFPMA members realize that developing pediatric formulations is important, however sometimes strong international and non-governmental advocacy is needed to drive successful introduction and uptake of pediatric formulations.

“Improving drug management must be a priority for countries. If Coartem doesn’t reach patients, it can’t cure them”

Mr. Silvio Gabriel, Exec VP Malaria Initiatives, Novartis
Challenges for the global research and development of pediatric medicines are technical, ethical and financial.

Early collaboration among all stakeholders is required to identify treatments to be developed and how to develop them, to ensure safety, efficacy and timely global access.

A balanced approach to the provision of assured quality pediatric medicines based on scientific and risk/benefit considerations may not always lead to a ‘gold standard’ product, but will provide better access to pediatric medicines which meet the patient’s and the practitioner’s needs.

Medicines for children in developing countries should meet the same universal quality standards as for the developed world, thereby ensuring safety and efficacy of the drug treatment.
Many of the essential medicines for child survival are off-patent and so there may be a role for other stakeholders in addition to R&D companies in the manufacture and supply of those medicines.

IFPMA members welcome new sustainable proposals, such as PPPs that have proven to be effective means of bringing public-sector, academic and private-sector research institutions together to contribute their respective expertise and strengths.

Finding sustainable and sufficient funding for such PPPs has been a significant challenge – more funds from bilateral and multilateral donors are needed.