Challenges along the paediatric ARV pipeline

Summary: IAS-ILF Industry Roundtable on Paediatric ARVs

Presented by Shaffiq Essajee (CHAI, USA)

INDUSTRY LIAISON FORUM
Engaging Experts in HIV

CIPHER
Paediatric HIV Matters

International AIDS Society
Stronger Together Against HIV

25 YEARS OF COMMITMENT

Optimize paediatric ARVs and shape the market

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PADO
- New drugs, mid- and long-term priorities
- New formulations

WHO Guidelines
- Existing drugs
- Existing formulations

PAWG
- Critical technical enabler for formulation development and dose ratios

IATT Formulary
- Optimized formulations for procurement
- Minimum number of products to build regimens recommended by guidelines

PAPWG
- Coordinated procurement of paediatric ARVs

Adapted from:
IAS-ILF Industry Roundtable on Paed. ARVs, 2013

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Paediatric Antiretroviral Drug Optimization conference (October 2013, Dakar, Senegal)

Identify medium- and long-term priorities for the development of paediatric ARVs

1. Accurate forecasting of demand for paediatric ARVs are critical to ensuring adequate supply
2. Accelerating the approval of new paediatric ARVs and formulations is essential
3. Patent-sharing agreements are needed for DTG, TAF, LPV/r and RTV for development of FDC
4. Developing a triple fixed-dose combination of ABC + 3TC + EFV for use 3–10 years old is a medium-term priority
5. Developing fixed-dose combinations of DTG and TAF is a long-term priority
6. Innovating to generate age-appropriate PK data to facilitate earlier treatment initiation among infants and more potent postnatal prophylaxis regimens.

For this, collective engagement between researchers, manufacturers, funders and policy-makers is critical.

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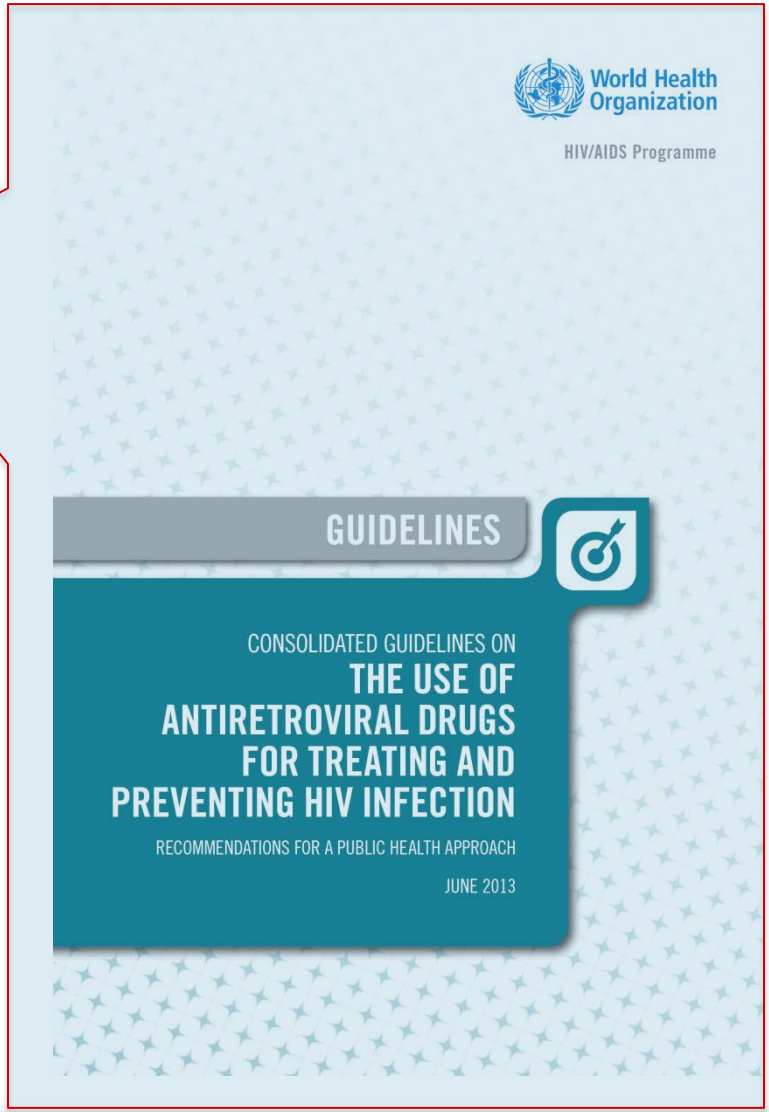

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- Develop FDC based on approved target dose
- Explore weight-based ratios and dosing schedule
- Validation of options identified with the target dose
- PK-PD to explore clinical relevance of PK parameters
- Bio-stability studies
- Bio-equivalence studies
- Clinical studies to with PK sub-studies to validate dosing and formulations based on PK parameters, efficacy, safety and acceptability
- Submission to SRAs / FDA / WHOPQ

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Drug class (or FDC)	Product	Formulation	Dosage	Rationale for list
OPTIMAL				
NRTI	AZT	Oral liquid	50 mg/5 ml	For infant prophylaxis as part of PMTCT
NNRTI	EFV	Tablet (scored)	200 mg	
NNRTI	NVP	Tablet (dispersible, scored)	50 mg	
NNRTI	NVP	Oral liquid	50 mg/5 ml	For infant prophylaxis as part of PMTCT
PI	LPV/r	Tablet (heat stable)	100 mg/25 mg	
PI	LPV/r	Oral liquid	80/20 mg/ml	
FDC	AZT/3TC	Tablet (dispersible, scored)	60/30 mg	
FDC	AZT/3TC/NVP	Tablet (dispersible, scored)	60/30/50 mg	
FDC	ABC/3TC	Tablet (dispersible, scored)	60/30 mg	
FDC	ABC/3TC/AZT	Tablet (non-dispersible, scored)	60/30/60 mg	

Drug class (or FDC)	Product	Formulation	Dosage	Rationale for list
LIMITED-USE				

...

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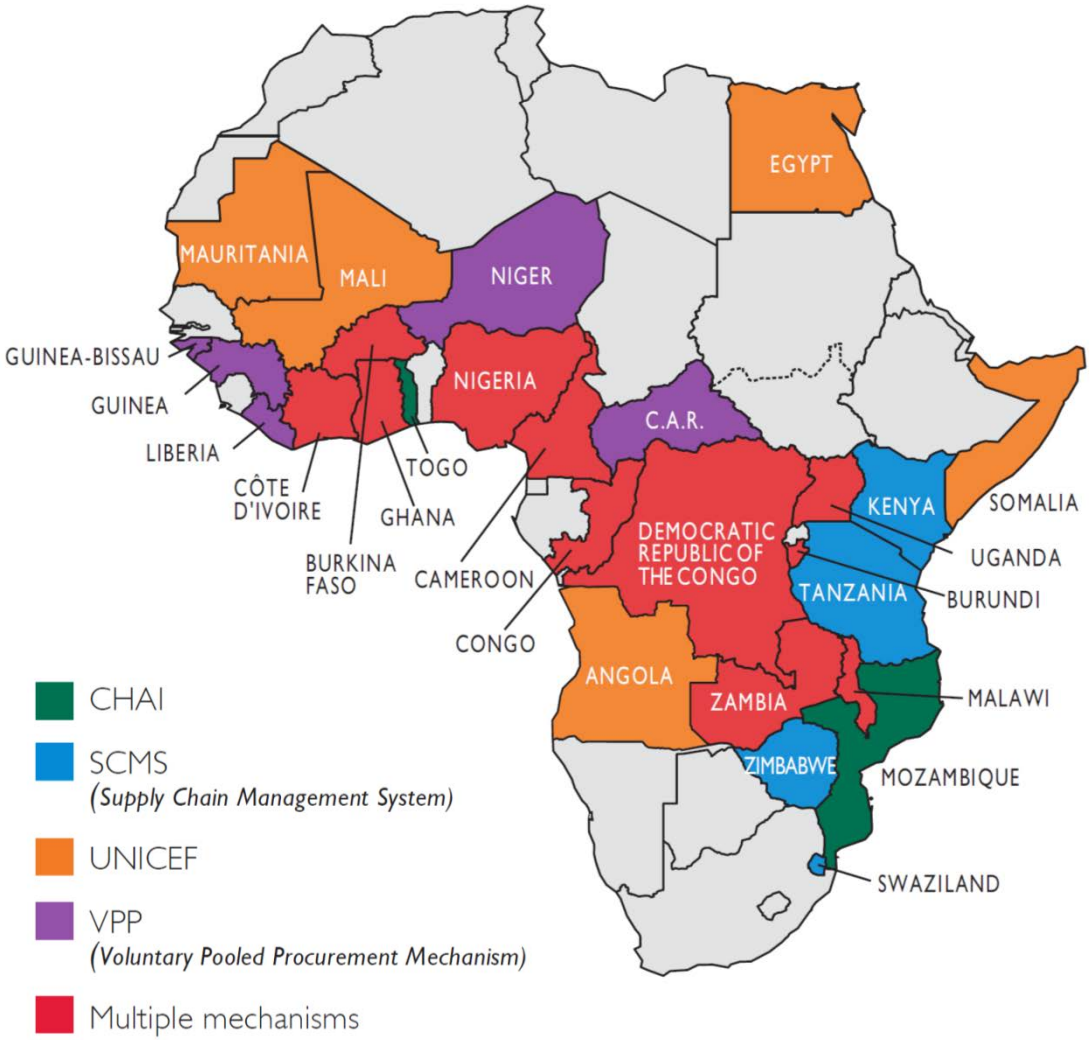

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Several recent paediatric ARV consultations have included industry

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- **WHO ARV Manufacturers & Stakeholders' Meeting**
  - Bring industry and selected stakeholders together for a briefing by WHO on current ARV use and future directions for ARVs
- **CHAI Annual Industry consultation**
  - Informs industry of CHAI forecasts for adult and ped ARVs
- **DNDi Paediatric ARV Roundtable**
  - Provide an overview of paediatric HIV market dynamics and drugs in the pipeline, identify priority drugs/formulations and develop roadmap for access to paediatric ARVs
- **Global Fund and PEPFAR ARV Manufacturers Meeting**
  - Provide an update on future ARV procurement strategies

IAS-ILF Thematic Roundtable on Paediatric HIV

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- **IAS-ILF Thematic Roundtable on Paediatric HIV**
  - Bring industry and other stakeholders together to discuss gaps
  - Provide a platform where industry can interact with the processes in place (going beyond what is possible in more formal forums where industry is commonly left out by fear of conflicts of interest, and often only informed instead of consulted)
  - November 2013, Geneva

Thematic roundtables convene scientific and technical experts from industry and non-industry organizations in an independent forum to discuss topics where a multi-stakeholder approach can lead to solutions.

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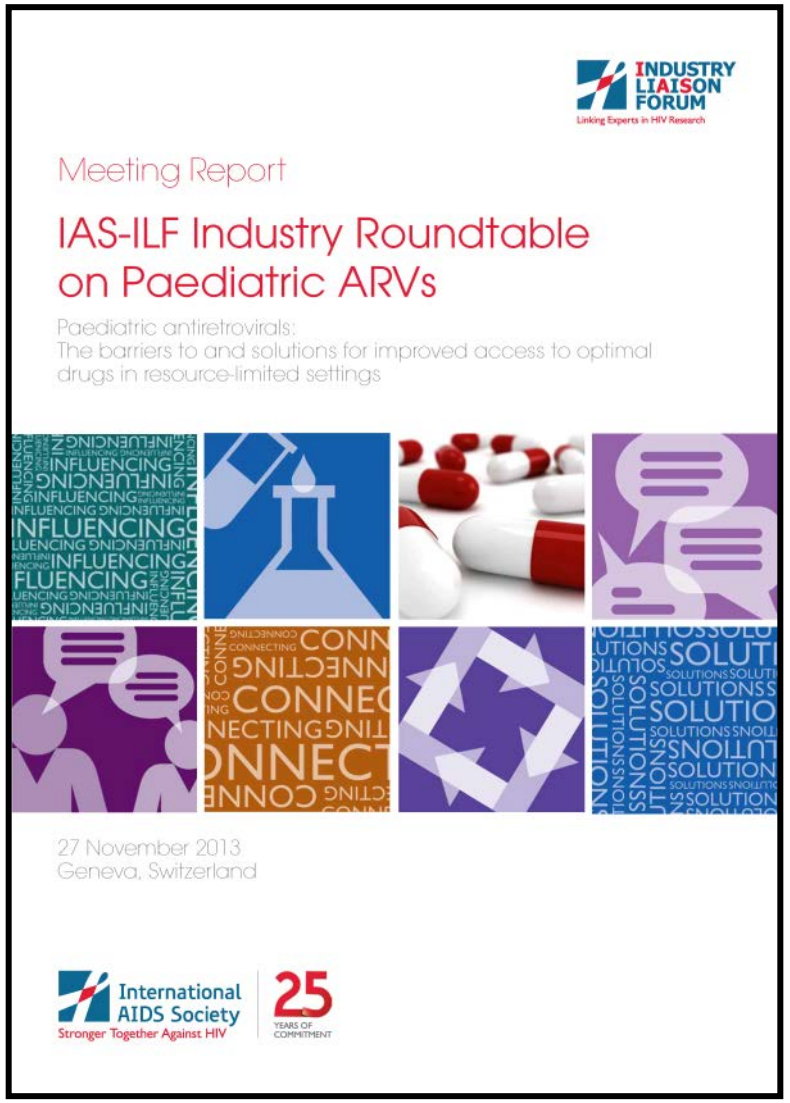
IAS-ILF Thematic Roundtable on Paediatric ARVs



The barriers and solutions for improved access to optimal drugs in resource-limited settings

Co-chairs: *Shirin Heidari (IAS, Switzerland)*
Martina Penazzato (WHO, Switzerland)

- New paediatric treatment recommendations
  Martina Penazzato (WHO, Switzerland)
- IATT optimal paediatric formulary
  Marianne Gauval (CHAI, USA)
- Paediatric ARV Procurement Working Group
  Martin Auton (Global Fund, Switzerland)
- Paediatric ARV Optimization Meeting
  Martina Penazzato (WHO, Switzerland)
- Discussion on creative solutions to overcome barriers to development and delivery of optimal paediatric ARV formulations
  Facilitator: Shaffiq Essajee

- 13 ARV manufacturers + 12 international organizations
- Report available at: http://www.iasociety.org/ilf.aspx

Challenges along the paediatric ARV pipeline

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Challenges identified during the
IAS-ILF Industry Roundtable on Paediatric ARVs

A. Research and development
B. Development of normative guidelines and guidance on appropriate formulations and, if needed, FDC ratios
C. Regulatory approval and commercial production
D. Reliable forecasting and funding to stabilize the market
E. Post-marketing surveillance

Challenges

- Developing child-friendly formulations
- Recruiting children under 12 in clinical trials

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Challenge

- Consulting industry during the revision process without the perceived conflicts of interests
  - Most appropriate formulations
  - Most appropriate FDC ratios

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Challenges

- Harmonizing of regulatory processes, particularly with regards to product specifications
  - Different age bands
  - Different weight bands
  - Need to provide clinical data (e.g., PK) for generic production or formulations

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Challenges

- Producing and disseminating accurate forecasts (for production planning)
- Focusing on a limited range of products for procurement to ensure market stability

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Challenges

- Producing and disseminating accurate post-marketing surveillance data to inform countries and policy makers

Removing barriers and seizing opportunities

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Can collaboration between cohorts and industry tackle some of these challenges?