The Global Accelerator for Paediatric Formulations (GAPf): Updated framework for collaboration

CTA Partners
Geneva December 5th, 2016
Developing and delivering paediatric formulations through collaborative and coordinated action

Key formulations are prioritised in the context of a public health approach

Priority formulations are reliably supplied to countries

Priority formulations are procured via a pooled mechanism

Priority formulations are included in optimal formulary for selection

Technical/research work is undertaken to support development of the priority formulations
Developing and delivering paediatric formulations through collaborative and coordinated action

**Clinical work**

**Development and introduction**

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Drug optimization

PADO

PAWG

PROGRAMS

PAPWG

PHTI

IATT
Global Accelerator helps us to simplify

- Prioritisation (PADO/PAWG)
- Development and introduction of priority products

(children image)
Global Accelerator helps us to simplify

Prioritisation (PADO/PAWG) → Development and introduction of priority products → GAPf

UPSTREAM
- Research
- Development
- Regulatory (SRAs)

DOWNSTREAM
- Procurement
- Introduction
- Regulatory (NRAs)
Durban helped us moving forward

- Promote simultaneous enrolment of different **age** groups and parallel development of paeds formulations with new adult drugs
- Earlier and more frequent **interaction** between regulators, companies and PAWG for making the PIP/PSP more efficient.
- Improved collaboration and **regulatory alignment** to make PIP/PSP modifications less burdensome and challenging.
- Better **dissemination of PADO** outcomes to regulators and industry
- PADO priorities to be recognized by **National regulators** (ie DCGI)
- **Strategic financing** potentially useful at different stages (ie. clinical research, advance market commitment and mitigation of financial risk.
- As a model for **other disease** areas facing similar challenges.
Additional consultations enabled further refinement of the GAPf

- Industry
- FDA and EMA
- PENTA
- CTA partners
Theory of change

1. Reduce time for approval of paediatric formulations of new drugs

<table>
<thead>
<tr>
<th>Goals</th>
<th>Outcomes</th>
<th>Activities</th>
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<tbody>
<tr>
<td>Reduce time to obtain regulatory approval from FDA/EMA for paediatric formulations</td>
<td>Reduce time to complete paediatric investigation plans (compared with the current average of 8 to 10 years)</td>
<td>Make the existing Pediatric Study Plan (PSP)/Paediatric Investigation Plan (PIP) mechanisms more targeted, rapid and efficient</td>
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<td>Engage with the innovators to simplify, target and accelerate required studies</td>
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2. Reduce time to develop, approval and introduction of optimal FDCs

<table>
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<tr>
<th>Outcomes</th>
<th>Activities</th>
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<tbody>
<tr>
<td>Timely prioritization of optimal FDCs and guidance on dosing by weight bands</td>
<td>➢ Ensure timely update and dissemination of PADO recommendations</td>
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<tr>
<td>Licence of the drugs in FDCs available to generic manufacturers</td>
<td>➢ Maximize generation of evidence through innovator studies to inform optimal use of the formulation in the population of interest (LMICs)</td>
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<tr>
<td>The appropriate number of generic manufacturers are committed and adequately supported to get a viable return on their investment on development and manufacturing</td>
<td>➢ Transfer of licence for novel drugs for innovator to generic manufacturers has been well covered under the current MPP mandate and should continue without duplication</td>
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<tr>
<td>Resolve technical hurdles faced by generic manufacturers for FDCs requiring specialized formulation technology</td>
<td>➢ However, additional activity can explore possibility of including an incentive to develop paediatric formulation as part of the licencing process</td>
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<tr>
<td></td>
<td>➢ Reliable information on market size, target pricing</td>
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<td>➢ Demand generation in large-volume countries to support commercialization</td>
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<td>➢ Support to expedite and harmonize in-country product registration</td>
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<td>➢ Evaluate the need to provide incentives such as funding for part of development cost, buy down, pricing subsidy on initial supplies</td>
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<td>➢ Develop a team of experts to meet the unique challenges of a formulation</td>
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<td>➢ Create an independent not-for-profit formulation technology development platform</td>
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Proposed staged approach: GAPf development and implementation

1. Activities that require little or no additional funding, but advance the Global Accelerator agenda.

2. Global Accelerator hosted by UNITAID as an evolution of PHTI in its scope, mission and operationalization.

3. Full development of the Global Accelerator with broad focus on paediatric formulation to be included in existing PPP or as an independent entity. (Pending successful completion of stage 1 and 2)
Today we would like your endorsement on the key activities of stage 1

**STAGE 1 (1-2 years)**
- Continue the current mechanism with the present structure
- No/negligible funding required
- Specific activities described in Stage 1 will make impact and progress towards the goal
- Key activities will be extended to TB and hepatitis where appropriate and feasible
- Deliverables:
  - Regulatory efficiencies in place
  - Revised PADO priority list

**End of Stage 1 review**
- Impact of Stage 1 activities
- Future product portfolio to develop

**STAGE 2 (~3 years, many activities in parallel to Stage 1)**
- Create a core group of experts to be members of the Global Accelerator
- Funding required for activities such as PK studies, additional clinical studies and administrative support to manage the activities
- To be hosted by another organization with matching strategic objectives
- Current grants in paediatric HIV space to inform additional activities
- Scope will have major focus on ARVs, but also include other diseases
- Moderate exit cost
- Deliverables:
  - Completion and implementation of PADO formulations currently under development
  - Synergies with other disease areas identified
  - Moderate Exit Cost

**End of Stage 2 review**
- Impact of Stage 2 activities
- Future product portfolio to develop
- Assessment of market need

**STAGE 3**
- Expansion of scope and mission (potential creation of an independent entity or inclusion in an existing PPP)
- Develop Global Accelerator Advisory Board and funding activities
- Possibility to expand to other disease areas beyond HIV
- Very high exit cost

Vision for Stage 3

Input for refinement of stage 2
Stage 1 Actions

1. FDA/EMA initiative to impact faster pediatric studies – WHO, in collaboration with other relevant CTA partners to set up meetings with the FDA Division of Antiviral Products and the EMA PDCO to discuss and agree on key recommendations to innovators

   • Include adolescents in initial registrational adult efficacy trials or in parallel with adult studies
   • Engage with WHO PAWG and engage pediatric HIV clinical trials networks to develop simplified, efficient pediatric trials.
   • Use WHO weight bands and use weight-based dosing (rather than age-based dosing) in designing pediatric PK and safety studies
   • Enroll all other ages/weight bands concurrently and not as sequential cohorts for the remaining (pre-adolescent) paediatric population
   • Begin formulation development appropriate for clinical trials for pediatric populations as soon as evidence of potential public health benefit to pediatric patients is evident
   • Ensure acceptability and palatability data is also provided
Stage 1 Actions (cont’d)

1. FDA/EMA initiative to impact faster pediatric studies – ...to discuss and agree on three to five key recommendations to innovators

2. FDA/EMA should guide the innovators to simplify and harmonise the PSP/PIP document
   • simplified, efficient pediatric trials

3. Develop a "master protocol" for pediatric clinical trials of ARVs designed to collect similar (required) PK and safety data for any desired pediatric product

4. WHO will further engage with strengthening the paediatric regulatory network and to promote a more coordinated approach to in-country drug registration

5. Explore the possibility of including additional incentives for pediatric formulation development when granting license for novel drugs.

6. Improve assessment of market needs and the staging/duration of each PADO priority product in the marketplace.
Stage 2 “The Proof of concept”

• Global Accelerator could reside in PHTI during its incubation period (3 years)
• Stage 2 would start during Stage 1 activities and, during this time, the concept will be tested for feasibility and results
• Broad set of stakeholders will be part of the group advising the Global Accelerator
• PHTI would expand membership to develop a core Global Accelerator team drawing experts from PAWG, PHTI, APWG, and other key stakeholder organizations
  – Skillsets such as clinical safety, clinical pharmacology, Chemistry/Manufacturing/ Controls, regulatory, market analysis, patient advocacy, demand generation, coordinated procurement and supply.
• Coordination with ongoing activities to address similar challenges in tuberculosis and viral hepatitis will be ensured and, where required, jointly addressed.
Stage 2 Activities

- Engage with the innovators and paediatric HIV clinical trials networks early on at the design stage of the initial paediatric studies.
- Incentivize generic development of priority products as needed.
- Ensure timely notification of optimal FDCs recommended by PADO, including an ongoing assessment of order of priority.
- Promote earlier collaboration between innovators and generics so that the generics can potentially be part of innovator’s development team and take up some of the work on early formulation development.
- Characterize and triangulate the future demand for priority products. Coordinate with various organizations involved in forecasting, including WHO, UNAIDS, CHAI, MPP, The Global Fund, PEPFAR and Department of Health of South Africa.
- Initiate demand generation activities during development.
- Work with country partners for developing and rolling out scale-up plans.
- Create a formulation technology development platform.
CHAI-UNITAID project will be key...

UPSTREAM
- Raw material sourcing and process chemistry optimization
- Product commercialization plans
- Incentive Pool/Accelerated Development Contracts (when necessary)
- Product Development
- SRA/NDRA filings

DOWNSTREAM
- Clinical value proposition development
- WHO guidelines analysis and budget impact tools
- In-country HIV guideline revision
- National forecasting & quantification
- In country product uptake/Early adopter market research
- Transition monitoring and stock management

Civil Society Engagement

Key:
- Denotes upstream activities
- Denotes downstream activities
...but additional support might be required

- Funding key additional PK studies and clinical studies
- Formulation technology platform
- Additional IP to be overcome
- Administrative support of a small team is required to actively manage the initiative, coordinate between partners, track progress and flag delays.
Stage 3 “The expansion”

• This stage will be initiated subject to assessment of
  – Portfolio of products
  – Impact of previous stages
  – Market needs and potential for efficiencies with other diseases areas

• It could be included within an existing, well-established PPP or become independent

• Fundraising will be a critical activity
Industry Comments - Regulatory/Normative

• In general, positive comments received on the concept and staged approach to development of Global Accelerator
• Closer links between PADO priorities, WHO guidelines and actual procurement would be useful
• Early engagement and harmonization with NDRAs was stressed as of importance, with special emphasis on DCGI and MCC and NDRAs in high burden countries
• Advance commitments for inclusion of new regimens in guidelines, especially if a time frame was given
Industry Comments – Clinical

• Trial designs for ARVs in children should be standardized via a “Master Protocol” for a streamlined approach that will produce meaningful results that will support timely approval.

• Explore potential for filings to be based upon short-term safety and PK analysis rather than a full 24 week analysis of safety/efficacy. The full report would follow.
Industry Comments – Technical/Development

• Technology platform for development of pediatric dosage forms was supported

• Further clarity on the priorities for the development of pediatric ARVs is needed through better dissemination of PADO priorities and further prioritization within the PADO list.
Industry Comments – Licensing

- Exploring routes to paediatric licenses negotiated by MPP. There is also a good scope of having paediatric formulation for MDR TB drugs and licenses should be negotiated.
Industry Comments – Demand & Procurement

• Many industry participants stressed the need for better market characterization/assurance of procurement once new formulations available versus the need for development funding.

• Advance procurement commitments from large buyers for specific formulations could help

• Closer links between PADO priorities, WHO guidelines and actual procurement would be useful

• Support to generic manufacturers especially on volume guarantees
In summary

- **Special efforts** are required for development and introduction of the most critical paediatric formulations for HIV and beyond.
- The ideal mechanism to ensure the sustainability of the Global Accelerator will be assessed during the **three stages** of the project;
- **Neutrality and flexibility** to work with a variety of stakeholders will be key to its success and longevity.
- *The first stage* comprises those activities that can be taken up by key stakeholders with little or no additional funding.
- *The second stage* will require hosting of the Global Accelerator by another organization.
- *The third stage* will see it established in its final structure with sustainability and broader impact across orphaned paediatric medication development as its goal.
- It is crucial that a **review of critical parameters**, such as product portfolio, prevailing market need and impact analysis of the previous stages, is undertaken before moving to the third stage.
Thank you All for your input!!