The Global Accelerator for Paediatric Formulations (GAP-f):

Ensuring children have accelerated access to optimal drug formulations

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HCV burden in the paediatric population

- Global prevalence estimation: 3.5 million children between 1-15 years are HCV-viraemic
- Mother-to-child is the main transmission route
- Iatrogenic transmission through unsafe injection
- Histological course of chronic HCV is unpredictable
- Risk of cirrhosis: 1-2%
- Few HCV-infected children with HCC described

Challenges for paediatric drug formulation development

- Drug absorption, distribution, metabolism and elimination changes lead to different PK/PD at different ages
- Taste-masked, scored tablets in dispersible/chewable/crushable forms are desirable to cover the entire age spectrum, but are difficult to develop
- Sequential enrolment of different age groups into PK studies and clinical trials delays process
- Need to shift from age to weight-based drug dosing in paediatrics
- Small market in high-income countries not stimulating development of formulations adapted to paediatric needs
- Limited interaction between industry and research community on paediatric study plans (PSP/PIPs)
- Fast moving HCV therapeutic advances making paediatric development even less able to keep up with adults

Importance of treating paediatric HCV infection

- Important burden of infection in some settings
- Reduce development of chronic liver disease (cirrhosis and HCC)
- Reduce horizontal transmission within families and school
- Avoid stigma and psychological consequences
- Reduce economic burden of managing chronic liver disease in adults
- Fewer co-morbidities, good compliance and tolerance, evidence for comparably high SVR rates as in adults

Target product profile for paediatric HCV drug formulations

- High efficacy (>95%)
- High barrier to resistance
- Few drug-drug interactions
- Optimal safety profile
- Short duration
- Pan-genotypic
- Use in all patients (regardless of cirrhosis, HIV or treatment history)
- Simplified monitoring schedule with single SVR assessment
- Easy to administer (age-specific formulation)
- Fixed-dose combination, one pill once daily

Too few HCV regimens approved for children

- 2 for >12 y.
- 0 for <12 y.
- 6 studies ongoing

The Global Accelerator for Paediatric Formulations

The GAP-f builds on the HIV experience and formalizes collaboration across sectors to ensure accelerated development and uptake of the most needed drugs and formulations for children. Its initial focus is on HIV, but will expand to HCV and TB.

Three stages of implementation building on lessons learned from the Paediatric HIV Treatment Initiative

The GAP-f is a pilot project currently focused on HIV, with the intention to address similar challenges in HCV and other disease areas in the near future.

Stage 1 – 2017

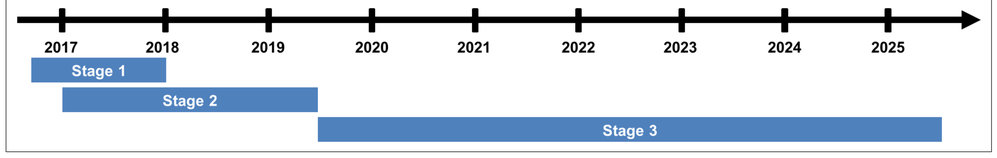
- Streamline regulatory activities and coordinate clinical protocols using existing funds within existing organizations
- Develop a research toolkit for paediatric formulations
- Push forward specific recommendations:
  - ✓ Using weight-based dosing in designing paediatric PK and safety studies
  - ✓ Including adolescents in initial registrational adult efficacy trials or in parallel with adult studies
  - ✓ For new drugs in development, beginning paediatric formulation work as soon as evidence of potential public health benefit
  - ✓ Enrolling all ages/weight bands concurrently (>4 weeks)
  - ✓ Ensuring acceptability and palatability data obtained early
  - ✓ Making initial PSP/PIP submissions less detailed to simplify the process for subsequent revisions

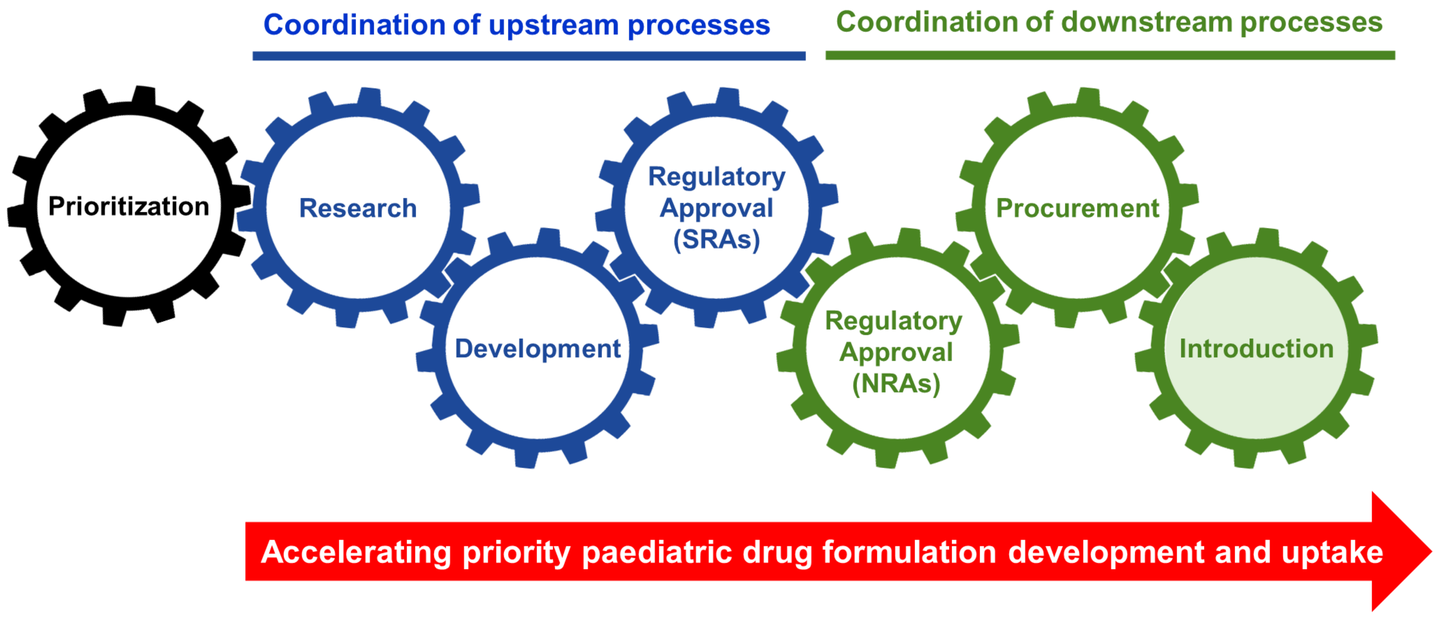
Stage 2 – 2017-2019

- Develop a mechanism to prioritize products for low- and middle-income countries
- Improve paediatric drug formulation forecasting
- Accelerate product development through incentives (potentially including strategic financing and market shaping approaches)

Stage 3 – 2019 and beyond

- Full development of the GAP-f model to coordinate and accelerate all stages of a portfolio of products
- Potential formalization as an independent nonprofit organization





SRAs: Stringent regulatory authorities
NRAs: National regulatory authorities (in high-burden countries)

Focusing on the most needed paediatric drug formulations for HIV and beyond

The current approach to paediatric drug formulation development (for HIV and other diseases) results in a delayed situation with children suffering and dying unnecessarily.

The GAP-f builds on the HIV experience, but aims to fast-track development of optimal paediatric drug formulations in a number of other diseases facing similar challenges, including tuberculosis and viral hepatitis. It brings together a coordinated and purposeful clinical, product development, and commercialization strategy, as well as an implementation plan for paediatric products.

The GAP-f will prioritize products to improve the treatment portfolio; support formulation development (or reformulation of existing drugs); help alleviate intellectual property barriers; generate clinical evidence meeting regulatory requirements; support regulatory approval globally and nationally; secure prioritized commitments from manufacturers; accelerate product introduction by early engagement with MoHs, healthcare workers, and community advocates; incentivize suppliers and coordinate procurement to catalyse uptake; and establish pharmacovigilance and enhanced monitoring of paediatric patients.

The GAP-f drug development consortium will optimize resources and accelerate the timelines for paediatric drug formulation development in a number of disease areas – starting with HIV, and expanding through HCV, TB and other diseases as needed.

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Contact

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