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 HCV 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 formulations
- High efficacy (>95%)
- High barrier to resistance
- Few drug-drug interactions
- Optimal safety profile
- Short duration
- Pan-genotypic

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
  ✓ Enrolling in parallel with adult studies
  ✓ For new drugs in development, beginning paediatric formulation work as soon as evidence of potential public health benefit
  ✓ 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

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