FDA Pediatric Stakeholder Meeting

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Pediatric Drug Regulations: Positive Impact on the Pediatric Population

- A balance of requirements and incentives have led to an increase in pediatric research, pediatric indications and product approvals, and approved labeling for pediatric populations.
  - The Pediatric Research Equity Act (PREA)
  - Best Pharmaceuticals for Children Act (BPCA)
  - Rare Pediatric Disease Priority Review Voucher

Challenges Remain for Pediatric Drug Development

- Pediatric drug development remains challenging:
  - Limited patient populations and parents may not be willing to consent
  - Numerous other feasibility constraints (e.g., formulation development)
  - Incomplete scientific understanding of many pediatric diseases and conditions
  - Differing health authority requirements

- The above challenges are compounded in the context of rare pediatric diseases.

- Guidance, scientific dialogue, reflection, and evaluation of the impacts of PREA requirements and BPCA is needed to continue to support pediatric drug development.

Outline

- Updates to Guidance or New Guidance Development
- Evaluation of the Impact of PREA Requirements and BPCA
- Areas for Further Stakeholder Discussion

Updates to Guidance or New Guidance Development

- BIO appreciates FDA's recent work to develop guidance addressing issues in pediatric drug development and review:
  - Rare Pediatric Priority Review Vouchers
  - Inclusions of Adolescents in Adult Oncology Clinical Trials
  - Post-Marketing Pediatric-Focused Product Safety Reviews
  - Drugs for Treatment of Partial Onset Seizures: Full Extrapolation of Efficacy From Adults to Pediatric Patients 2 Years of Age and Older
  - General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products
  - Cancer Clinical Trial Eligibility Criteria: Minimum Age for Pediatric Patients

Updates to Guidance or New Guidance Development

- To continue to support pediatric drug development, BIO requests that the FDA consider developing or updating existing guidance pertaining to:
  - General Considerations for the Clinical Evaluation of Drugs in Infants and Children (1977)
    - Consider updates to content including terminology (e.g., "school-aged children", "special problems") and the addition of references to other pediatric guidance released since 1977
  - Complying with the Best Pharmaceutical for Children Act (BPCA) to replace FDA's FAQ website
  - Complying with PREA as modified by new pediatric oncology requirements (FDARA 504), implementation that allows global alignment in vulnerable pediatric oncology patients
    - Guidance was to be made public in August 2019

Evaluation of the Impact of PREA Requirements and BPCA

- As outlined in Section 508 of the Food and Drug Administration Safety and Innovation Act (FDASIA), FDA is required to submit to Congress a report concerning pediatrics.
  - The requirement now also mandates that the FDA report on metrics pertaining to pediatric oncology studies.
- FDA statements indicate that the new FDARA Section 504 requirement are aimed at a accelerating the timeline for initial evaluation of agents that appear to be promising for the pediatric population.
- BIO requests that the FDA consider mechanisms to confirm pediatric oncology studies are being considered earlier in drug development:
  - Timing of submission of Pediatric Study Plans (PSPs)
  - Number and timing of discussions among Sponsors and FDA on pediatric oncology drug development
  - Use of FDARA Section 503 meetings to discuss pediatric oncology development programs

Areas for Further Discussion: Aligned Pediatric Scientific Advice

- It is the goal of BIO member companies to get safe and effective therapies to pediatric patients as quickly as possible.
- To support pediatric drug development there is a clear need for alignment and consistency both within the Agency and across health authorities.
  - Within Agency: Need for a consistency on the use of innovative approaches (e.g., use of innovative clinical trial designs, real-world evidence, extrapolation, external controls)
  - Across Health Authorities: Need for aligned advice from major global health authorities as represented in the pediatric cluster
    - BIO requests FDA work with the stakeholder community (including Sponsors) to achieve the goal of aligned scientific advice on pediatric programs.

Areas for Further Discussion: Best Pharmaceuticals for Children Act (BPCA) Written Requests

- The FDA has made statements that in order to fulfill a Written Request, Sponsors must conduct studies in all applicable age groups, in all possible indications for a given therapy.

- While BIO fully supports BPCA and the use of additional marketing exclusivity to incentivize the conduct of studies, BIO requests that:
  - Written requests be based on scientific rationales and should address unmet medical needs in a feasible manner and timeframe that incentivizes conduct of such studies, otherwise the number of sponsors conducting such studies will likely decrease.

Areas for Further Discussion: Drug Development and Review for Neonates

- BIO appreciates FDA's General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products Guidance.
- There remains a need for additional guidance and clarity as it pertains to endpoints, biomarkers, and natural history for neonates.
- Given the great difficulty of conducting interventional trials in neonates, alternative means of gathering data should be encouraged.
- BIO requests that:
  - FDA's internal neonatologist/SMEs engage in Division communications with sponsors and that the Agency consult with additional external experts in order to reach the most scientifically sound decisions regarding assessments and studies.

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