Global Pediatric Development: Comparison of PSP and PIP

Hari Cheryl Sachs, M.D.
Team Leader, Pediatric and Maternal Health Staff
Brief Glossary

- PREA: Pediatric Research Equity Act
- BPCA: Best Pharmaceuticals for Children Act
- PeRC: Pediatric Review Committee
- PSP: Pediatric Study Plan
- PIP: Pediatric Investigation Plan
- EMA: European Medicines Agency
- PDCO: Paediatric Committee
**PREA and BPCA**

- **Pediatric Research Equity Act (PREA)**
  - Requires companies to assess safety and effectiveness of new drugs/biologics in pediatric patients (Pediatric Assessment)

- **Best Pharmaceuticals for Children Act (BPCA)**
  - Provides a financial incentive to companies to voluntarily conduct pediatric studies
PREA vs. BPCA

**PREA**
- Drugs and biologics
- **Mandatory** studies
- Requires studies only on indication(s) under review
- **Orphan indications** exempt from studies
- Pediatric studies must be labeled

**BPCA**
- Drugs and biologics
- **Voluntary** studies
- Studies relate to entire moiety and may expand indications
- Studies may be requested for orphan indications
- Pediatric studies must be labeled
Pediatric Review Committee (PeRC)

- Established by legislation to carry out the activities described under PREA and BPCA

- Intended to increase the consistency of implementation of provisions of PREA and BPCA across FDA

- Committee membership
  - Expertise in Pediatrics, Neonatology, Pediatric Ethics, Biopharmacology, Statistics, Chemistry, Law required
  - Appropriate expertise pertaining to the product under review
Brief History of PSP

- Requirement under PREA as amended by FDASIA (Section 506)
  - FDA encourages inclusion of all pediatric plans including those plans as may be studied under BPCA (i.e., under WR)

- Encourage sponsors to identify pediatric studies as early as possible in product development

- When appropriate, conduct pediatric studies prior to the submission of the NDA or BLA

- Implemented January, 2013
  - 292 Initial PSPs received
  - 193 Initial PSPs reviewed
  - 74 Agreed initial PSPs
PSP: Goals of Pediatric Development

• Obtain sufficient data to support the dosing, safety and efficacy in the pediatric population

• Communicate that data in the product labeling

• Judicious use of medication in the pediatric population
Contents of PSP

- Overview of Disease and Overview of Product
- Plan for Extrapolation
- Plans for requests for Waivers
- Summary of Planned clinical and nonclinical studies
- Formulation development
- Nonclinical studies
- Clinical data to support planned studies
- Planned clinical studies
- Timeline
- Plans for request for Deferrals
- Agreements with other Regulatory Authorities
- Guidance suggests no more than 60 pages total
European Medicines Agency

- EMA coordinates member states activities with respect to medicines
- Single application to the EMA to obtain marketing authorization in all EU member states
How is the EMA organised?

- Committee for Herbal Medicinal Products
- Committee for Advanced Therapies (CAT)
- Paediatric Committee (PDCO)
- Committee for Human Medicinal Products (CHMP)
- Committee for Orphan Medicinal Products (COMP)
- Committee for Veterinary Medicinal Products
- Pharmacovigilance Risk Assessment Committee

Management Board

33+ National Competent Authorities + 3000 European experts

EU institutions: Commission - Parliament

Committee for Human Medicinal Products (CHMP)

Committee for Orphan Medicinal Products (COMP)

Committee for Veterinary Medicinal Products

Pharmacovigilance Risk Assessment Committee

Committee for Advanced Therapies (CAT)

Paediatric Committee (PDCO)
Brief History of PIP

• Pediatric Regulation instituted in EU January, 2007
  – Established the PDCO
  – Required submission of a PIP at filing

• Encourage sponsors to identify pediatric studies as in product development

• Five year report published
  – 600 PIPs agreed upon
  – 453 for products not yet authorized in EU
  – 147 for products already authorized (new indication)
PIP: Goals of Pediatric Development

- Ensure that the necessary data are obtained in children, when safe to do so
- Support the authorization of a medicine for children
Contents of PIP

• Description of studies and measures to adapt the medicine’s formulation so that acceptable in children

• Cover the needs of all age groups (birth to adolescents)

• Define the timing of studies in children compared to adults
  – Studies may be deferred and/or waived as appropriate

Note: PIP may be modified
PIP Application Summary

- Active substance(s), class and mechanism of action
- Product Name
- MAH/applicant
- Planned indication(s) in adults
- Condition
- Proposed indication(s) in children
- Potential benefit for children
- Clinical development
- Pharmaceutical form
- Nonclinical plans
- Extrapolation
- Waiver(s), deferrals
Contents of PIP

- Part A: Administrative and product information
- Part B: Overall development of the medicinal product including information on the conditions
- Part C: Applications for product specific waivers
- Part D: Paediatric investigation plan
- Part E: Applications for deferrals
- Part F: Annexes

- EMA website suggests that Parts B-E should be limited to 50 pages of less
Similarities

• Goal of each program is the same
• Scientific elements of PSP and PIP are consistent
  – Descriptions of product, disease and alternative treatments
  – Plans for requesting waivers, deferrals and developing pediatric formulations
  – Need for nonclinical studies
  – Timing of studies and role of extrapolation
## Comparison: PSP and PIP

**Part B - Overall development of the medicinal product**

| B. and B.1.1-2 Discussion on similarities and differences of the disease/condition between populations and pharmacological rationale | 1. Overview of Disease/Condition in the Pediatric Population  
2. Overview of Drug or Biological Product  
3. Overview of Extrapolation |
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<tbody>
<tr>
<td>B.3. Significant therapeutic benefit/fulfilment of need</td>
<td>2. Overview of the Drug or Biological Product(s)</td>
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**Part C - Applications for product-specific waivers**

| C.1. and C.2.1-3 Waiver overview and grounds for product waiver | 4. Request for Drug-Specific Waiver(s) |

**Part E - Applications for deferral**

| Part E Applications for deferral | 11. Plan to Request Deferral  
12. Agreements for Other Pediatric Studies  
VI. Contents of Requested Amendment to Initial PSP |
<table>
<thead>
<tr>
<th>Part D Paediatric investigation plan</th>
<th>D.1. Existing data and overall strategy for development</th>
<th>8. Clinical Data to Support Pediatric Studies</th>
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<tbody>
<tr>
<td>D.1.1. PIP indication</td>
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<td>2. Overview of the Drug or Biological Product.</td>
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<td>D.1.2. Paediatric subset(s)</td>
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<td>11. Plan to Request Deferral</td>
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<td>D.1.3. Information on existing quality/ non-clinical/clinical data</td>
<td>8. Clinical Data to Support Studies in Pediatric Patients</td>
<td>Overview of Planned Extrapolation</td>
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<td>Address need to demonstrate efficacy or extrapolate efficacy</td>
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<td>D.2. and D.2.1 Quality aspects</td>
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<td>6. Pediatric Formulation Development</td>
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<td>D.2.2. Outline of planned/ongoing studies and steps in the pharmaceutical development</td>
<td>5. Summary of Planned Nonclinical and Clinical Studies</td>
<td>6. Pediatric Formulation Development</td>
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<tr>
<td>D.3., D.3.1-3 Non-clinical aspects and planned/ongoing studies, including study(ies) summary</td>
<td>5. Summary of Planned Nonclinical Studies and 7. Nonclinical Studies</td>
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<td>D.4, D.4.1-3. Clinical aspects and planned/ongoing studies, including study(ies) summary; list key elements of modeling/ simulation and extrapolation</td>
<td>5. Summary of Planned Clinical Studies</td>
<td>9. and 9.1-2 Planned Pediatric Studies: PK and efficacy/ safety</td>
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Important Differences

• Regulatory requirements
  – distinct incentive (BPCA) and requirement (PREA) programs in US; combined incentive and requirement program in EU (PIP)
  – focus on indication (PREA) vs. condition (PIP)

• Review processes and timelines in each agency
Pediatric Drug Development Plans: alignment with the adult drug development process

* Start thinking about pediatric drug development as soon as possible

Pediatric Drug Development
Conclusions

• **Goal of each program is the same**
  – Sound and efficient global pediatric development

• **Scientific elements of PSP and PIP are consistent**

• **Process to encourage consistent scientific advice**
  (EMA cluster calls)
Resources

• PSP
  Guidance for Industry: Pediatric Study Plans

• PIP
  Pediatric investigation plans, waivers and modifications