Examination of FDA Pediatric Regulations: Inclusion of Pediatric Participants in Clinical Trials (2016-2018)

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Objective
Assess the effectiveness and impact of the Best Pharmaceuticals for Children Act (BPCA)

Background
- 2002: Best Pharmaceuticals for Children Act (BPCA)
- 2003: Pediatric Research Equity Act (PREA)
- 2012: Food and Drug Administration Safety and Innovation Act (FDASIA)
- 2016: Report to Congress: BPCA and PREA Status
- 2019: Report to Congress: Pediatric Labeling of Orphan Drugs

Figure 1. Timeline of Key Pediatric Guidances, Regulations, and Laws

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>Best Pharmaceuticals for Children Act (BPCA)</td>
</tr>
<tr>
<td>2003</td>
<td>Pediatric Research Equity Act (PREA)</td>
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</tr>
</tbody>
</table>

Table 1. Pediatric Age Breakdown from Center of Drug Evaluation and Research (CDER)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Approximate Age Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>Birth to &lt; 1 Month</td>
</tr>
<tr>
<td>Infants</td>
<td>1 Month to &lt; 2 Years</td>
</tr>
<tr>
<td>Children</td>
<td>2 to &lt; 12 Years</td>
</tr>
<tr>
<td>Adolescents</td>
<td>12 to &lt; 17 Years</td>
</tr>
</tbody>
</table>

Methodology
- Names of Drugs Approved under BPCA in 2016, 2017, and 2018 were gathered
- Each drug was searched for in clinicaltrials.gov
- Studies were categorized as follows:
  - Pediatric and Adult Eligible Studies
  - Pediatric Only Eligible Studies
  - Specific Pediatric Population Only Eligible Studies
- Studies were assessed for similarities and trends.

Findings

Studies Breakdown for Acetaminophen Approved under BPCA in 2016

- Trials (Combined%): n = 13, 13.3% (9 trials)
- Of these trials, n = 7 had < 1% pediatric representation
- Total studies eligible for adult and pediatrics: n = 13

2 Drugs Approved in 2016
- Total studies eligible for adult and pediatrics: n = 8
- Of these trials, n = 2 had < 1% pediatric representation

11 Drugs Approved in 2017
- Total studies eligible for adult and pediatrics: n = 38
- Of these trials, n = 31 had < 1% pediatric representation
- Total trials with < 1% pediatric representation: n = 31

13 Drugs Approved in 2018
- Total studies eligible for adult and pediatrics: n = 89
- Of these trials, n = 84 had < 1% pediatric representation
- Total trials with < 1% pediatric representation: n = 84

Figure 2: Pediatric Representation in Drugs Approved under BPCA

Conclusions and Implications
For the 26 drugs approved under the BPCA from 2016 to 2018 where both pediatric and adult populations were eligible, 154 studies were conducted. Due to ambiguous data presentation, 19 studies (12.3%) were excluded. Examining the remaining 135 studies revealed:

- There is a lack of standardization regarding which ages constitute a specific pediatric sub-population although guidelines exist (Table 1, Figure 2).
- There is a lack of pediatric representation in clinical trials involving both adult and pediatric populations (Figure 2).
- These findings are consistent with 2019 Report to Congress: Pediatric Labeling of Orphan Drugs (Figure 1).

Pediatric drug labeling guides doctors, healthcare providers, and caretakers of children on optimal drug utilization. Better pediatric representation in clinical trials will provide further safety, efficacy, and dosage information for pediatric labeling.

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Moving Targets
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Annie Ly, MS ‘21, is currently pursuing a Master of Science degree in Regulatory Science. Annie completed her Bachelor of Arts in Health and Human Sciences with a minor in English at USC. As an undergraduate, Annie was a Provost First Generation Undergraduate Research Fellow. She has been assisting and conducting research in the Department of Regulatory and Quality Sciences within the USC School of Pharmacy since Spring 2018. She worked on the Clinical Trials Monitoring Modules project by conducting a literature review and creating standard operating procedures (SOPs). Currently, she is looking into the inclusion and representation of pediatric populations in clinical trials. The inspiration and motivation for this project came from her summers as a Recreation Leader for the City of Westminster Parks program. She facilitated sports, crafts, and educational enrichment for children in local neighborhoods, and her interactions with children who were on ADHD medications sparked questions concerning the efficacy of pediatric products in general. Outside of research, Annie can be found volunteering at local schools as a tutor and as a mini-course instructor, leading her educational enrichment student organization, SplashSC, and attending monthly Grand Rounds at the Children’s Hospital Los Angeles. lyannie@usc.edu