A Brief History of the Best Pharmaceuticals Act (BPCA) and the Pediatric Research Equity Act (PREA)

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Disclosure Statement

- I have no financial relationships to disclose relating to this presentation

- The views expressed in this talk represent my opinions and do not necessarily represent the views of FDA

Historical Milestones (Pre-1970)

1902	• The Biologics Control Act enacted following the death of 22 children from tainted anti-toxins
1938	• FD&C Act: Drugs must be Safe: enacted after 100 deaths, many in children, after use of sulfanilamide elixir
1962	• Following thalidomide tragedy in Europe; Kefauver–Harris amendments require effectiveness
1962	• The FD&C Act amended: Drugs not tested in children should not be used in children

Historical Milestones (1970's)

1974
- AAP Committee on Drugs issues guidelines for evaluating drugs for pediatric use

1977
- AAP issues guidelines for ethical conduct in pediatric studies

1979
- FDA requires sponsors to conduct pediatric clinical trials before including pediatric information in the labeling

Historical Milestones (1990's)

1990
- Institute of Medicine holds workshop regarding the lack of labeling for pediatric drugs

1992
- FDA proposed Pediatric Labeling Rule and proposes extrapolation of efficacy from other data

1994
- Final Rule on Pediatric Labeling. Formalizes Extrapolation of Efficacy; manufacturers to update labeling if pediatric data existed; HOWEVER, it allowed a disclaimer to the labeling for drugs not evaluated in children

1994
- Pediatric Plan to encourage voluntary development of pediatric data

Historical Milestones: Legislation

1997	• FDAMA creates pediatric exclusivity provision (voluntary), provides 6-month exclusivity incentive
1998	• Pediatric Rule (mandatory): products are required to include pediatric assessments if the drug is likely to be used in a ‘‘substantial number of pediatric patients’’ (50,000) or if it may provide a ‘‘meaningful therapeutic benefit’’
2002	• Pediatric Rule declared invalid by DC Federal Court; the rule exceeded FDA’s authority
2002	• FDAMA pediatric exclusivity provision reauthorized as BPCA. Maintains 6-month exclusivity added to patent life of the active moiety. Mandates pediatric focused safety reviews.
2003	• PREA re-establishes many components of the FDA’s 1998 pediatric rule. Orphan products are exempted

Historical Milestones: Recent Advances

2007
- FDAA Reauthorizes BPCA & PREA for 5 years : Pediatric Review Committee (PeRC) formed. Negative and positive and inconclusive results of pediatric studies must be placed in Labeling.

2012
- FDASIA legislation makes permanent BPCA and PREA

2017
- RACE for Children Act: PREA changed to address challenges in pediatric cancer development by requiring for studies in molecular targets substantially relevant to the growth or progression of a pediatric cancer

2022(?)
- 1000th pediatric-specific labeling change under BPCA and PREA expected to be approved

Best Pharmaceuticals for Children Act

- Originally introduced in 1997 as “Better” Pharmaceuticals for Children Act
  - Senate sponsors: Chris Dodd (R-OH) and Mike DeWine (D-CT)
  - House sponsors: Jim Greenwood (R-PA) and Henry Waxman (D-CA)
- Passed as part of Food and Drug Administration Modernization and Accountability Act (FDAMA) in November 1997
- Best Pharmaceuticals for Children Act
  - Passed Senate with amendment by Unanimous Consent on December 12, 2001
  - Passed House on motion to suspend the rules and pass the bill Agreed to by voice vote on December 18, 2001
  - Signed by President George W. Bush and became Public Law 107-109 on January 4, 2002

Brief History of Legislative Efforts

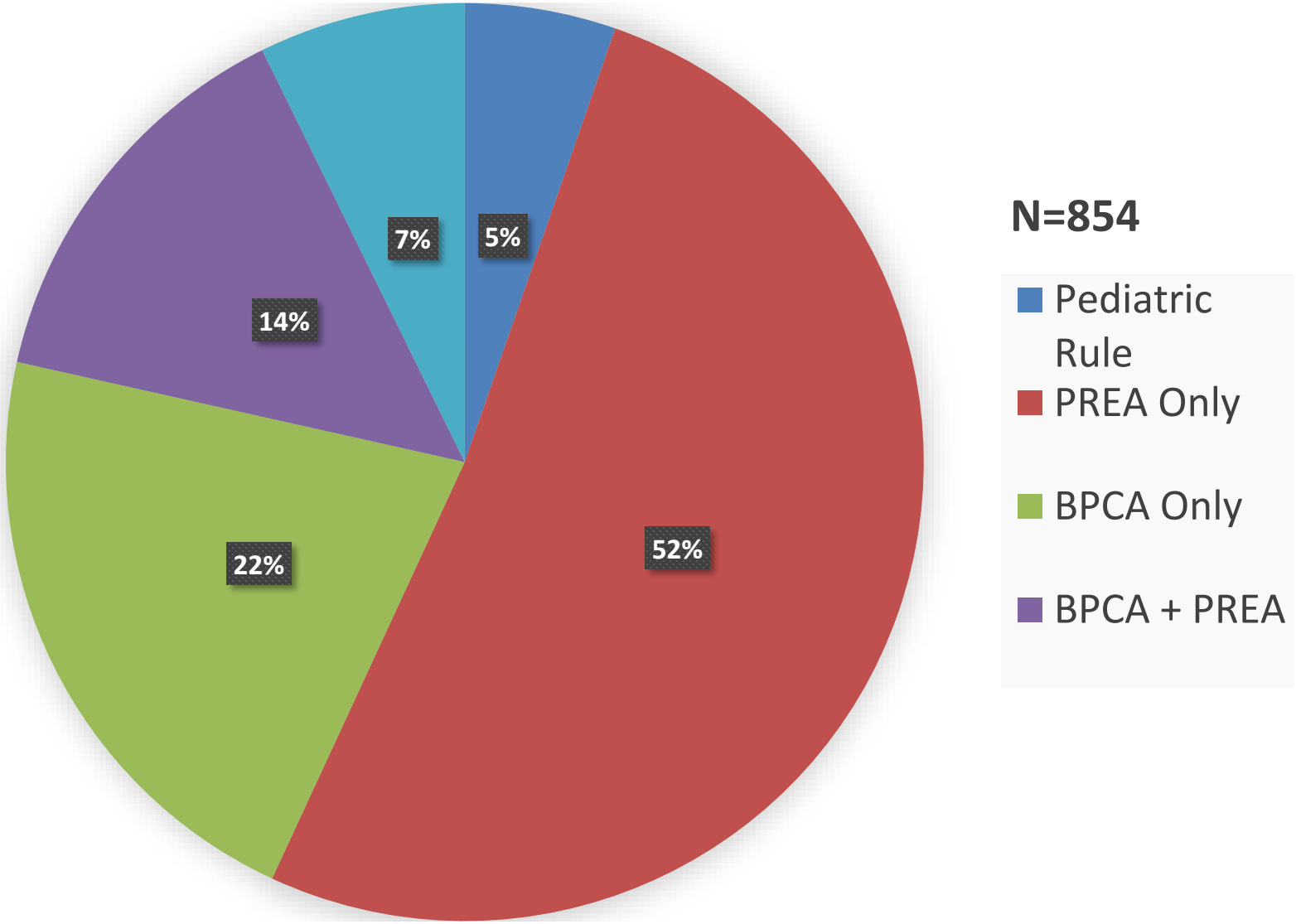
- Hilary Clinton (D-NY) originally introduced PREA in the Senate in 2002 and passed out of committee but was not passed by the Senate
- Hillary Clinton and Mike DeWine (R-OH) re-introduced the Pediatric Research Equity Act in March 2003
- Jim Greenwood (R-PA), Anna Eshoo (D-CA), and Deborah Pryce (R-OH) introduce the legislation in the House of Representatives
- PREA passed in the Senate with amendments by Unanimous Consent
- PREA passed in the House after motion to suspend the rules and pass the bill Agreed by voice vote
- Signed by George W. Bush and became Public Law No. 108-155 on December 3, 2003

PREA vs. BPCA

- **PREA**
- Drugs and biologics
- **Required studies**
- Studies may only be required for approved indication(s)
- Products with orphan designation are exempt from requirements except molecular targets relevant to pediatric cancers
- 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 products with orphan designation
- Pediatric studies must be labeled

Pediatric Labeling Changes 1998-2020



My Thoughts

- The health of the child begins with the health of the mother
- Statutory requirements to conduct and incentive pediatric therapeutics development have been successful
- Data required for pregnancy and lactation are different
  - Therapies that have been approved for adults of reproductive potential are also approved for use in pregnancy unless specifically contraindicated
- Legislative efforts could be more fraught compared to early 2000's
- Careful consideration and collaboration with stakeholders in moving forward with any legislative efforts would be important