Drug Development in Pediatric Heart Failure: Extrapolation, Clinical Trial Design, and Endpoints

FDA-University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI)

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

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- FDA has developed collaborations with academic institutions to advance regulatory science through innovative research, education, and scientific exchanges
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- CERSI collaborations include:
  - Workshops, Lectures, Webinars, Publications
  - Research projects
  - Fellowship opportunities
  - Scholars program

UMD-CERSI and Pediatric Product Development

- Drug development in pediatric heart failure: extrapolation, clinical trial design, and endpoints (October, 2017)
- UCSF CERSI: ACDRS Workshop: pediatric drug development (March 2017)
- Pediatric master protocols workshop (September, 2016)
- Challenges and strategies to facility formulation development of pediatric drug products (June, 2016)
- Quantitative assessment of assumptions to support extrapolation of efficacy in pediatrics (June, 2016)
- Pediatric drug development: Use of exposure matching and exposure-response for extrapolation of efficacy in pediatric product development (January, 2015)

Pediatric Drug Development
General Principles

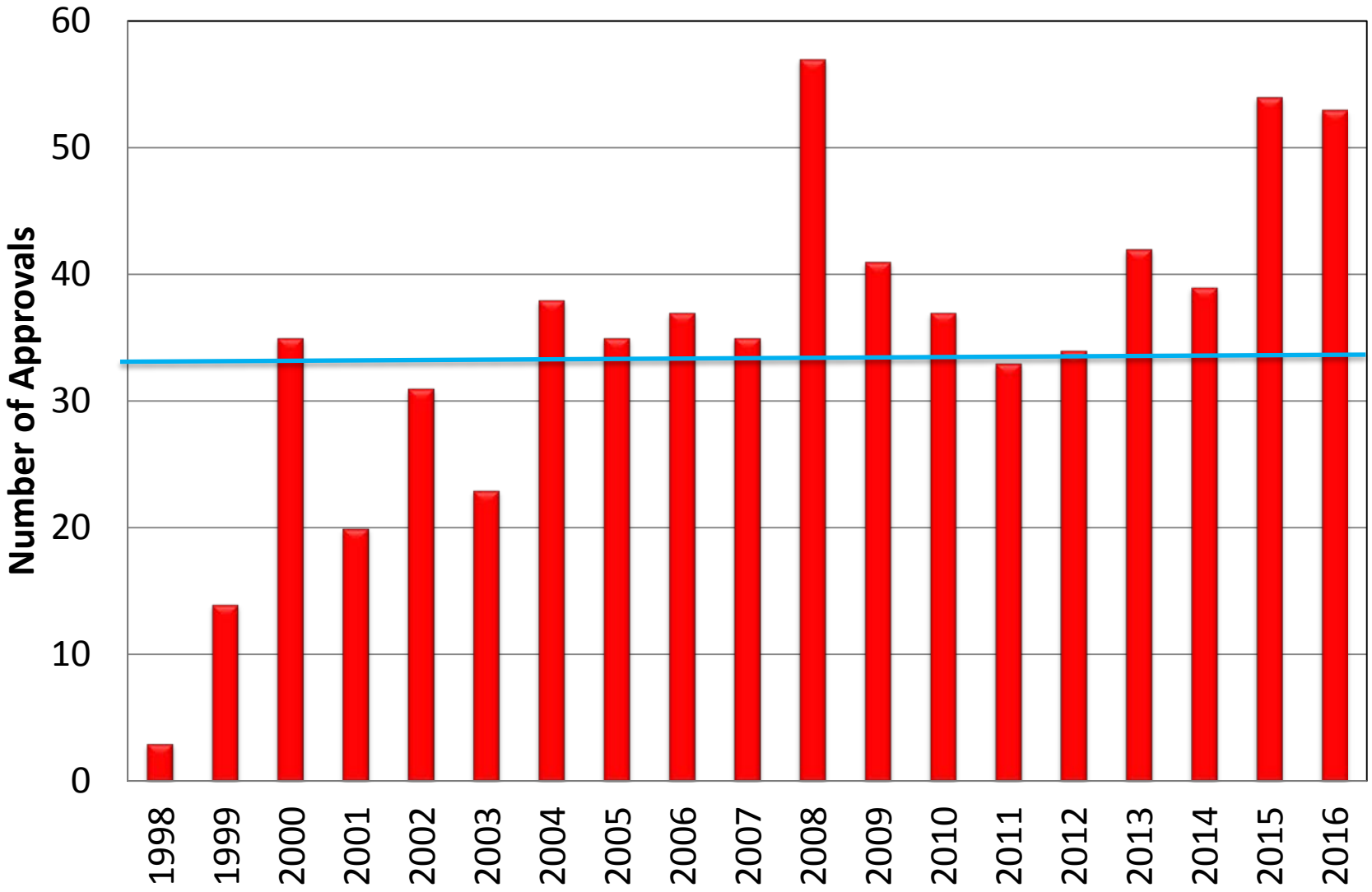
- Children first described as the therapeutic orphan in 1963 by Harry Shirkey, M.D.
- Pediatric patients should have access to products that have been appropriately evaluated
- Product development programs should include pediatric studies when pediatric use is anticipated

From FDA guidance to industry titled *E11 - Clinical Investigation of Medicinal Products in the Pediatric Population,* December 2000

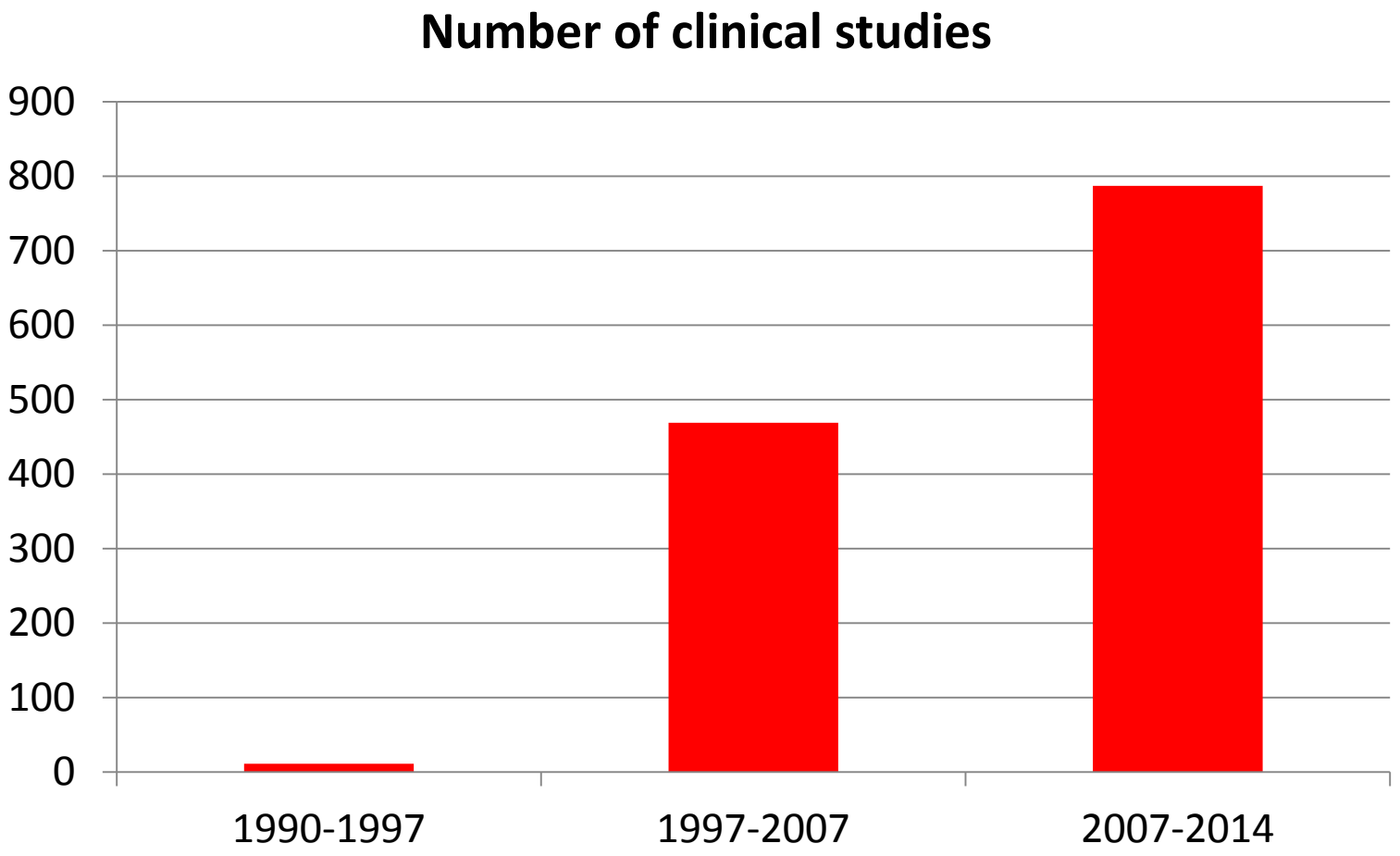
U.S. Pediatric Drug Development Laws

- Best Pharmaceuticals for Children Act (BPCA)
  - Section 505A of the Federal Food, Drug , and Cosmetic Act
  - Provides a financial incentive to companies to voluntarily conduct pediatric studies
  - FDA and the National Institutes of Health partner to obtain information to support labeling of products used in pediatric patients (Section 409I of the Public Health Service Act)
- Pediatric Research Equity Act (PREA)
  - Section 505B of the Federal Food, Drug , and Cosmetic Act
  - Requires companies to assess safety and effectiveness of certain products in pediatric patients

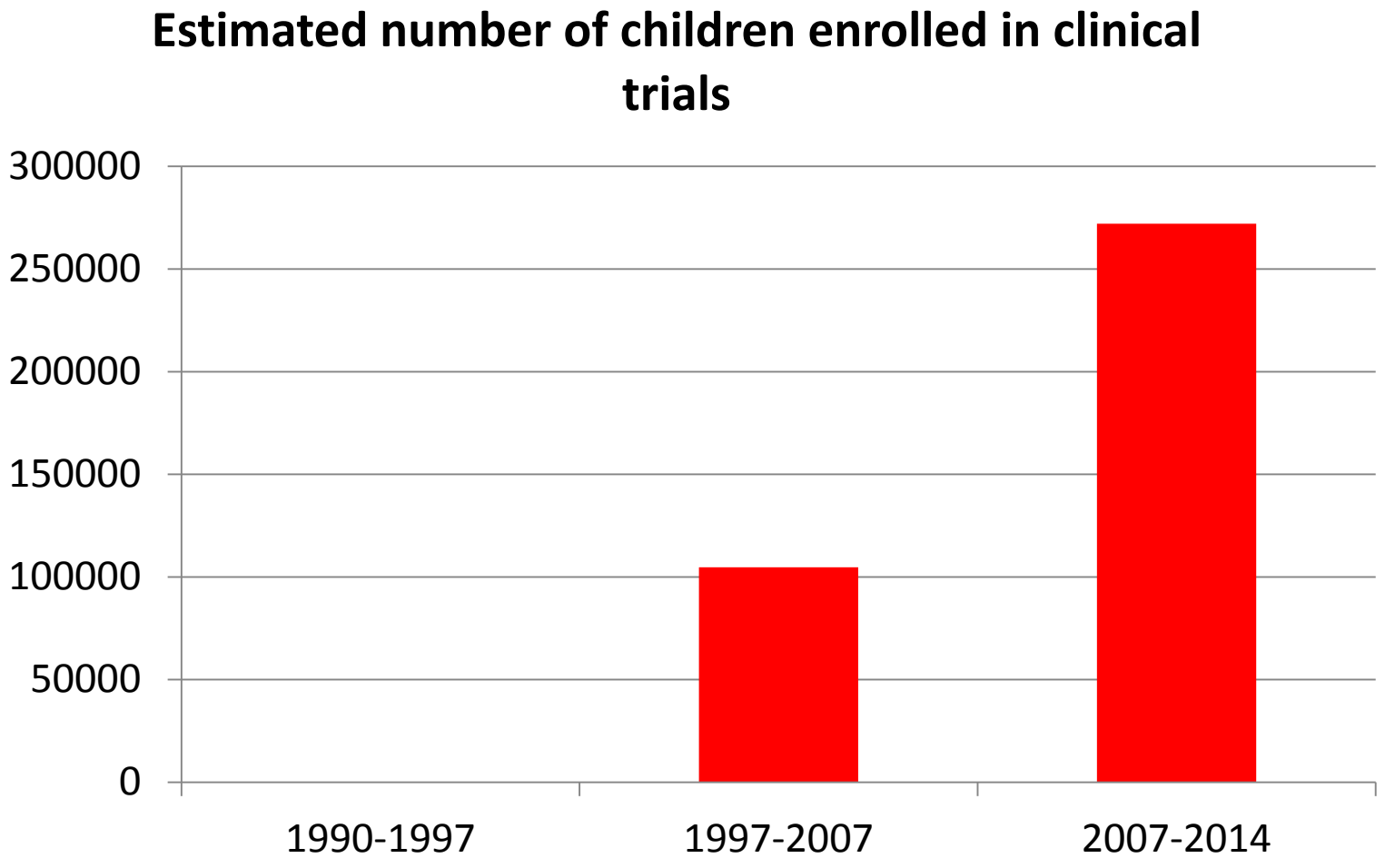
Pediatric Labeling Changes 1998-2016



Number of Studies Completed under BPCA and PREA



Number of children enrolled in trials under BPCA and PREA



Challenges in the 21st Century

- BPCA and PREA work together to accomplish goal of obtaining adequate pediatric efficacy and safety data for labeling
- Still time between adult approval and incorporation of pediatric information in labeling is substantial
- Easy product development has already been done
  - Recognition that pediatric product development must incorporate innovation and collaboration

Pediatric Heart Failure

- Over 20 drugs approved for treatment of heart failure in adults
- No drugs approved for treatment of pediatric heart failure
- Only one drug studied under BPCA/PREA for heart failure
  - Carvedilol failed to demonstrate efficacy

Goals for Today

- Review the current state of knowledge of natural history and management of pediatric heart failure
- Discuss possible trial designs/trial design issues in pediatric heart failure
- Identify potential paths forward for successful treatment trials in pediatric heart failure

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