

# **Development of Over the Counter Drugs for Adolescent Patients: What is Known and What is Needed**

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# Objectives

- **Review Pediatric Legislation**
- **Describe Adolescent Data**
- **Describe Challenges in Drug Development for the Adolescent**



# Pediatric Legislation

Legislation passed 27 September 2007

- **Voluntary**
  - **Best Pharmaceuticals for Children Act (BPCA)**
    - Renewed pediatric exclusivity incentive originally in FDAMA, BPCA
- **Mandatory**
  - **Pediatric Research Equity Act (PREA)**
    - Restored some important aspects from the Pediatric Rule, enjoined in 2002, and PREA



# Early Assumptions

- **No significant differences in dosing, absorption, metabolism, elimination, toxicity**
- **Adult-like size of adolescents**
  - **50<sup>th</sup> percentile weight for a 12 year old female is 50 kg**
  - **Once menarche occurs, adolescents are considered adults**



# Early Assumptions

- **Adolescents are about the same size as adults, so we can simply extrapolate down to age 12 years, and get studies on younger children**
  - **Examples of extrapolation**
    - **Singulair (montelukast\*)**
    - **Codeprex Extended-Release Suspension (chlorpheniramine; codeine)**
    - **Tirosint capsules (levothyroxine)**



# Child vs. Adolescent vs. Adult



# What Studies Have Revealed

- **SSRIs**
  - Adolescents and young adults using SSRI antidepressants have increased rate of suicidal ideation when compared to older adults
  - Difficult to establish efficacy in pediatric depression (mostly adolescents enrolled)
- **Sumatriptan**
  - Five clinical trials evaluating oral sumatriptan in pediatric patients ages 12 -17 years with migraines did not establish the safety and effectiveness when compared to placebo
- **Zolmitriptan**
  - Clinical trial evaluating zolmitriptan in pediatric patients ages 12 -17 years with migraines did not establish the safety and effectiveness when compared to placebo



# What Studies Have Revealed

- **Betamethasone and Betamethasone/  
Clotrimazole**
  - the treatment of tinea pedis (athletes foot), 17 of 43 (39.5%) evaluable patients (ages 12-16 years) demonstrated adrenal suppression as determined by cosyntropin testing
  - Lotrisone cream for the treatment of tinea cruris, 8 of 17 (47.1%) evaluable patients (ages 12-16 years) demonstrated adrenal suppression by cosyntropin testing
- **Methylphenidate**
  - Increase in age resulted in increased apparent oral clearance



# Why Are Adolescents Different?

- **Physical development (puberty)**
  - May need to reassess endpoints (adolescent migraines and depression may be different from adult conditions)
  - Clinical pharmacology is different
- **Cognitive and psychological development**
  - Going from concrete thinking to abstract
  - Do not feel immortal, feel vulnerable
  - Regress when placed under stress
- **Social development**
  - Friends take precedence over family obligations
  - Committed to academics, athletics, arts, clubs

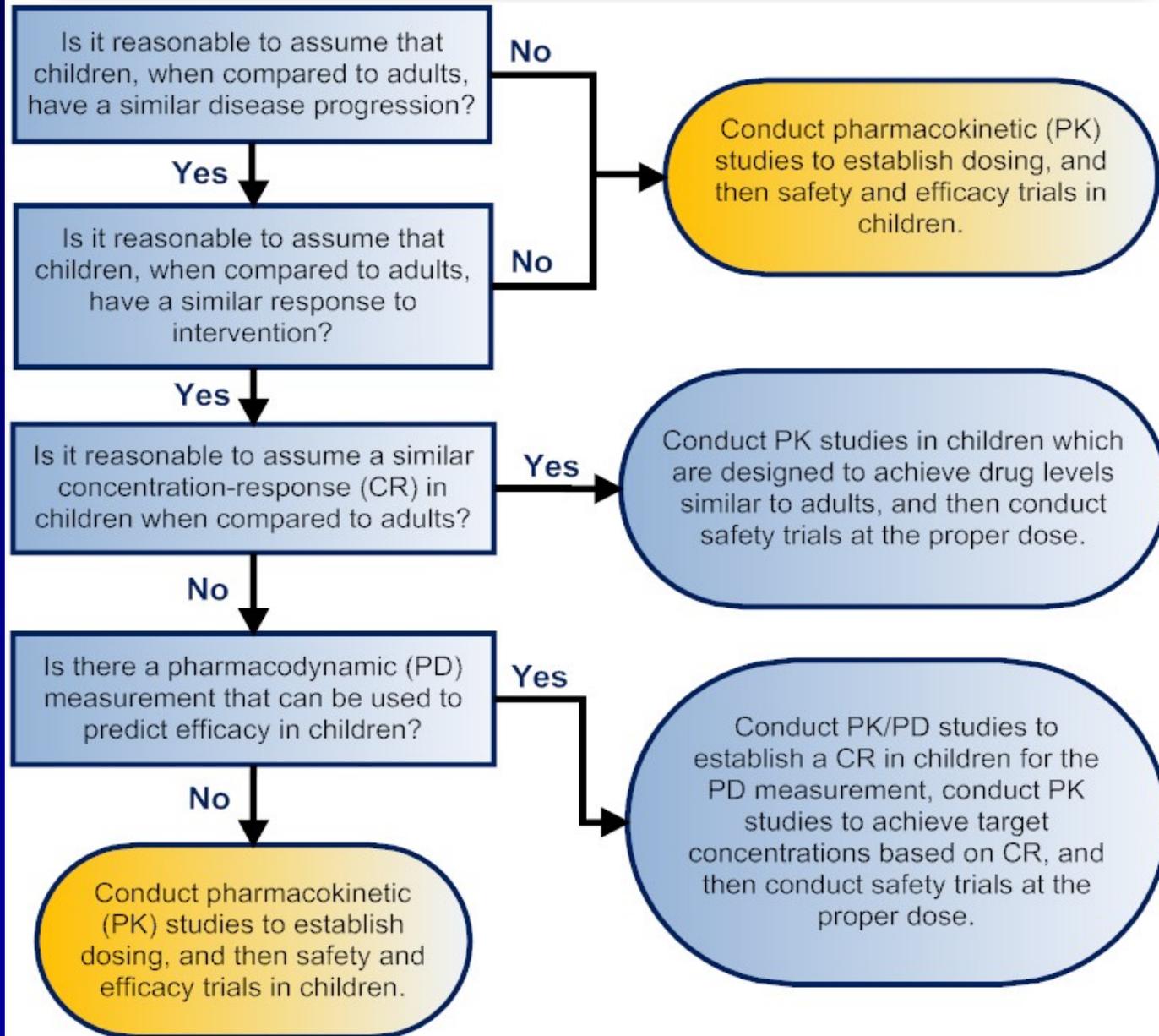


# Assumptions

- **Given previous information learned from studies of prescription drugs, can we assume similar pharmacologic effects?**
  - **Extrapolation must be supported by scientific rationale and supportive studies\***



**FDA algorithm for determining need for pediatric studies using the principle of scientific necessity/extrapolation (under BPCA or PREA)**



# Assumptions

- **Given behavioral issues with OTC drug use, can we assume that adolescents (12 – 16 years) are the same as adults?**
  - **Neurocognitive differences known**
  - **Interpretation of labeling may be different**
  - **Understanding of how instructions apply to condition may vary**



## **Conclusion (con't)**

- **The FDA has been given tools to encourage and require studies in the pediatric population**
- **Studies have demonstrated that adolescents are different from smaller children and adults**
- **Greater efforts must be made to assess differences in physical, cognitive and psychological, and social development in order to meet medical needs of adolescents**



## Conclusion (con't)

- **Additional information needed regarding**
  - **adolescent development, behavior, decision making**
  - **how these developmental differences effect actual use of adolescents**
  - **if adolescents must be studied separately from adults, and if this age group should be subdivided even more (e.g. 12-14 yrs, 14-16 years, >16 years)**
  - **factors that will help promote appropriate use of OTC medications, including communication**

