Priorities from the Cold and Cough Therapeutics Working Group

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Upper Respiratory Infections (URIs)

- Most common reason for acute care physician visits in the U.S.; #2 for children
- No cures available, but many OTC medications claim symptomatic relief
- **Billions** of dollars are spent each year in the United States on OTC cough & cold medications
- 10% of children use cough and cold medications each week in the U.S. (Vernacchio L et al. *Pediatrics*, 2008)

4 Classes of PO Drugs Marketed for URIs*

- Antitussives – Dextromethorphan
- Decongestants – Pseudoephedrine
  Phenylephrine
- Antihistamines – Diphenhydramine
  Brompheniramine
  Chlorpheniramine
  Doxylamine
- Expectorants – Guaifenesin

*Numerous other topical or nasal products

Safety Concerns

- >7000 ED visits/year in US children <12 years old due to adverse events associated with cough/cold medications (Schaefer MK et al. *Pediatrics*, 2008)

Efficacy Concerns

- 1997 – American Academy of Pediatrics:

  "No well-controlled scientific studies … support the efficacy & safety of narcotics or dextromethorphan as antitussives in children. Indications for their use in children have not been established."

Efficacy Concerns

- 2006 – American College of Chest Physicians:

  "There is no evidence for using medications for the symptomatic relief of cough … In children with cough, cough suppressants and other OTC cough medicines should not be used as patients, especially young children, may experience significant morbidity and mortality."

Problems Interpreting Data

- Unclear endpoints for efficacy
- Lack of validated tools for measuring outcomes
- Are the doses right?
- Single dose vs. multiple dose outcomes?

Working Group Questions in Determining Priorities

- Where is the evidence gap?
- Which ages are affected?
- What research is being done, what should be done, and who should do it?
- What is achievable within BPCA?
- What areas will have the highest impact?
- What areas will move science AND clinical care forward?

Priority Area #1

- "Development of clinically meaningful endpoints and validated tools to measure them"
  - subjective and objective
  - all ages <12 years (may differ by age grouping)
  - single and multiple doses

Priority Area #2

- "Pharmacokinetic studies of orally administered cough and cold ingredients in children including the study of pharmacogenetic variability"
  - all ages <12 years *including* infants <2 years
  - may duplicate some ongoing industry efforts

Priority Area #3

- "Efficacy studies of orally administered OTC cough and cold ingredients"
  - all ages <12 years
  - randomized, masked, placebo controlled trials
  - dependent on priority areas 1 & 2

Priority Area #4

- "Studies to better elucidate the primary biochemical mediators of cough and cold symptoms to identify new targets for drug therapy"
  - longer term research priority

Moving Forward – Cough/Cold Medication Research

- These drugs will continue to be used by a large percentage of children despite lack of science to justify use or doses administered

- Surveillance and safety efforts currently being performed by industry and CDC for OTC medications should continue

Moving Forward – Cough/Cold Medication Research

- Funding needed to determine PK, dose, pharmacogenetic impact, efficacy → fits within BPCA since drugs are off-patent and have no market exclusivity

- Most of the drugs included in the monograph are >50 years old. Innovative tools for symptom & outcome measurement are required, new targets for treatment are needed, and new drugs need to be developed → fits within BPCA's pre-clinical data collection mission