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ARRA Grand Opportunities FOA: Bisphenol A: Research to Impact Human Health

Jerrold J. Heindel PhD
Scientific Program Administrator
National Institute of Environmental Health Sciences
National Institutes of Health/DHHS

heindelj@niehs.nih.gov

U.S. Department of Health and Human Services
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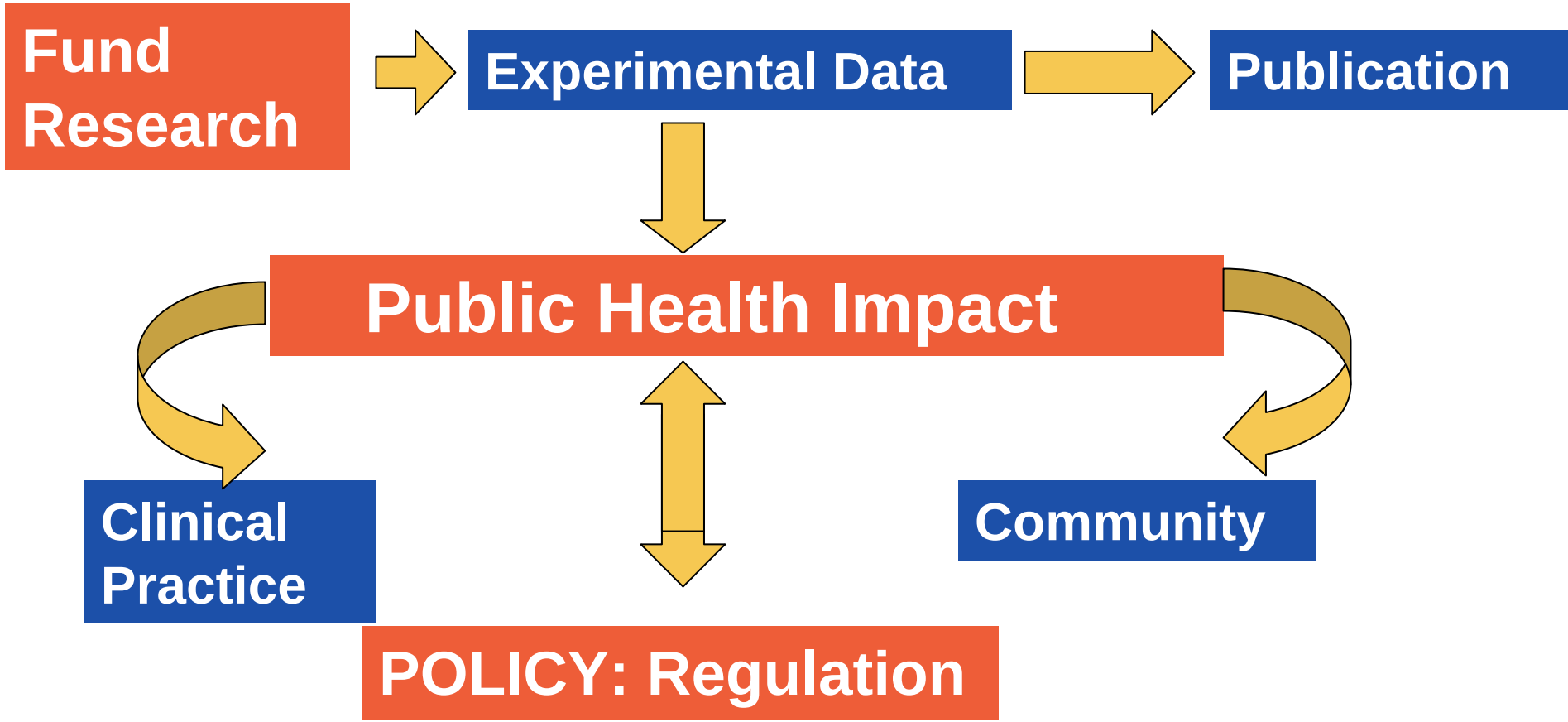
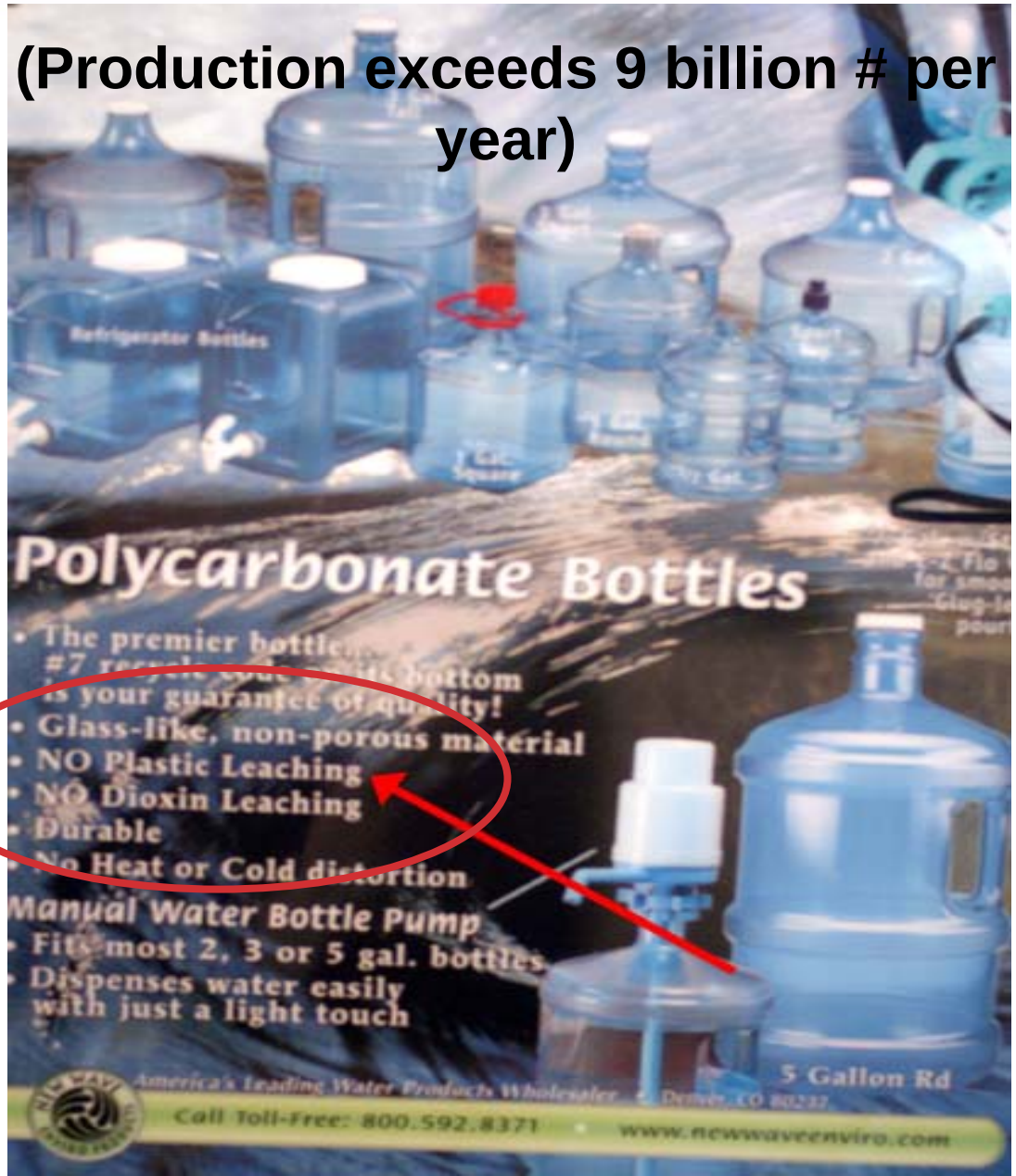
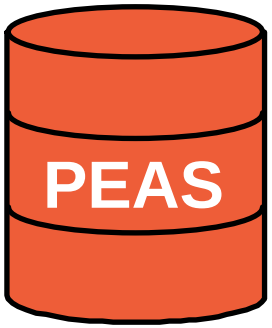
Challenge: IMPACT Human Heath and Policy !



Bisphenol A

(Production exceeds 9 billion # per year)





Current Situation

- Over 900 published manuscripts on BPA .
- Major BPA effects noted in rats and mice
    - Abnormal urethra
    - Prostate hyperplasia & cancer and Mammary gland cancer
    - Sperm count decrease
    - Early puberty in females
    - Hyperactivity/Impaired learning
    - Abnormal Chromosomes in oocyes
    - Body weight increase
- Many effects at low environmentally relevant doses

Current Situation

- Two NIEHS sponsored meetings examined the data
  - **Chapel Hill Consensus statement (2006)**
    - BPA exerts cellular and tissue-type specific effects and non-monotonic dose response at low physiologically-relevant concentrations.
  - **CERHR/NTP Final Report (2008):**
    - Some concern BPA exposure during development to affect prostate cancer and sexually dimorphic behavior at low physiologically-relevant concentrations.
- **FDA Report (2009)**
  - BPA is safe based on focus on GLP guideline studies
- **FDA/NIH Committee (2009)**
  - NTP/NCTR research, NIH research (human and animal studies)

Bisphenol A: Research to Impact Human Health Animal Studies

- Valid models/species and strain/diet
- Larger numbers of animals/repeat experiments
- Examine both males and females
- Measure internal dose of environmental chemical
- Dose response curves (environmentally relevant exposures)
- Extrapolate to humans (PBPK models, mechanisms)
- Keep primary data sets for use in regulatory assessment
- Focus on disease endpoints

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Bisphenol A: Research to Impact Human Health
Animal Studies

Research Focus (Developmental exposures)

- behavior
- obesity/diabetes/metabolic syndrome
- reproductive disorders including age at puberty
- development of prostate, mammary gland and uterine cancer
- Asthma, infections and autoimmune diseases
- cardiovascular diseases
- transgenerational effects
- physiologically-based pharmacokinetic models for animals and humans to facilitate cross species extrapolations

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Bisphenol A: Research to Impact Human Health
Human Studies

- Established cohorts, extant datasets and banked specimens
- Focus on development
- Existing longitudinal studies to add new analyses on health effects of BPA
- Blood and or urine measurements of BPA to correlate with disease outcomes

Additional "Grand Opportunities" Requirements

RC2: Not the usual R01

- Budget of >$500,000
- Collaborative team approach
- No preliminary data
- Two year awards

Results

- Forty-two applications (41 responsive)
- Review conducted by Leroy Worth, SRO
- Twenty-four applications discussed and scored, 17 not discussed
- Scores ranged from 20-65
- Funded applications: priority scores of 35 or less

Funding Strategy

Name	Project	Priority Score
Shana Swan Bernard Weise	Human and animal study of behavior	26
Kim Harley	Human study of cognitive function at 5 yrs and body mass and metabolic syndrome at 9 yrs	31
Beverly Rubin	Mouse model of obesity and metabolic syndrome	27
Robin Whyatt	Human study of airway inflammation and asthma	28
Paige Lawrence	Mouse model of susceptibility to infection later in life	35

Funding Strategy

Cheryl Walker Shuk Mei Ho Michael Mancini	Reprogramming of epigenome and risk of prostate cancer in mouse model	20
Gail Prins	Novel human prostate model and epigenetic alterations and prostate cancer	25
Fred vom Saal	Mouse model of obstructive voiding disorder and prostate cancer	35
Scott Belcher	Cardiovascular function in mouse strains with differing sensitivity	26
Ana Soto	Rat model of breast cancer	32

How to Move Forward?

Meeting of newly funded “GO” grantees along with other BPA funded researchers to assure maximum IMPACT of the research

- Encourage Coordination protocols, models, endpoints, diets, BPA measurements
- Encourage collaboration and sharing of tissues among animal researchers and epidemiologists
- Present FDA/NTP research program and possibilities for collaboration
- October 6, NIEHS

Questions