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

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Challenge: IMPACT Human Heath and Policy!

- Fund Research
- Experimental Data
- Publication
- Public Health Impact
- Clinical Practice
- Community
- POLICY: Regulation
Bisphenol A

(Production exceeds 9 billion # per year)
• 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 oocytes
  • Body weight increase
• Many effects at low environmentally relevant doses
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)
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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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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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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
<table>
<thead>
<tr>
<th>Name</th>
<th>Project</th>
<th>Priority Score</th>
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<tbody>
<tr>
<td>Shana Swan</td>
<td>Human and animal study of behavior</td>
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<td>Bernard Weise</td>
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<td>Kim Harley</td>
<td>Human study of cognitive function at 5 yrs and body mass and metabolic syndrome at 9 yrs</td>
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<tr>
<td>Beverly Rubin</td>
<td>Mouse model of obesity and metabolic syndrome</td>
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<td>Robin Whyatt</td>
<td>Human study of airway inflammation and asthma</td>
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<td>Paige Lawrence</td>
<td>Mouse model of susceptibility to infection later in life</td>
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<tr>
<td>Name</td>
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<td>Cheryl Walker</td>
<td>Reprogramming of epigenome and risk of prostate cancer in mouse model</td>
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<td>Shuk Mei Ho</td>
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<td>Michael Mancini</td>
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<td>Gail Prins</td>
<td>Novel human prostate model and epigenetic alterations and prostate cancer</td>
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<td>Fred vom Saal</td>
<td>Mouse model of obstructive voiding disorder and prostate cancer</td>
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<tr>
<td>Scott Belcher</td>
<td>Cardiovascular function in mouse strains with differing sensitivity</td>
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<tr>
<td>Ana Soto</td>
<td>Rat model of breast cancer</td>
<td>32</td>
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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