# PROGRAM OVERVIEW

## HHRP 2009 BOSC Subcommittee

## First Conference Call, October 10, 2008

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National Program Director (Acting)

Acknowledgement: Hugh Tilson, NPD 2005-7
HHRP Writing Team

# Human Health Research Coordination Team

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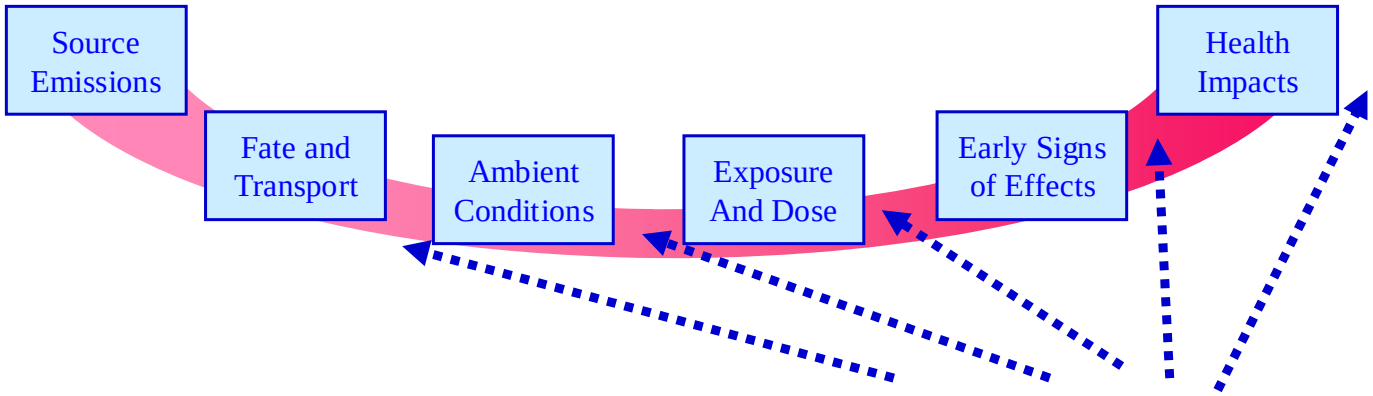
# Objectives of this Overview

- Orient the BOSC HHRP Subcommittee to the HHRP including its history and strategic future directions
- Review HHRP Multi Year Plan (MYP-2006) for relevance, balance and scope
- Summarize changes in emphasis or direction in response to the mid-cycle BOSC review and other influences
- Provide background and context for 2nd conference call that will expand in more detail upon scientific progress and future plans

# Over-arching goal: Help EPA to protect human health




- Human health research develops the methods, models, & data to characterize and reduce uncertainty in the 'critical links' across the exposure-to-effect paradigm;
- and, explores fundamental determinants of exposure and dose, and the basic biological changes (effects) that result from exposure to environmental contaminants and lead to adverse health outcomes

# Context of 4 LTGs: Risk assessors and risk managers USE ORD's methods and models to…

- LTG-1 … Understand and reduce uncertainty in risk assessment using mechanistic (mode of action) information

- LTG-2 … Characterize aggregate & cumulative risk in order to manage risks to humans exposed to multiple environmental stressors

- LTG-3 … Characterize and provide adequate protection for susceptible populations

- LTG-4 … Evaluate the effectiveness of risk management decisions

Human Health Research Program
Multi-Year Plan
(FY 2006-2013)

Office of Research and Development
US Environmental Protection Agency

2 June 06

# Timeline: Where we've been… Where we are now…

HH Research Strategy

National Center for Computational Toxicology 2005

Human Health Risk Assessment MYP 2005

NAS: Tox Testing 21st Century, NAS 2007

'90s — 2003 — 2005 — 2006 — 2007 — 2008 — 2009

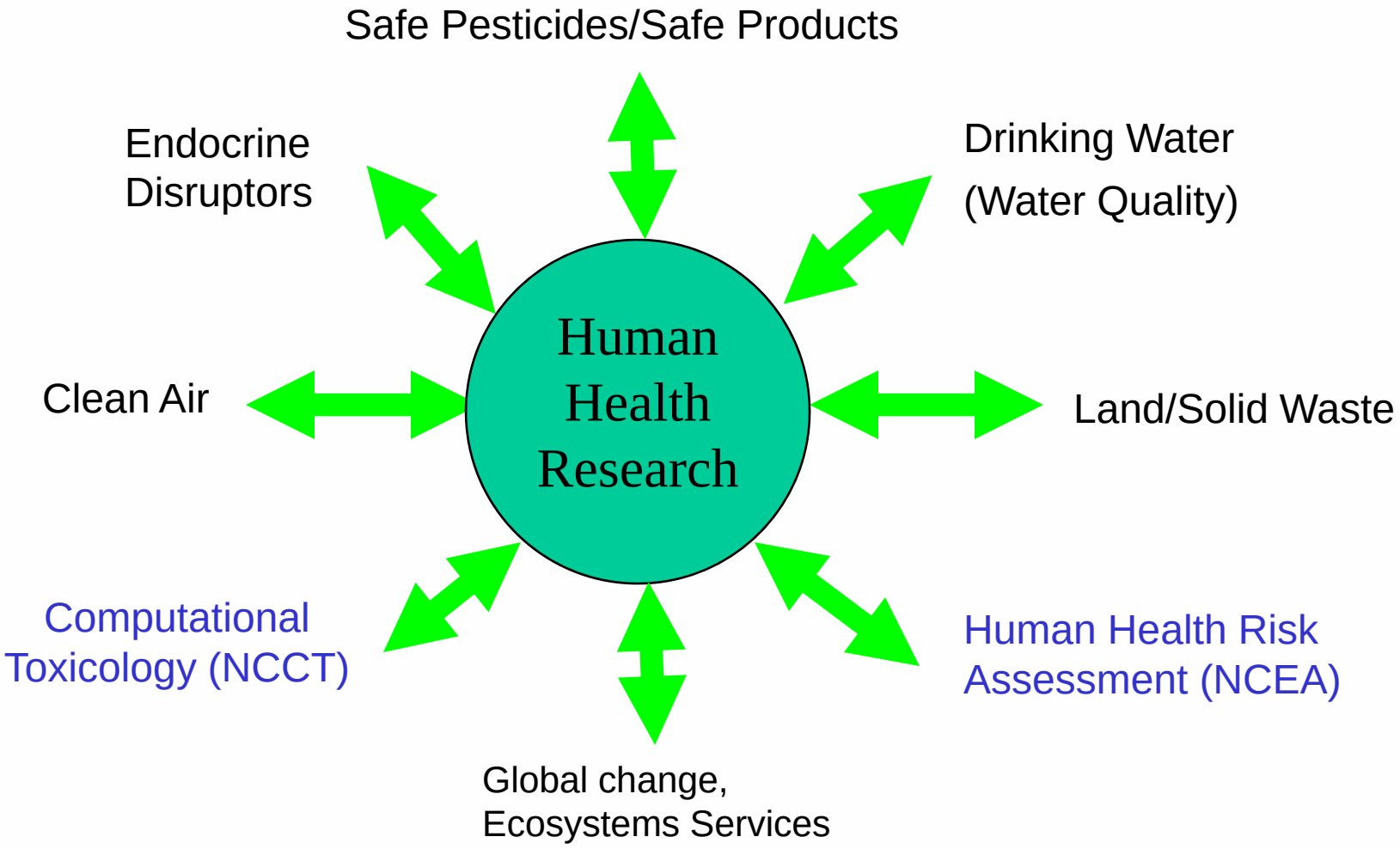
BOSC 1st full

BOSC Mid-cycle

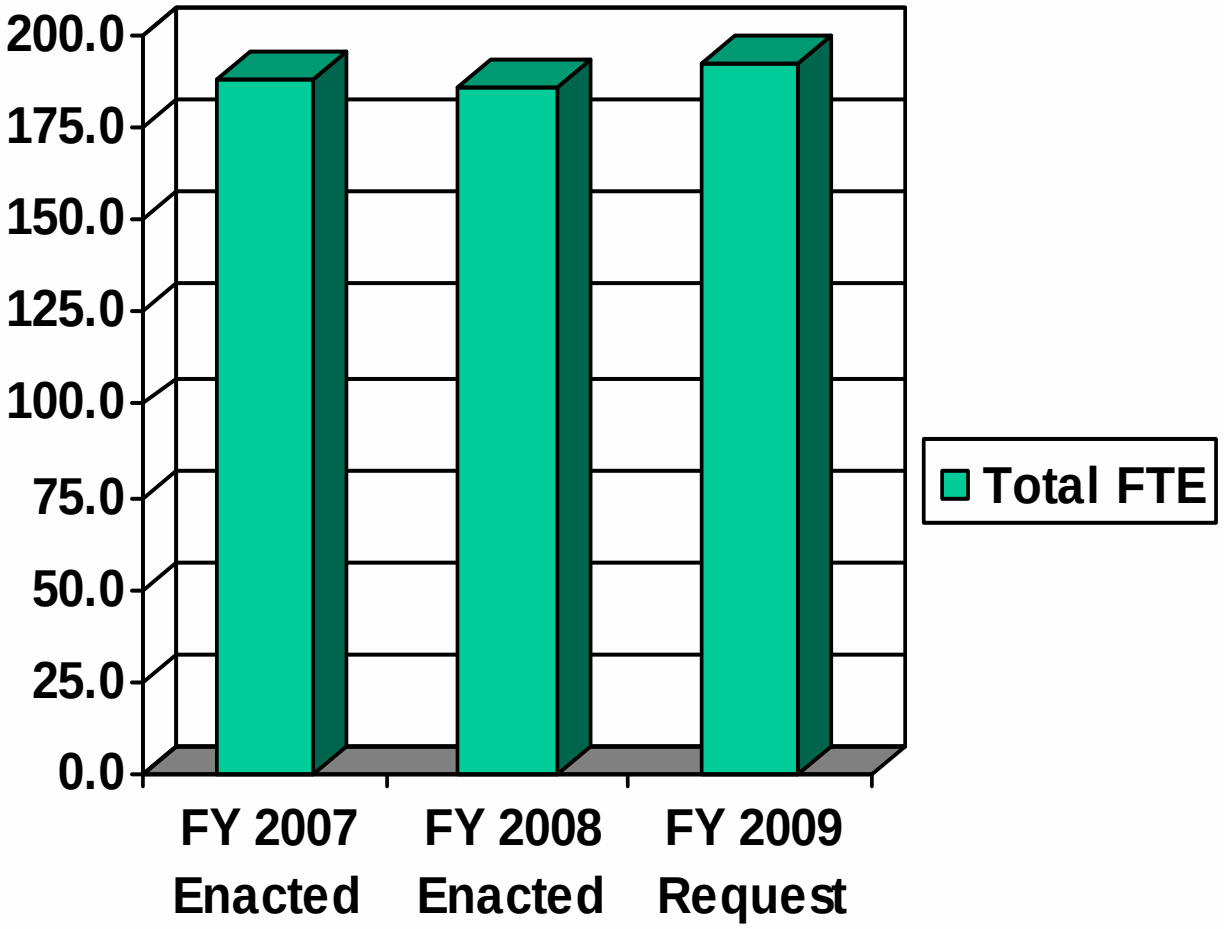
MYP 2003

**MYP 2006**

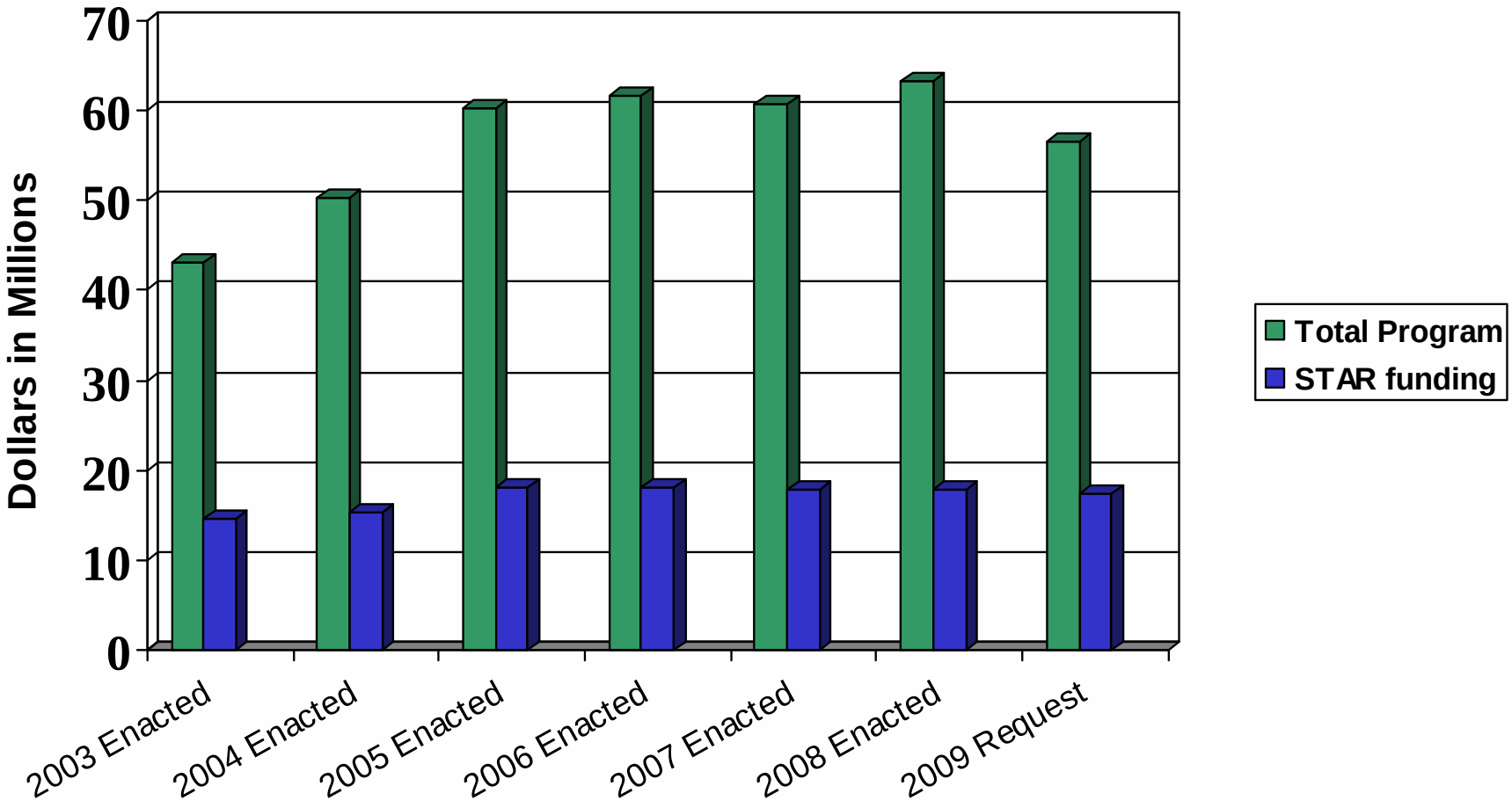
# Interdisciplinary, Cross-Program ("Core") Research



# A large program…



# Past and current resources, ~25% for extramural grants




Funding levels reflect total program including payroll, travel, working capital fund, and operating expenses. STAR: Science to Achieve Results extramural grants

# *HHRP products are broadly applicable to many partners and stakeholders*

- EPA Program Offices (OAR,OPPTS, OW, OSWER)
- EPA Regions (States) and Tribes
- EPA's Office of Children's Health Protection and Environmental Education (OCHPEE)
- Other Federal Groups
  - NIH/CDC – Interpretation of Biomonitoring Data; Public Health priorities and impact; diseases (asthma, autism)
  - NIH/NICHD – Participation in the National Children's Study (ICC with NIEHS & CDC); Application of methods and models
  - NIH/NIEHS – Centers for Children's Environmental Health and Disease Prevention, since 1998
- International: WHO, OECD, IPCS

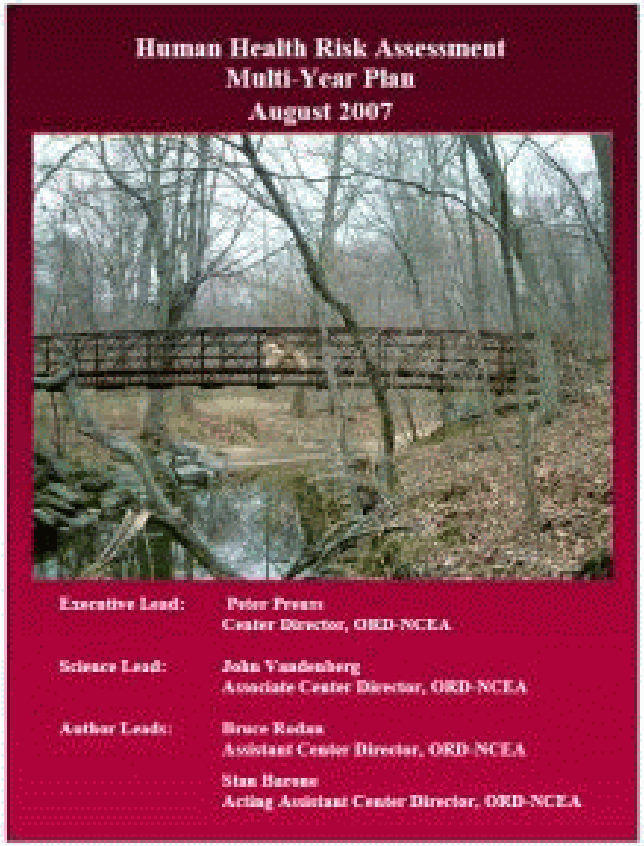
## *Participants to Partners*

NCCT


www.epa.gov/comtox

Implementation Plan 2006

NCEA

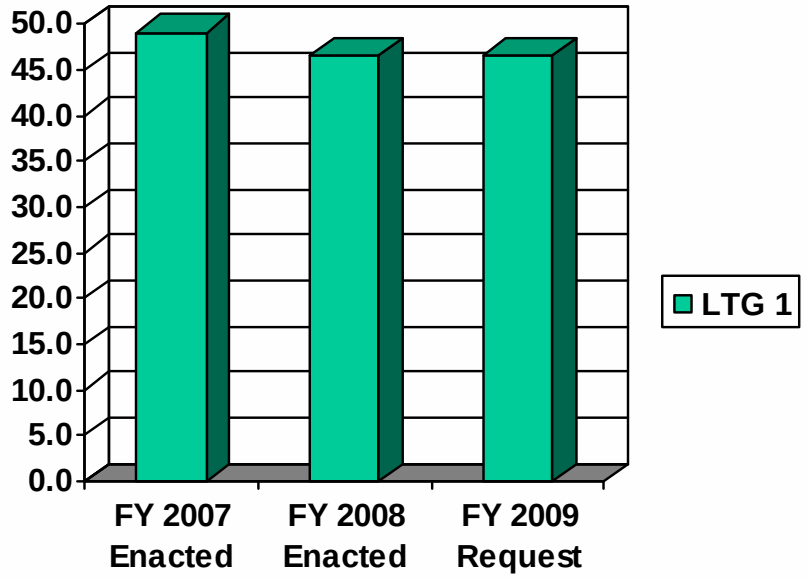



www.epa.gov/ncea

MYP 2005 & 2007

# LTG 1 Mode of Action

- Julian Preston, LTG Lead
- Methods & Models to Characterize MOA: cancer vs. non-cancer; oxidative stress pathways; neuroendocrine modes of action
- Linkages between PK and PD models
- MOA information to address extrapolation in risk assessment
- MoA models and biomarkers are used in LTG 2 (Cumulative Risk) and contribute to NCCT's computational toxicology goals
- Strategic direction: Increasing emphasize on systems approaches
- Responsive to NRC: Tox Testing 21st Century

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# *LTG1 Research in partnership with NCCT*

- Using toxicogenomics to explore mode(s) of action of conazole pesticides
- Linking pharmacokinetic and pharmacodynamic models for use in risk assessment (extrapolations)
- Identifying & using toxicity pathways
- Using Systems approach:
  - Virtual liver
  - Virtual embryo

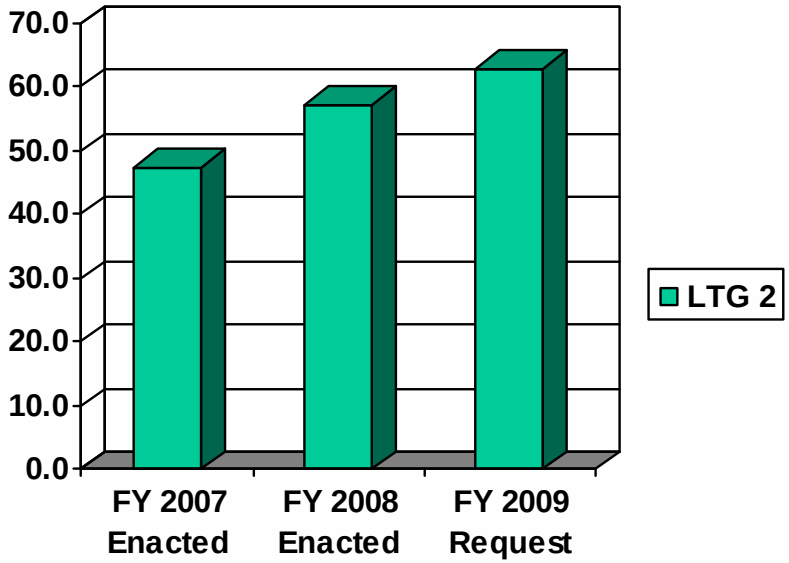

www.epa.gov/comtox

Implementation Plan 2006

# LTG 2 Cumulative Risk

- Linda Sheldon and Ross Highsmith, LTG Leads

- Develop Biomarkers of exposure and effect for use in cumulative risk assessment
- Develop source to dose models for cumulative risk
- Create tools for cumulative risk of chemical mixtures…
- and for identifying and assessing communities at risk

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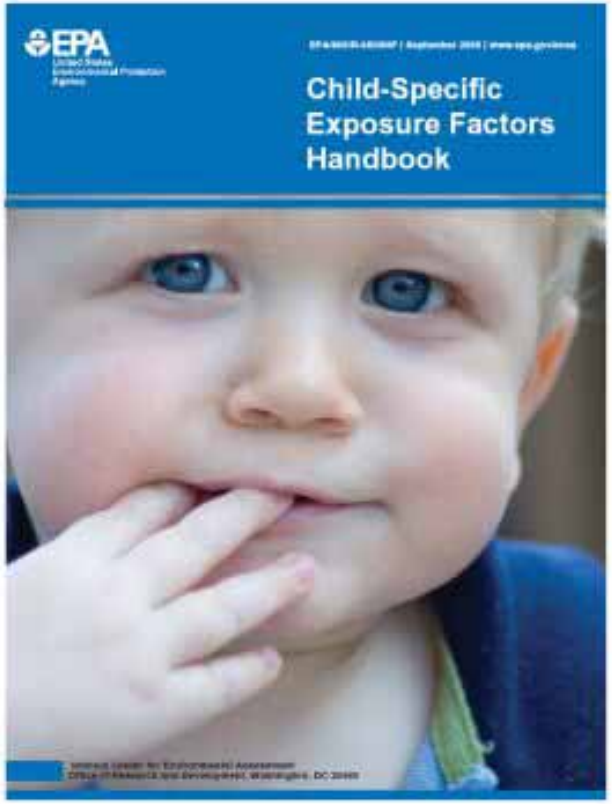
# *LTG 2 Cumulative Risk Research…*

- Elucidates determinants of exposure including life stage (informs LTG 3, NCS)
- Uses biomonitoring and observational studies to learn about exposure factors and test biomarkers (informs LTG 3 and 4, and NCS)
- Contributes to NCEA's Exposure Factor handbooks used by PO, Regions, States
- Builds models: SHEDS-Multimedia exposure model for use in risk assessment by OPPTS and states
- Contributed to NCER Workshops on Community Risk Assessment and Biomarkers, 2007

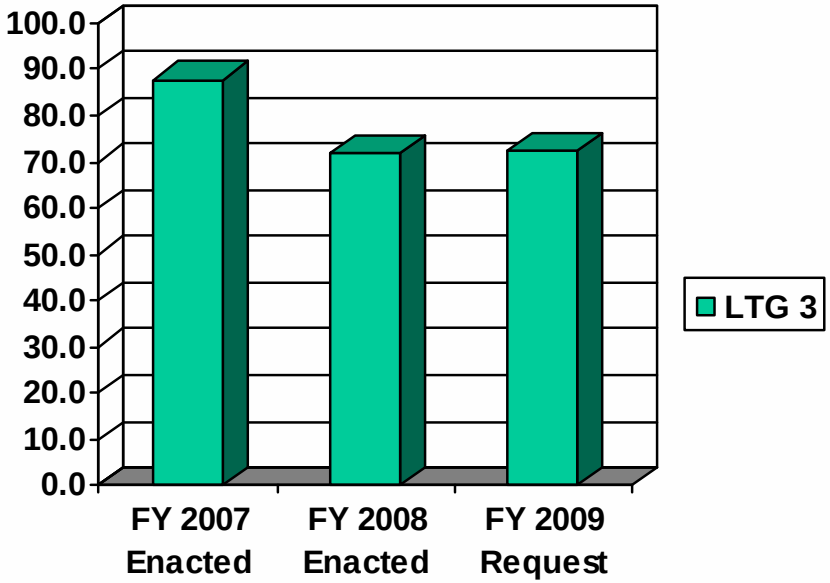



www.epa.gov/hhra

2008

# LTG 3 Susceptible Populations

- Devon Payne-Sturges, LTG lead
- Life stage research
  - Children
  - Older Americans (aging factors)
- Methods for longitudinal research
  - Children's Environmental Health Centers
  - National Children's Study
- Research on Asthma
  - Induction vs. Exacerbation
  - Factors: Age, Biologicals (mold), inflammation, Diesel

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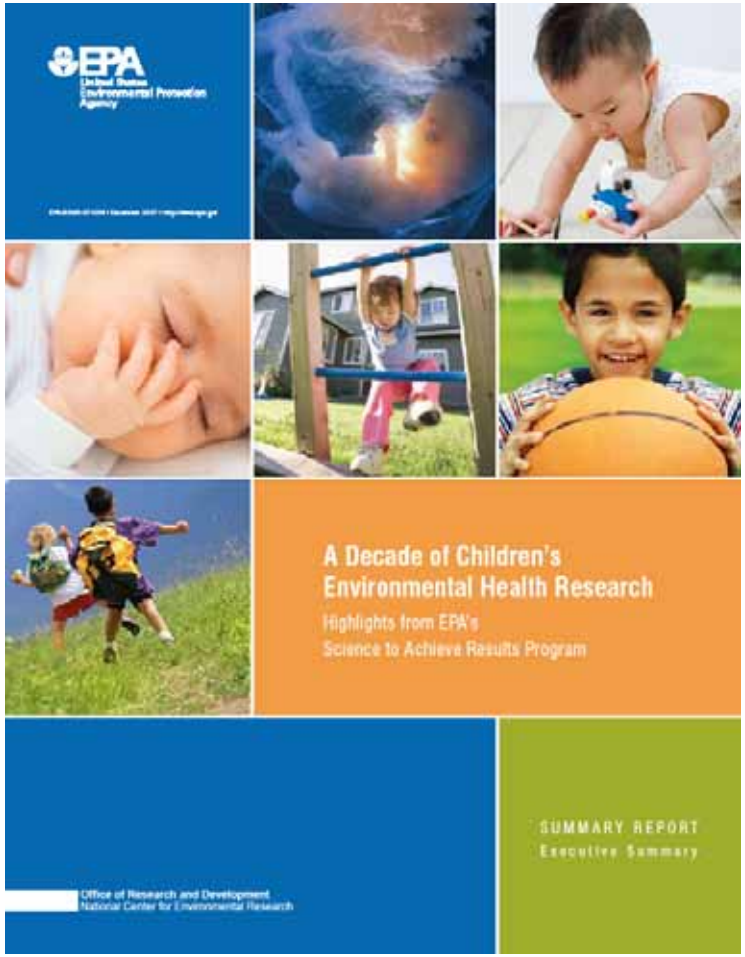
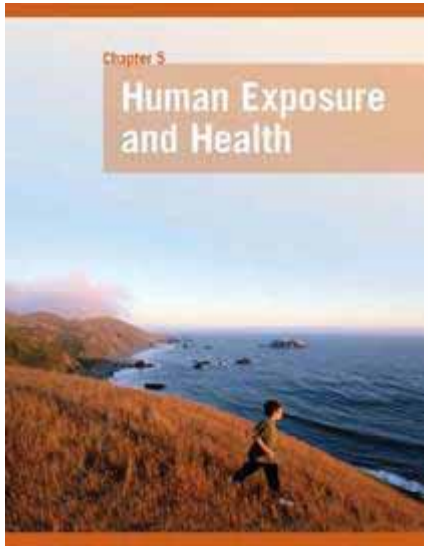
# *Children's Health Research Combines:*

- LTG 2 –
  - Susceptibility/vulnerability based on exposure – changes with place (home/school)
  - Other factors: behaviors, activity, SES
- LTG 3 –
  - Susceptibility based on life stage: in utero, infant (breast milk), toddler, child, adolescent
  - Possible long term effects of in utero exposures (epigenetics)
  - Genetic factors
  - Asthma

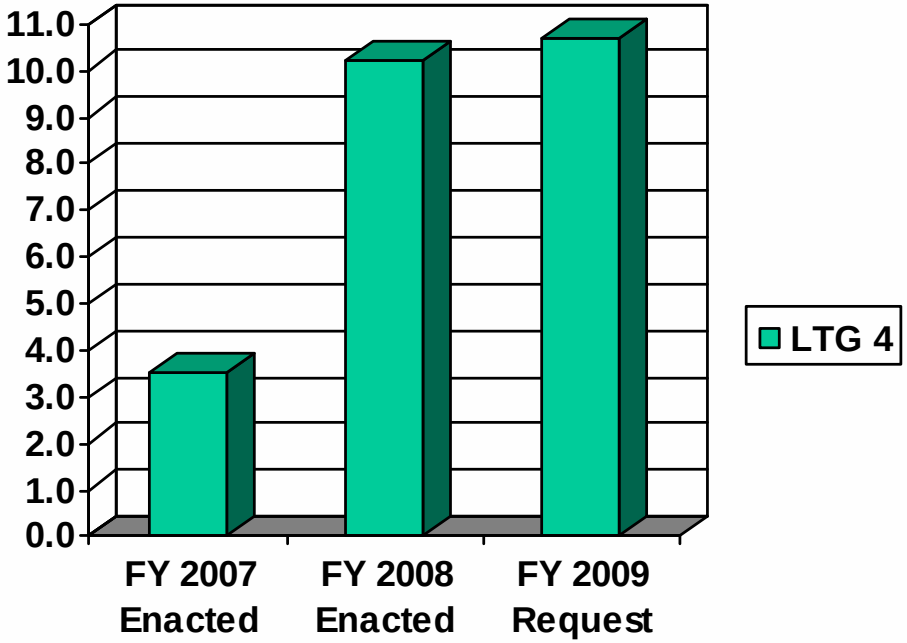



NCER 2007 Report

- Andrew Geller and Rebecca Calderon, LTG leads
- Approaches to evaluate risk management decisions
  - Informed by LTG 1, 2 & 3 (biomarkers, biomonitoring, community risk assessment)
- Health Chapter for 2008 Report on Environment




## *LTG 4 Evaluation of Risk Management Decisions*

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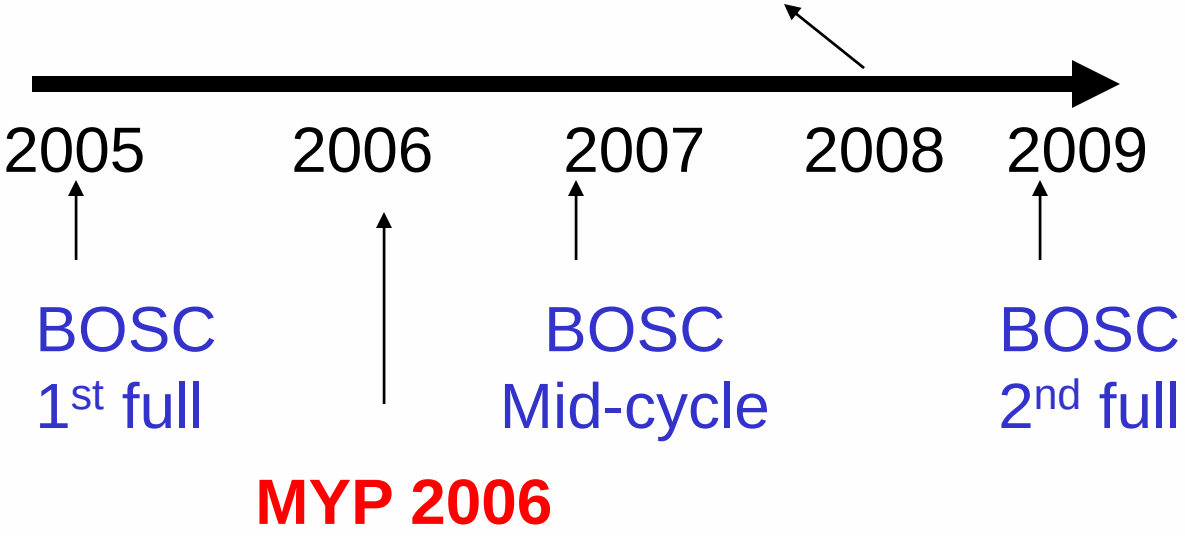
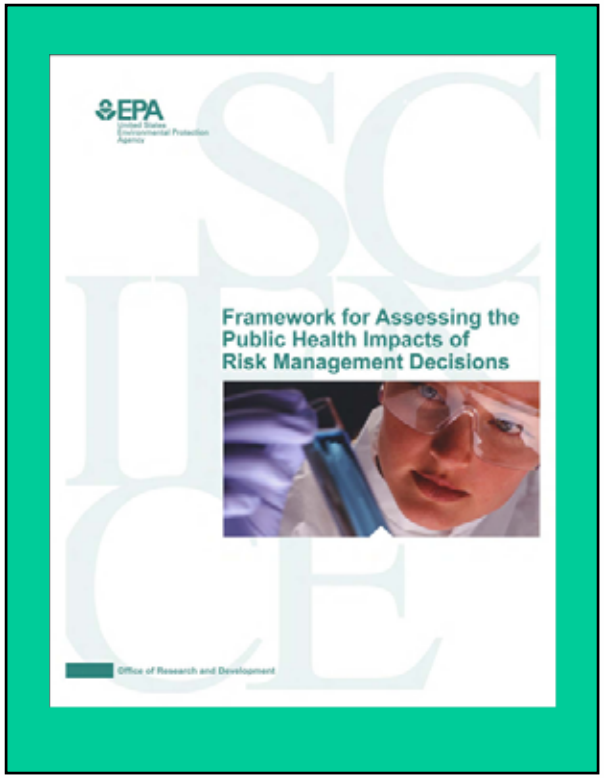
# LTG 4 -- in response to 2007 mid-cycle review

- "Framework for Assessing the Public Health Impacts of Risk Management Decisions," 2007
- "Accountability" Pilot Projects, underway in collaboration with Region 1
- Environmental Health Outcome Indicators grants, 2007
- NCER Workshop January 2008

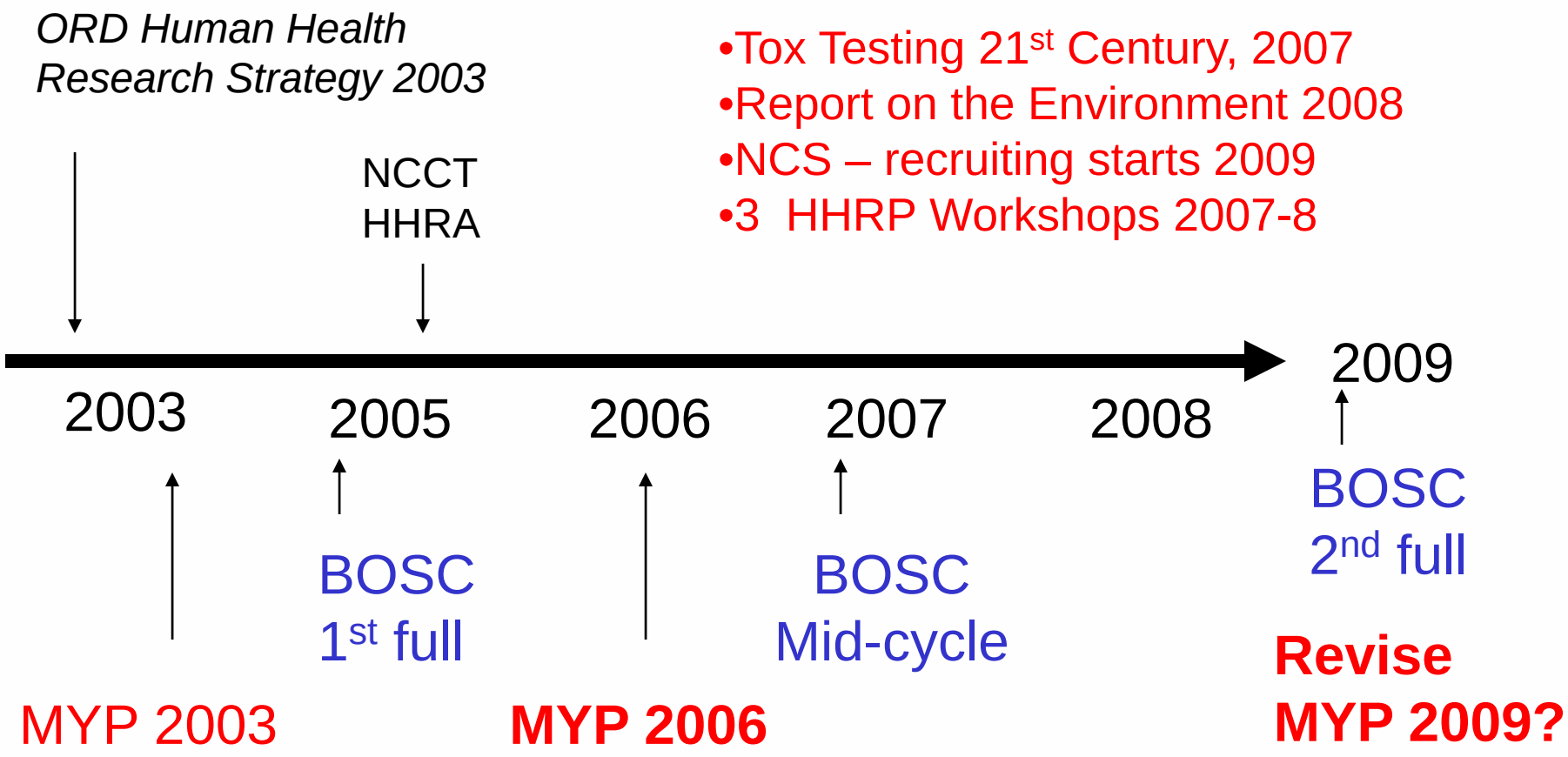


# *STAR RFAs in HHRP: Integrated Themes*

- Centers for Children's Environmental Health & Disease Prevention, 1998, 2001, '03, '05, '09 (LTG 3, supports all LTGs)
  - Decade of Children's Environmental Health Research, 2007
- Children's Vulnerability to Toxic Substances in the Environment, 2001 (LTG 2&3)
- Complex Mixtures, 2000 (LTG 1)
- Issues in Human Health Risk Assessment, 2001
- Biomarkers for the Assessment of Exposure & Toxicity in Children, 2002 (LTG 3)
- Lifestyle & Cultural Practices of Tribal Populations & Risks from Toxic Substances in the Environment, 2002, 2007 (LTG 2&3)
- Application of Biomarkers to Environmental Health & Risk Assessment, 2004 (LTG 1&2)
- Early Indicators of Environmentally Induced Disease, 2004 (LTG 1, 2)
- Interpretation of Biomarkers using Physiologically Based Pharmacokinetic Modeling, 2007 (LTG 2)
- Development of Novel Environmental Health Outcome Indicators, 2007 (LTG 4)
- Planned: Community-based Cumulative Risk Assessment
- Planned: Novel Approaches for Assessing Exposure for School-Aged Children in Longitudinal Studies

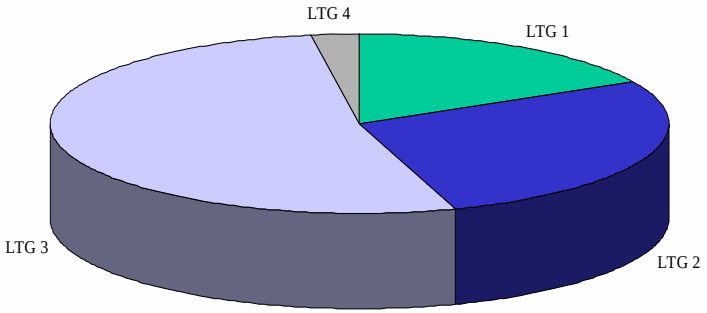
# *Timeline: Where are we going?*
# *Apply what we've learned to have Impact*



# Reality check: HHRP Resources by LTG

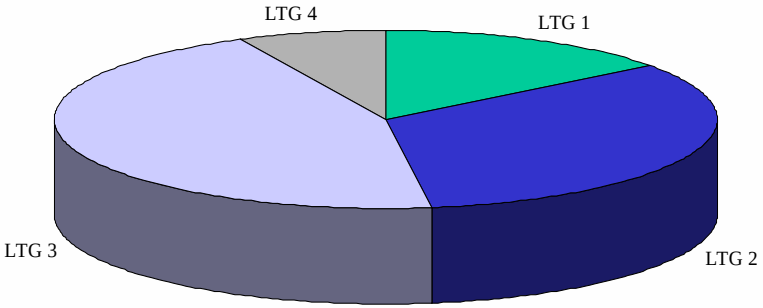
**FY 2007 Enacted**

**$60.9 M**



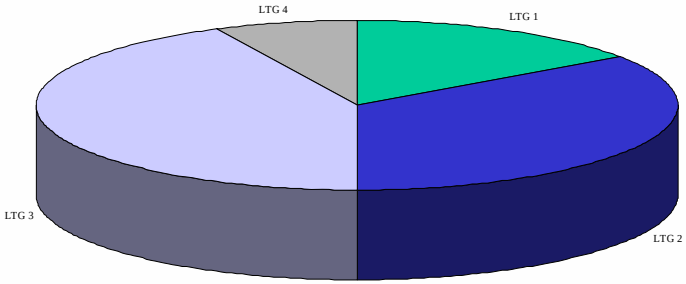

**FY 2008 Enacted**

**$63.2 M**




**FY 2009 President's Budget**

**$56.3 M**



# *Reality check: Program Resources & Implications*

- Trend: Relatively flat with decrease in FY09 anticipated
  - Increasing PC&B (people are not retiring as anticipated)
  - Result is decreases in operating funds
  - And funds for extramural programs: STAR grants and field studies
- Therefore, build upon existing data and partner with others (CDC, NICHD-NCS) to do:
  - Field studies on exposure & community risk assessment
  - Research to interpret biomonitoring data
  - Contribute to epidemiology studies and “mine” the data

- Focus on research issues where we can have greatest impact with our unique capabilities and available resources

**EPA Mission**
**EPA & ORD Strategic Plans**
**Report on the Environment**
**HHRP BOSC Review**
**Stakeholder Feedback**
**ORD Senior Management**

Mode of Action

Susceptibility

Cumulative Risk

Address uncertainty and characterize variability to improve risk assessment

Assess the public health impacts of risk management decisions

To help EPA protect human health



Andrew Geller