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ENDOCRINE **DISRUPTORS** RESEARCH PROGRAM

BUILDING A SCIENTIFIC FOUNDATION FOR SOUND ENVIRONMENTAL DECISIONS

Strategic Directions:

Endocrine Disruptors and Safe Pesticides/Safe Products Research Programs

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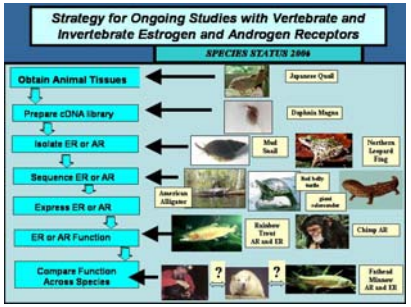
Strategic Directions (1)

- Provide a better understanding of the science underlying the effects, exposure, assessment, and management of endocrine disruptors
- Determine the extent of the impact of endocrine disruptors on humans, wildlife, and the environment
- Support Agency's screening and testing program



Strategic Directions (2)

- Consistent with Administrator's priority areas:
  - Managing chemical risks. Protecting America's waters. Vulnerable subpopulations, specifically children
- Leveraging with other research partners
- Addressing SAB Recommendations:
  - Apply newer molecular tools to develop subsequent generations of screening assays, increase efforts on cumulative risk, incorporate newer "computational" approaches to CAFOs research
- **Major Changes**
  - Acceleration/augmentation of certain research areas as a result of FY09 Omnibus Bill increase of $1.5 M more than FY08 enacted budget
    - Competitive internal RFPs with emphasis on integrated multi-disciplinary research
  - FY08 Appropriations requested a proposal and budget for extramural grants program – not known whether this will be considered in future

- **Major recent program accomplishments**
  - Completed research in developing assays for Tier 1 of the Agency's EDSP
  - Began integrated multi-disciplinary effort across all of ORD's Laboratories in collaboration with grantees, scientists from Programs/Regions and other Agencies to characterize the environmental impact of hormones (natural and synthetic) from CAFOs; held workshops in '07 and '08
  - Completed project with GWRC where assays, including one developed by EPA, were used to determine estrogenicity of WWTP effluents from around the world
  - Summary report on 10 years of accomplishments
  - Research on prenatal effects of phthalates (individual and mixtures of) considered in NAS report, PL 110-314, assessments in US, Canada, Europe
  - Report on whole lake study dosed with EE2 (one of *Discover*'s top 100 papers of '07)
- **Major program accomplishments anticipated in the near-term**
  - Completion of last 2 assays for Tier 2 of EDSP using fish and amphibian models
  - Short term screen to predict developmental neurotoxicity of thyrotoxic agents
  - STAR grantee reports on characterization of low dose effects
  - Characterization of predictive value of *in vitro* aromatase assays
  - Improved biomarkers of exposure and development of other novel approaches for monitoring endocrine activity in complex environmental media
  - Analytic methods to quantify EDCs and determine treatability of selected EDCs
  - Approach for utilizing genomics data in EPA risk assessments
  - Completion of 5 epidemiology studies on developmental/reproductive effects

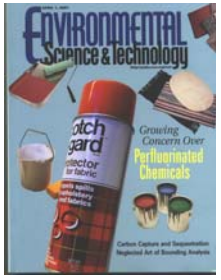
Significant Anticipated Products and their Intended Use by Partners

- Comprehensive battery of "next generation" assays using several classes of vertebrates
  - Used by OPPTS and others for chemical prioritization and screening
- Cross-Lab/Center/Program/Office/grantees/interagency/state/city efforts to develop/apply new analytical & *in vitro* methods & other tools to evaluate environmental samples for endocrine activity & determine potential impact on fish & human health using lab & field studies; determining efficacy of operations to reduce endocrine activity
  - Used by Program/Regional Offices, States, municipalities, and industry to assess and mitigate environmental impact of endocrine activity
- Frameworks for: cross-species models of TH and aromatase disruption; improved linkages between TH alternations in short term screens and adverse outcomes; cumulative risk assessments; characterization of impact of EDCs on toxicity pathways associated with neuroendocrine regulation of puberty and epigenetic mechanisms of transgenerationally induced reproductive effects
  - Used by EPA and others to improve risk assessments of EDCs
- Training of Programs/Regions, States, Tribes on molecular assays and exposure methods for environmental assessment; further application of methods, e.g., characterize impact of CAFOs, endocrine active pharmaceuticals in WWTPs on fish populations
  - Used by Programs/Regions, States, Tribes for environmental assessment

Strategic Directions (1)

OPPTS and/or other organizations use the results of ORD's research on methods, models, and data as scientific foundation for:

- 1) prioritization of testing requirements, 2) enhanced interpretation of data to improve their human health and ecological risk assessments, and 3) decisionmaking regarding specific individual or classes of pesticides and toxic substances that are of high priority.
- probabilistic risk assessments to protect natural populations of birds, fish, other wildlife, and non-target plants.
- decisionmaking related to products of biotechnology.



Strategic Directions (2)

- Consistent with Administrator's priorities:
  - Managing chemical risks. Protecting American's waters. Vulnerable subpopulations, specifically children.
- Leveraging with other research partners
- Addresses SAB Recommendations: extension of program to develop ecological risk assessment tools
- **Major changes**
  - Additional FTEs brought in to develop integrated effects-exposure ecological risk assessment tools
  - Determine feasibility of having a viable biotechnology program with resources that are now 50% of the original initiative; Can expertise be applied to biofuels program? Can unmet priorities be addressed through/leveraged with biofuels program?

- **Major recent program accomplishments**
  - Issued joint RFA with NIAID on factors contributing to food allergenicity – funded 16 grantees; held session at SOT; workshop & publication
  - Developed novel methods to detect pest resistance to GM crops: 1) Partnered w/NASA & developed remote sensing capability; 2) developed/applied methods for genetic characterization; 3) developed & evaluated exposure monitoring protocol
  - Brought together 180 scientists and managers for international workshop on PFCs where ORD's multidisciplinary research was showcased
  - Developed novel method to screen chemicals using HTPS and whole zebrafish approaches and contributed chemical analysis to ToxCast program
  - Developed ecological models Web-ICE and ACE to support pesticide assessments
  - Established ORD NMR-based Metabolomic Research Facility
- **Major program accomplishments anticipated in the near-term**
  - Additional data on effects, exposure and fate of PFCs
  - Support to Agency assessment of potential risks in Decatur from PFCs
  - Tools and data on the fate of pesticides and PFCs following drinking water treatment
  - Compendium of AHS Pesticide Exposure Study results for use in exposure classification
  - Population-level models for risk assessments for aquatic and avian populations
  - Metabolite & degradate simulator model for rapid/efficient identification of chemicals
  - Evaluation of the next generation of lead test kits

Significant Anticipated Products and their Intended Use by Partners

- Assays to screen chemicals for their potential toxicity across a number of end points & multiple modeling approaches for prioritizing chemicals
  - Used by OPPTS and others to prioritize and screen chemicals
- Advanced methods/modeling approaches for extrapolating integrated toxicological and exposure data across wildlife, media, and individual- and population- level
  - Used by OPP and others to characterize individual- & spatial population-level exposures & effects in aquatic and other wildlife for use in addressing ESA
- Multiple models to assess potential allergenicity to GM crops & guidelines/tools to mitigate gene-transfer, non-target effects & development of resistance in targeted pest populations
  - Used by OPP to improve data requirements for registrants & aid management of potential human and ecological risks from GM crops
- Completion of multidisciplinary research on the toxicity, environmental pathways and fate of PFCs, including their characterization in environmental and biological species
  - Used by OPPT and other organizations in their assessments on potential risks of PFCs