

# Chemical Producers and Distributors Association Adjuvants and Inerts Conference

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A. M. Rohde



# Topics

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- **Background**
- **Elements of the Endocrine Disruption Screening Program (EDSP)**
- **Summary**

# Endocrine Disruption Screening Program (EDSP)



- **Food Quality Protection Act of 1996**  
Federal Food, Drug and Cosmetic Act
  - Congress mandated EPA to develop a screening program using validated assays to identify pesticides that may have estrogenic effects in humans
  - Authorizes EPA to include other endocrine effects and non-pesticide chemicals that “have an effect cumulative to that of a pesticide” and to which a substantial human population may be exposed (discretionary authority)
  
- **Safe Drinking Water Act Amendments**
  - Allows EPA to require testing of chemical substances found in sources of drinking water, if a substantial human population may be exposed
  
- **EDSP established in 1999**
  - Following the recommendations of the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC)

# EDSP is a Two-Tiered Approach

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## **Tier 1 “Screening”**

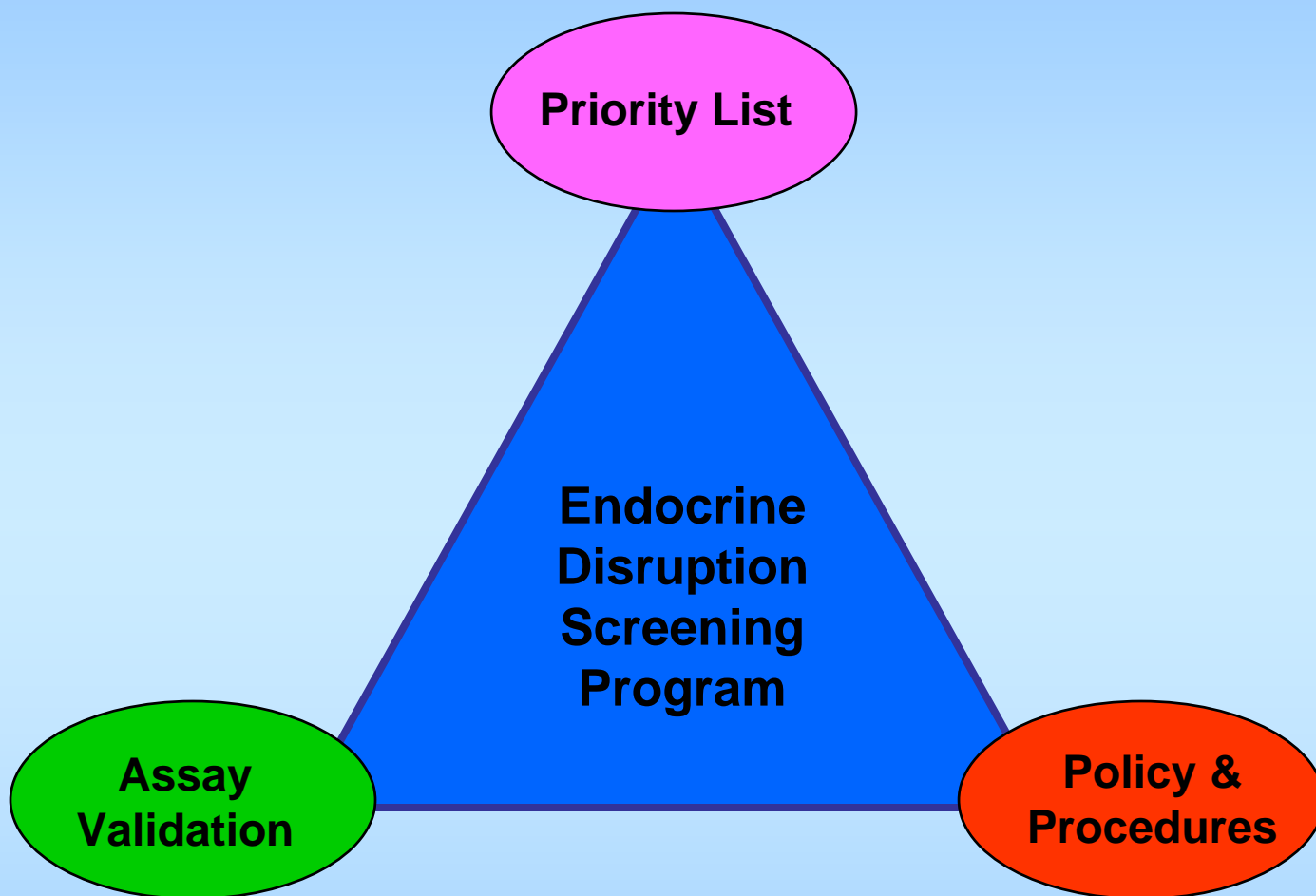
**identify substances that have the potential to interact with the estrogen, androgen, or thyroid hormone systems using a battery of assays**

## **Tier 2 “Testing”**

**identify and establish a dose-response relationship for any adverse effects that might result from interactions identified through Tier 1 assays**

# Three Elements of the EDSP

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# Draft Initial Priority Screening List

## 64 Active Ingredients

## 9 HPV Inerts

2, 4-D  
 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-  
 Abamectin  
 Acephate  
 Aldicarb  
 Allethrin  
 Atrazine  
 Azinophos-Methyl  
 Benfluralin  
 Bifenthrin  
 Captan  
 Carbamothioic acid, dipropyl-S-ethyl ester  
 Carbaryl  
 Carbofuran  
 Chlorothalonil  
 Chlorpyrifos  
 Cyfluthrin  
 Cypermethrin  
 DCPA (or chlorthal-dimethyl)

Diazinon  
 Dichlorbenil  
 Dichlorvos  
 Dicofol  
 Dimethoate  
 Disulfoton  
 Endosulfan  
 Esfenvalerate  
 Ethoprop  
 Fenbutatin oxide  
 Fenvalerate  
 Flutolanil  
 Gardona (cis-isomer)  
 Glyphosate  
 Imidacloprid  
 Iprodione  
 Linuron  
 Malathion  
 Metalaxyl  
 Methamidophos  
 Methidathion  
 Methiocarb  
 Methomyl

Methyl parathion  
 Metolachlor  
 Metribuzin  
 Myclobutanil  
 Norflurazon  
 O-Phenylphenol  
 Oxamyl  
 Permethrin  
 Phosmet  
 Piperonyl butoxide  
 Propachlor  
 Propargite  
 Propiconazole  
 Propyzamid  
 Pyridine, 2-(1-methyl-2-(4-phenoxy phenoxy)ethoxy)-  
 Quintozene  
 Resmethrin  
 Simazine  
 Tebuconazole  
 Triadimefon  
 Trifluralin

Acetone  
 Butyl benzyl phthalate  
 Dibutyl phthalate  
 Diethyl phthalate  
 Dimethyl phthalate  
 Di-sec-octyl phthalate  
 Methyl ethyl ketone  
 Toluene  
 Isophorone

**“This list should not be construed as a list of known or likely endocrine disruptors.”**

(EPA-HQ-OPPT-2004-0109, June 18, 2007)

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# Initial Screening List Based on Potential Exposure

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- **Human exposure potential determined from exposure databases**
  - Pesticide active ingredients based on presence in food, water, residential, occupational exposure databases
  - HPV chemicals used as pesticide inerts present in human and eco biomonitoring, water and indoor air exposure databases
- **Screening list inclusion criteria based on a “hit” in exposure databases**
- **Exposure databases were not the most recent or up-to-date**
- **No consideration for chemicals naturally present in foods and/or a human metabolite**
- **Many chemicals on the initial screening list have been extensively tested**
  - Some chemicals have data from Tier 2 studies

# Assay Validation – SAB Reviewed Tier 1 Assays

## Tier 1 Screening Assays

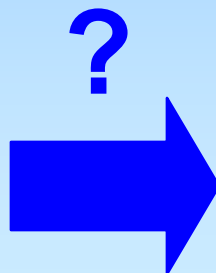
### In vitro

Estrogen receptor binding – rat uterus  
Estrogen receptor transcriptional activation – human cell line  
Androgen receptor binding – rat prostate  
Steroidogenesis – human cell line  
Aromatase – human recombinant

### In vivo

Uterotrophic (rat)  
Hershberger (rat)  
Pubertal female (rat)  
Pubertal male (rat)  
Amphibian metamorphosis (frog)  
Fish short-term reproduction

~ 500K\$ per chemical



## Tier 2 Tests

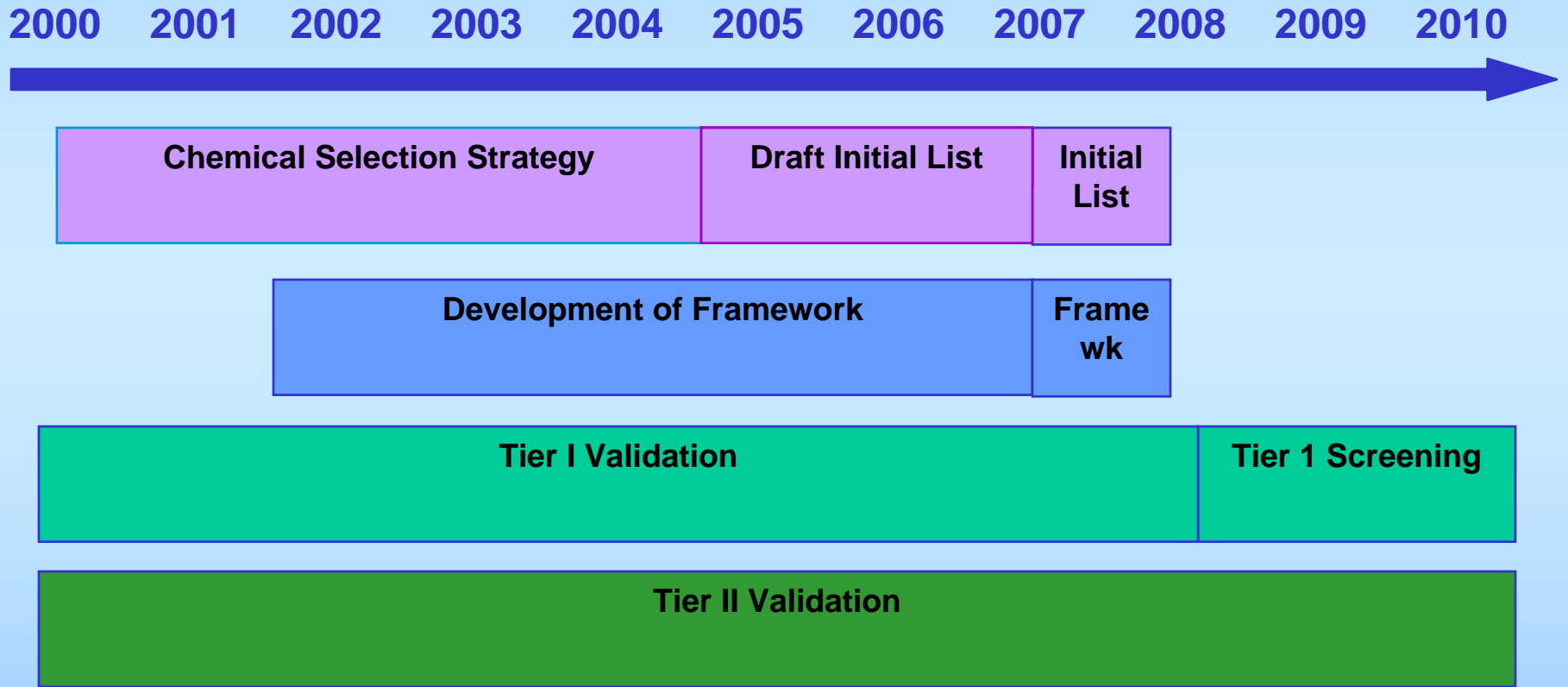
### Multi-generational tests in

Mammals  
Birds  
Amphibians  
Fish  
Invertebrates

- SAB proposed Tier 1 Assays
- EPA expected to release final Tier 1 assays by August 08
- Validation of some assays in question – appropriate negative controls ?
- EPA plans to publish results of Tier 1
- Interpretation of results ? ?
- Weight of Evidence – what are the triggers for Tier 2 ?

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# EDSP Timeline (USEPA Public Workshop on the EDSP, Dec 17, 2007)



# Summary

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- **Endocrine testing is mandated by law – not a voluntary testing program**
  - **Consequences of non-compliance**
    - If a registrant fails to comply with the EDSP order, EPA may suspend any affected registrations
    - If a non-registrant fails to comply, EPA may impose fines under TSCA
- **Tier 1 testing cost per chemical ~ 500k\$**
- **Initial EDSP initiatives will set precedent**
  - **Test orders for commodity chemicals**
  - **Interpretation of Tier 1 results ?**
    - **Positive in one assay or one endpoint ?**
  - **Weight of evidence approach**
    - **What triggers a “Positive” in Tier 1 ?**
    - **What triggers Tier 2 testing ?**
- **For subsequent EDSP phrases**
  - **All pesticide chemicals (actives and inerts) are in bounds**
  - **Commodity and specialty chemicals – any substance that may be found in sources of drinking water with potential for substantial exposure**
- **Policy and procedures not fully developed**
  - **CBI, data compensation issues for inert ingredients**
  - **Undefined process to challenge test orders or opt out**



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