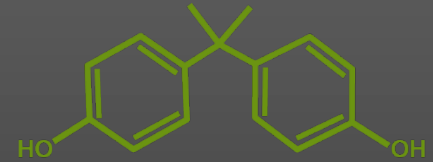# CLARITY-BPA:
Data integration, analysis and interpretation of eight academic studies

Jerrold J. Heindel, Scott Belcher, Jodi A. Flaws, Gail S. Prins, Shuk-Mei Ho, Jiude Mao, Heather B. Patisaul, William Ricke, Cheryl S. Rosenfeld, Ana M. Soto, Frederick S. vom Saal, R. Thomas Zoeller

Jerrold J. Heindel PhD
Healthy Environment and Endocrine Disruptor Strategies (HEEDS.ORG), Commonweal

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CLARITY-BPA: Overview

Consortium

Linking

Academic and

Regulatory

Insights on the

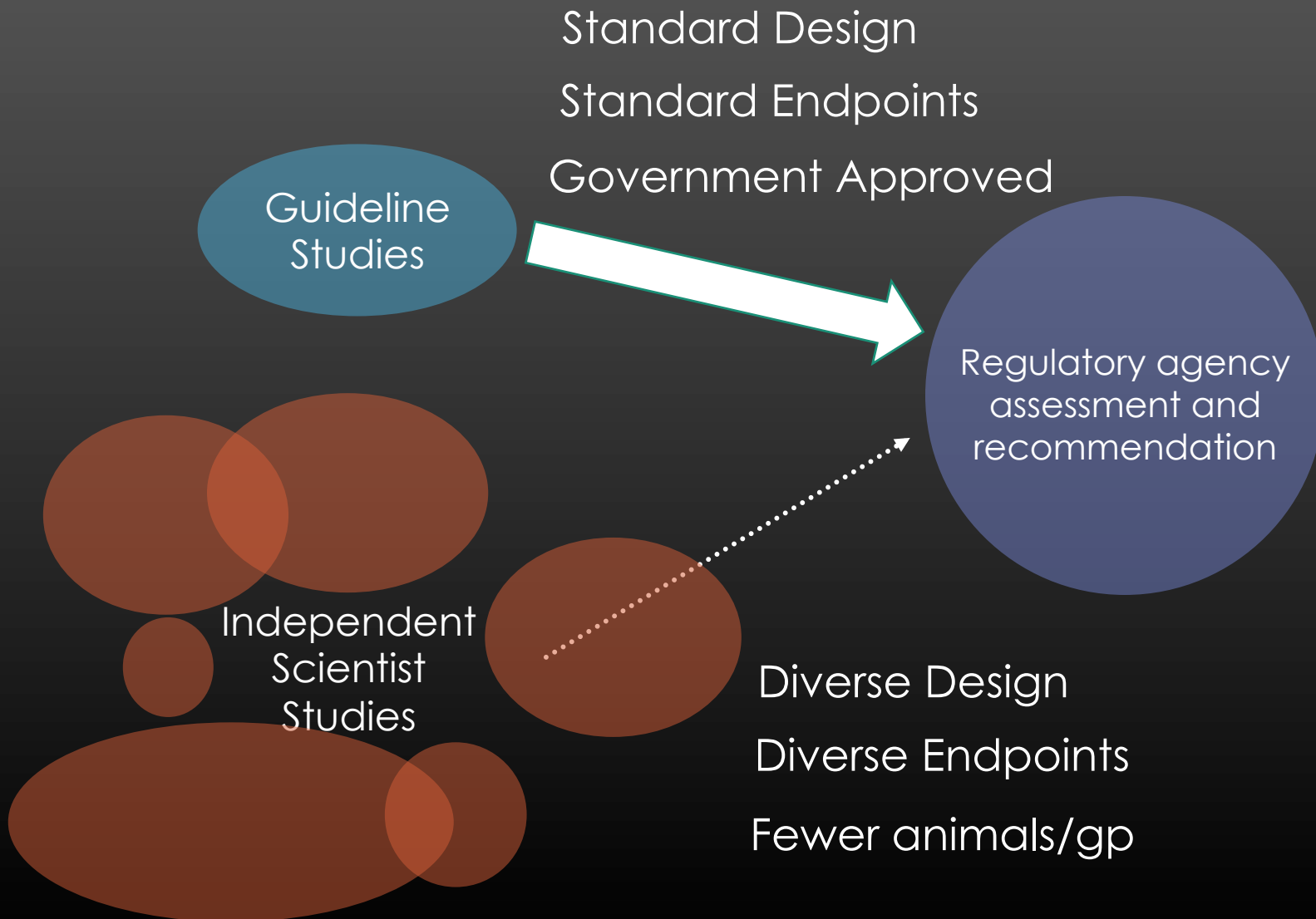**T**oxicit**y** of

BPA

- A new collaborative model

Goals:

- Integrate strength of guideline study with molecular and disease associated endpoints from independent scientists into one study.
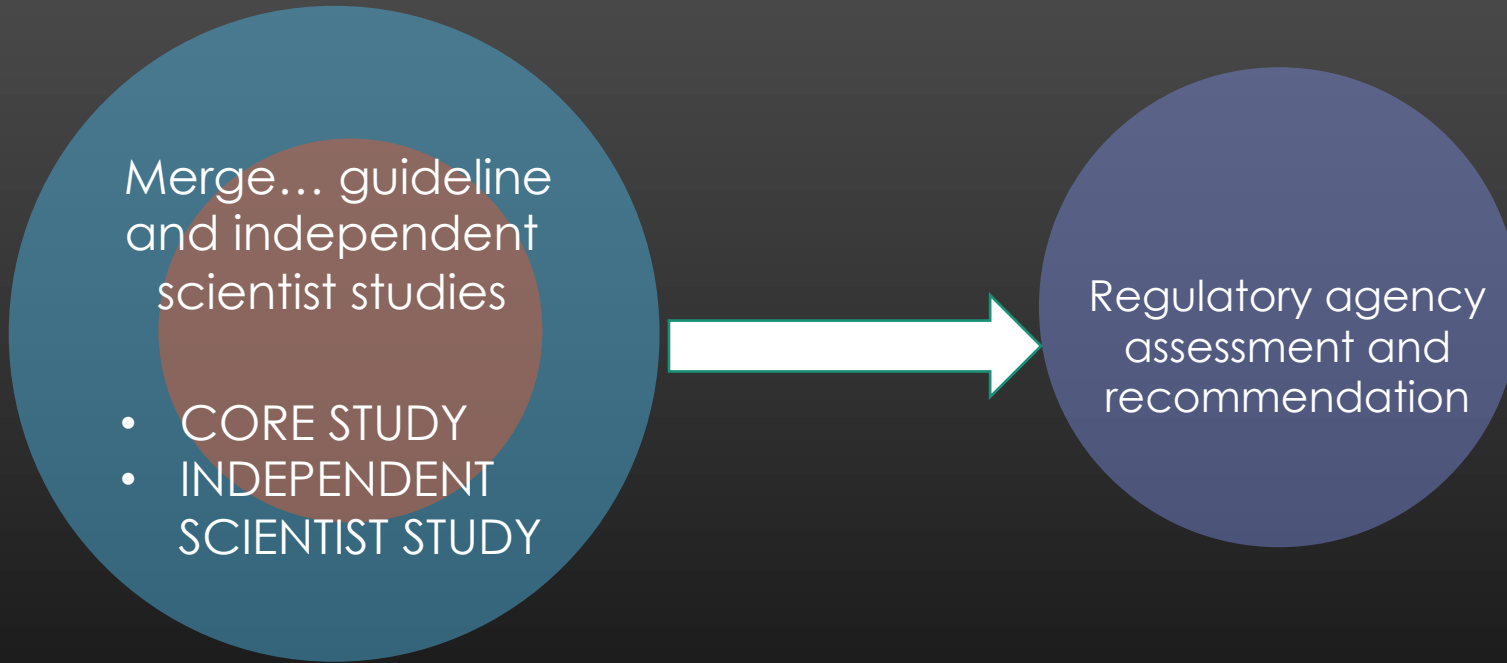
- To improve safety assessment.

Partners:

- NIEHS NTP and Extramural Grants Program

- FDA NCTR and CFSAN

- 14 NIEHS-funded academic grantees

Current Approach to Risk Assessment

Standard Design

Standard Endpoints

Government Approved

Guideline Studies

Regulatory agency assessment and recommendation

Independent Scientist Studies

Diverse Design

Diverse Endpoints

Fewer animals/gp

CLARITY Approach to Risk Assessment

Merge… guideline and independent scientist studies

- CORE STUDY
- INDEPENDENT SCIENTIST STUDY

Regulatory agency assessment and recommendation

Government approved design

More comprehensive assessment of toxic effects

CLARITY-BPA: Study Details

Sprague Dawley rat

FDA-Core Study

50 animals/dose

Independent Scientist Studies

~10 animals/dose

Dose Groups
(μg/kg bw/day)

Vehicle only

BPA

2.5
25
250
2,500
25,000

EE$_2$

0.05
0.5

Route of Administration

Gavage: GD 6-Birth, PND 1 to PND 21 OR 2 years

CLARITY-BPA: Study Design

FDA-CORE STUDY

1 YEAR

2 YEARS

Mating E6   Birth   P21

Continuous - 1 year

Continuous - 2 year

Stop Dose - 1 year

Stop Dose - 2 year

Gavage daily
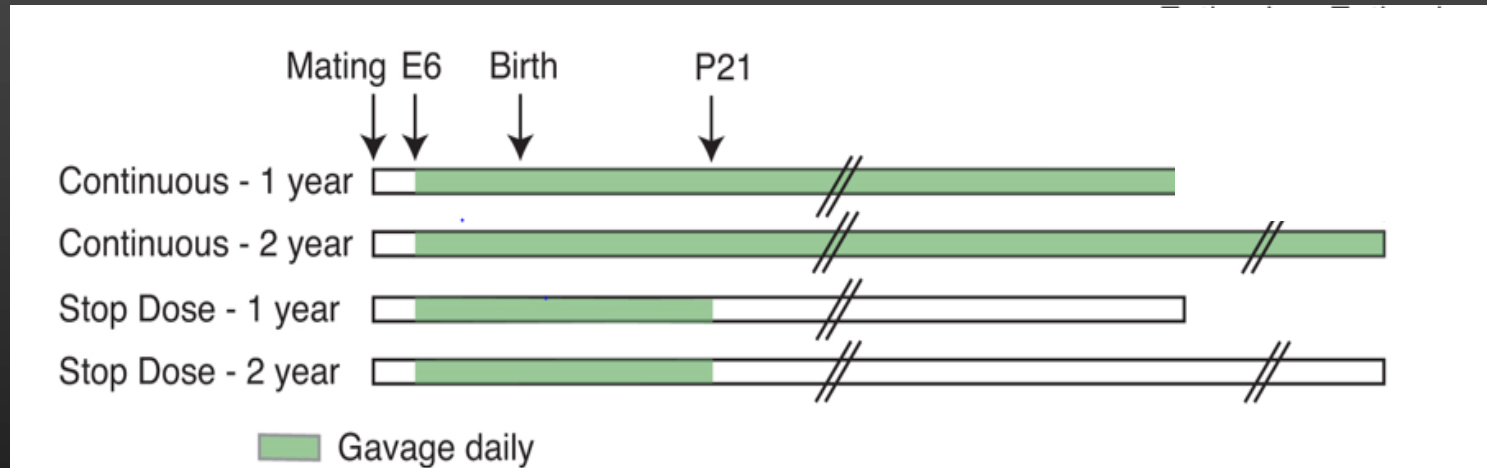
INDEPENDENT SCIENTIST STUDIES

1 15 21   90   180   1 YEAR

Endpoints

FDA-Core Study

Clinical chemistry

Sperm parameters

Histopathology of all tissues

Estrus cyclicity

Body weight

Organ weights of selected

tissues

Prostate
Fred vom Saal
Gail Prins

Testis function
Kim Boekelheide

Penile dysfunction
Nestor Gonzalez-
Cadavid

Cardiovascular
Scott Belcher

Immune function
Norbert Kaminski

Breast cancer
Ana Soto

Uterine cancer
Shuk Mei Ho

Ovarian function
Jodi Flaws

Obesity
Nira Ben Jonathon

Diabetes/liver
Andrew Greenberg

Thyroid function
Tom Zoeller

Brain development
Cheryl Rosenfeld
Heather Patisaul

Publication Status

- Core guideline study
- 10/14 independent/academic studies
- No integrated publication of all the independent studies
- No integrated publication of all CLARITY-BPA data, core and independent scientist

Today: Unique Manuscript

- This is a final report of 8 independent/academic studies that presents their data and puts it in perspective to previously published data

AND

- Integrates all the findings and interprets them as a whole.

Independent Scientist Studies Published, NOT INCLUDED

Independent Scientist Studies NOT PUBLISHED

Testis function
Kim Boekelheide

Immune function
Norbert Kaminski

Diabetes/liver
Andrew Greenberg

Obesity
Nira Ben Jonathon

Penile dysfunction
Nestor Gonzalez-Cadavid

Uterine cancer
Shuk Mei Ho

Independent Studies Included

Prostate Cancer/Stem cell Progenitor numbers
Gail Prins

Male Urogenital abnormalities
Fred vom Saal, William Ricke

Cardiovascular Function
Scott Belcher

Mammary Gland Development/Cancer/ Nature of Dose Response
Ana Soto

Ovarian function
Jodi Flaws

Thyroid Function
Tom Zoeller

Learning and Behavior/transcriptomics
Cheryl Rosenfeld, Shuk Mei Ho

Behavioral Changes/Brain transcriptomics
Heather Patisaul

Data Integration Across Organs/Dose and Time
Cheryl Rosenfeld, Juide Mao

Manuscript Organization

- For Each Organ System
  - Previous Publications
  - Hypothesis
  - Methodology
  - Data Summary
  - Discussion
    - Major Findings
    - Compare to Previous Publications
    - Study Differences
- Data Integration across organs, dose, time
- Discussion of data integration
- Final integrated Discussion

Presentations…

- Gail Prins, U Illinois Chicago

Prostate Cancer/Stem Cell Progenitor number

- Ana Soto, Tufts University

Mammary Gland Development/Cancer/Nature of the dose response

- Cheryl Rosenfeld, University of Missouri

Integrated Data Across Organs/Doses/Times

- Gail Prins, U Illinois Chicago

Summary and Key Messages