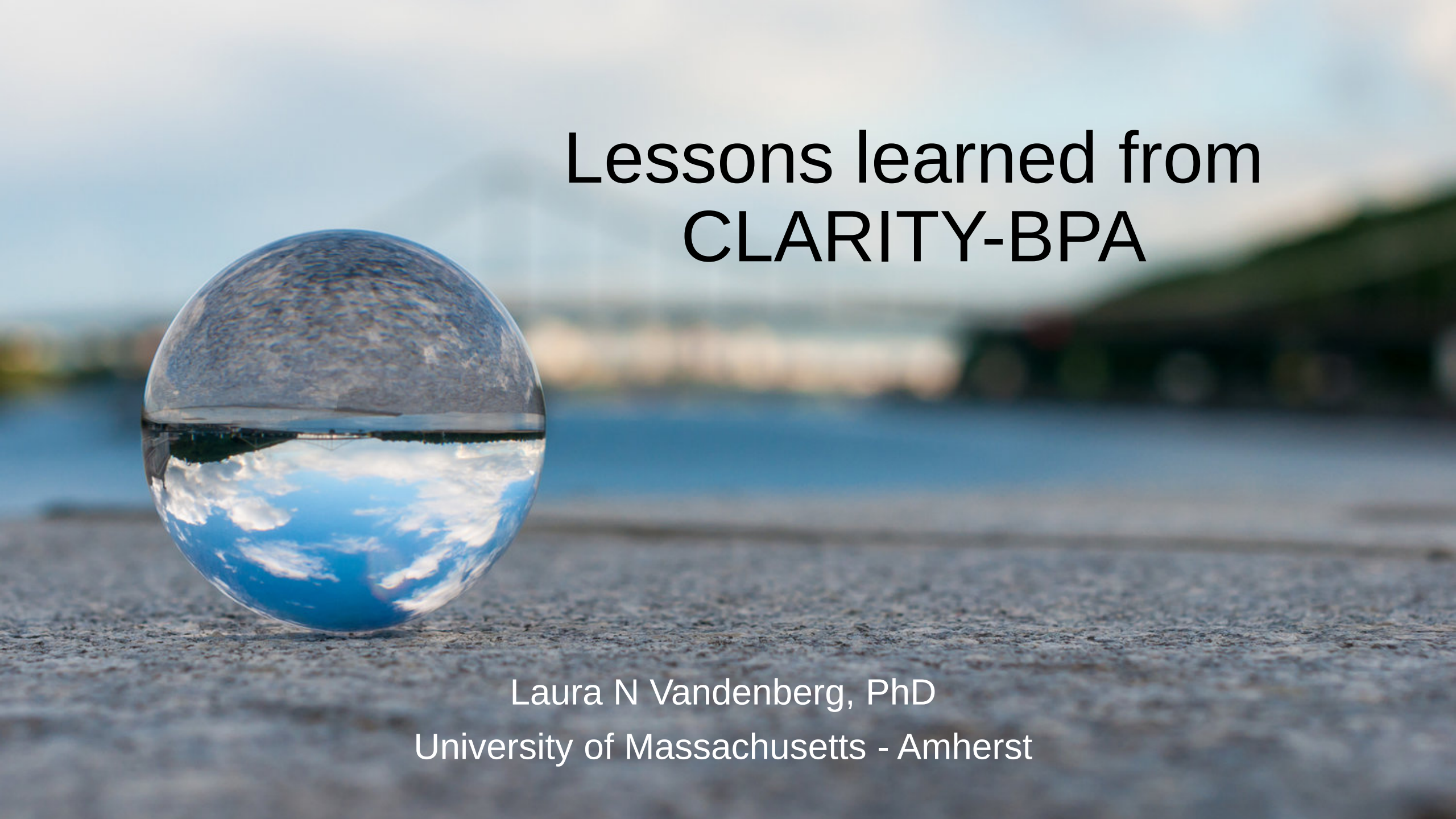
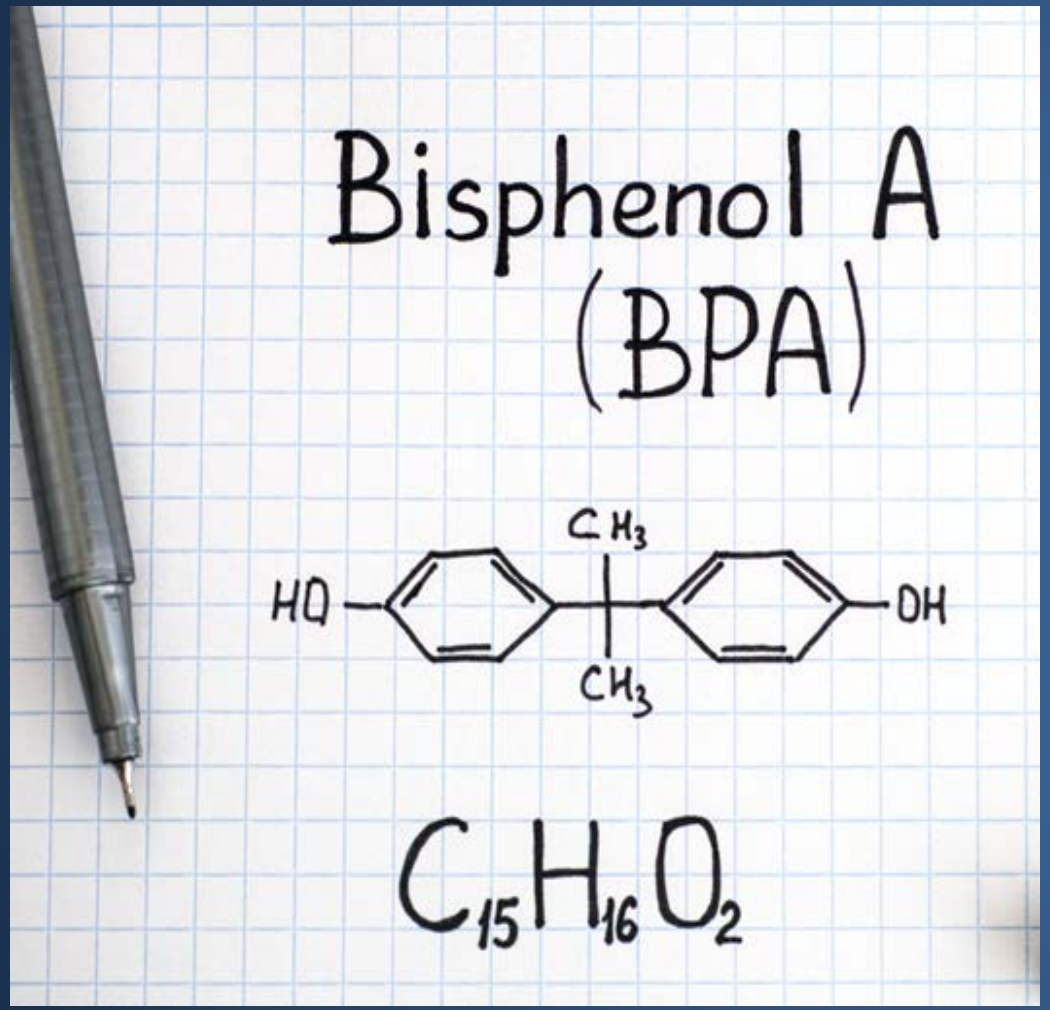


Lessons learned from CLARITY-BPA

Laura N Vandenberg, PhD

University of Massachusetts - Amherst



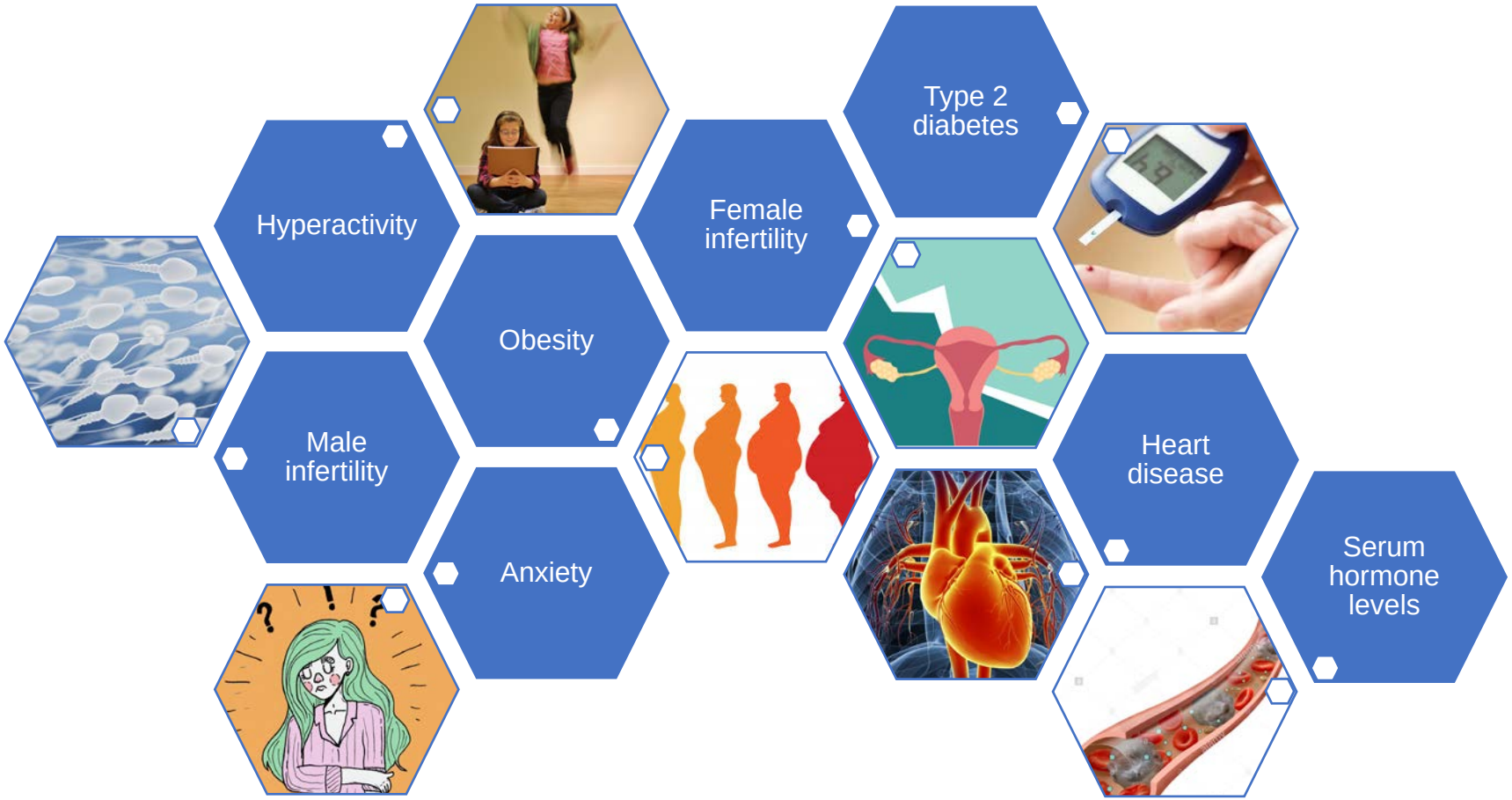
Canned foods & beverages

Consumer plastics

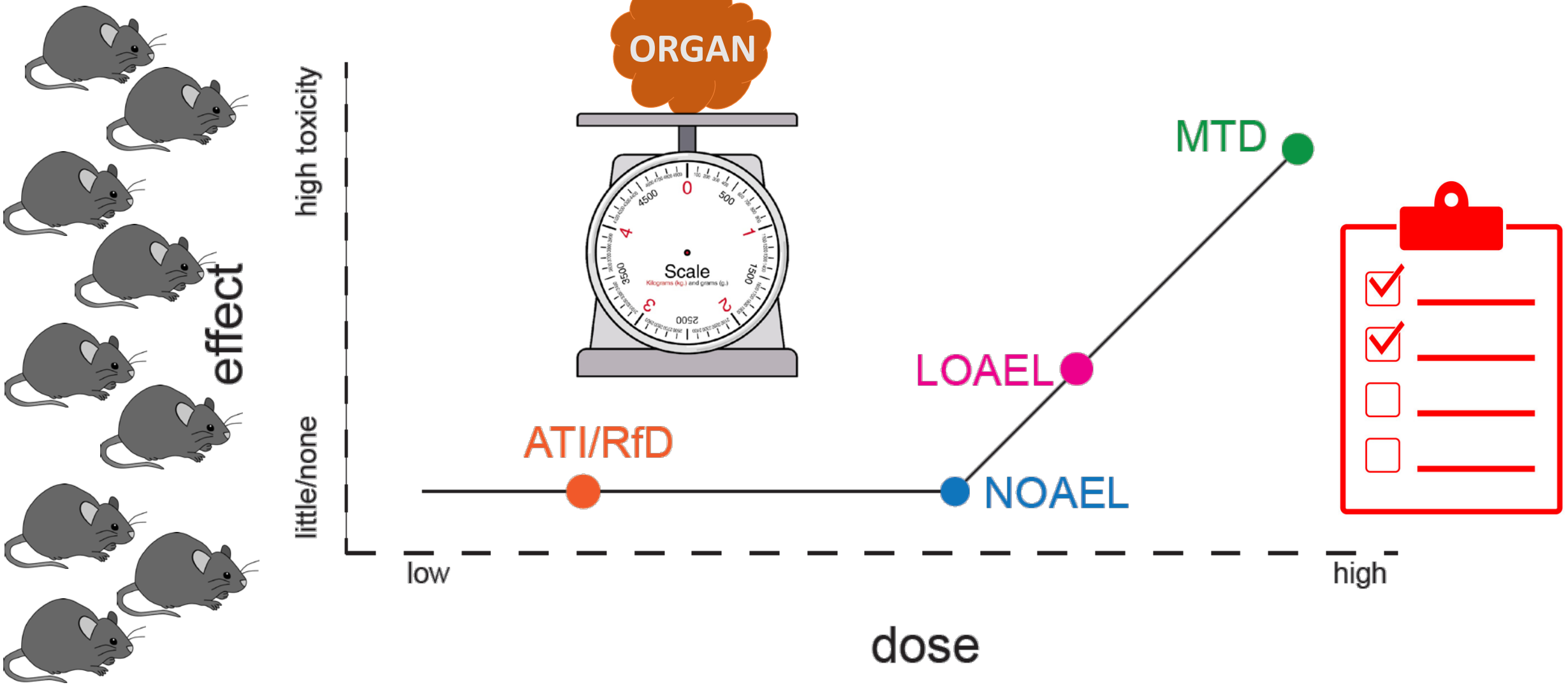
Thermal receipt paper

Sports & medical equipment

More than 100 human studies suggest associations between BPA and human disease

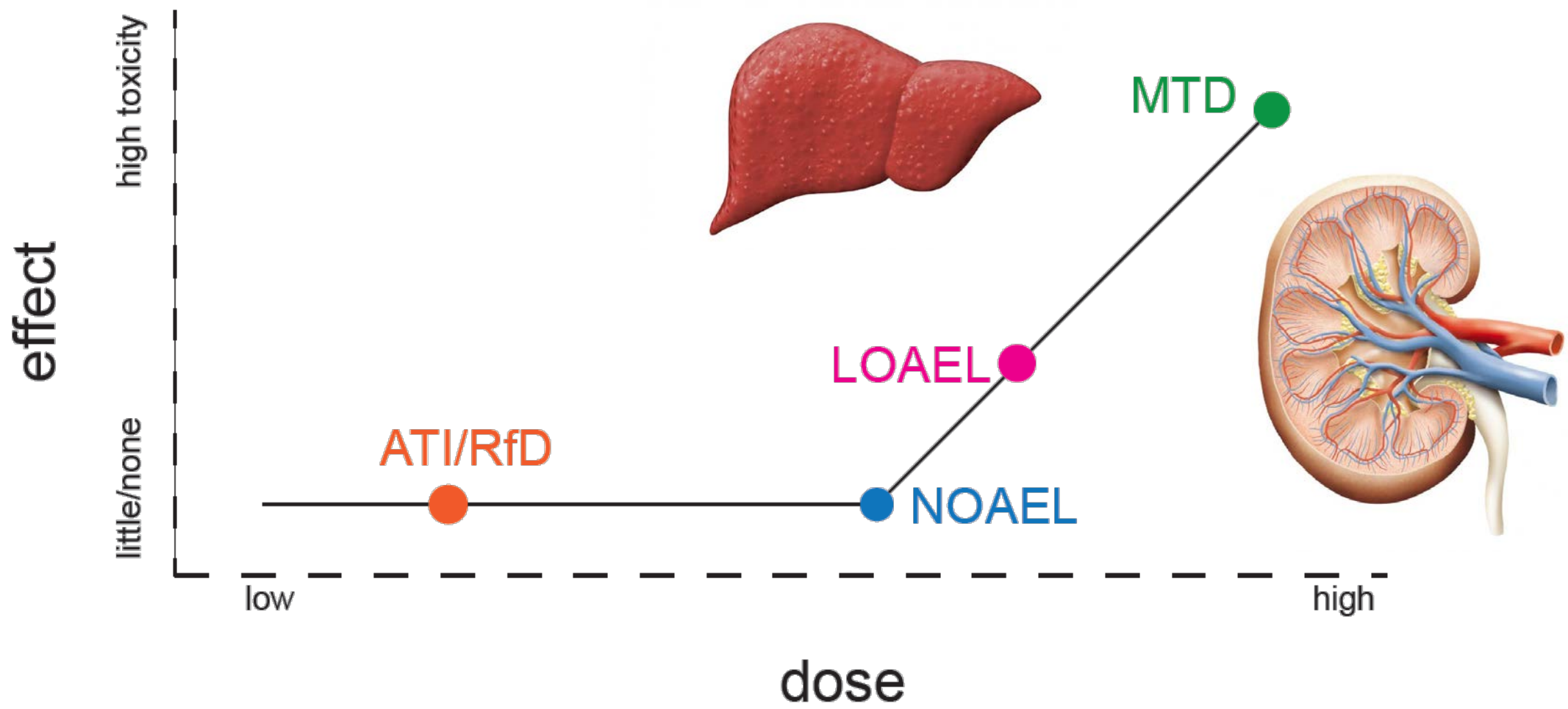


A 2-minute crash course in chemical safety testing



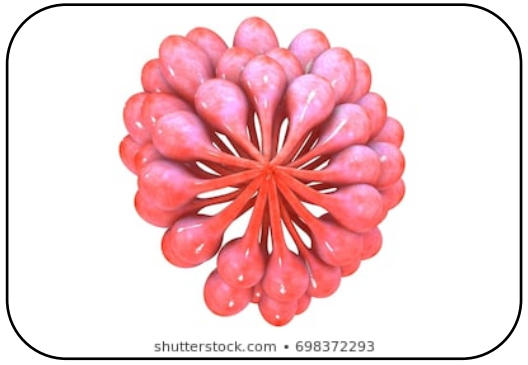
Prior to the CLARITY study...

Guideline studies suggested that only high doses of BPA were toxic.

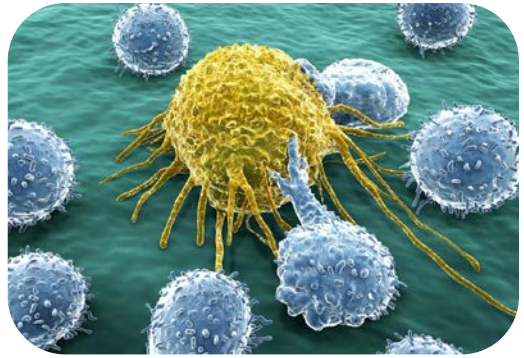


In contrast, hundreds of academic studies revealed effects of BPA on a wide range of hormone-sensitive outcomes

Reproduction

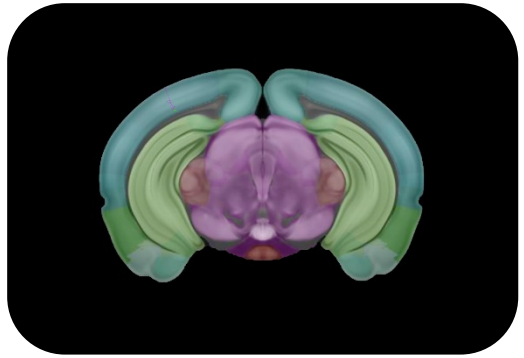


Mammary gland



Immune system

Metabolic endpoints



Brain & behavior

Why would guideline and academic studies show vastly different effects of BPA (and other chemicals)?

Differences in sample sizes

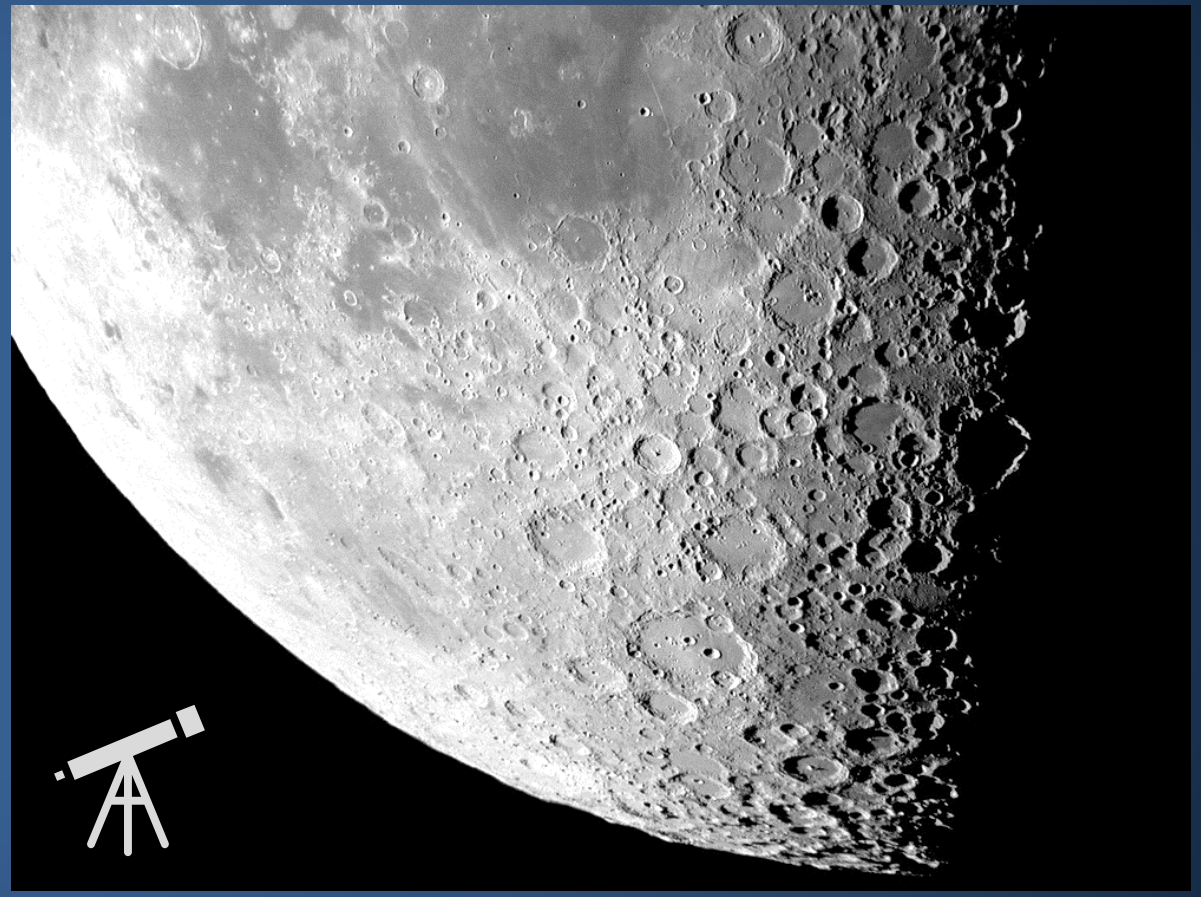
Differences in sensitivity

Differences in relevance to disease

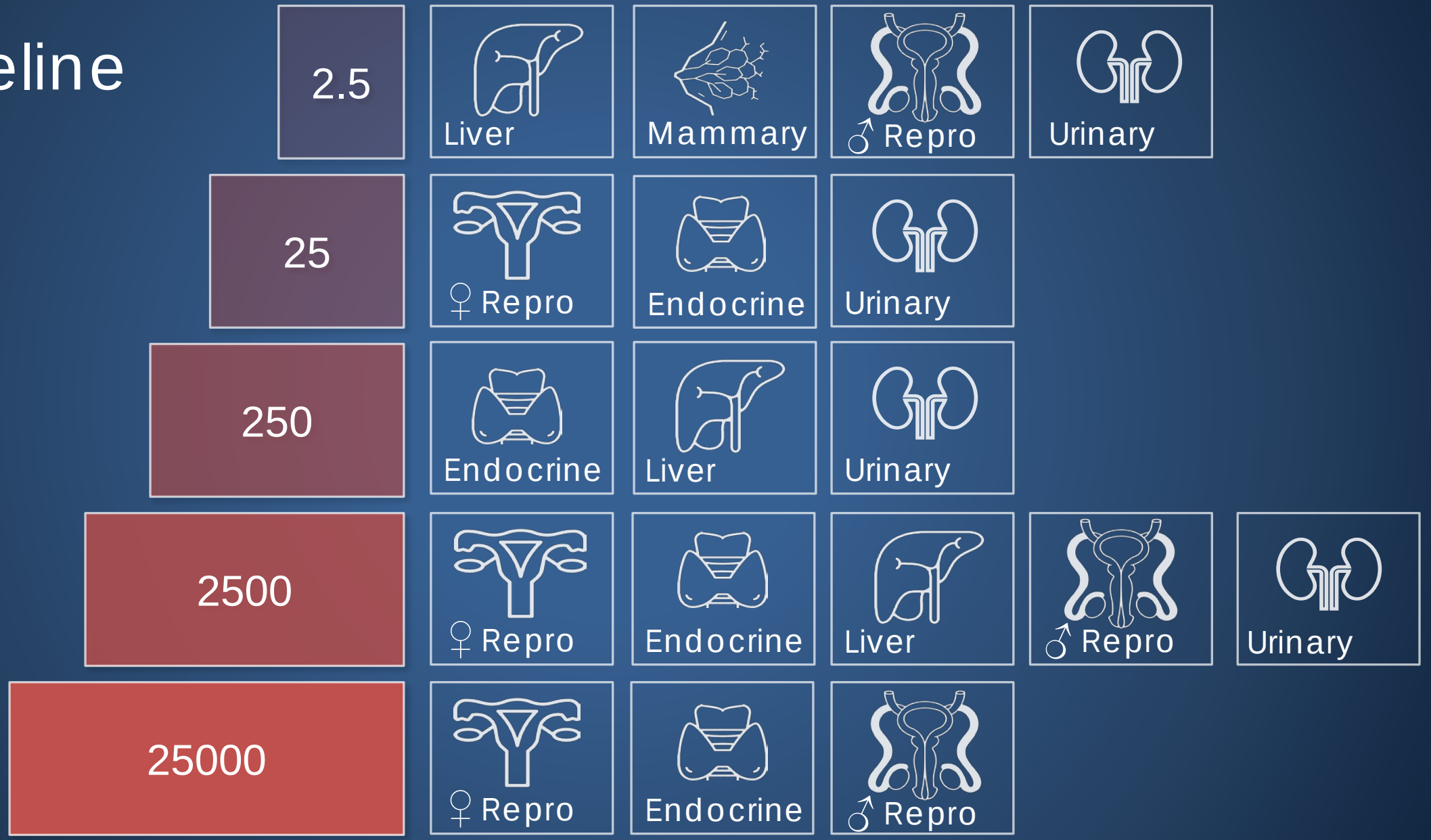
Differences in study reliability

CLARITY-BPA: bringing together a guideline study with academic endpoints

Consortium Linking Academic and Regulatory Insights of Toxicity of BPA



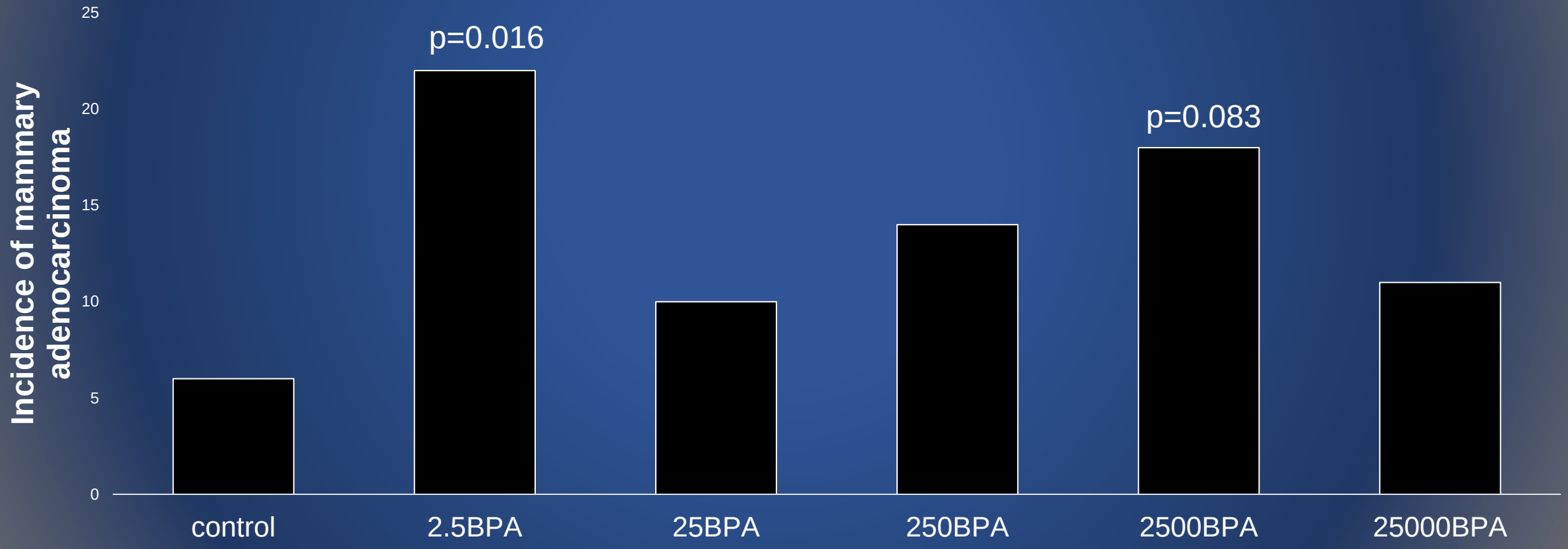
Guideline study



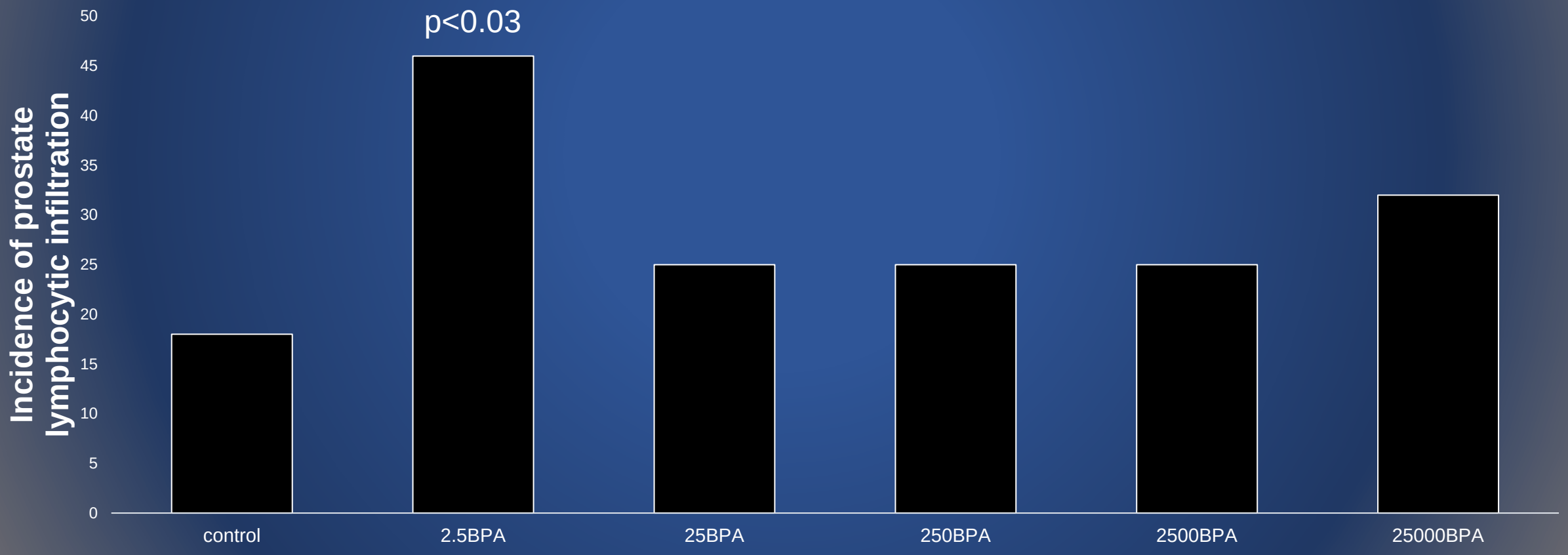
Several serious adverse effects of BPA were observed in the FDA-Core study at low doses

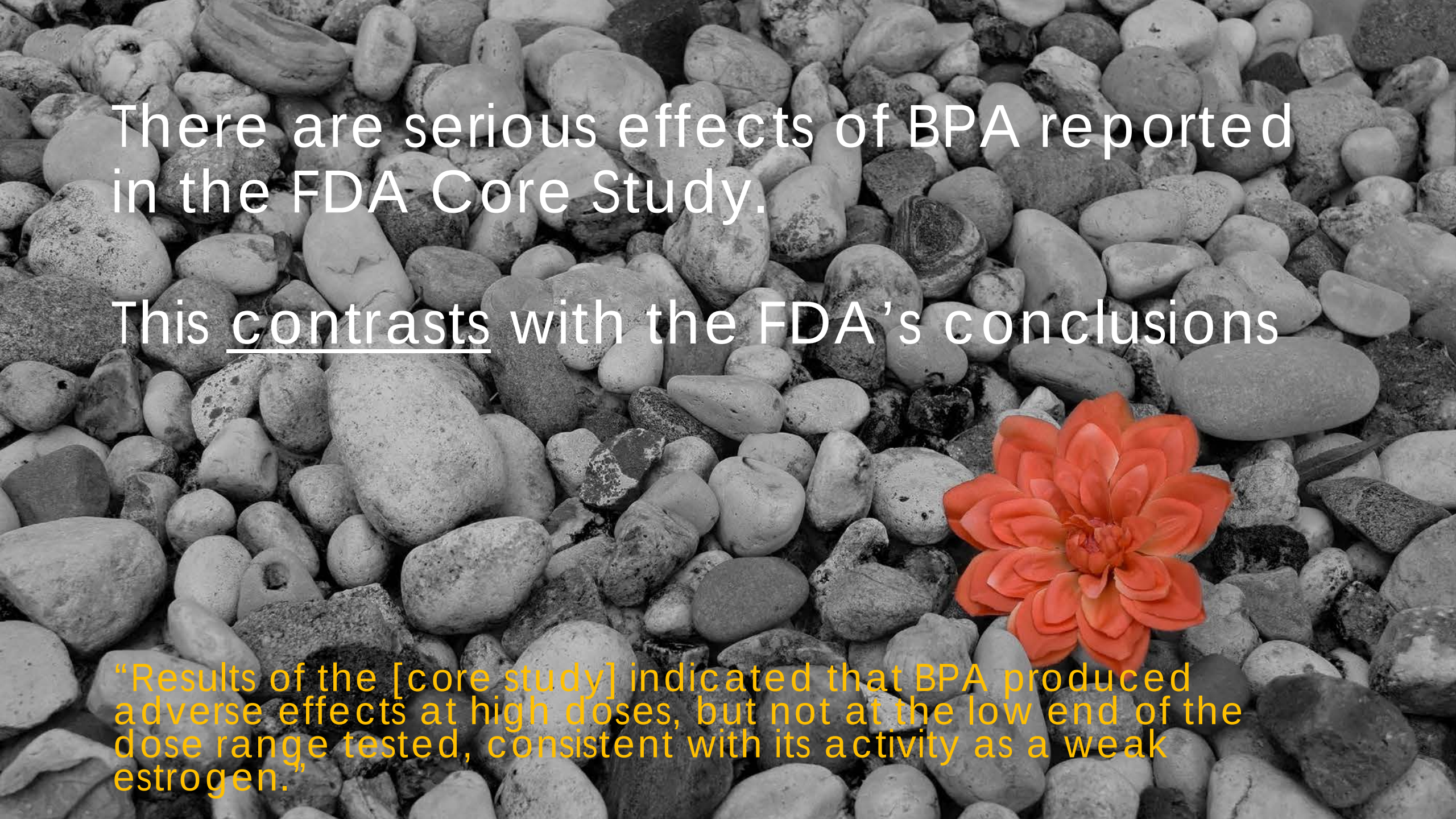
- increases in the incidence of mammary adenocarcinoma (at 2.5 µg/kg/day in the STOP group)
- inflammation of the dorsal and lateral lobes of the prostate (at 2.5 µg/kg/day in the CONTINUOUS group)
- kidney nephropathy in females (at 2.5 µg/kg/day in the CONTINUOUS group)
- increased body weight in adult females (at 250 µg/kg/day in the CONTINUOUS group)

Example 1: Low dose BPA exposure increased mammary cancer



Example 2: Low dose BPA exposure increased prostate inflammation (a cancer risk factor)





There are serious effects of BPA reported in the FDA Core Study.

This contrasts with the FDA's conclusions

"Results of the [core study] indicated that BPA produced adverse effects at high doses, but not at the low end of the dose range tested, consistent with its activity as a weak estrogen."

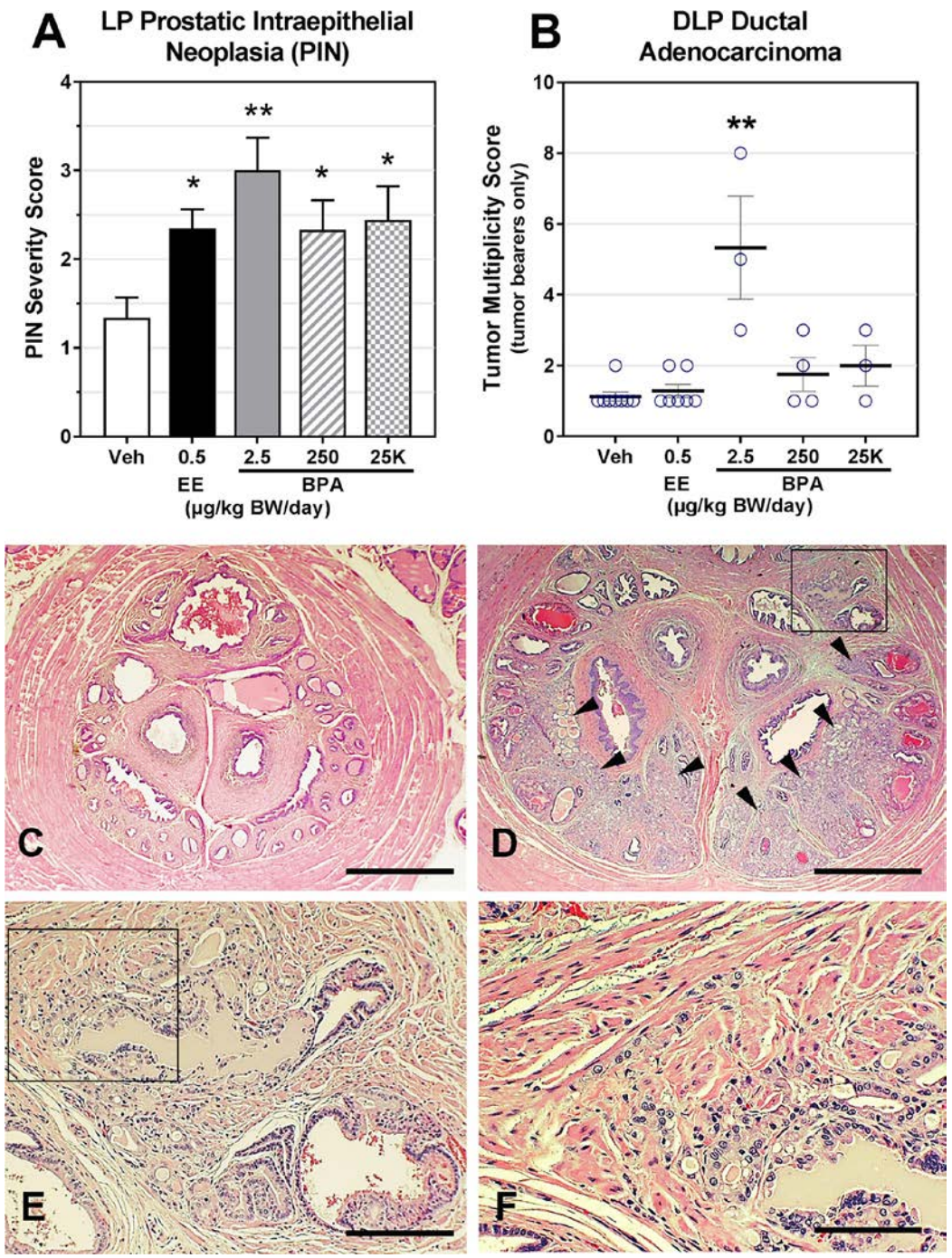
Why does the FDA ignore low dose effects of BPA observed in the FDA-Core study?

Finding anything in the low dose groups of the guideline study is surprising, based on the prior guideline studies on BPA!!

Academic studies

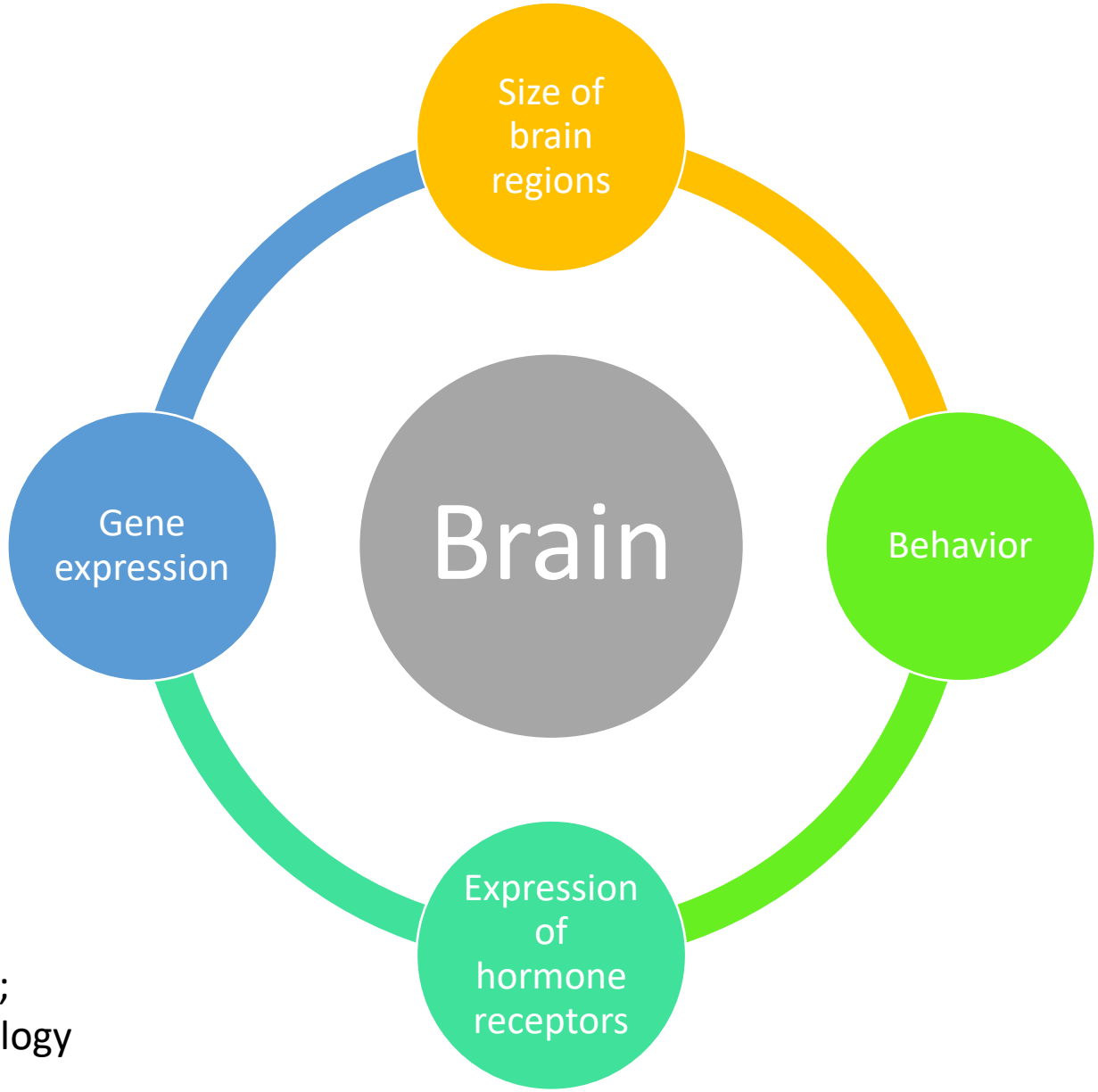
2.5	Brain	♀ Repro	Heart	Endocrine	♂ Repro	
25	Brain	Heart	Endocrine	♂ Repro		
250	Brain	♀ Repro	Heart	Endocrine	Mammary	
2500	Brain	♀ Repro	Endocrine			
25000	Brain	♀ Repro	Heart	Endocrine	♂ Repro	

Example 1: Low dose BPA exposure induces neoplasia (PIN) and adenocarcinoma in the prostate



Prins et al., EHP 2018

Example 2: Seven academic CLARITY publications document effects of BPA on brain and behavior



Rebuli et al. Tox Sci 2015; Arambula et al. Endocrinology 2016; Johnson et al. Horm Behav 2016; Arambula et al. Neurotoxicology 2017; Cheong et al. Epigenetics 2018; Arambula et al. Neurotoxicology 2018; Witchey et al. Neurotoxicology 2019

CLARITY was an imperfect study

Vandenberg, Hunt & Gore, Nat Reviews Endocrinol 2019

What can we conclude from the CLARITY study?

Differences in sample sizes

Differences in sensitivity

Differences in relevance to disease

Differences in study reliability

CLARITY is not
about looking at the
same data
and
drawing different
conclusions


The patterns tell a story…


21st Century Analyses
for 21st Century Data

CLARITY-BPA

Traditional and modern methods

Low dose effects