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Bisphenol A: Sufficient evidence of possible harm?

EFSA's health effects assessment
Brussels meeting April 2014

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Talk overview: Focus on 2 issues

- **Transparency + accessibility**
- **Effects on mammary gland**

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Issue 1: Transparency + accessibility

- Summary = vital.
- The uncertainties in the hazard identification are clear.
- But hidden are potential implications of being wrong in areas with high uncertainty.

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Eg. For metabolic effects – EFSA acknowledge high uncertainty

- Methodology used in RA only takes forward to risk assessment those doses for which there is confidence in the effect.
- But still useful – to be able to compare existing exposures with dose levels reported to cause such adverse effects.

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For all endpoints which are ‘likely’ or where there is high uncertainty

Summary should include a table to show the lowest dose levels (in animals) which are reported to cause effects, so that comparison with current exposures can be made.

Could public possibly be at risk?
EFSA can still indicate studies not justified.

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Given the high uncertainties – summary needs to portray the implications if EFSA Panel's judgment is wrong.

But the summary gives no indication of whether or not there is any margin of safety if the reported effects in the studies it dismisses were in-fact real.

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Issue 2: What happened to risk assessment of effects on mammary ?

Only US FDA/NCTR 2013 study is used for dose response modelling – ‘uncertainty for the robustness of BMD modelling for this end-point’.

- anyway higher than kidney effects.

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BPA

BPA

+ chemical carcinogen

Mammary gland morphology
Gene expression
Pre-neoplastic & neoplastic lesions

Tumor latency, incidence

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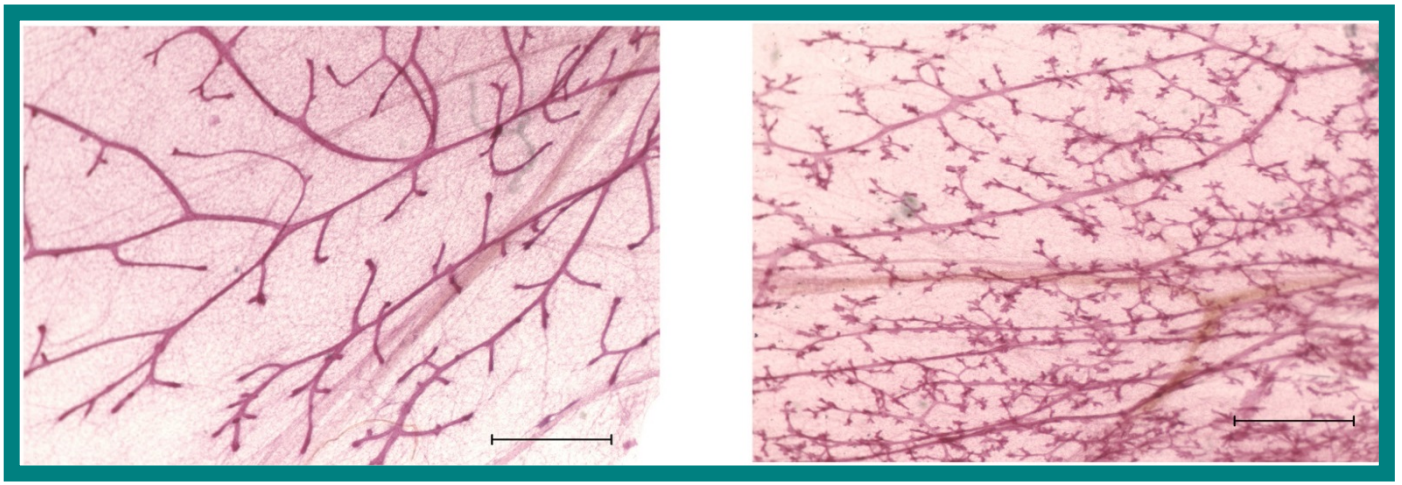
control

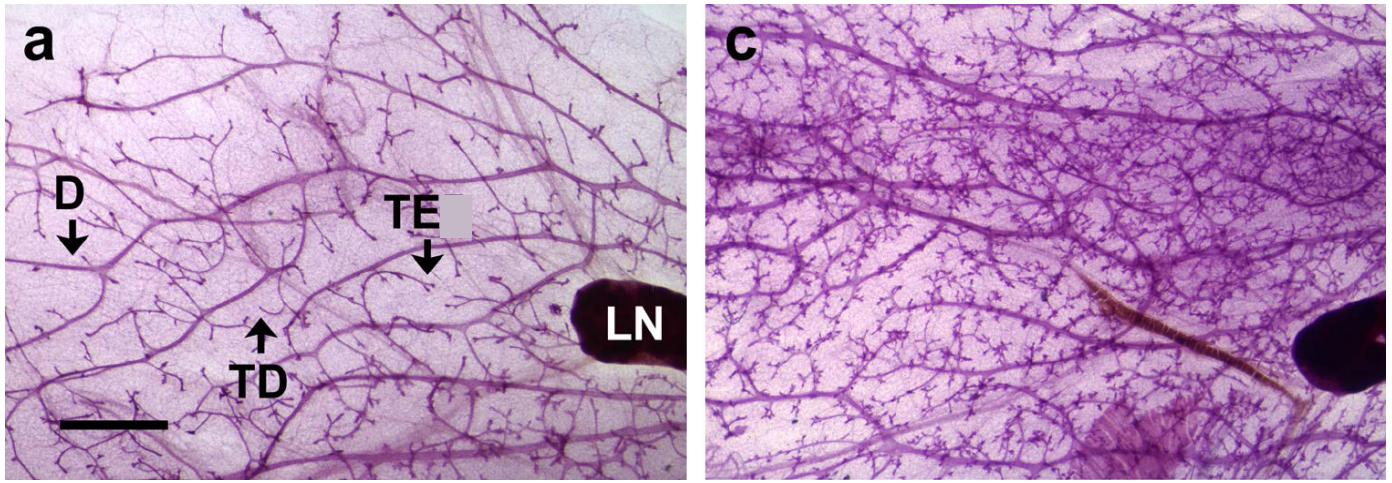
BPA

4 months



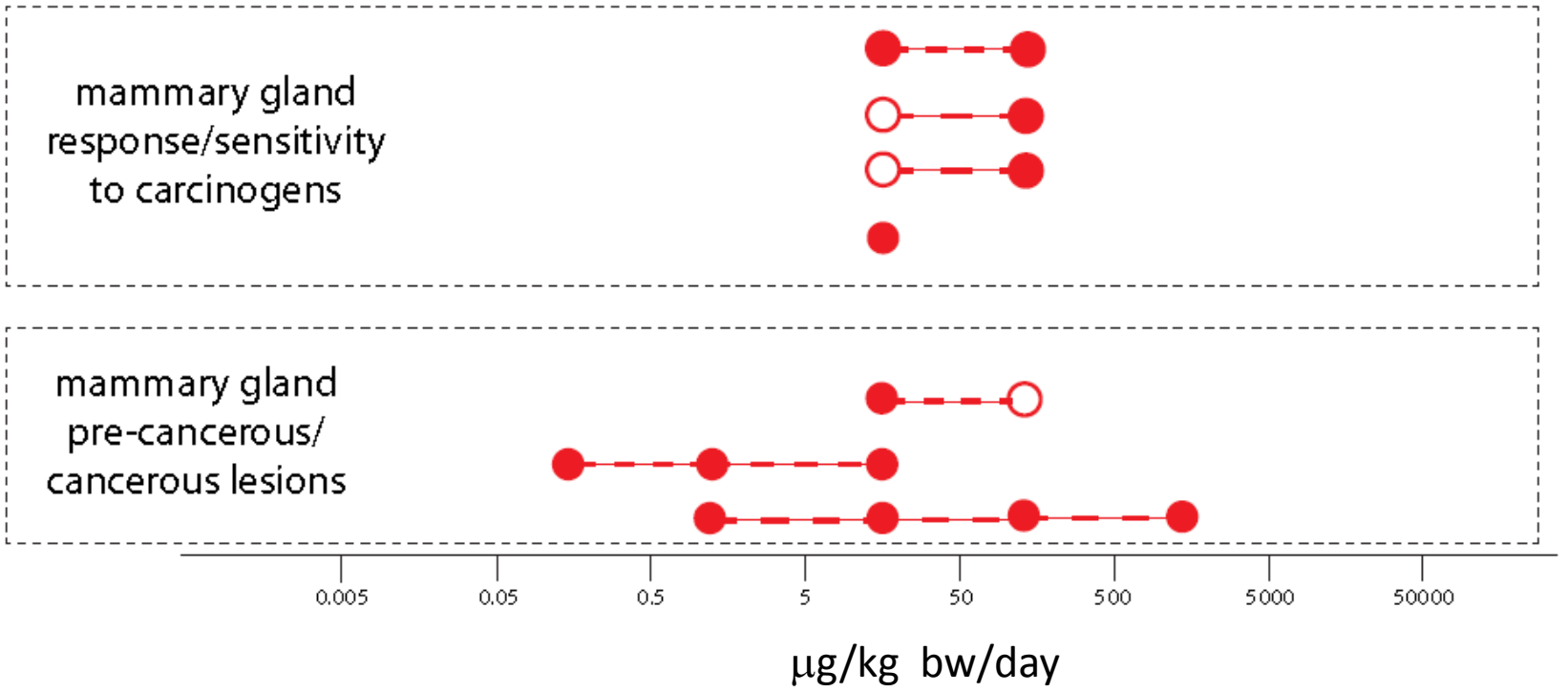
Munoz de Toro et al, 2005

6 months



Markey et al, 2001

Effects of developmental BPA exposure on mammary cancer



Vandenberg et al. 2013

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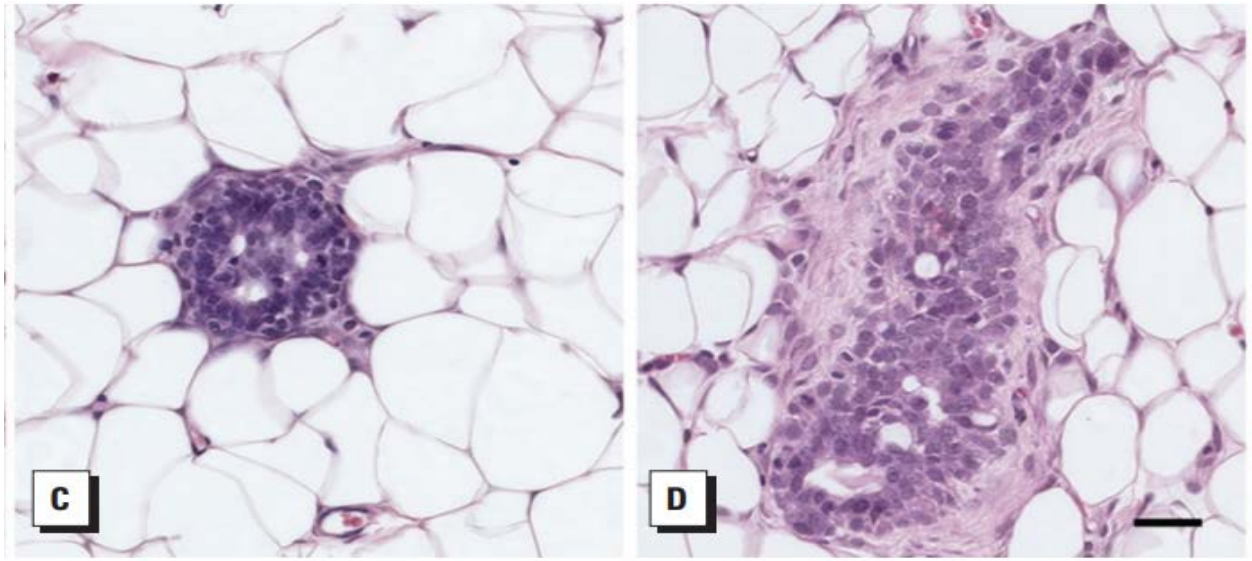

Acevedo et al. 2013

Rats: at PND 50 after gest/lact 25 µg/kg bw/day

Ductal hyperplasia and DCIS

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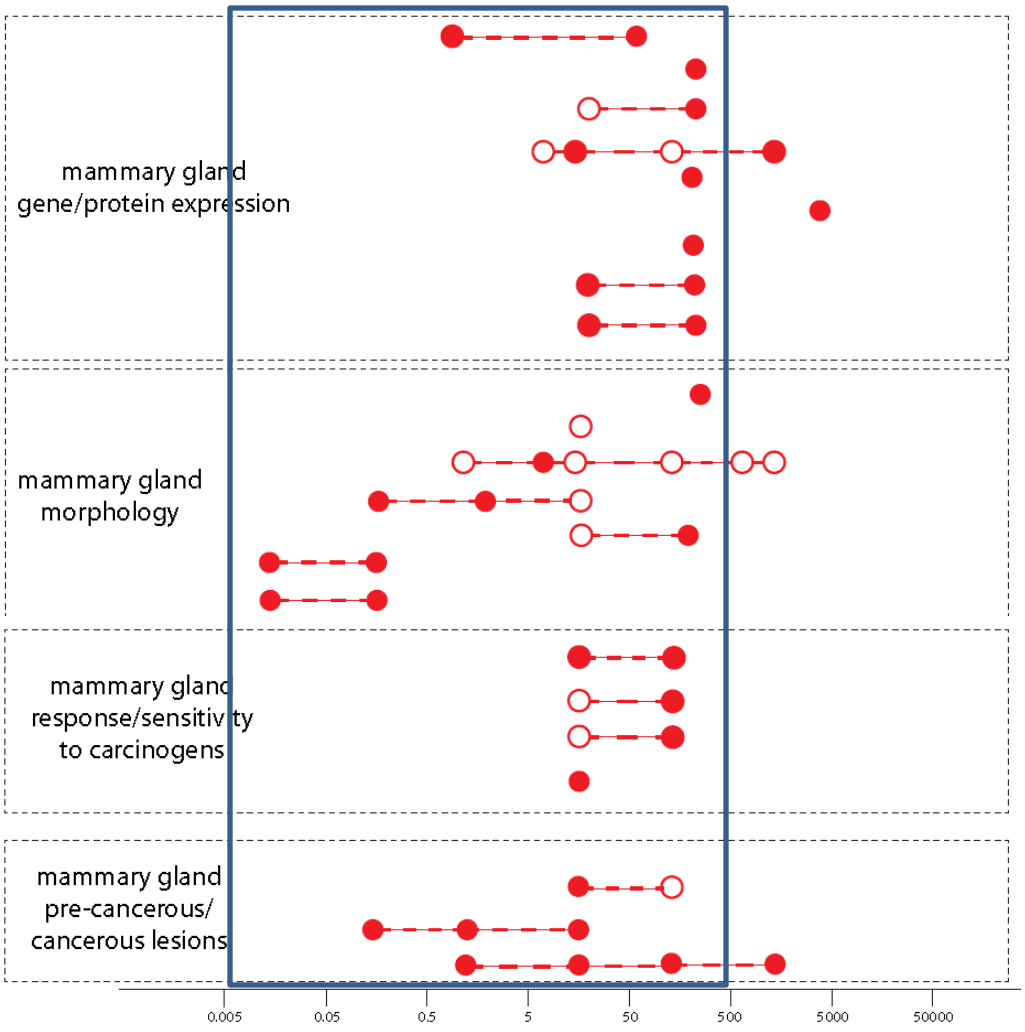
Are these end-points adverse?

YES!

"A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, **or reduces an organism's ability to respond to an additional environmental challenge**."

There are consistent effects of BPA on the mammary at doses below 500 µg/kg/day



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Calculating a TDI

Using 25 µg/kg/day as the NOAEL (as per ANSES) apply 2x10 assessment factors for inter and intra variability

TDI = 0.25 µg/kg/day or 250 ng/kg/day

Using 250 ng/kg/day as LOAEL (Vandenberg 2007)

apply 3x10 assessment factors

TDI = 0.25 ng/kg/day

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Conclusions

EFSA's report inappropriately dismisses many studies reporting low dose effects.

Instead puts too much weight on some 'flawed' studies.

And the summary is lacking, because it does not portray the controversy and does not transparently show that there may not be a MOS if their analysis is wrong.

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