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# Identifying BPA as a reproductive toxicant



Avinash Kar  
Senior Attorney



Johanna Rochester, PhD  
Research Associate

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Contents lists available at [ScienceDirect](#)

## Reproductive Toxicology

journal homepage: [www.elsevier.com/locate/reprotox](http://www.elsevier.com/locate/reprotox)



Review

### Bisphenol A and human health: A review of the literature

Johanna R. Rochester\*

*The Endocrine Disruption Exchange (TEDX), P.O. Box 1407, Paonia, CO 81428, United States*



A comprehensive review of all the human literature exploring BPA and health effects

- 91 studies
- 75 showed effects
- Multiple adverse health effects

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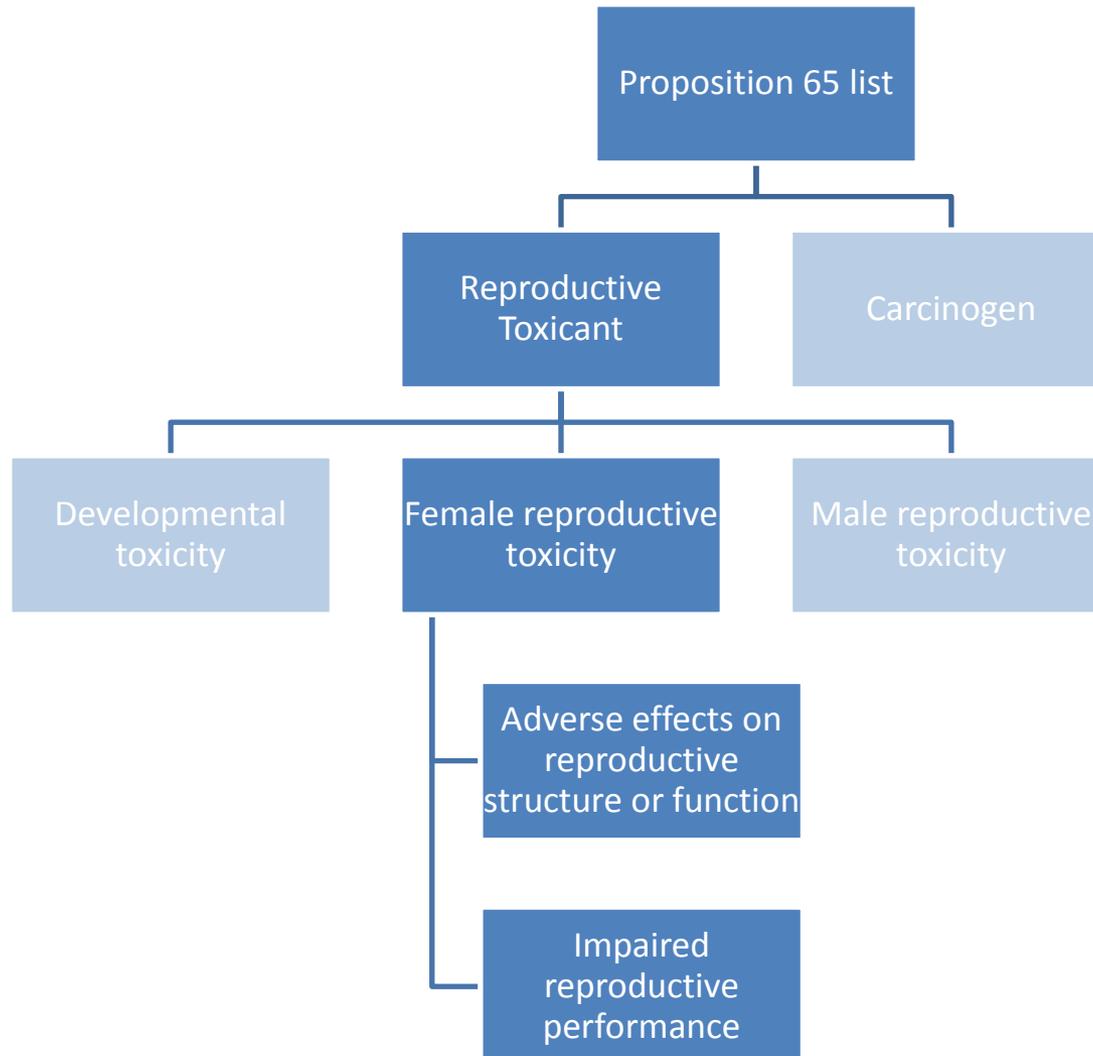
# Outline

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**(Nov. 1993) CRITERIA FOR RECOMMENDING CHEMICALS FOR LISTING AS  
"KNOWN TO THE STATE TO CAUSE REPRODUCTIVE TOXICITY"**

- What is listed
- Criteria for listing
- Scientific evidence on BPA

# What is listed



For listing, ONE of these criteria has to be met

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1

Sufficient evidence of  
reproductive toxicity in  
humans

OR

2

Sufficient evidence of  
reproductive toxicity in  
animals (mammals)

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# Other considerations

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1

Sufficient evidence of  
reproductive toxicity in  
humans

OR

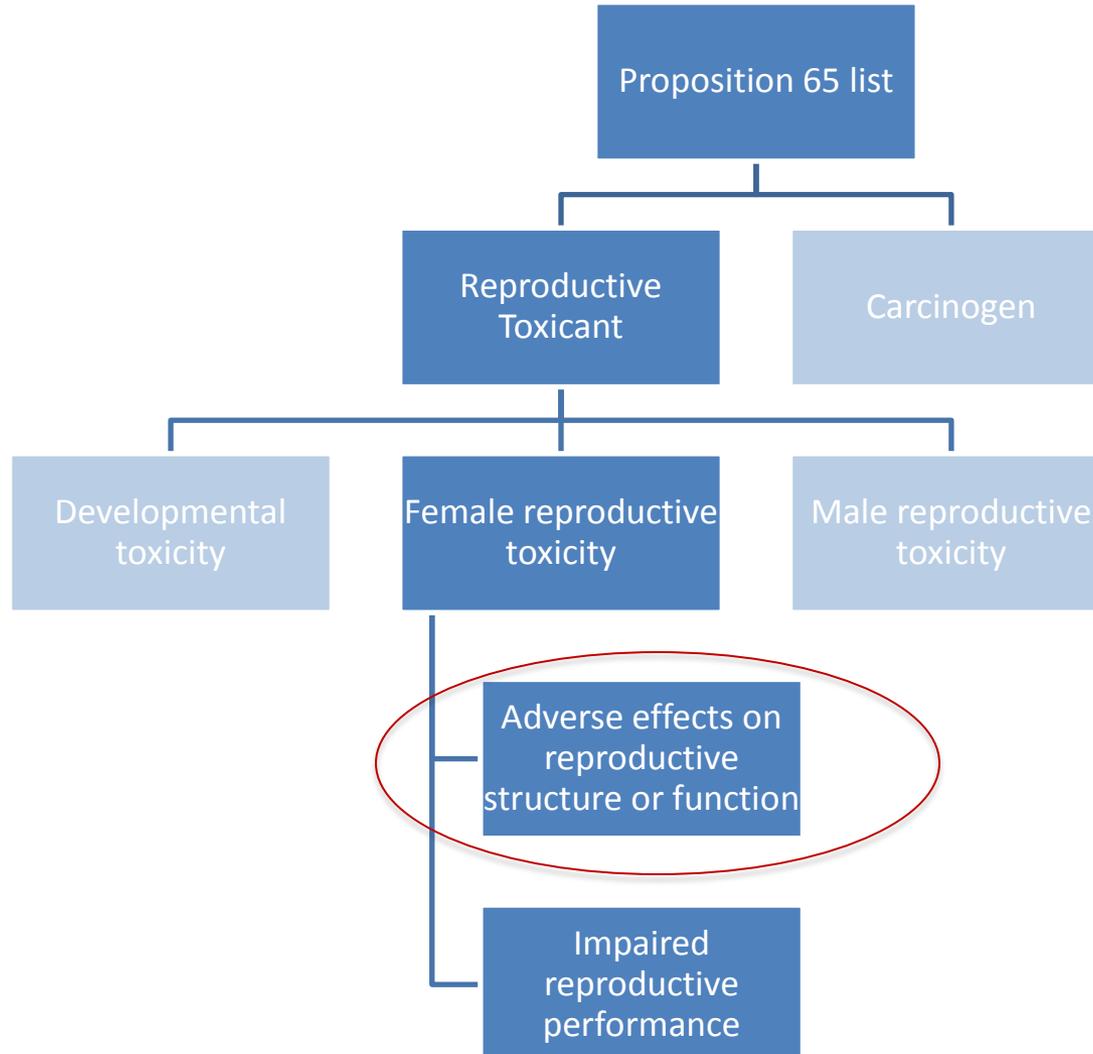
2

Sufficient evidence of  
reproductive toxicity in  
animals (mammals)

Statistical  
considerations

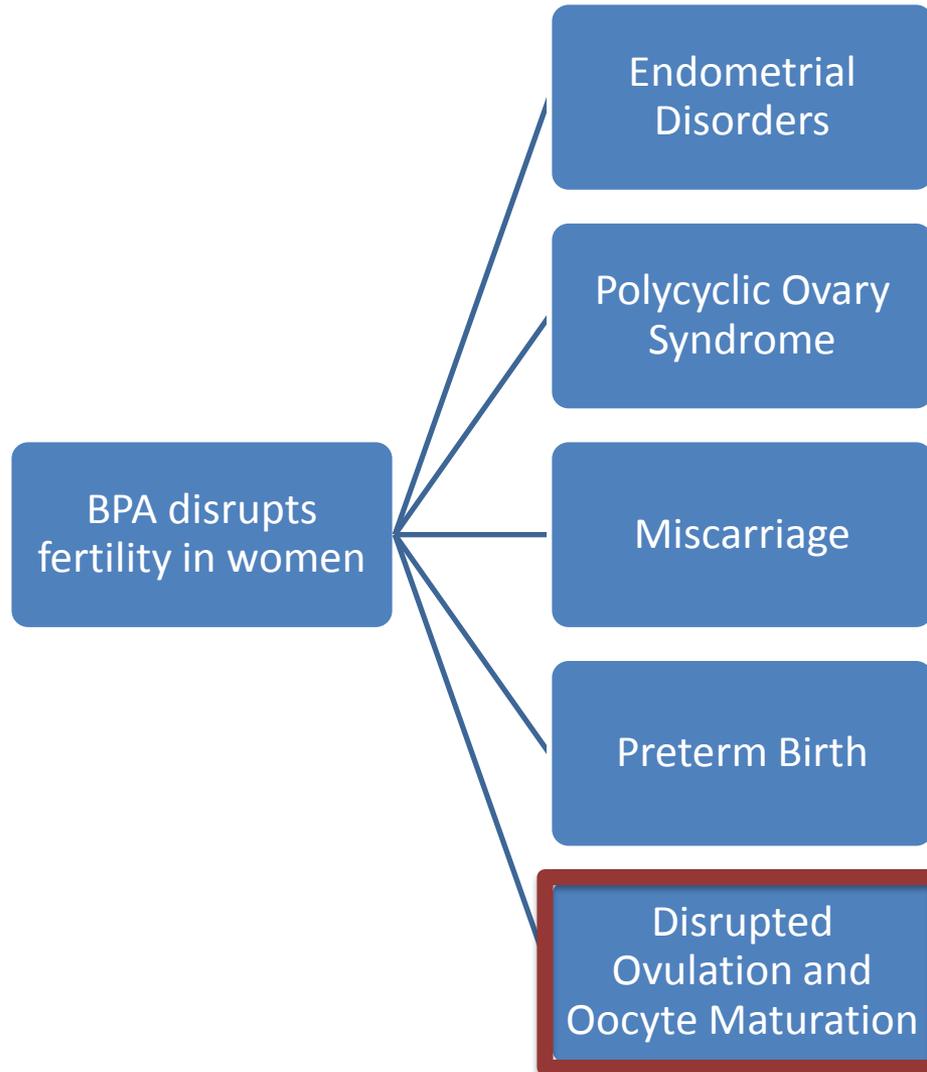
Biological  
Plausibility

# What is listed



# One example of reproductive effects in women

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# Adverse effects on **reproductive structure or function**: Evidence of reproductive toxicity in humans

Adverse effects on reproductive structure include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

Genetic damage to the ovum or its precursors

**Ehrlich 2012**

Reduced number of mature and fertilized oocytes

**Fujimoto 2011**

Reduced number mature oocytes

Alterations in ovulation, menstrual cycle/  
menstrual disorders

**Ehrlich 2012**

Poor ovulation response

**Mok-Lin 2010**

Poor ovulation response

**Bloom 2011a**

Poor ovulation response

Impaired or altered endocrine function

**Ehrlich 2012**

Low estrogen response

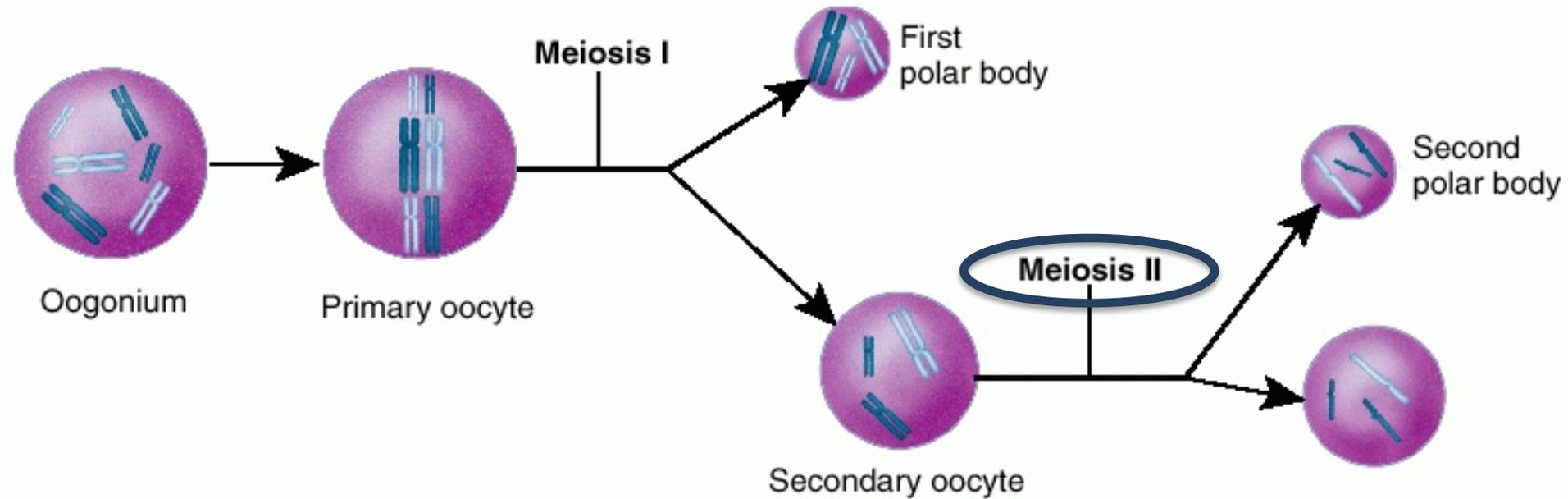
**Mok-Lin 2010**

Low estrogen response

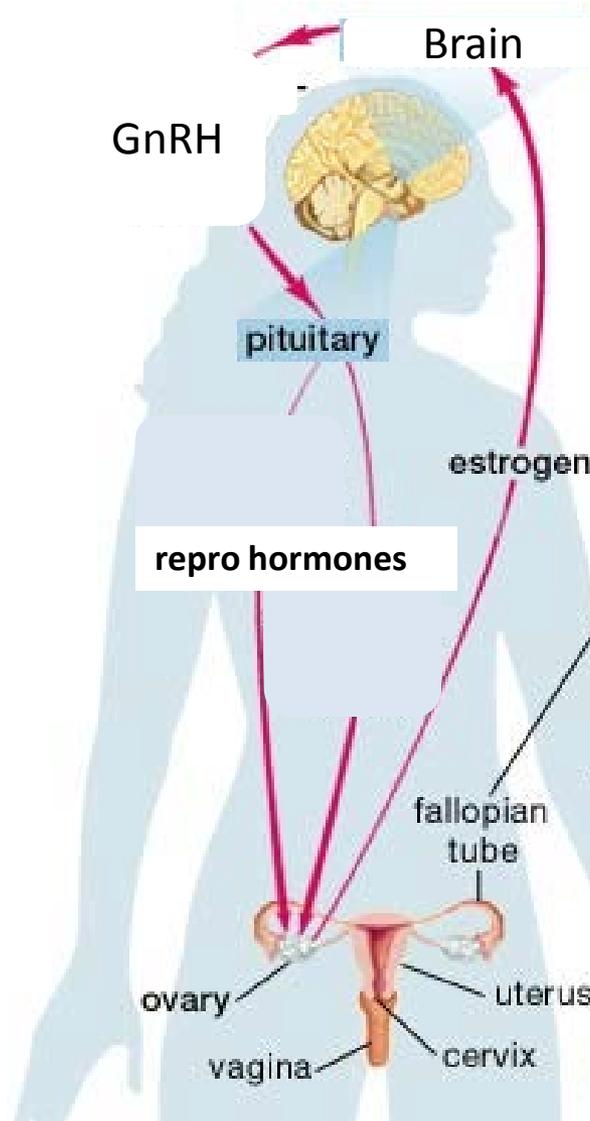
**Bloom 2011a**

Low estrogen response

# Normal oocyte development



# Normal ovulation



# Adverse effects on **reproductive structure or function**: Evidence of reproductive toxicity in animals

Adverse effects on reproductive structure include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

Genetic damage to the ovum

**Zhang 2012**

Mice: Disrupted oocytes and follicles

**Hunt 2012**

Macaques: Disrupted oocyte meiosis

Alterations in ovulation, menstrual cycle/ menstrual disorders

**Ziv-Gal 2015**

Mice: Delayed time of first estrus

**Nah 2011**

Mice: Decreased estrus cycles and days

Impaired endocrine function

**Kawai 2007**

Mice: Alterations in estrogen receptor

Adverse effects on **reproductive structure or function**:  
In vitro/mechanistic evidence showing biological plausibility

Adverse effects on reproductive structure include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

### Genetic damage to the ovum

**Lenie 2008**

Oocyte disruption and spindle aberrations  
(in vitro)

**Can 2005**

Oocyte cell cycle and spindle disruption  
(in vitro)

### Alterations in ovulation and estrous

**Adewale 2009**

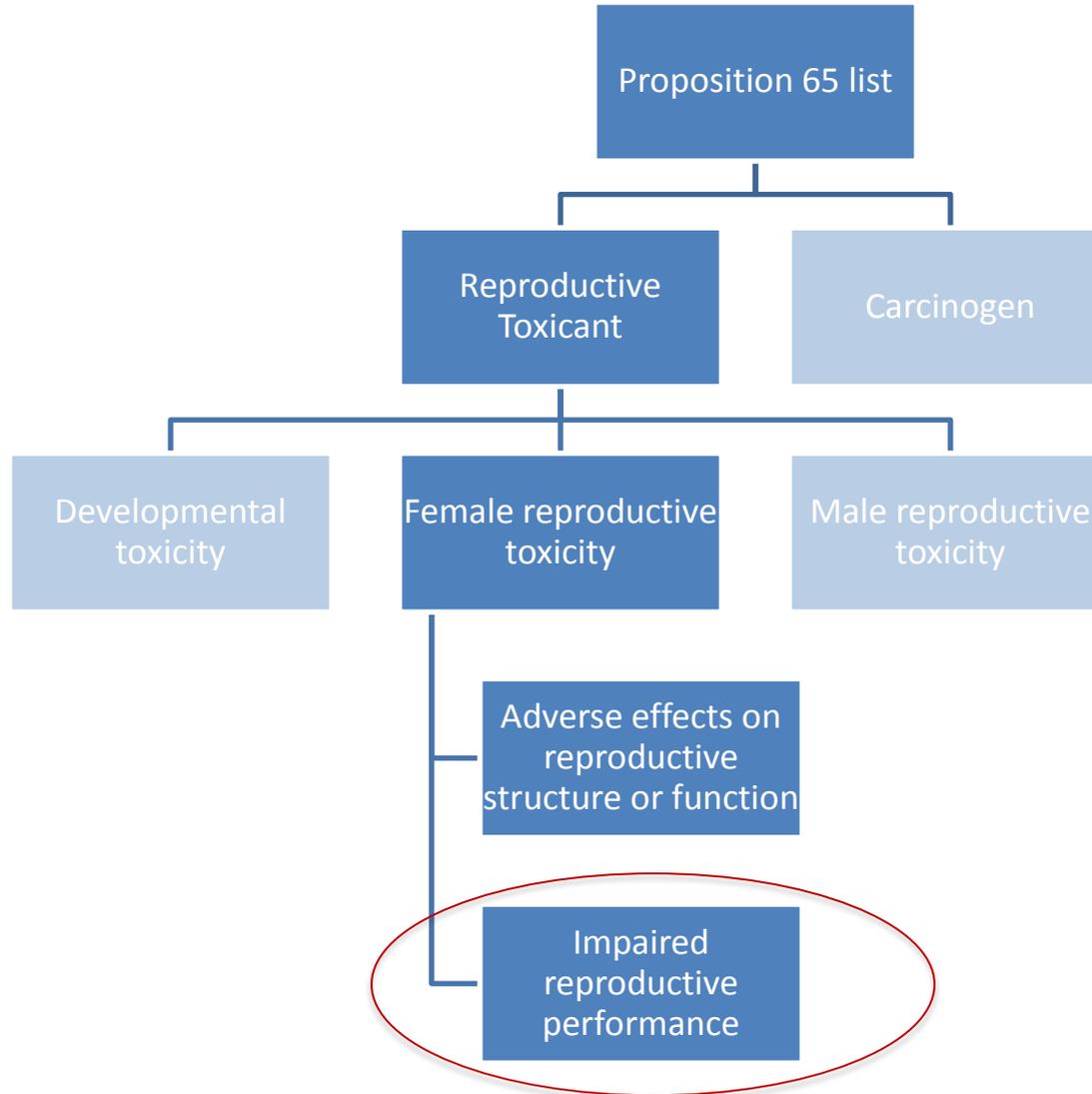
Disruption of ovarian development but not brain hormone neurons  
(in vivo)

### Impaired endocrine function

**Kitamura 2005**

BPA binds to the estrogen and androgen receptors and has estrogenic and anti-androgenic activity  
(in vitro)

# What is listed



# Impaired reproductive performance:

## Evidence of reproductive toxicity in humans

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Adverse effects on reproductive structure

include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

Increased pregnancy wastage (e.g., miscarriage)

**Lathi 2014**

Increased rates of miscarriage

**Sugiura-Ogasawara 2005**

Increased rates of miscarriage

Inability/decreased ability to conceive

**Ehrlich 2012**

Increased implantation failure

**Caserta 2013**

Higher rates of infertility in women

Adverse effects on sexual behavior, gestation, lactation, etc.

**Cantonwine 2010**

Increased premature delivery

# Impaired reproductive performance: Evidence of reproductive toxicity in animals

Adverse effects on reproductive structure

include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

Increased pregnancy wastage (e.g., miscarriage)

**Kim 2001**

Mice: Pregnancy failure and pre- and post-implantation failure

**George 2012**

Rats: Increased fetal death and malformation

Inability/ decreased ability to conceive

**Cabaton 2011**

Mice: Reduction in fertility in females

Adverse effects on sexual behavior, gestation, lactation, etc.

**Farabollini 2002**

Mice: Altered female sexual behavior

**Matsumoto 2004**

Mice: Exposed mothers had reduced lactation

## Impaired reproductive performance:

In vitro/mechanistic evidence showing biological plausibility

Adverse effects on reproductive structure include (but are not limited to):

Evidence of any one of these effects is sufficient for listing

Increased pregnancy wastage (e.g., miscarriage)

**Ozlem 2008**

BPA is toxic to embryos  
(in vitro)

**Hwang 1986**

BPA is toxic to embryos  
(in vitro)

Inability/decreased ability to conceive

**Newbold 2007**

Disruption of reproductive tract morphology  
(in vivo)

Adverse effects on sexual behavior, gestation, lactation, etc.

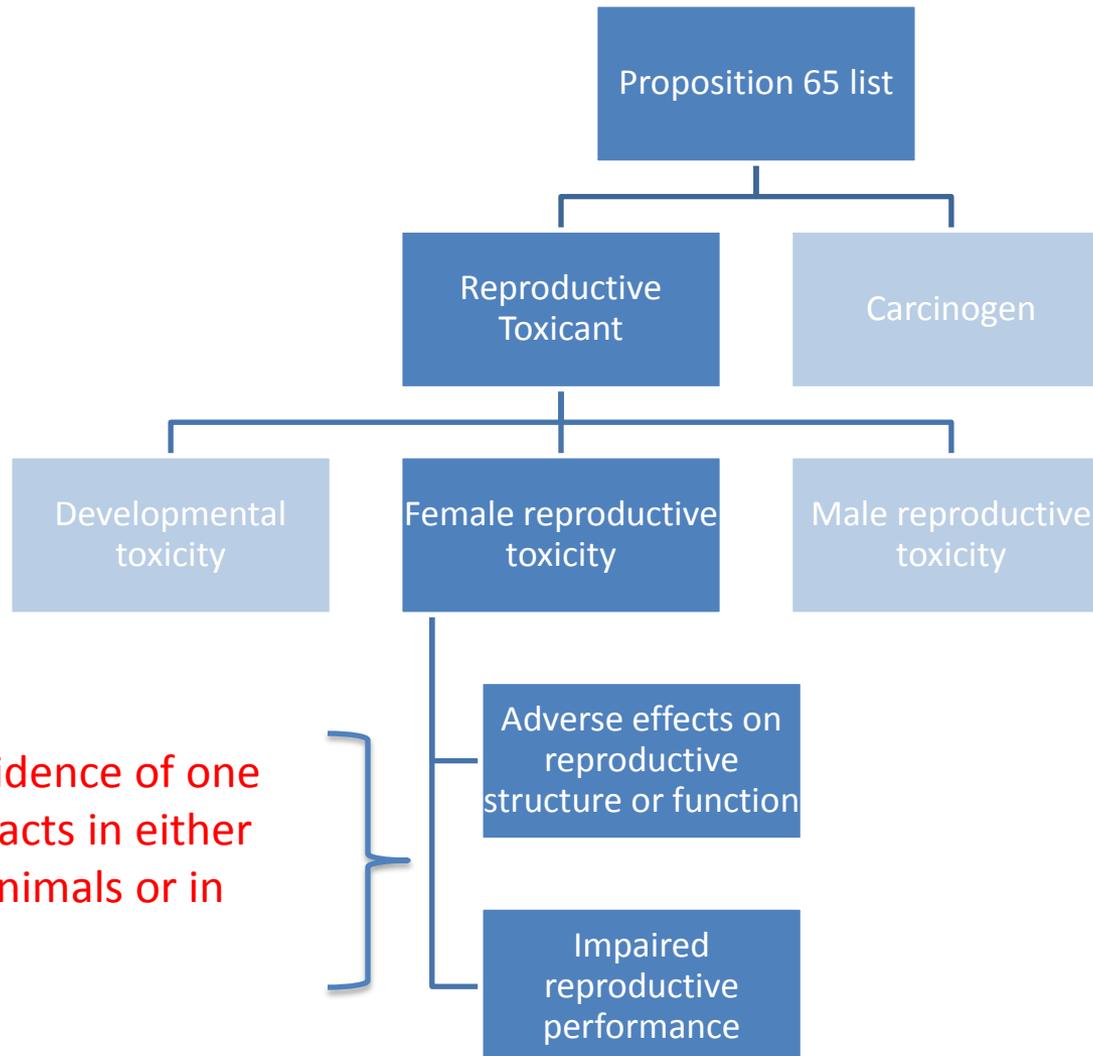
**Chun 2000**

BPA alters prolactin (lactation hormone) release  
(in vitro)

**Monje 2009**

BPA altered brain mechanisms that drive female sexual behavior  
(in vivo)

# What is listed



Sufficient evidence of one of these impacts in either humans or animals or in combination

# Conclusion

Unlike some other bodies that have reviewed BPA, the DART IC's inquiry is focused on whether there is sufficient evidence of reproductive toxicity, guided by the criteria we just discussed

- The scientific literature demonstrates **sufficient evidence of female reproductive toxicity**

The decision reflects the DART IC's independent judgment as the State's experts on the science and responding to Proposition 65's specific criteria

Risk and exposure issues are addressed at a later stage

- The committee will have an opportunity to review and comment on OEHHA's assessment of risk and exposure and any proposed action at that stage