

BPA – Bisphenol A

Margin of Exposure

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Wrong Question

Wrong Question: Is KRYPTONITE safe?



Right Question

Right Question:

What is the KRYPTONITE margin of exposure?



Margin of Exposure

- What is margin of exposure?
- Why is it important?
- How do we figure out what it is?



BPA - Human Margin of Exposure

- **99% of human BPA exposure is dietary**
(Wilson et al., 2007)
- **The larger the margin of exposure, the higher the safety factor**
- **10 is good, but 100 is better**



Risk Assessment in the Federal Government: *Managing the Process* *

- Hazard Identification
- Dose-Response Assessment
- Exposure Assessment
- Risk Characterization



* National Research Council (1983)

BPA Standardized Studies

- Cancer
- Genetic toxicity
- Developmental toxicity
- Multi-generation reproduction toxicity



Cancer Studies *



No cancer risk
for male or female rats or mice



* National Toxicology Program (1982)

Genetic Tests

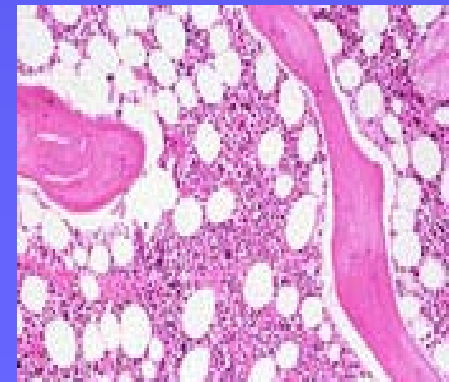
Negative in
Salmonella bacteria



Negative in chromosomal aberrations



Negative in mouse bone marrow



Reproduction and Developmental Toxicity Test Guidelines *

- Oral administration in animals unless human exposure dictates other routes
- Three or more dose groups and control
- Twenty-plus animals per dose group



* U.S. EPA

Rat and Mouse Reproduction Studies

No Observable Effect Level

equals

5 milligrams/kilogram per day

or

0.005 gram per 1,000 grams



Accounting for Uncertainty

- ✓ 10 x for interspecies extrapolation
- ✓ 10 x for intraspecies extrapolation
- ✓ 1 x subchronic to chronic
- ✓ 1 x for LOEL to NOEL
- ✓ 3 x for database deficiencies

Total uncertainty factor = 300 x



From NOEL to Oral Reference Dose

No Observable Effect Level

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Total Uncertainty (Safety) Factor

=

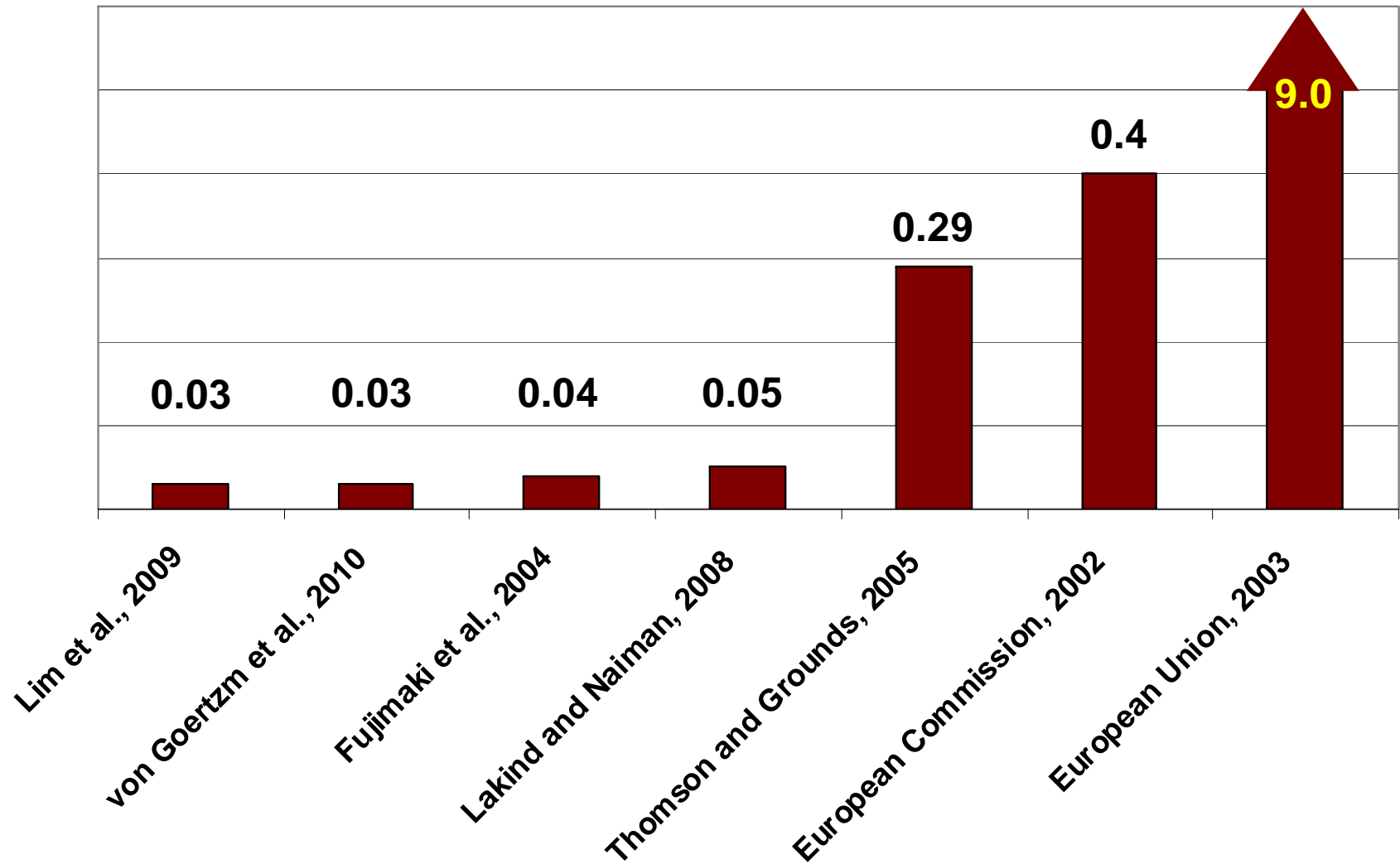
Reference Dose

20 micrograms / kilogram per day



Adult BPA Exposure

micrograms/kilogram per day



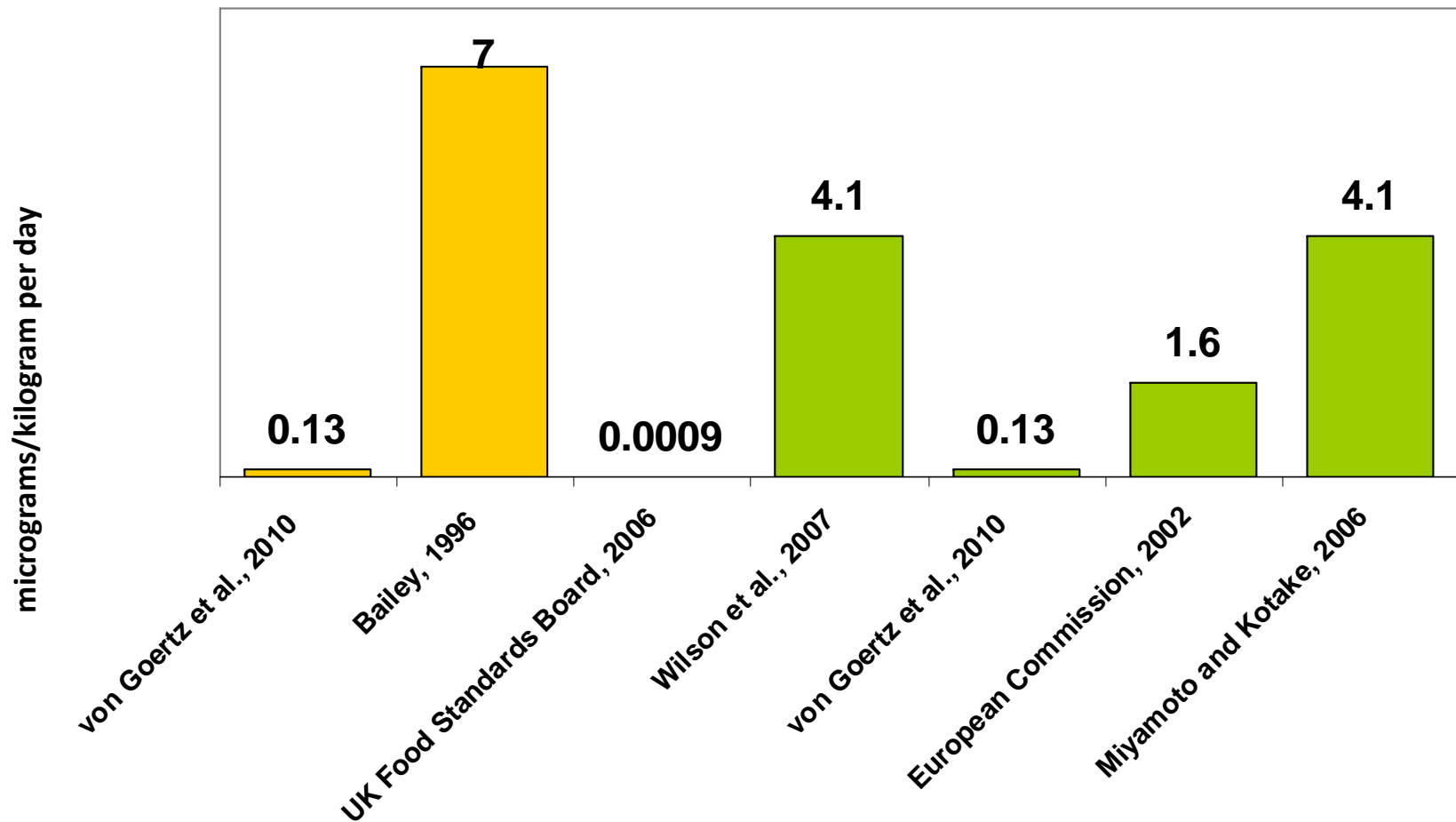
Adult BPA Margin of Exposure

- Aggregate average margin of exposure = 2 to 2,500
- U.S. (urinary) margin of exposure = 58 and 550
- German and Japanese (urinary) margin of exposure = 260 to 2,200



Infant BPA Exposure

Child BPA Exposure



Polycarbonate Baby Bottles

- Highest BPA formula concentration plus BPA migration from bottle =
infant dose $7.0 \mu\text{g}/\text{kg}\text{-day}$ *
- BPA in formula to BPA migration from bottles boiled for 1 hour =
infant dose $0.8 \mu\text{g}/\text{kg}\text{-day}$ **

* Bailey (1996)

** von Goertz et al. (2010)



Infant BPA Margin of Exposure

- Oral Reference Dose = 20 $\mu\text{g}/\text{kg}\text{-day}$
- Infant exposure = 0.8 to 7.0 $\mu\text{g}/\text{kg}\text{-day}$
- Infant daily BPA margin of exposure = 3 to 25
- Worst case human BPA exposure is at least 700 times less than rodent oral no effect level



So, Now What?

- **Enforceable maximum limits on BPA levels in canned foods and polycarbonate containers**
 - **European Union and Korean maximum limit = 0.6 milligram/kilogram**
 - **Maximum limit restricts human BPA exposure to not more than 0.03 microgram/kilogram - day**
- **Margin of BPA exposure = 666**

