

**Comments on
“EPA’s Reanalysis of Key Issues Related to
Dioxin Toxicity and Response to NAS
Comments”**

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2006 National Academy of Science report on 2003 EPA Dioxin Reassessment

NAS emphasized that, “If significant differences in the REP of dioxins, other than TCDD, and DLCs are found between humans and other species, then adjustments should be made in the TEFs, and these should be acknowledged in the Reassessment.” (NAS, 2006, page 87)

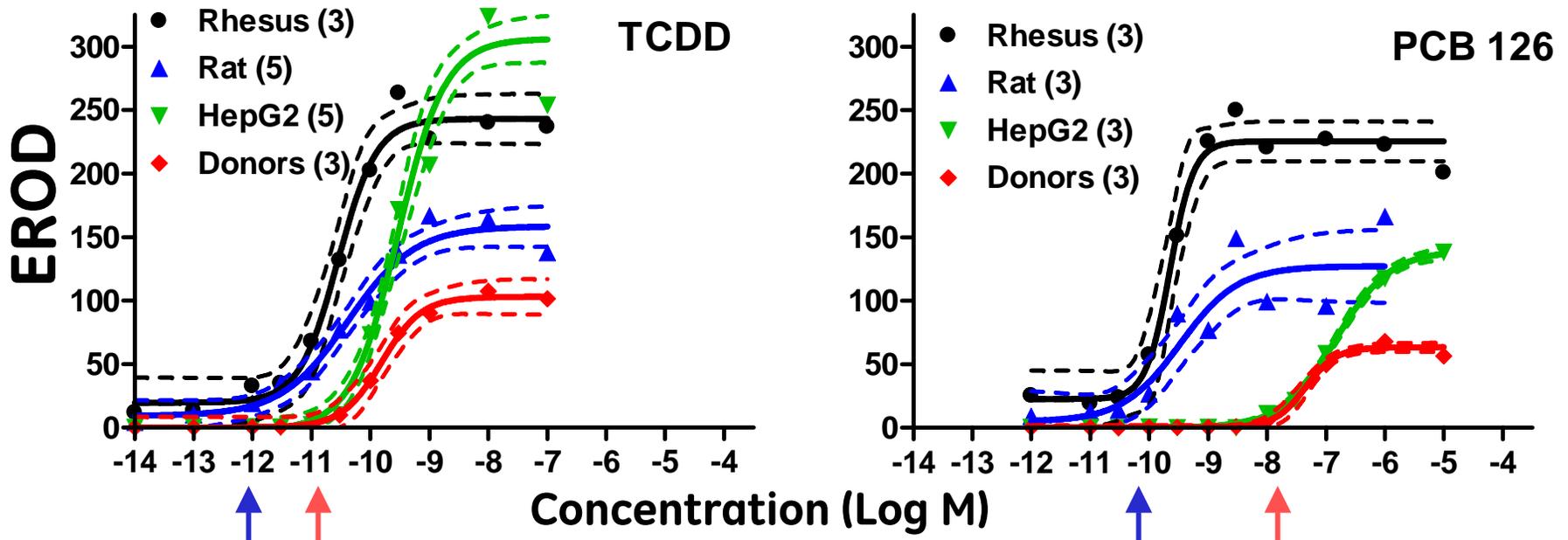
From “Health Risks from Dioxin and Related Compounds: Evaluation of the EPA Reassessment”, National Research Council of the National Academies, 2006.

Application of inconsistently derived risk values

- The Draft Reanalysis uses human data to derive new RfD and CSFs for TCDD only.
- To apply these values to real world mixtures of DLCs, EPA proposes to apply the current WHO TEFs which are derived from rodent studies.
- But, NAS recommends 'adjusting for species differences' if evidence available.
- Some human *in vitro* derived factors are available, e.g., PCB 126 (0.1 in rodents and rodent cells) is 0.002 in human cells. More are coming.

Human cells far less sensitive to PCB 126

Primary human hepatocytes*



Observed PCB 126 REP

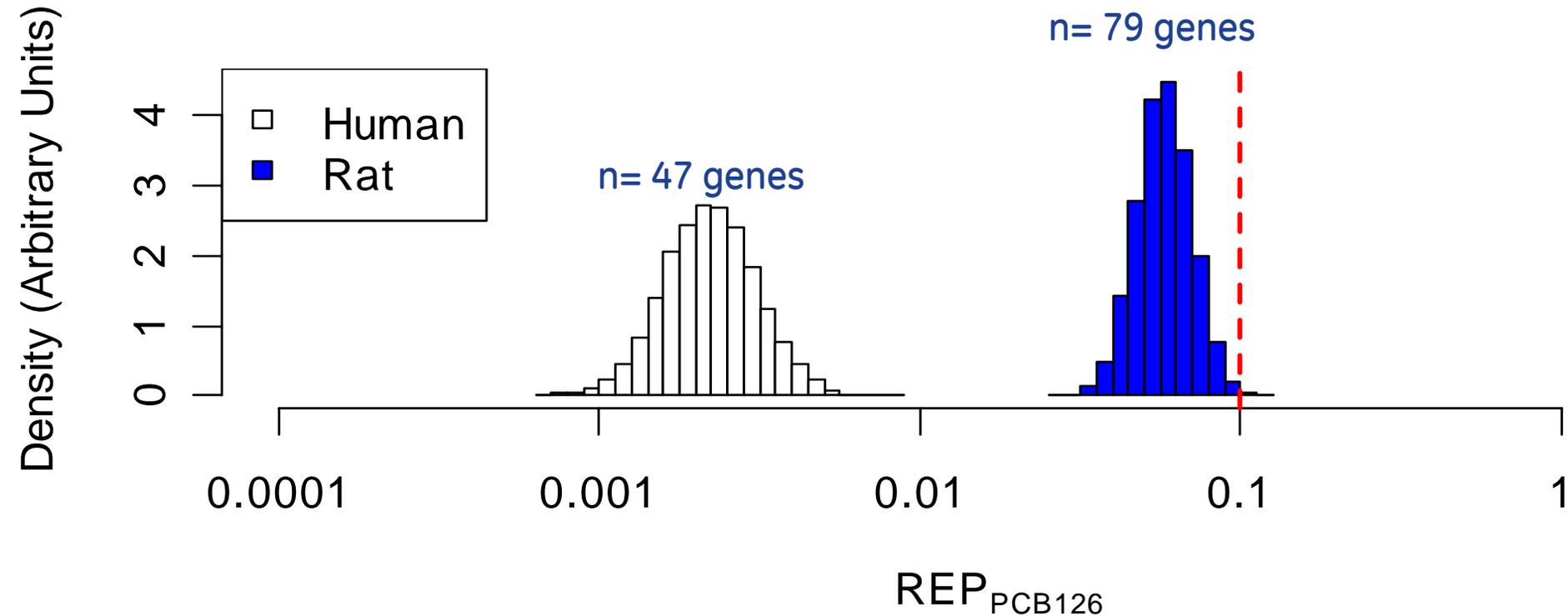
0.1 for Rhesus & Rats

~0.003 for Human cells

*Adapted from Silkworth *et al.* (2005). *Toxicol Sci.* 87(2), 508-519

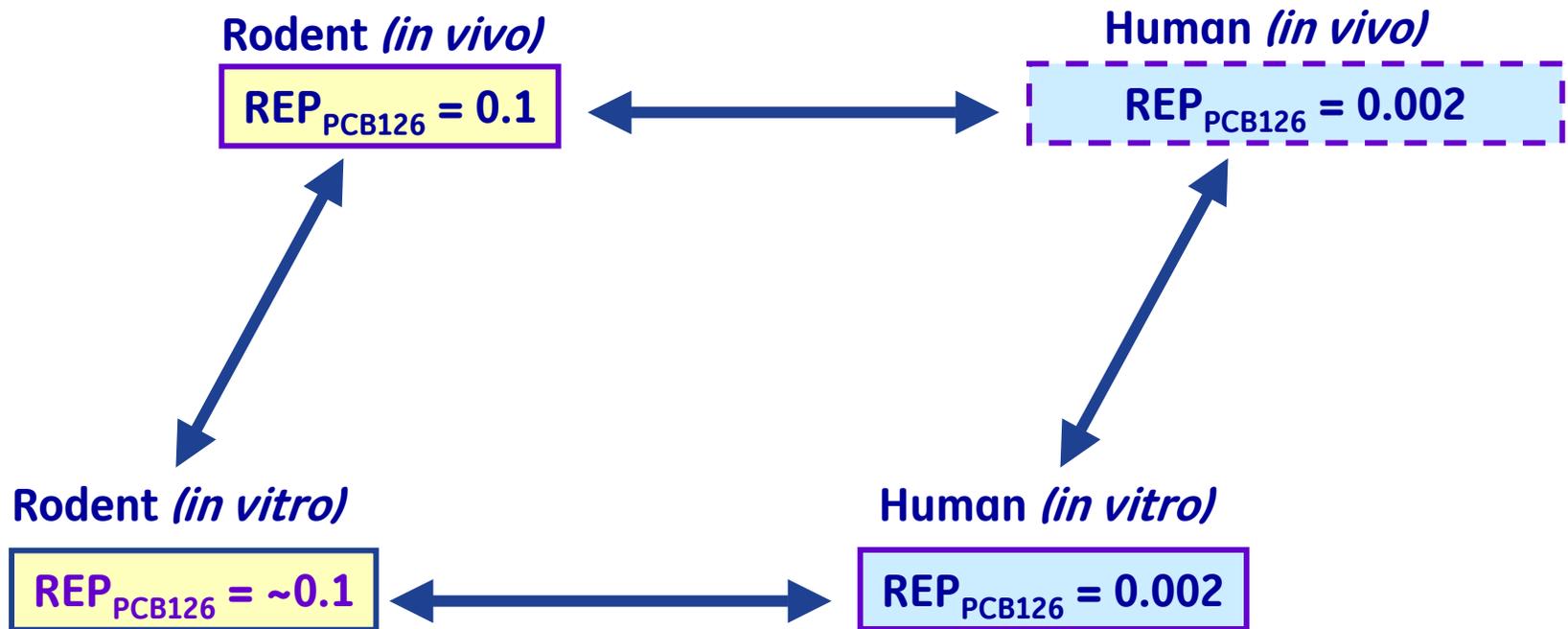
Human cells far less sensitive to PCB 126

Toxicogenomic REP modeling



Monte Carlo analysis of distribution around geomean REP_{PCB126}

Modern risk assessment guidelines encourage the use of *in vitro* data in human health risk assessment



SAB should recommend that the EPA refrain from applying dioxin risk values to PCBs

Unless or until the EPA:

- Implements NAS recommendations relating to TEFs;
- Revises TEFs to incorporate into the analysis newer and more accurate estimates of the human-specific relative potency of DLCs, particularly PCBs, when assessing human health risk.