# U.S. Consumer Product Safety Commission
## LOG OF MEETING

**SUBJECT: Chris Wallace, Exxon Mobil Chemical Company requested to meet with CPSC technical staff to provide information about a chemical composition of household dust review article, as well as to present Exxon Mobil's analysis of the NHANES 2013/2014 phthalates data.**

**DATE OF MEETING: March 21, 2017**

**LOG ENTRY SOURCE: Alice Thaler**

**DATE OF LOG ENTRY: March 22, 2017**

**LOCATION: 5 Research Place, Rockville, MD 20850**

**CPSC ATTENDEE(S): Dr. Alice Thaler, Associate Executive Director for Health Sciences; Dr. Michael Babich, Director Division of Toxicology and Risk Assessment; Dr. Kent Carlson, Toxicologist; Dr. Melanie Biggs, Toxicologist; Kris Hatlelid, Toxicologist; Kathleen Stralka, Associate Executive Director for Epidemiology; Dr. Stephen Hanway, Statistician; Wioletta Szeszel-Fedorowicz, Epidemiologist; Sarah Garland, Epidemiologist; David DiMatteo, General Council.**

**NON-CPSC ATTENDEE(S): Exxon Mobil Chemical Company attendees: Chris Wallace, Manager Global Advocacy & Regulatory Affairs Intermediates; Elissa Sterry, Global Vice President Intermediates; Matthew Crocker, Dr. Jennifer Foreman, Toxicology Associate. Ann Claassen, Latham & Watkins LLP.**

**SUMMARY OF MEETING: Exxon Mobil will submit everything presented today as a written comment to the CPSC analysis of the 2013/2014 NHANES phthalate data. Elissa Sterry started the meeting by announcing she would retire from Exxon Mobil Chemical Company April 1, 2017, and introduced Matthew Crocker as her replacement. Ms. Sterry has been involved with the phthalate issue for many years. She then introduced Dr. Jennifer Foreman who presented her conclusions about the NRDC Dust Study article. She stated that phthalates are expected to be found in dust and the environment, because they are used in a variety of consumer products. However, the levels of phthalates in dust are well below the conservative tolerable daily intake (assumes 100% bioavailability). Also the impact of phthalate exposure is already captured in human biomonitoring data so this article does not inform the CPSC phthalate rulemaking.**

**She then presented the Exxon Mobil Chemical Company's analysis of the 2013/2014 NHANES phthalate biomonitoring data. Arguments included: use of data at the 99$^{th}$% overestimates the risk and is not scientifically appropriate both mathematically and biologically; Individual HQs and HIs from NHANES data cannot be used to draw conclusions about the population; NHANES uses spot urine samples which are not representative of phthalate exposure over time; Case 2 should be disregarded because it derived PODs based on the POD established for DEHP, which are not further refined by experimentally derived NOAEL; Case 3 is the only approach that would support regulatory action because it is based on experimental data; cummulative risk assessment requires a common mechanism of action, specifically testosterone reduction; using a different approach to uncertainty analysis would lower the risk from DINP; margin of exposure for DINP is in the range that the CHAP states is generally accepted as safe; contribution of toys to cummulative risk at the 95$^{th}$% is negligible; increased use of DINP to replace the use of other low molecular weight phthalates would further reduce the risk from phthalates, because DINP would be replacing more potent phthalates.**

**She argued that human risk from phthalates is lower than that estimated using rodent studies, citing a recent Earl Gray study showing a 70% reduction in testosterone is needed before adverse effectes on male reproductive organs are observed; the phthalate cummulative risk assessment is the first time this has been used for an industrial chemical; a 2014 Spade paper on DBP exposure shows human testes are not affected the same as are rodents.**

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March 21st, 2017

# CPSC Science Staff

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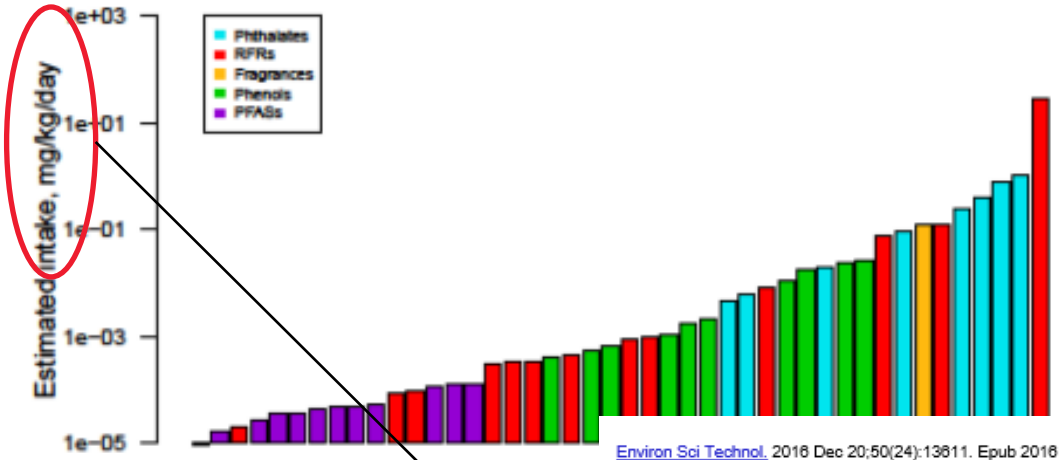
# NRDC Dust Study

# The units for the estimated intake levels reported in the publication were updated in a correction

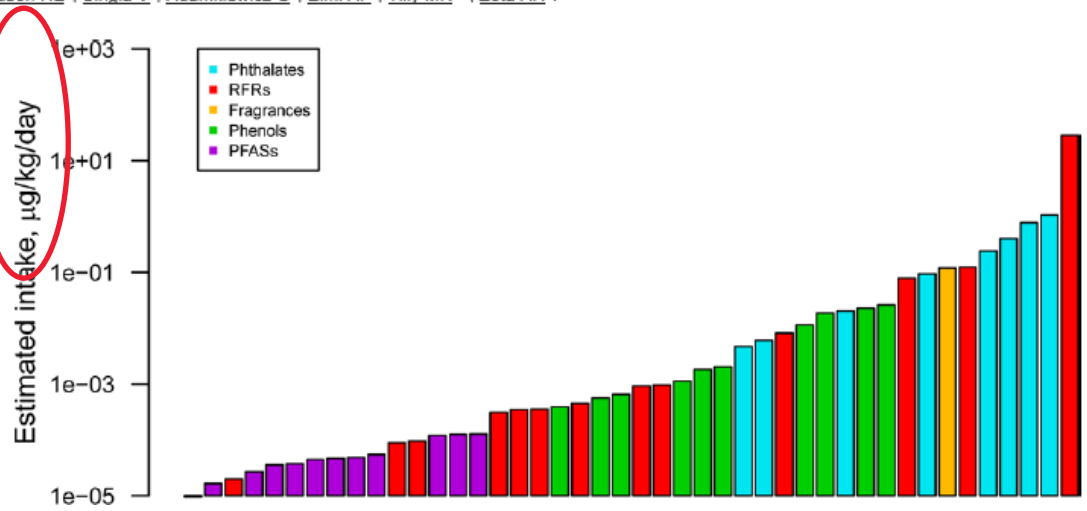



Difference in intake is 3 orders of magnitude.

Environ Sci Technol. 2016 Dec 20;50(24):13611. Epub 2016 Nov 29.

**Correction to Consumer Product Chemicals in Indoor Dust: A Quantitative Meta-Analysis of U.S. Studies.**

Mitro SD[1], Dodson RE[2], Singla V[3], Adamkiewicz G[4], Elmi AF[1], Tilly MK[3,5], Zota AR[1].

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# Soil screen levels are not an appropriate comparator for dust risk conclusions

- Soil screening levels are estimated using extremely conservative approaches
  - EPA recognized soil and dust are not equivalent
- Conclusions based on soil screening levels are not appropriate for dust

Volume for equivalent mass

$$\text{Screening Level (mg/kg)} = \frac{THQ \times BW \times AT \times 365\,d/yr}{(EF \times ED \times 10^{-6}\,kg/mg)\left[\left(\frac{1}{RfD_o} \times IR\right) + \left(\frac{1}{RfD_{ABS}} \times AF \times ABS_d \times EV \times SA\right)\right]}$$

From EPA RAGS document, 1996

**Table 5-1. Recommended Values for Daily Soil, Dust, and Soil + Dust Ingestion (mg/day)**

| Age Group | Soil[a] | | | | Dust[b] | | Soil + Dust | |
|---|---|---|---|---|---|---|---|---|
| | | High End | | | | | | |
| | General Population Central Tendency[c] | General Population Upper Percentile[d] | Soil-Pica[e] | Geophagy[f] | General Population Central Tendency[g] | General Population Upper Percentile[h] | General Population Central Tendency[c] | General Population Upper Percentile[h] |
| 6 weeks to <1 year | 30 | | | | 30 | | 60 | |
| 1 to <6 years | 50 | | 1,000 | 50,000 | 60 | | 100[i] | |
| 3 to <6 years | | 200 | | | | 100 | | 200 |
| 6 to <21 years | 50 | | 1,000 | 50,000 | 60 | | 100[i] | |
| Adult | 20[j] | | | 50,000 | 30[j] | | 50 | |

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# Implications of analysis of chemicals in indoor dust

- Impact of this paper on phthalate assessments for CPSC rule makings should be negligible. Does not add additional information as exposure from dust is already incorporated into biomontoring data
  - Biomontoring data accounts for bioavailability of substances and aggregate exposures

# Estimated Phthalate Exposure and Risk to Women of Reproductive Age as Assessed Using 2013/2014 NHANES Biomonitoring Data

# Some concepts brought forward from the CHAP should be amended

"CPSC staff's risk analysis demonstrates that a number of women of reproductive age (WORA; ages 15-45 years) had phthalate hazard quotients (DEHP and DINP) and hazard indices that exceeded one in the 2013/2014 National Health and Nutrition Examination Survey (NHANES) data set. As many as one percent of WORA exceeded an HQ or HI of one. These estimates, however, are statistically unstable, meaning that there are too few cases used as the basis of this estimate to be confident in their magnitude." (Page ii CPSC 2017)

- Data from NHANES cannot be used to derive individual risk.

- Risk estimates from Case 2 are scientifically inappropriate and should be discarded.

Spot samples cannot be used to determine individual risk

# Identification of individual risk is inappropriate

| Table 6. Estimated Percentage of Women of Reproductive Age with Hazard Index >1 by PEAA (NHANES 2013/2014) | |
|---|---|
| PEAA Case | 2013-2014 |
| Case 1 | <1%* |
| ~~Case 2~~ | ~~1.2%*~~ |
| Case 3 | <1%* |
| 1% = 604,000 | |
| *Marked estimates have a coefficient of variance that is considered high; these estimates are not considered stable. | |

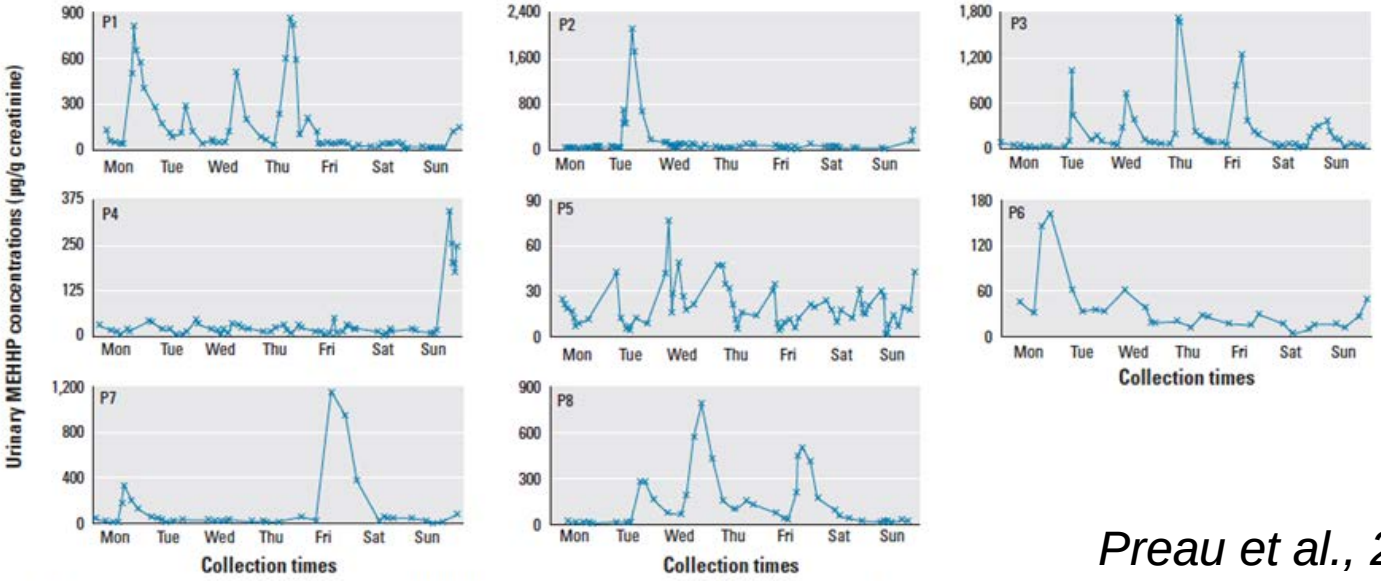
Not at risk

- NHANES dataset is developed with spot samples. They represent the variability of exposure in the population. Limitations for short lived chemicals with large intra-individual variability are such that they are inappropriate for use to determine individual risk. With a large enough sample size, only population risk can be estimated.

- An HI value for each subject can be generated, however it is not biologically representative of subject's risk level.

# Levels of phthalates in the urine fluctuate throughout the day

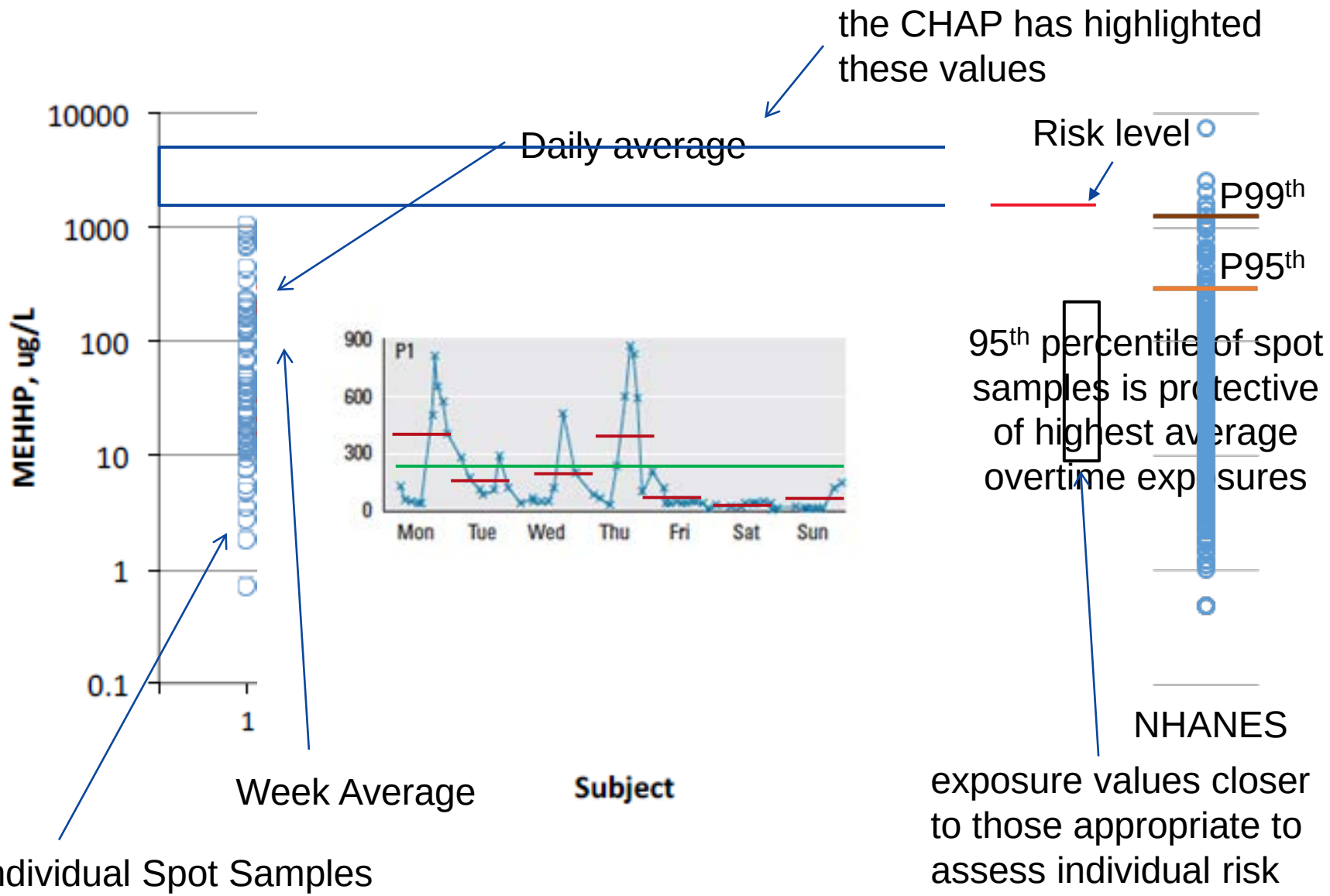
- Internal concentrations vary due to rapid clearance of phthalates
- The 95$^{th}$ percentile of spot urine samples likely overestimates the upper percentiles of multiday average concentrations among individuals (and therefore longer-term average intake rates) for most transient analytes (Aylward *et al*. 2016)
- The data are appropriate for population based estimates only




*Preau et al., 2010*

ExxonMo Figure 2. Creatinine-corrected concentrations of MEHHP (µg/g creatinine) for all study participants (P1–P8) during 1 week.

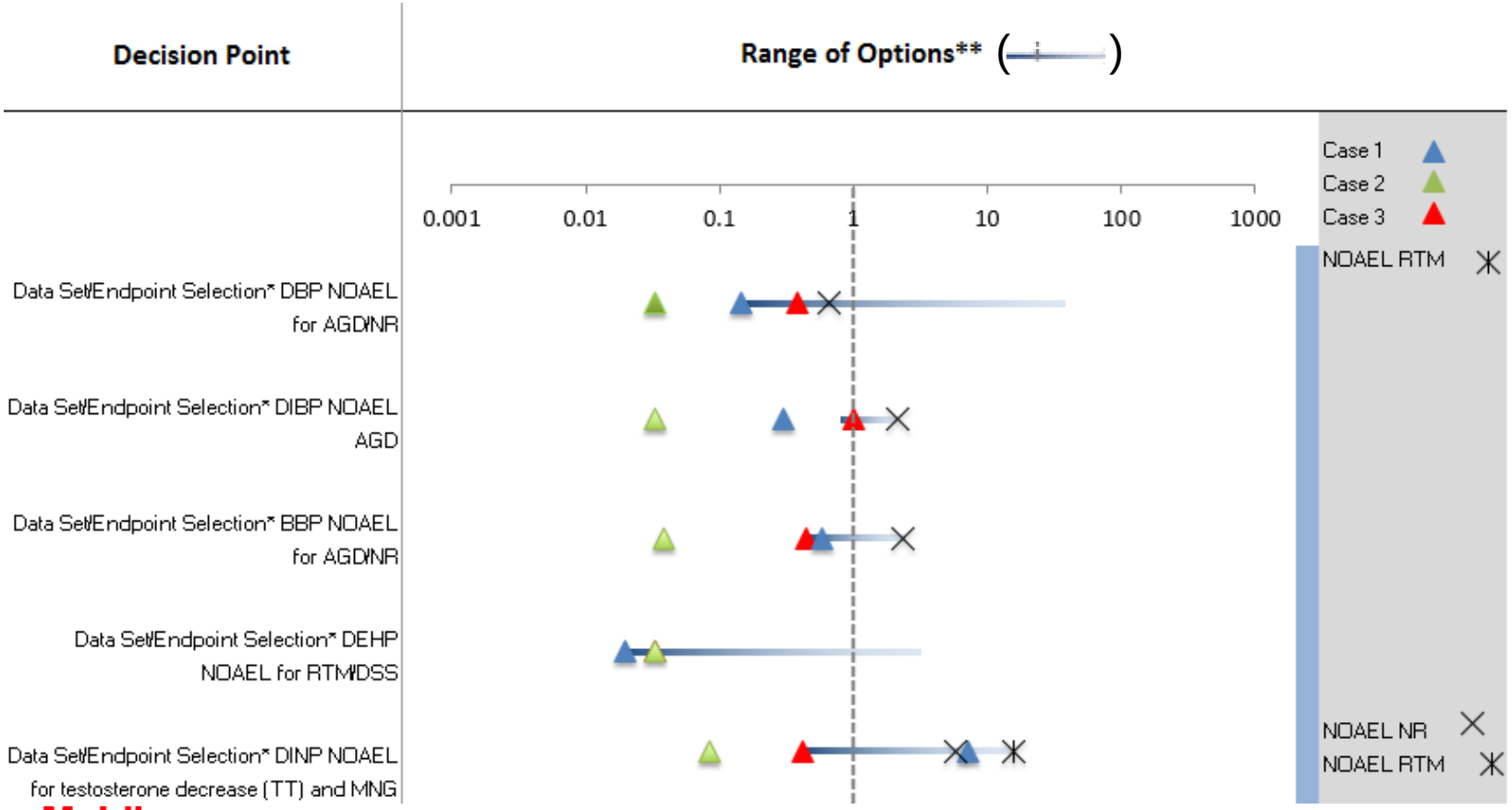
# A single spot sample is not representative of an individuals exposure over time



Case 2 is scientifically inappropriate for regulatory decision making

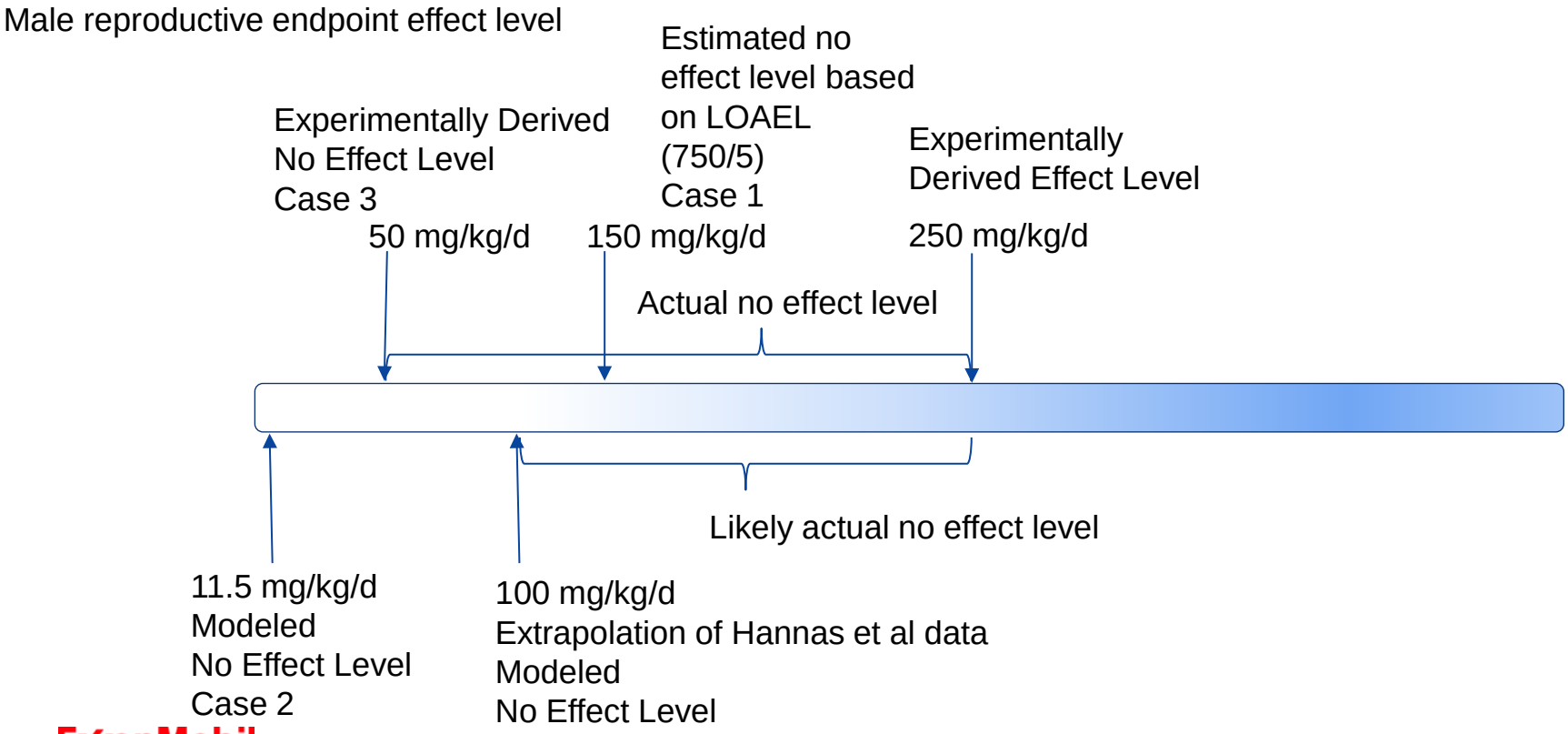
# Estimates for Case 2 fall outside the observable range

- Case 2 is modeled based on DEHP data and approximations based on *ex vivo* potency estimates (Hannas et al). Case 2 NOAELs are not supported by *in vivo* test data.



# Risk levels developed with Case 2 values fail a reality check

- In-vivo data suggests actual no effect level between 50 and 250 mg/kg/d
- CHAP modeled no effect level from modeled ex-vivo data 100 mg/kg/d
- Case 2 point of departure for DINP of 11.2 mg/kg/day has no basis in the toxicological data set: every indication points to an effect level greater than 50 mg/kg/d



2013/2014 NHANES analysis reconfirms no cumulative risk concern

# Calculation for Daily Intake (DI) should be updated

$$DI(\mu g/kg_{bw}/day) = \frac{UE_{sum}(\mu mole/g_{crt}) \times CE(mg_{crt}/kg/day)}{F_{UE} \times (1000 mg_{crt}/g_{crt})} \times MW_{parent}(g/mole)$$

Metabolites used is indicated in Table D1

- DIBP – MIBP
- DBP – MBP
- BBP – MBZP
- DEHP – SUM (MEHP, MEHHP, MEOHP, & MECPP)
- DINP – cx-MINP (MCOP)

Metabolites using all available

- DIBP – MIBP
- DBP – MBP
- BBP – MBZP
- DEHP – SUM (MEHP, MEHHP, MEOHP, & MECPP)
- DINP – SUM (MCOP, & MINP)

# Using all metabolites to calculate DI for DINP decreases intake values ~17%

- Using all available metabolites for DI calculation gives slightly different , and likely more accurate, values

| DINP Daily Intake Estimates (ug/kg-d) for Women of Reproductive Age (NHANES 2013/2014) | | |
|---|---|---|
| CPSC Staff* – CHAP method | EMBSI** – CHAP method | EMBSI** – All metabolites |
| Median | | |
| 4.97 | 4.67 | 3.9 |
| 95$^{th}$ Percentile | | |
| 53.19 | 53.72 | 44.33 |

*Data extracted from Table 2, N = 538 nonpregenant WoRA
**N=563, did not exclude pregnant WoRA

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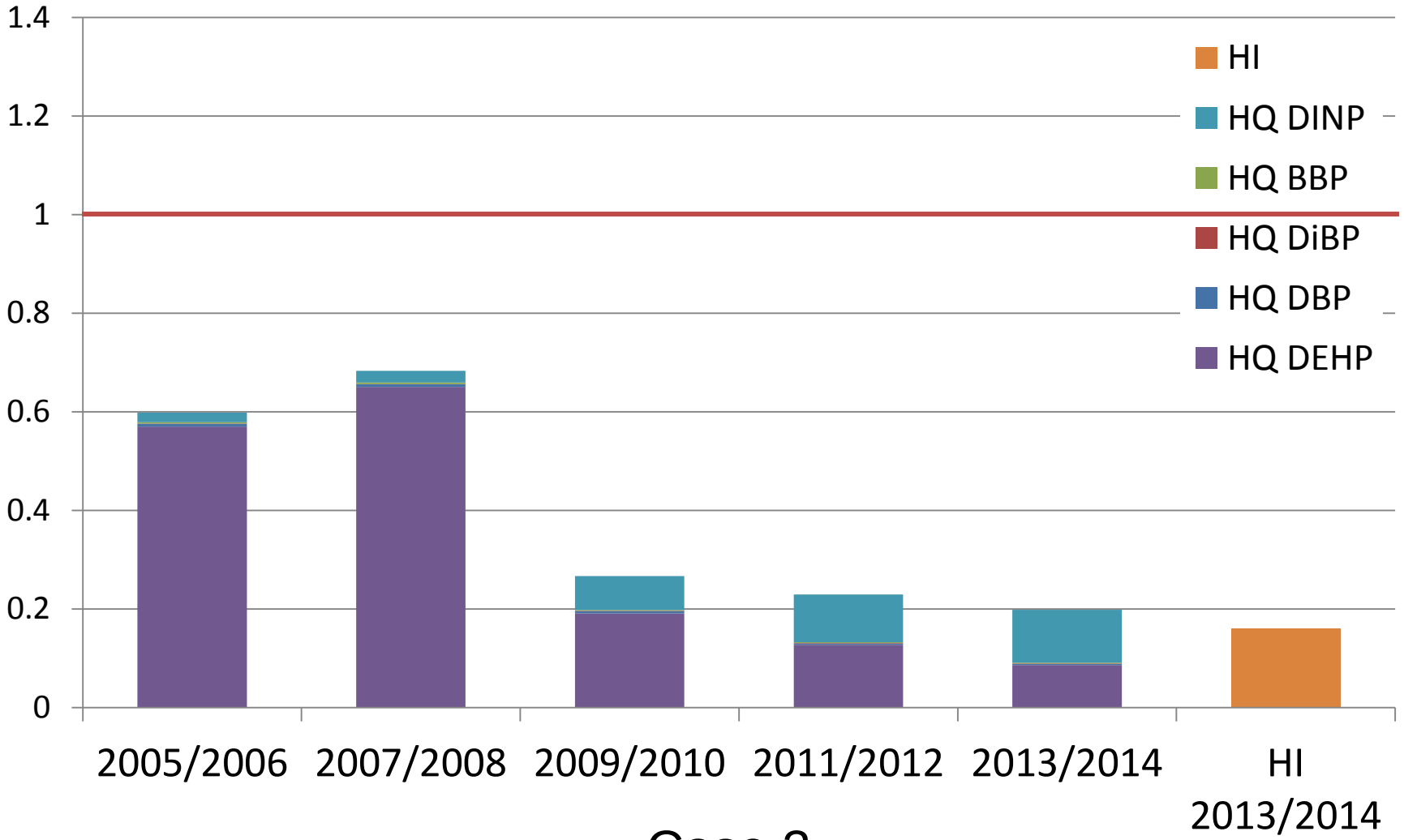
# 2013/2014 data confirms there is no cumulative risk concern

| Table 5. Hazard Index Estimates for Women of Reproductive Age (NHANES 2013/2014) | | | |
|---|---|---|---|
| Percentile | PEAA Case | Hazard Indices | EMBSI HI's |
| Median | Case 1 | 0.057 | 0.06 |
| | ~~Case 2~~ | ~~0.102~~ | ~~0.09~~ |
| | Case 3 | 0.044 | 0.04 |
| 95th Percentile | Case 1 | 0.171 | 0.17 |
| | ~~Case 2~~ | ~~0.587~~ | ~~0.50~~ |
| | Case 3 | 0.180 | 0.16 |

# At the 95th Percentile, there is No Risk – All Below 1




Case 3

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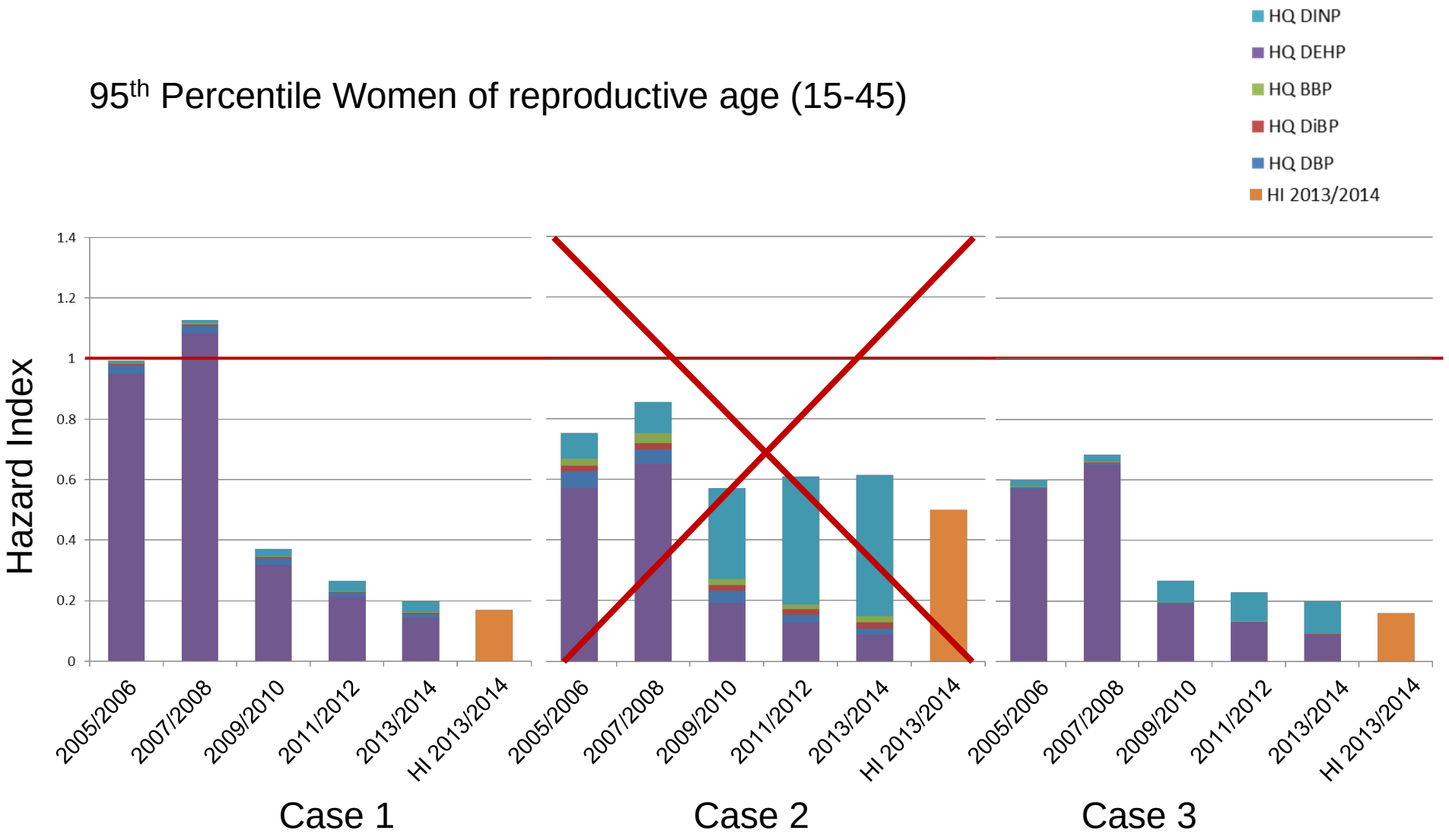
# 95th Percentile Women of reproductive age (15-45)



# No individual risk for DINP

# 2013/2014 Reanalysis highlights “HQ>1” by Phthalate

| Table 4. Estimated Percentage of Women of Reproductive Age with Hazard Quotient >1 by Phthalate and PEAA (NHANES 2013/2014) | | |
|---|---|---|
| Phthalate | PEAA Case | 2013-2014 |
| DEHP | Case 1 | <1%* |
| | Case 2 | <1%* |
| | Case 3 | <1%* |
| DINP | Case 1 | --* |
| | ~~Case 2~~ | ~~<1%*~~ |
| | Case 3 | --* |
| 1% = 604,000 | | |
| *Marked estimates have a coefficient of variance that is considered high; these estimates are not considered stable. | | |

# Conservative CHAP methodology for determining individual risk

- Margin of Exposure (MoE) Example DIDP (pg 104 CPSC 2014):
  - Used median and 95th percentile exposure values compared to selected Point of Departure to make determination of individual safety

| DIDP – Example | DINP – CHAP Method | DINP – All Metabolites |
|---|---|---|
| CHAP selected Point of Departure (mg/kg/d) | | |
| 15 | 50 | 50 |
| | Median MoE | |
| 2,500 - 10,000 | 10,000 – 11,500 | 12,000 - 13,700 |
| | 95th MoE | |
| 586 - 3,300 | 800 - 1,100 | 1,000-1,300 |

- CHAP states Margins of Exposure from 100-1,000 are generally accepted as safe

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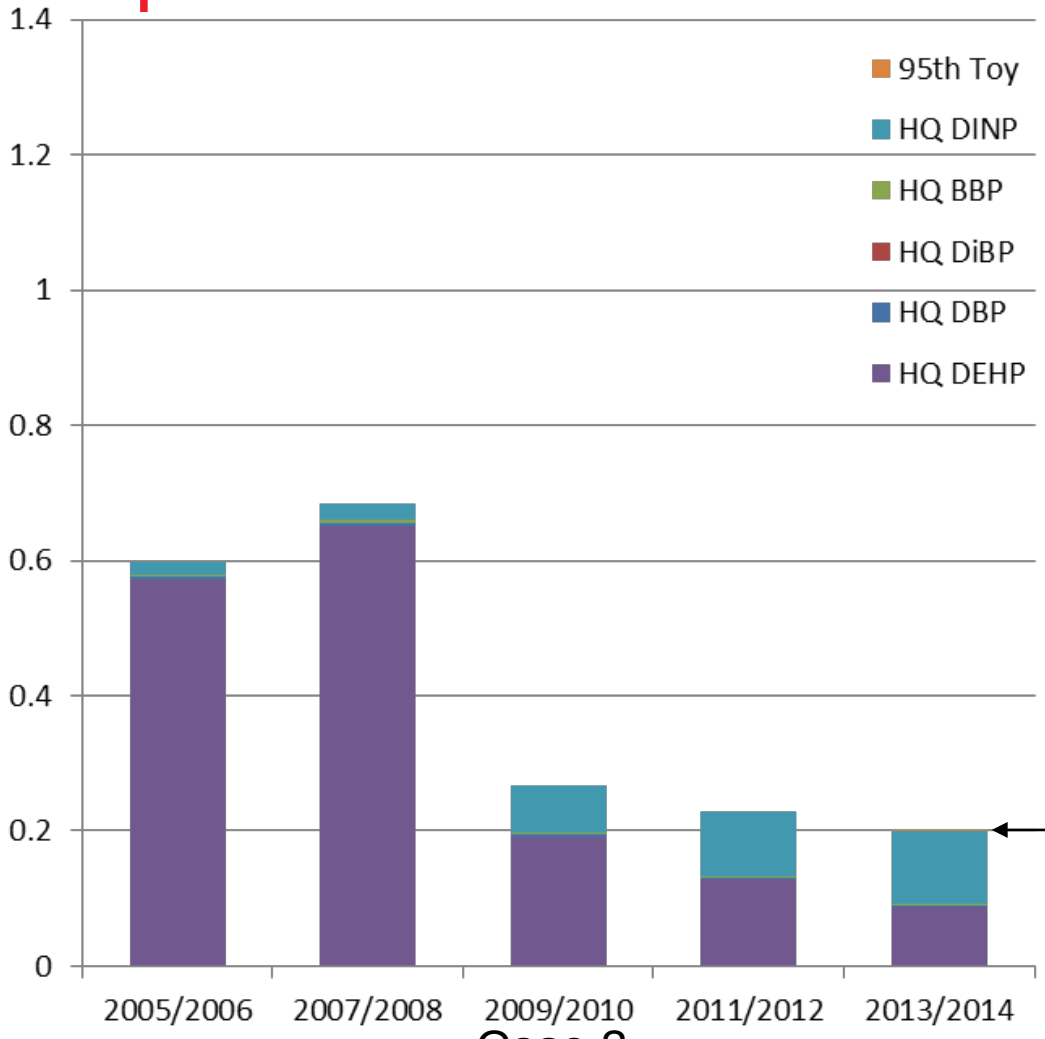
*MoE rounded to the nearest hundred

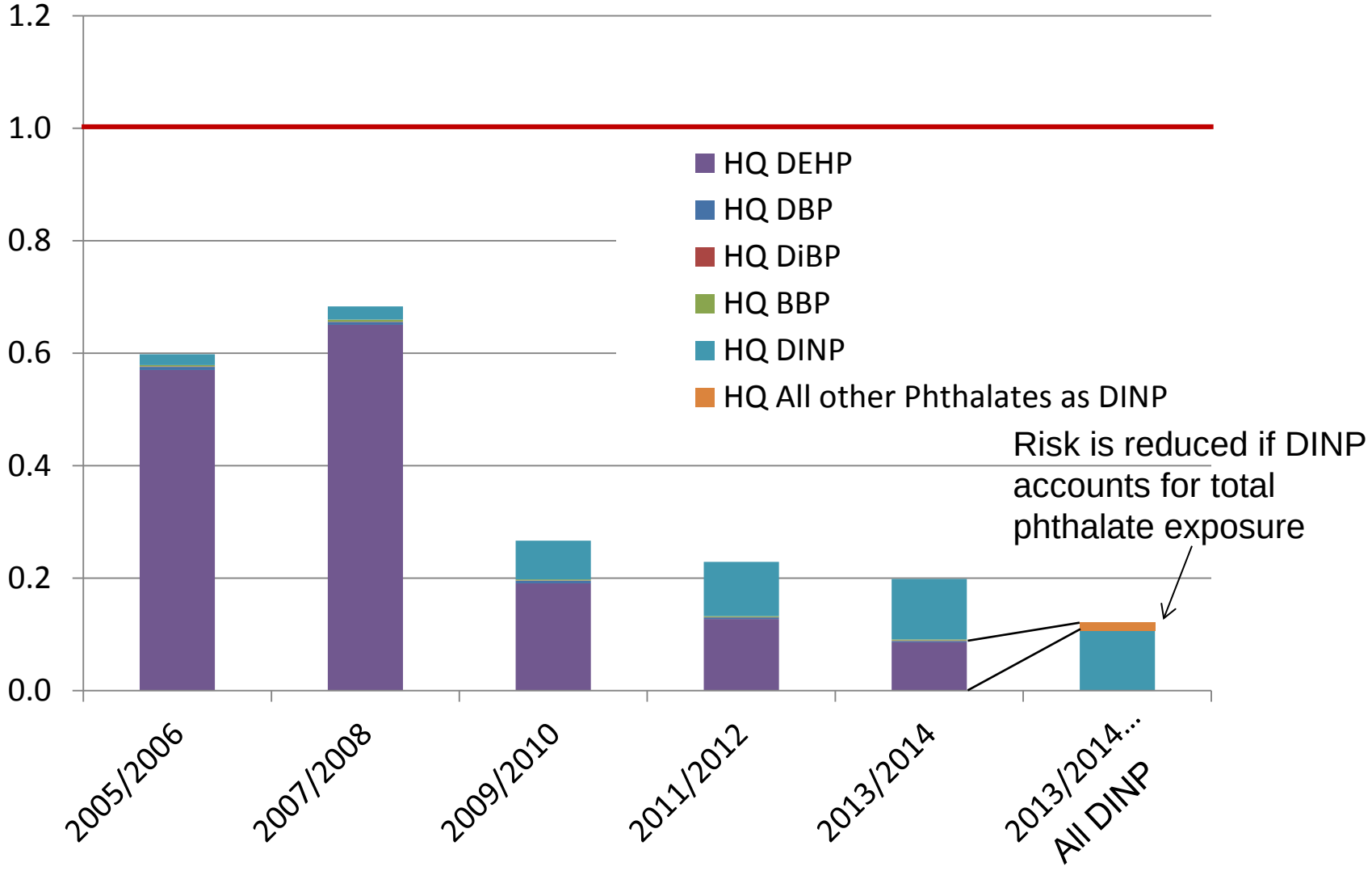
# Including the 95th percentile estimate of exposure to DINP in toys to women has a negligible impact on risk




Impact of exposure from toys (orange)

Case 3

# Further replacement of LMW phthalates by DINP will continue to decrease risk



# Strong Scientific Support to Meet Standard of Reasonable Certainty of No Harm for DINP

- Individual MoE's for DINP ≥ 1,000
- CRA have HI's < 1 in all Cases
- Further increase in DINP would likely mean further risk reduction as it would replace higher hazard LMW phthalates
- Additional exposure from DINP in toys has negligible impact on risk
- The most appropriate Case study for regulatory decision making is Case 3

# Additional Topics

- Data on sensitivity in humans indicate human risk is lower than that calculated
- Points of departure are inconsistent with basis for the cumulative risk assessment
  - Common MOA (testosterone reduction) provides the biological basis for the cumulative risk approach
  - Selected points of departure are lower than identified NOELs for testosterone reduction
- Uncertainty Analysis indicates actual risks likely lower