Analysis of the Report to the US CPSC by the CHAP on phthalates and phthalate alternatives

July 2014

http://www.cpsc.gov/PageFiles/169902/CHAP-REPORT-With-Appendices.pdf

Introductory comments

- CHAP Confirms DINP & DIDP are Safe
  - Recommends lifting interim restriction on DIDP
  - Individually, found DINP safe too
- Precedent Setting Cumulative Risk Assessment (CRA) Applied
  - No regulatory body in the world uses this CRA approach
  - US EPA is developing its approach – data call-in mid-2013 – policy not yet developed
- Highly Flawed Cumulative Risk Assessment Methodology
  - Major data errors and data selection throughout the report
- Used Outdated Exposure Data – new data show no risk
  - CHAP applied 2005/2006 NHANES Data rather than more recent, readily available data
- Cumulative Effect Demonstrates DEHP/DBP are the Drivers, not DINP
  - Appropriately applied CRA methodology would focus on the drivers, not a minute contributor
- CHAP Failed to Robustly Assess Alternative Plasticizers

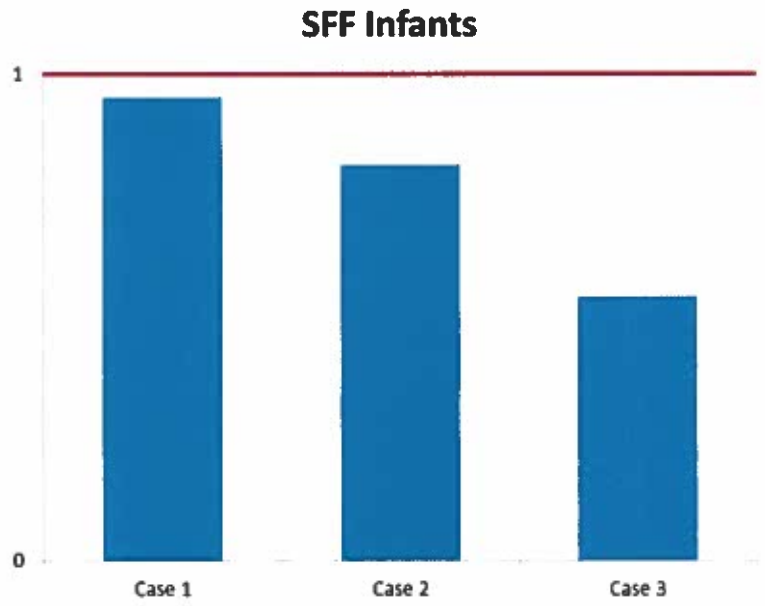
Analysis Overview

- Report conclusions
  - DINP and DIDP safe in current applications
  - Cumulative assessment for children indicates no cumulative risk
- CRA is superficial and dangerously precedent setting
  - Screening assessment of cumulative risk
  - Inappropriately conservative in approach
  - Demonstrates DEHP is major contributor to cumulative risk
  - DINP contribution within safe limits
  - Conclusions and recommendations for risk management inappropriate based on the evidence
- Newer biomonitoring data demonstrates reduced overall risk
- Report quality

CHAP Report Conclusions

- DINP and DIDP present no risk to infants and children through exposure to toys and child care articles
  - Conclusion in line with previous CHAP report (2001)
  - Different health endpoint in focus in 2014 but same conclusion (no risk)
- DINP urinary metabolite data for young children were taken from SFF study
  - Not peer reviewed (data submitted directly to CHAP)
  - Estimated exposures are higher than those from other investigators
  - Use of unpublished, unviewed, information here is concerning as the estimated exposures relate directly to the CHAPs recommendation on DINP

- CRA of population of concern (infants and children) to DINP and four other phthalates from all sources indicates no risk
  - Hazard indices of combined exposure were all under 1, indicating no combined risk
  - Cumulative risk assessment driven by DEHP component



Cumulative Risk Assessment (CRA) Conduct

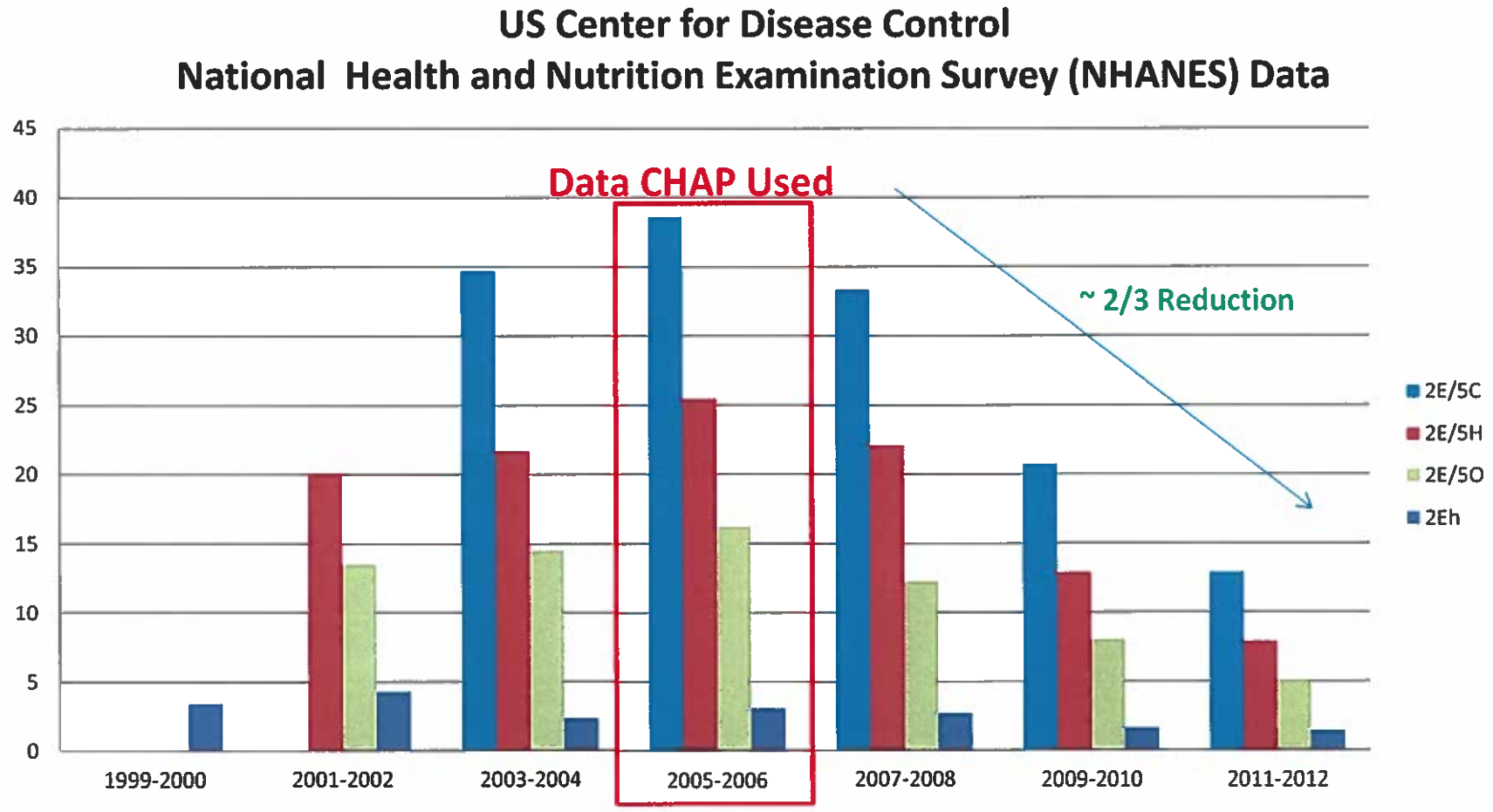
- Dangerously precedent setting use of this CRA approach in risk management
- CRA is overly simplistic and refrains from using recent advances and frameworks
- CHAP CRA is a preliminary screening level assessment
  - Only addresses whether a cumulative risk could exist from exposure to phthalates
  - This approach is a means to determine if further steps are needed
  - Multiple frameworks (i.e. WHO) exist to determine next steps, but were not used by the CHAP
- CHAP CRA is ultra-conservative in determination of risk and estimates of both hazard and exposure
- CHAP estimates of cumulative risk for phthalates differ from estimates derived by other researchers
- DEHP drives cumulative risk from phthalates

If the CHAP had used the best available CDC NHANES data, the CRA would show no risk

Newer Biomonitoring Data

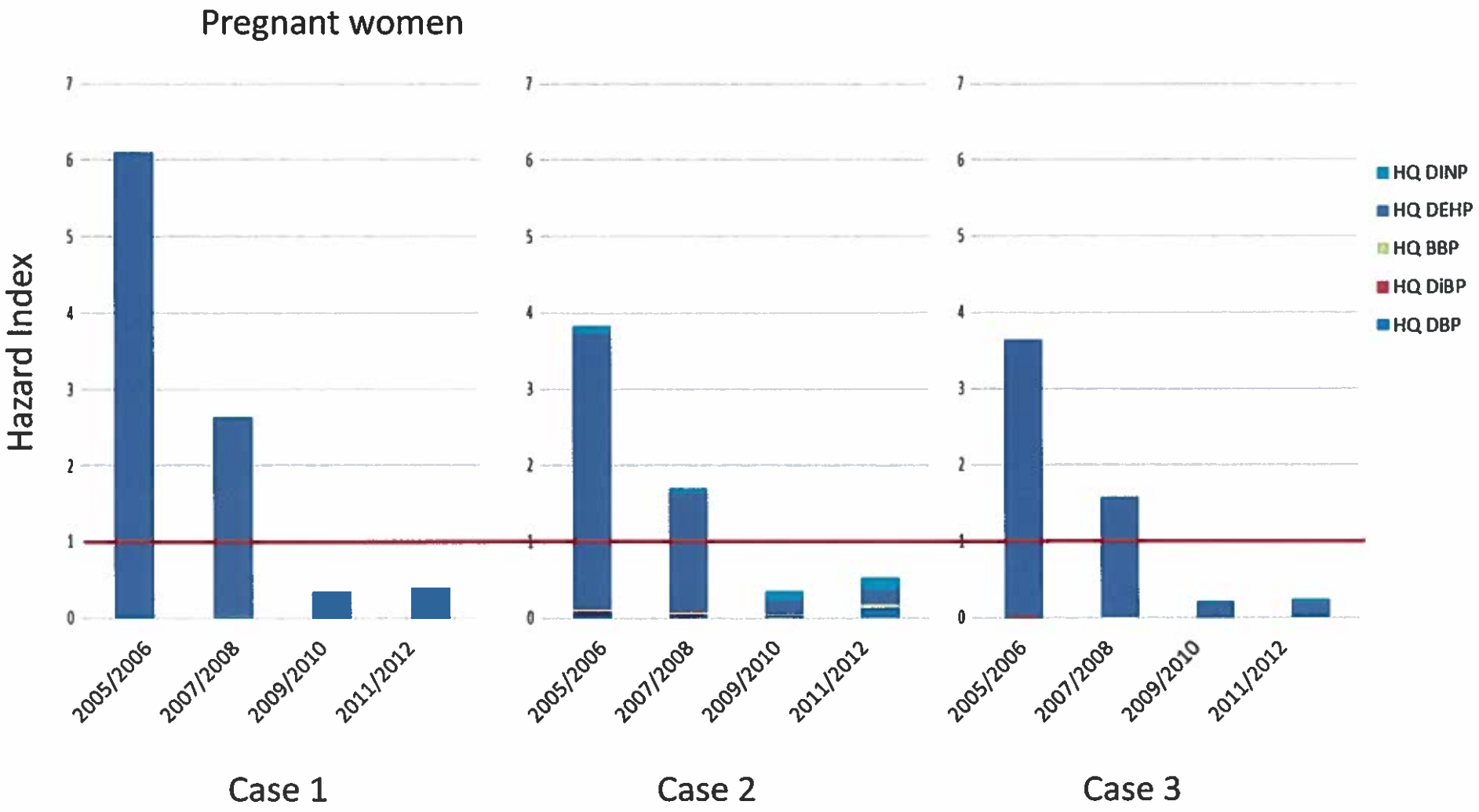
- CHAP chose the NHANES data set from 2005/2006 to conduct assessment
  - Exception is use of SFF biomonitoring data for young children
- Newer NHANES data set were available to the CHAP (2007-'08; 2009 –'10) and additional data set exists (2011- '12)
- Utilizing newer data with CHAP conservative methods and parameters indicates no population-based risk for either women of reproductive age or pregnant women
- Cumulative risk primarily driven by DEHP Hazard Indices (HI)
  - <1 for both pregnant women in 2009 –'10 and 2011- '12 data sets;
  - reduction in risk observed between 2005-'06 and 2007-'08 data sets (HI << below 1)
- HI is at or below 1 for women of reproductive age in all NHANES data sets
- DINP contribution to cumulative risk is less than DEHP and within safe limits

Ignored Significant Downward Exposure Trend



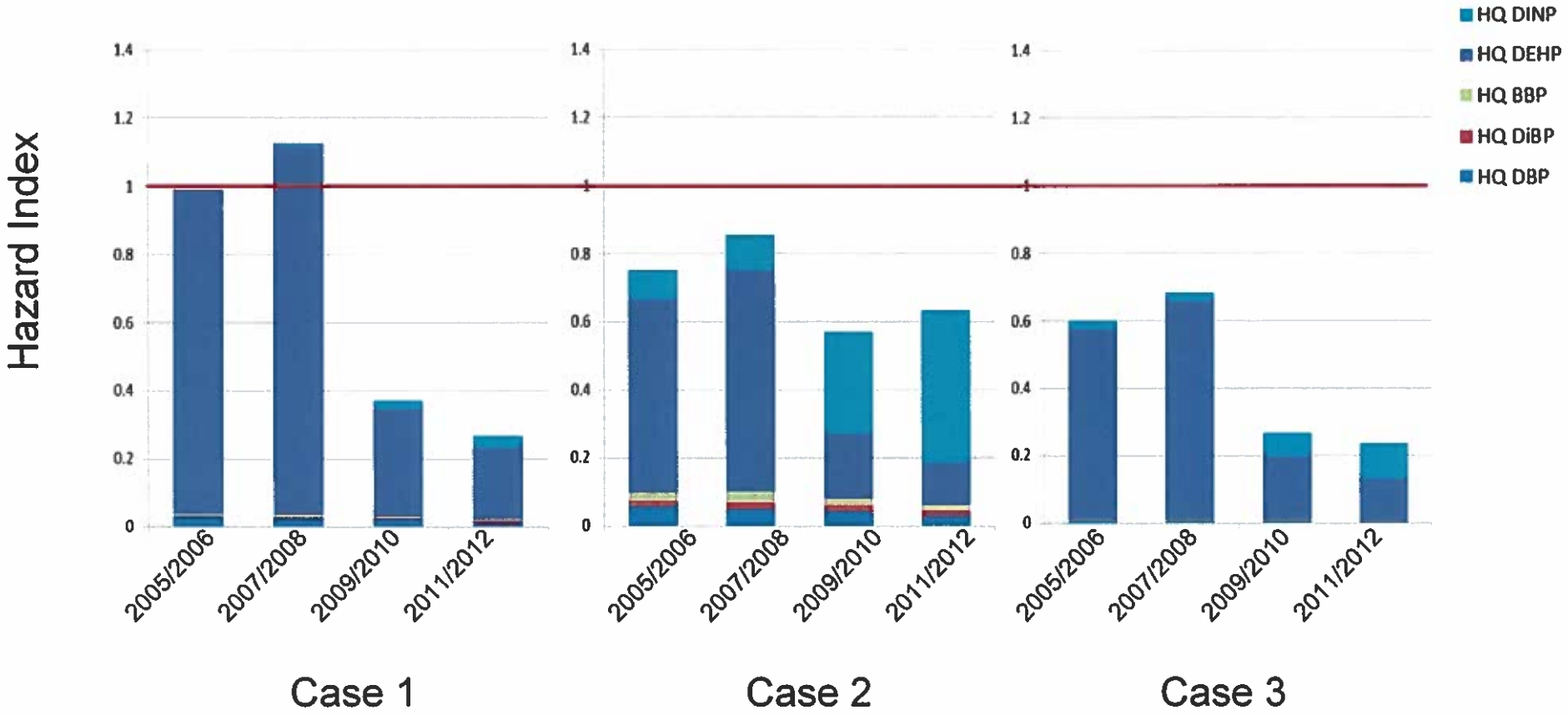
2005-2006 CDC NHANES data published February 2010
2007-2008 CDC NHANES data published October 2010
2009-2010 CDC NHANES data published September 2012
2011-2012 CDC NHANES data published November 2013

Evaluation of All NHANES Data Sets



Evaluation of All NHANES Data Sets

Women of reproductive age (15-45)



Report Quality

- Preliminary screening level CRA and does not meet the standards of a robust risk assessment
  - Not a systematic evaluation of available data
    - CHAP admits it did not conduct a systematic review
    - Conclusions mis-identified as following a "systematic evaluation"
  - No objective weight-of-the-evidence evaluation
  - Inadequate assessment of uncertainty and impact of uncertainty in overall conclusions/ recommendations

- Inconsistent in statements and conclusions
  - Lack of logic in continuing restriction of DINP
  - Uncertainty and inconsistency recognized in human effect data – but strong conclusions
  - Inconsistent with other major systematic reviews of human epidemiological data

- Inaccuracies and transcriptional errors in report content impact CHAP recommendations

Multiple flaws noted in peer reviewer comments but not addressed

Analytical Summary

- Report confirms safety of DINP and DIDP in toys and childcare articles
  - No risk to children
  - No cumulative risk for children

- CRA missed the mark
  - Superficial in its approach
  - Inappropriately conservative and at times erroneous
  - DEHP is major contributor to cumulative risk
  - Risk management recommendations for DINP are not appropriate based on this CRA

If the CHAP had used the best available CDC NHANES data, the CRA would show no risk

Concluding comments

- What the Commission must do now – as required by the Statute
  - Determine whether to continue the interim restriction on DINP
  - In addition to the CHAP report, draw on CPSC scientific staff and other more recent scientific input

- What the CHAP Report provides the Commission
  - Data demonstrating no significant risk from exposure to DINP or DIDP in toys and child care articles (indeed, in all consumer products)

- What the CHAP Report does not provide the Commission
  - A well-reasoned basis for its recommendation to continue the interim ban (which was not the recommendation it was to make)
    - Used a non-standard CRA methodology
    - Relied on non-peer-reviewed data
    - Ignored newer data that show no risk
    - Clear errors with some DINP data used for analysis
    - Indicates DEHP as the risk driver: but even if DINP replaced all DEHP, no cumulative risk under its approach
    - Any consideration of whether replacement of DINP by alternatives would reduce or increase risk to human health

Science supports that the CPSC promulgated rule should end the interim ban on DINP, DIDP and DnOP

Back up

DIDP conclusion

CHAP conclusions confirm the Margins of Exposure (MOEs) for DIDP are adequate i.e. no significant risk

> ***5.3.3.4.3 Risk***
>
> Based on the lowest POD (15 mg/kg-day) the MOEs range from 2500 to 10,000 for median intakes and from 586 to 3300 for 95th percentile intakes.

These DIDP MOE's (586-10,000) are comparable with those for DINP (640-68,000)

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DINP conclusion

CHAP conclusions confirm the Margins of Exposure (MOEs) for DINP are adequate i.e. no significant risk - including for anti-androgenicity (male developmental effects).

5.3.2.4.3 Risk

5.3.2.4.3.1 Male Developmental Effects

In infants in the SFF study, the MOE for total exposure ranged from 640 to 42,000 using 95th percentile estimates of exposure. For pregnant women, the MOE for total DINP exposure ranged from 1000 to 68,000. Typically, MOEs exceeding 100–1000 are considered adequate for public health; however, the cumulative risk of DINP with other antiandrogens should also be considered.

5.3.2.4.3.2 Systemic Effects (Liver)

In infants in the SFF study, the estimated total DINP exposure ranged from 3.6 to 18.0 µg/kg-d (median and 95th percentile) (see Table 2.7). For women in NHANES (2005–2006), the estimated total exposure ranged from 1.0 to 9.4 µg/kg-d (Table 2.7). Using the NOAEL of 15 mg/kg-d for systemic toxicity, the MOE for infants ranged from 830 to 4,200. The MOE for women ranged from 1600 to 15,000. Typically, MOEs exceeding 100–1000 are considered adequate for public health.

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CRA conclusion

CHAP data confirm 95th percentile exposure data show HI below 1 for infants

Only 67/258 SFF infants had calculable DINP daily intake levels (Table 2.7)

Table D-9 Summary percentiles from the hazard index distributions using five phthalates for pregnant women and children from NHANES (2005–06) and from SFF (Sathyanarayana *et al.*, 2008a). The NHANES estimates infer to 5.1 million pregnant women in the United States.

Hazard Index	AA set		PEAA Case	Percentiles			
				Median	75th	95th	99th
Pregnant Women	NHANES		1	0.14	0.26	6.1	12.2
			2	0.13	0.23	3.7	7.4
			3	0.08	0.15	3.6	7.3
	SFF	Prenatal	1	0.11	0.19	0.57	2.39
		Postnatal		0.10	0.19	0.73	1.51
		Prenatal	2	0.10	0.16	0.41	1.54
		Postnatal		0.09	0.16	0.46	0.92
		Prenatal	3	0.06	0.11	0.33	1.40
		Postnatal		0.06	0.11	0.43	0.91
Infants	SFF Infants		1	0.22	0.40	0.95	3.71
			2	0.20	0.34	0.81	2.32
			3	0.12	0.22	0.54	2.21

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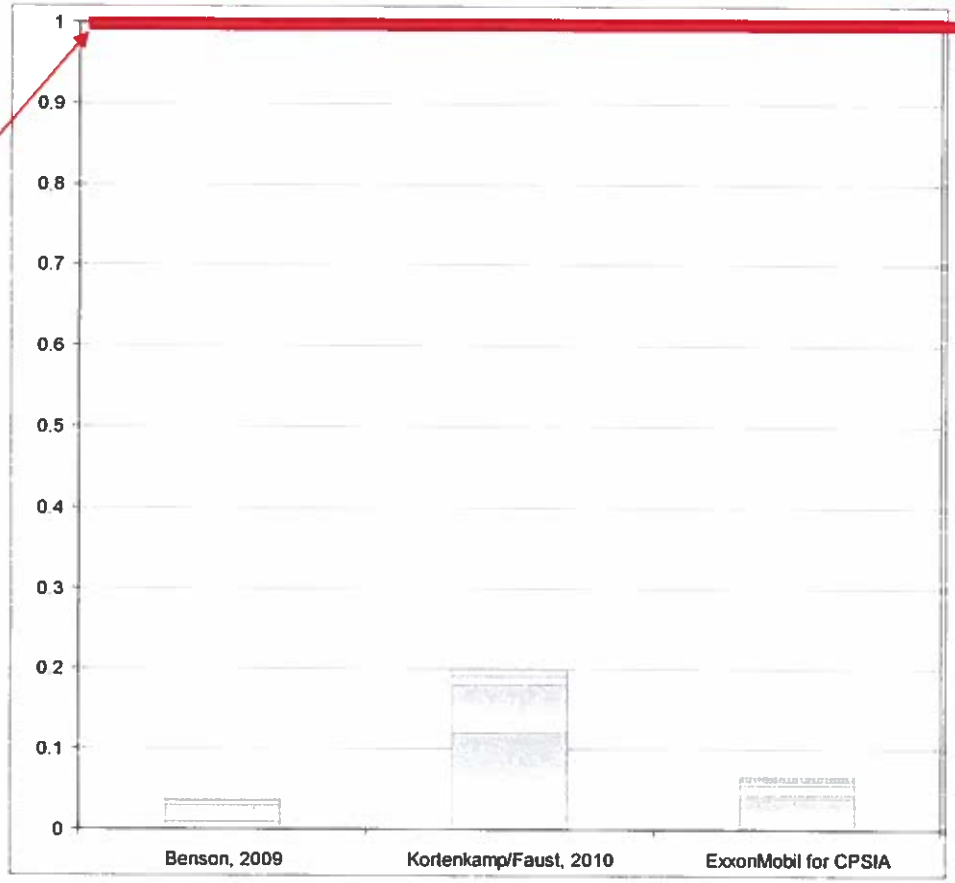
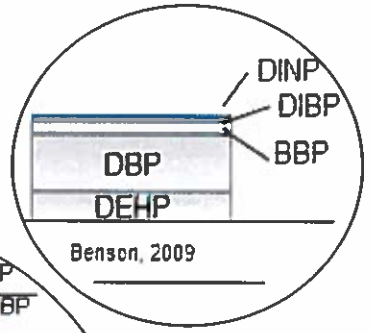
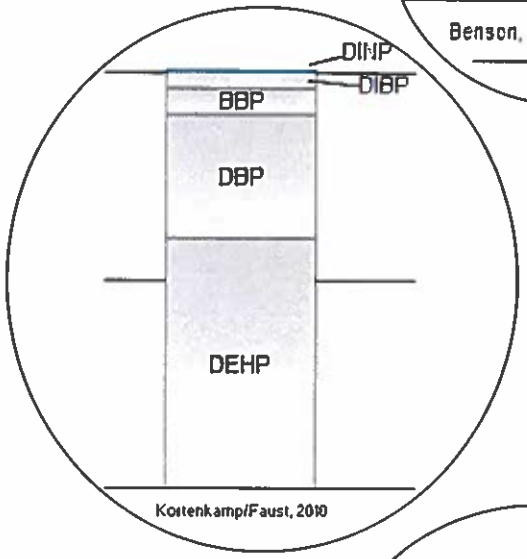
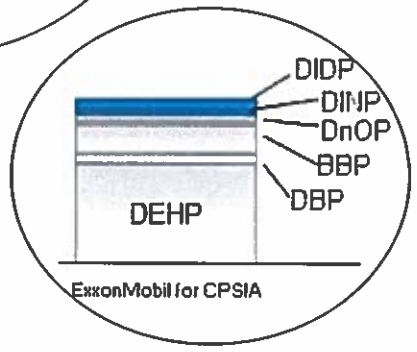
DINP and DIDP are Minor Contributors to Cumulative Risk









As the HI methodology likely overestimates risk, further efforts to develop a more complex assessment are not justified

[1]In addition to HI limitations, common toxic effect was broadly defined; calculation of point of departure (POD) was inconsistent
[2]In addition to HI limitations, common toxic effect was broadly defined; included additional chemicals other than above listed phthalates
[3]While not relevant to humans, increased liver weight and Palmitoyl CoA induction are the only common endpoints among LMW and HMW phthalates in CPSIA; therefore, was used by ExxonMobil to illustrate a conservative (overestimate of risk) screening for cumulative effect consideration; based on children's biomonitoring data