

Natural Resources Defense Council (NRDC) comments to CPSC CHAP

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Overview of comments

- Reasonable Certainty of No Harm
- PPAR- α and PPAR- γ
- Phthalates of concern
- Cumulative Risk assessment of phthalates



“Reasonable Certainty of No Harm”

- Defined the Food Quality Protection Act, 1996.
 - Amended how U.S. EPA evaluates and regulates pesticides.
- Establishes the standard of “safe” for tolerances for pesticide chemical residues in or on food.
- Intent of Congress was to apply a similar standard in phthalate provision of CSPIA



“Reasonable Certainty of No Harm”

- “safe” means there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue.
- “aggregate exposure” to the pesticide chemical residue to include dietary exposures under all tolerances for the pesticide chemical residue, and exposure from other non-occupational sources as well.
- Legislative History, p. 41-42, of FQPA in the Energy & Commerce Committee's report



“Reasonable Certainty of No Harm”

Non-threshold and threshold effects.

- “ if any increase in lifetime risk based on negligible.”
- “It is the Committee’s understanding that, under current EPA practice, utilizing quantitative risk assessment to calculate Potency Factors called “Q star”, **EPA interprets a negligible risk to be a one-in-a-million lifetime risk.**”



“Reasonable Certainty of No Harm”

- “Statutory language does not preclude EPA from changing its risk assessment methodology as the science of risk assessment evolves”
“should be at least equally protective of public health”
- Sets a high bar for confidence that exposure will be “safe” in all populations
- Considers exposures from multiple sources



Peroxisome proliferation PPAR α

- Hypothesized that there is no single hallmark event but a combination of the molecular signals and multiple pathways, contribute to the formation of tumors. (Rusyn, 2006 and Guyton, 2009)
- IARC is re-evaluating DEHP, based on evidence of PPAR- α independent carcinogenesis



Recent NAS comments

PPAR- α

- **There is evidence that the hepatic, testicular, and pancreatic cancers associated with phthalate exposures “may be mediated by mechanisms independent of PPAR α ”** [Phthalates and Cumulative Risk Assessment, 2008]
- **Ito et al. (2007a) “calls into question” conclusions regarding DEHP’s carcinogenic risk to humans** [Science and Decisions, 2009]
- **“Important knowledge gaps remain to be addressed... the committee is not yet convinced of the proof of the hypothesis that the PPAR α MOA is the sole MOA... premature to draw definitive conclusions regarding the relevance of the PPAR α MOA to human hepatocarcinogenesis”** [Tetrachloroethylene, 2010]



Phthalates and Liver Toxicity

- Non-human primate studies have found persistent changes in liver histology with IV dosing of DEHP (Kevy, S.V., Jacobson, M.S., 1982)
- Cholestasis and hepatoblastoma in infants has been associated with DEHP exposure from medical devices in NICU (von Rettberg, 2009 and Latini, 2010)



Peroxisome proliferation

PPAR γ

- PPAR- γ - adipogenesis and adipocyte differentiation
- Endocrine disruptors – tributyl tins increase fat mass in rodent students. (Grun, 2006)
- Single or perhaps episodic exposure - permanent changes in adipocyte differentiation and increased cell number (Grun, 2006)
- Phthalates activators of PPAR γ



Links to obesity and metabolic syndrome

- Phthalate metabolites BBzP and DEHP correlated with increased waist circumference in men.
(Stahlhut, 2007)
- Metabolites DBP, DEP, and BBzP were also associated with measures of insulin resistance



Other Phthalates of Concern

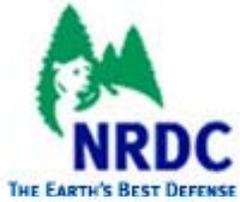
- Di-isobutyl phthalate (DiBP)
- Di-n-hexyl phthalate (DnHP)
- Di-isoheptyl phthalate
- Di-pentyl phthalate (DPP)
- Dicyclohexyl phthalate (DcHP)
- Di-isoheptyl phthalate

Air freshener testing – 2007

- 14 air freshener products tested
 - 8 aerosol sprays;
 - 5 continuously-emitting liquids;
 - 1 solid

- 12 found to contain phthalates
 - None were labeled
 - “unscented” and “all natural” products





NRDC Air freshener testing

- Concentrations ranged from 0.1 - 7,300 ppm
- Three samples >100 parts per million (ppm)
- Over half samples > 2 phthalates
- Major phthalates found were DBP, DEP, di-isobutyl phthalate (DIBP), and di-methyl phthalate (DMP)
- Di-isoheptyl phthalate (DIHP) was also found in a single sample

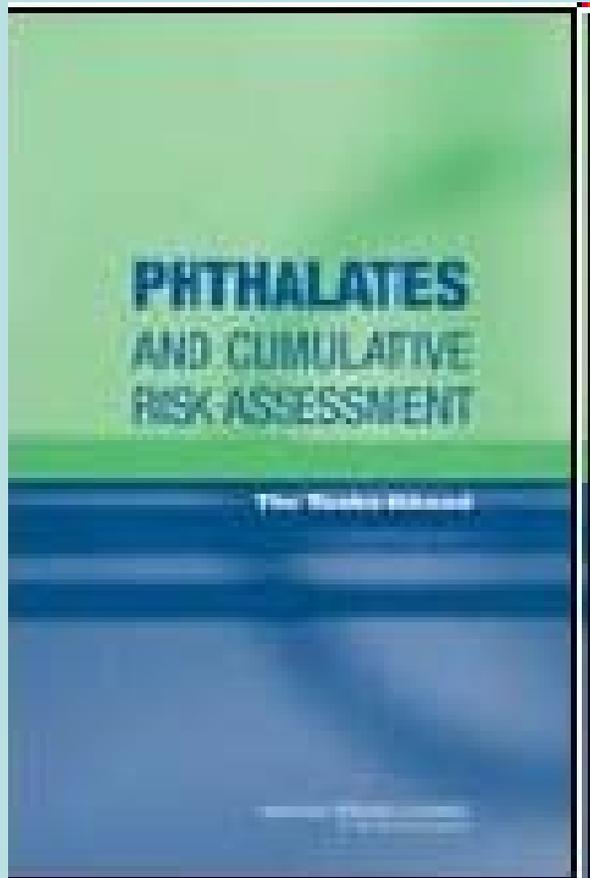


Sources of Exposure

- Toys
- Fragrances and Cosmetics
- Building materials
- Food and food packaging
- Automobile interiors
- Artificial leather
- Printing inks, paints and adhesives
- Shower curtains
- Garden hoses
- Medical Devices and Pharmaceuticals



NAS Report: Phthalates and Cumulative Risk assessment 2008



Conclusions:

Cumulative risk assessment based on common adverse outcomes is a feasible and physiologically relevant approach to the evaluation of the multiplicity of human exposures and directly reflects EPA's mission to protect public health.



Conclusions

- Congress has set a high bar for confidence in conclusions of safety.
- Important that CHAP fully consider the range of endpoint associated with phthalate exposure – liver toxicity, female reproductive effects, breast tissue, adipogenesis and metabolism
- Consider aggregate and cumulative exposures
- Sensitivity of vulnerable populations