Natural Resources Defense Council (NRDC) comments to CPSC CHAP

Sarah Janssen, MD, PhD, MPH
Senior Scientist
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email: sjanssen@nrdc.org

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 quantitative risk assessment using conservative assumptions, will be no greater than '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 PPARα"** [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 PPARα MOA is the sole MOA… premature to draw definitive conclusions regarding the relevance of the PPARα 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-isohexyl 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

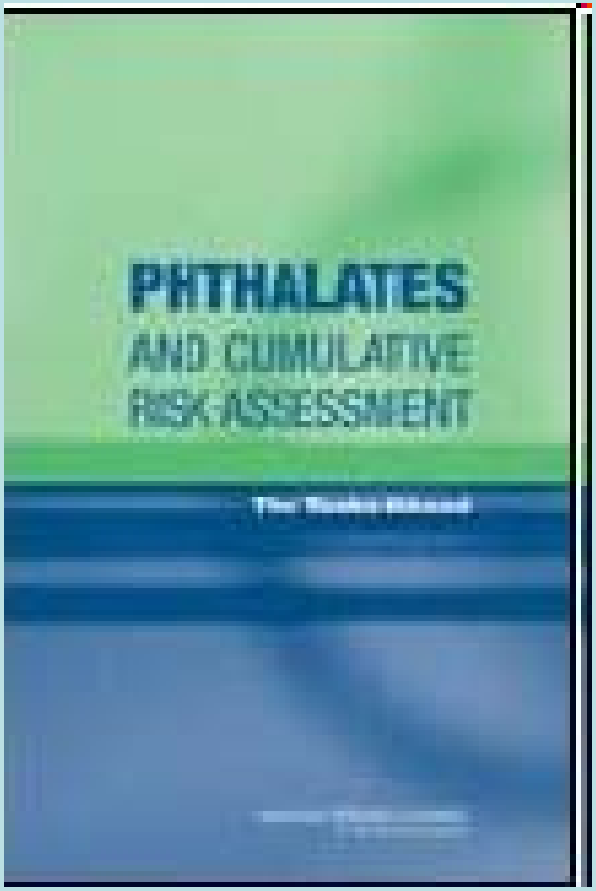
NRDC Air freshener testing

- 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-isohexyl 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