NATURAL RESOURCES DEFENSE COUNCIL

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Proposition 65 Implementation
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Submitted via email: coshita@oehha.ca.gov

Re: Prioritization of Chemicals for Carcinogen Identification Committee Review: Proposed Chemicals for Committee Consideration and Consultation.

Dear Members of the Carcinogen Identification Committee,

The following comments are submitted on behalf of the Natural Resources Defense Council (NRDC), a non-profit organization with over 1.2 million members and activists, 250,000 of whom are Californians. NRDC has no financial interest in any of the chemicals subject to the current comments. We urge the Carcinogen Identification Committee (CIC) to direct the Office of Environmental Health Hazard Assessment (OEHHA) to prioritize and develop hazard identification materials for the following seven chemicals: **Diisononyl phthalate (DINP), Methoxychlor, Perfluorooctanoic acid and its salts and transformation and degradation precursors, Permethrin, Tetrachlorvinphos, Triclosan and Tris(1,3-dichloro-2-propyl) phosphate.**

We are pleased that the revised prioritization process, which took so many years to develop, has resulted in a list of chemicals for review. It is feasible and reasonable to require a review of these chemicals of priority within the next year.

History of the Prioritization Process: More than Ten Years of Delay

For more than ten years, the scientific expertise of the CIC and the Development and Reproductive Toxicant (DART) IC has been underutilized. These two Committees have convened only annually (the minimum required by statute), and often have been given none or only one chemical to review each year. Yet the DART IC and the CIC are both charged by the California public with reviewing the science and making important decisions about whether or not chemicals should be listed pursuant to Proposition 65. The history of the process makes it clear why the current opportunity to move forward is so important.

In 1997, OEHHA implemented a process for bringing candidate chemicals before the Committees through random selection. This process was criticized for wasting the Committees' time on chemicals with little or no exposure concern, while leaving a

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growing backlog of widespread chemicals of concern unaddressed. In November of 1996, NRDC submitted comments on the draft random selection process stating in part that, "It seems apparent that random selection will increase the likelihood that lower-yield or less important chemicals will bypass others that the scientific community feels should be addressed….NRDC is greatly concerned that the proposed prioritization process will virtually halt the listing of chemicals under Prop. 65 by tying up the process in red tape."[1]

In fact, that is exactly what happened, and over the ensuing ten years, the DART IC and CIC have listed very few chemicals. Meanwhile the tracking database maintained by OEHHA contains hundreds of chemicals, many of which may merit listing, and all of which merit at least some level of review. By our calculations, it would literally take centuries at the current pace to bring all of these chemicals before the state's qualified experts for potential listing. Meanwhile, people are being exposed to many of these chemicals without benefit of the protection and information offered by the statute.

In 2002, the DART IC and the CIC identified problems with the slow pace of listing chemicals under Proposition 65, and with the lack of relevance of chemicals that were coming forward through random selection. The Committees directed OEHHA to develop a new and improved prioritization process for bringing relevant and important candidate chemicals before the Committees.

Clearing the Backlog of Chemicals for Listing

The decision before the CIC today represents an opportunity to open the pipeline of potential candidate chemicals for listing, and to prioritize chemicals with widespread human exposure and evidence of carcinogenicity based on the scientific evidence. OEHHA has reviewed 80 chemicals in the tracking database and identified a list of thirty-eight chemicals to be prioritized for further review. NRDC believes the seven chemicals we have identified should be prioritized because of their widespread use and continued exposure in California and because of the depth of scientific evidence that supports their listing. In particular, each of these chemicals has been entered into the tracking database, have become Candidate Chemicals as a result of relevant toxicity data and the potential for human exposure. It is not an unreasonable workload for OEHHA to further review all seven of these chemicals within the coming year.

Diisononyl phthalate (DINP)

Di-isononyl phthalate (DiNP) is a plasticizer used in children's toys and other consumer products that require a soft and flexible plastic. When children put toys containing DiNP and other phthalates into their mouths, the chemical leaches from the toy into their saliva and can be swallowed**.** DiNP also leaches from consumer products used by adults and can be ingested or inhaled through contact with contaminated dust particles. DiNP has temporarily been banned in children's toys but can continue to be sold in other products.

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[1] Solomon GM. Comments on: Procedure for Prioritizing Candidate Chemicals for Consideration Under Proposition 65 by the "State's Qualified Experts". Submitted to OEHHA November 27, 1996.

In 2000, Earl Gray and colleagues published a study showing DiNP caused male reproductive toxicity in a manner similar to the toxicity of another phthalate, DEHP, which is recognized as a carcinogen by the State of California.[2] Recent research has replicated this work and demonstrates the DiNP acts through a similar mode of action by reducing the production of testosterone.[3] DiNP is thus, a hormone-disrupting chemical. Post-natal exposure to the phthalate metabolites of DiNP and DBP in breast milk has been associated with alterations in male hormone profiles in baby boys and may make them more susceptible to hormone-mediated cancers later in life.[4] Finally, other animal studies identified by OEHHA have demonstrated that DiNP causes liver toxicity and liver tumors.

There is likely to be widespread exposure to DiNP in the general population. When the US CDC analyzed a cross section of the U.S. population for the DiNP monoester metabolite, MiNP in human urine, less than 16% of the samples were positive. However, as has been demonstrated for other phthalates such as DEHP, the monoester metabolite may not be the best indicator of exposure and the oxidative metabolites may be better because the urinary levels are higher and less subject to contamination[5].

When the CDC analyzed a pilot group of urine samples they found none of the 129 samples contained the detectable levels of the DiNP monoester metabolite MiNP but three oxidative metabolites, MCIOP, MHINP, and MOINP were detected in 97, 100, and 87% of the urine samples, respectively[6]. Therefore, the prevalence of human exposure to DINP has previously been underestimated by using MINP as the sole DINP urinary biomarker and future biomonitoring studies should use the oxidative metabolites for a more accurate assessment.

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[2] Gray, L. E., Jr., et al. (2000). Perinatal Exposure to the Phthalates DEHP, BBP, and DINP, but Not DEP, DMP, or DOTP, Alters Sexual Differentiation of the Male Rat. *Toxicol. Sci.* **58**, 350-365.

[3] Borch, J., et al.. (2004). Steroidogenesis in fetal male rats is reduced by DEHP and DINP, but endocrine effects of DEHP are not modulated by DEHA in fetal, prepubertal and adult male rats. *Reproductive Toxicology* **18**, 53-6.

[4] Main KM, et al. (2006) "Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in three months old infants." *Environmental Health Perspectives*, 114(2):270-6.

[5] Silva, M. J., et al. (2006). Measurement of eight urinary metabolites of di(2-ethylhexyl) phthalate as biomarkers for human exposure assessment. *Biomarkers* **11**, 1-13.

[6] Silva, M. J., et al. (2006). Oxidative metabolites of diisononyl phthalate as biomarkers for human exposure assessment. *Environ Health Perspect* **114**, 1158-1161.

Methoxychlor

Although methoxychlor has not been registered for use by the U.S. Environmental Protection Agency (U.S. EPA) since 2003, it is an organochlorine pesticide that is persistent and bioaccumulates in the environment. Methoxychlor has been associated with human epidemiological evidence of cancer, development of cancer in two different animal models and has structural similarities to DDT. Further there is evidence of exposure in vulnerable human populations. Because of on-going exposures and the strength of the cancer data, this chemical should be prioritized for further review.

Perfluorooctanoic acid and its salts and transformation and degradation precursors

Perfluorooctanoic acid (PFOA, C8) and its salts are perfluorinated organic compounds used as protective finishes to make non-stick cookware, food packaging and water- and stain- repelling textiles. There is evidence of widespread exposure in the population[7], and PFOA can cross the placenta. [8] PFOA has been associated with abnormalities in the development of the mammary gland and has been associated with mammary and other tumors.[9] Given the widespread exposure, widespread consumer awareness and evidence of harm, this chemical should be prioritized for further review.

Permethrin,

Permethrin is a general use pesticide commonly used by consumers and widely available. It has been associated with cancer in two or more animal models, causes genotoxicity and has structural similarities to other known carcinogens. Because of on-going exposures and the strength of the cancer data, this chemical should be prioritized for further review.

Tetrachlorvinphos

Tetrachlorvinphos (TCVP) is an organophosphate insecticide that's use in flea and tick control products, particularly flea collars, results in significant opportunities for residential exposure. Due to the mode of action of these products, which rely on the continuous presence of a pesticide residue on the fur of the pet, long term and repeated exposures would be expected for both children and adults in households with pets.

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[7] Calafat AM, Wong LY, Kuklenyik Z, Reidy JA, Needham LL. Polyfluoroalkyl Chemicals in the U.S. Population: Data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and Comparisons to NHANES 1999-2000. Environ Health Perspect 2007 Nov;115(11):1578-83.

[8] Transplacental exposure of neonates to perfluorooctanesulfonate and perfluorooctanoate: a pilot study. Midasch O, Drexler H, Hart N, Beckmann MW, Angerer J. Int Arch Occup Environ Health. 2007 Jul;80(7):643-8.

[9] Suzanne E. Fenton, Jason P. Stanko, Sally S. White, Erin P. Hines Latent effects of PFAA exposure during perinatal development. Reproductive Toxicology, Volume 27, Issues 3-4, June 2009, Pages 411-412

The US Environmental Protection Agency has classified tetrachlorvinphos as "Likely to be Carcinogenic to Humans."[10] This determination was made by the HIARC based on a reevaluation of the 1995 Carcinogenicity Peer Review of Gardona in accordance with the 1999 USEPA Guidelines for Carcinogen Risk Assessment. The 1995 review was based on "statistically significant increases in combined adenomas/carcinomas (predominantly carcinomas) in the female B6C3F1 mouse, suggestive evidence of the thyroid C- cell adenomas and adrenal pheochromocytomas in the rat, mutagenicity concerns, and SAR support."[11] In addition, OEHHA's 2009 evaluation of the animal carcinogenicity data determined that it passed the animal data screen due to two positive animal cancer bioassays. In two studies malignant liver tumors in male and female mice were associated with exposure to tetrachlorvinphos.

The review of the available animal studies, by OEHHA and USEPA, has determined a high level of concern for the carcinogenicity of tetrachlorvinphos. In addition, current registered uses present a significant opportunity for residential and occupational exposures. Therefore, tetrachlorvinphos should be a high priority for the development of hazard identification materials by OEHHA and the consideration for listing by the Carcinogen Identification Committee.

Triclosan

Triclosan is a broad spectrum anti-bacterial chemical found in many different consumer products where it is reported to kill bacteria, prevent odors, or act as a preservative. It is used in consumer products such as liquid hand soap, toothpaste, mouth rinse, cosmetics, pharmaceutical products, fabrics, plastics, textiles, and plastic kitchenware.

Residues of triclosan has been found in seventy-five percent of Americans (ages 6-65+) have been found to have triclosan in their urine. [12] Other studies also have detected triclosan in urine[13], blood[14], and breast milk[15] samples throughout the world.

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[10] HIARC report 2002 (I don't have the full citation yet -waiting for FOIA)

[11] US EPA Carcinogenicity Peer Review of Gardona (2nd) dated March 6, 1995.

[12] Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Urinary concentrations of triclosan in the U.S. population: 2003-2004. Environ Health Perspect. 2008. 116(3):303-7.

[13] Wolff, MS; Teitelbaum, SL; Windham, G; et al. Pilot study of urinary biomarkers of phytoestrogens, phthalates, and phenols in girls. Environ. Health Perspect, 2007. 115–117.

[14] Allmyr, M; Harden, F; Toms, LM; Mueller, et al. The influence of age and gender on triclosan concentrations in Australian human blood serum Sci Total Environ. 2008 393(1):162-7.

[15] Adolfsson-Erici, M., Pettersson, M., Parkkonen, J., Sturve, J., 2002. Triclosan, a commonly used bactericide found in human milk and in the aquatic environment in Sweden. Chemosphere 46, 1485–1489. Allmyr, M; Adolfsson-Erici, M; McLachlan, MS; Sandborgh-Englund, G. Triclosan in plasma and milk from Swedish nursing mothers and their exposure via personal care products. Science of the Total Environment. 2006. 372 (87-93). Ye X, Bishop AM, Needham LL, Calafat AM. Automated on-line column-switching HPLC-MS/MS method with peak focusing for measuring parabens, triclosan, and other environmental phenols in human milk. Anal Chim Acta. 2008 Aug 1;622(1-2):150-6.

Given the widespread exposure, widespread consumer awareness and evidence of harm, this chemical should be prioritized for further review.

Tris(1,3-dichloro-2-propyl) phosphate (TDCPP)

TDCPP is a flame retardant used in polyurethane foam, plastics, resins and in backcoating of fabrics. TDCPP was used briefly in children's sleepwear but was withdrawn in 1977. It is now being used a replacement for the banned PBDEs in furniture foam. TDCPP was detected in some water samples from 139 streams across the United States, some including California (Kolpin et al., 2002).
The U.S. Consumer Product Safety Commission concluded TDCPP was a probable human carcinogen based on sufficient evidence in animals.[16] TDCPP is structurally similar to TRIS and tris(2-chloroethyl)phosphate, which are both listed as causing cancer under Proposition 65. Given the widespread of use in consumer products and evidence of carcinogenity, this chemical should be prioritized for review.

In summary, we hope that the CIC will move forward on further assessing the science on these seven important and interesting chemicals, and make sound and independent decisions on whether or not these chemicals meet the criteria for listing under Proposition 65.

Thank you for the opportunity to comment on the list of priority chemicals.

Sincerely,

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Natural Resources Defense Council

Dayan, AD. Risk assessment of triclosan [Irgasan®] in human breast milk. Food and Chemical Toxicology. 2007. 45: 125-129.

[16] U.S. Consumer Product Safety Comission (2006). CPSC Staff Preliminary Risk Assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam. December 21, 2006.