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Re: Prioritization of Chemicals for Carcinogen Identification Committee Review--
DIISONONYL PHTHALATE (DINP)

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Far too often, policy decisions are made in a political vacuum with a clear disregard for scientific evidence. This is clearly the case currently in California, where officials are disregarding the facts on di-isononyl phthalate (DINP) as they move forward with the proposition 65 screening process.

OEHHA has announced their intention to review 38 chemicals, including DINP (di-isononyl phthalate), by the Carcinogen Identification Committee, in spite of the fact that this chemical has not been found to have carcinogenic effects in humans. In fact, there is significant scientific evidence shown that the mechanisms which show possible carcinogenic effects in rodents at high doses are not present in humans. Therefore, I strongly recommend that the CIC rank DINP as "no priority" for further study on this issue.

A recent Chronic Hazard Advisory Panel (CHAP) convened by the Consumer Product Safety Commission (CPSC) affirmed that DINP is not known to be a carcinogen in humans. The CHAP concluded that "humans do not currently receive DINP doses from DINP-containing consumer products that are plausibly associated with a significant increase in cancer risk." In addition, the panel's report found that while DINP has been found to develop liver tumors in rodents through a PPAR activation, this mechanism is not applicable in humans.

DINP is classifiable as a hepatic peroxisome proliferator and in that regard the liver tumors developing in rats and mice chronically exposed to DINP can be mechanistically related to PPAR α activation. The PPAR α -mediated mechanism of hepatocarcinogenesis is pronounced in rodents, but believed not readily induced in humans, especially at the doses resulting from current use of consumer products. The human risk was therefore seen as negligible or non-existent.¹

In addition, the kidney tumors found in rats after exposure to high levels of DINP were also found to be rat-specific after review by the CHAP panel.

The male rat $\alpha 2\mu$ -globulin mechanism of action for the production of rat kidney tumors has been postulated. Criteria for supporting an $\alpha 2\mu$ -globulin mechanism of action were applied and found to be met. The renal tumors in male rats at the high dose of DINP were therefore treated as rat specific and were not used to predict human risk.²

¹ <http://www.cpsc.gov/libravy/foia/foia01/os/dinp.pdf>

² <http://www.cpsc.gov/libravy/foia/foia01/os/dinp.pdf>



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DINP is a member of a class of compounds known as peroxisome proliferating compounds (PPC's)³. The implication of human risk from the mechanisms of action of PPC's has been greatly studied. The CPSC reviewed the carcinogenic risk of mechanisms from DINP exposures and found no hazard risk to humans:

Some previous studies have shown DINP to have potential carcinogenic effects in mice. Animal carcinogens are generally regarded as potential human carcinogens in the absence of convincing evidence to the contrary (CPSC, 1992; IARC, 1987). However, in the case of PPC's, it has been argued that the tumors are a secondary effect of PPN, primates and humans are less sensitive than the mice and rats in which PPN-induced tumorigenesis is observed, and, therefore, PPC's do not present a cancer hazard in humans (Cattley et al., 1998).⁴

DINP has not been classified as a carcinogen by The World Health Organisation's International Agency for Research on Cancer (IARC). In fact, IARC reversed its ruling on the carcinogenicity of DEHP and concluded that the mechanism PPAR α activation by which DEHP increased the incidence of liver tumors in rodents was not relevant to humans.⁵

A rat's metabolism differs significantly from that of a human. Although rat studies may be useful for suggesting what sorts of toxicity to look for in humans, often they do not predict effects on humans.

Listing DINP under Proposition 65 as a possible carcinogen would be misguided; there is simply insufficient evidence to support such an action. If DINP is listed as a carcinogen, manufacturers will inevitably be forced to turn to – and consumers will be exposed to – alternatives that are likely to be less well tested. Ingredients known to be safe may be replaced by less-tested and less-effective alternatives, creating greater net risk to the public.

Regulation of chemicals should be based on sound scientific evidence, rather than politics or "popular wisdom." DINP has been thoroughly and specifically studied by many government agencies. It should be categorized as "no priority" for further review.

A handwritten signature in black ink, appearing to read "H. Miller".

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³ <http://www.cpsc.gov/phth/risk.pdf>

⁴ <http://www.cpsc.gov/phth/risk.pdf>

⁵ International Agency for Research on Cancer (IARC). 2000. Di(2-ethylhexyl) phthalate. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Some Industrial Chemicals. 77.