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Working globally for a toxic free future

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Proposed Variations on Priority Existing Chemical - DEHP

The National Toxics Network (NTN) welcomes the opportunity to make a submission regarding the PEC – DEHP Draft Report. Unfortunately you do not provide the Form 4a in electronic format so it has not been included with this submission.

NTN supports Recommendations 1 & 2 and welcomes the announcement already made by the ACCC in relation to Recommendation 1.

NTN considers that another Recommendation must also be made in relation to how the problem of imported products arriving into Australia from countries with no restrictions on DEHP will be regulated.

NTN also considers that a biomonitoring program would provide useful data to ensure the Recommendations actually result in reduced exposures to DEHP.

The existing Recommendations should be strengthened to include:

1. DEHP should be banned from all products

NTN considers DEHP should be banned from all products, with compliance mechanisms put in place to protect the entire population, particularly women of childbearing age who are also at unacceptable risk from DEHP exposures. This would include other products such as adhesives, packaging, food wrapping, building and furnishing products, PVC flooring/ moulding, food containers, personal products, cosmetics, toys and childcare articles.

Exposure from PVC flooring to children is clearly demonstrated and leaching from other products has also been shown. Two studies in the late 1990s (Jaakkola et al. 1999 [1] and Øie et al 1997[2]) found that the presence of plasticizers in surface materials indoors can increase the risk of bronchial obstructions, asthma, and perhaps the susceptibility to respiratory infections. The later noted that indoor inhalation of DEHP-adsorbed particulate matter could be as or more important than inhalation of vapor phase DEHP.

[1] Jaakkola, J.J.K., Øie, L., Nafstad, P., Botten, G., Lødrup-Carlson, K.C., Samuelsen, S.O. and Magnus, P. (1999) Interior surface materials in the home and the development of bronchial obstruction in young children in Oslo, Norway, *Am. J. Public Health*, 89, 188–192

[2] Øie, L., Hersoug, L.G. and Madsen, J.Ø. (1997) Residential exposure to plasticizers and its possible role in the pathogenesis of asthma, *Environ. Health. Perspect.*, 105, 972–978.

These findings were supported by a Swedish study (Bornehag et al 2004), [3] which has linked a range of phthalates to asthma, allergic rhinitis (hay fever), and eczema. Researchers took dust samples from the moulding and shelves in the children's bedrooms. Samples containing higher concentrations of phthalates were associated with symptoms of asthma, hay fever, and eczema. Notably, PVC flooring in the children's bedrooms was associated with symptoms. The Swedish study found that children exposed to household dust with the greatest concentrations of DEHP were 2.9 times as likely to have asthma as were children exposed to the lowest concentrations of that phthalate. Similarly, children in homes with the greatest concentrations of butyl benzyl phthalate were 3.0 and 2.6 times as likely as the other children to have rhinitis and eczema, respectively.

DEHP enters the environment *via* a number of different routes: during plasticizer production; during plasticizer distribution; during incorporation into PVC resin; during disposal in industrial and municipal landfills; leaching from PVC products during use (e.g. floor tiles, greenhouse film) and leaching from PVC products after use as with *in situ* disposal. DEHP has been shown to migrate into food from certain food wraps during storage.[4]

2. Use of MOE inappropriate

In assessing the impacts on humans, particularly children, NGOs have been vocal in their rejection of standard risk assessment methodologies that are based on Tolerable Daily Intakes.

This approach ignores the need for assessment of cumulative exposure to groups of 'like' chemicals (e.g., all phthalates, all reproductive toxins) and fails to acknowledge the importance of pulse exposure both prenatally through mother to foetus and postnatal through breast milk.

The unique vulnerability of children to hazardous chemicals and the concept of "windows of susceptibility"[5] is well recognised by the World Health Organisation (WHO), the United Nations' Children's Fund (UNICEF) and the United Nations Environment Program (UNEP).

3. Other phthalates need urgent action

NTN considers that immediate action needs to be taken on other phthalates where toxicity and exposure have already been demonstrated.

While DEHP remains the most prevalent plasticizer in PVC formulations and is also the dominant phthalate found in the environment, it is not the only phthalate of concern to human and animal health. Rats and mice fed di-isononyl phthalate (DINP) also showed an increase in liver cancers [6] and in the 2003 study[7] linking urinary MEP, at environmental

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[3] Carl-Gustaf Bornehag, Jan Sundell, Charles J. Weschler, Torben Sigsgaard, Björn Lundgren, Mikael Hasselgren, and Linda Hägerhed-Engman (2004) The Association between Asthma and Allergic Symptoms in Children and Phthalates in House Dust: A Nested Case–Control Study *Environmental Health Perspectives* Volume 112, Number 14, 1393-1397

[4] Dept of Environment and Heritage, 2004 End of Life Environmental Issues with PVC in Australia, authored by Dr John Scheirs, August 2003

[5] Stephen S. Olin and Babasaheb R. Sonawane, Workshop to Develop a Framework for Assessing Risks to Children from Exposure to Environmental Agents, September 2003, *Environmental Health Perspectives* Vol.111/12 pp1524-1526

[6] Jacqueline H. Smith*, Jason S. Isenberg, George Pugh, Jr.*, Lisa M. Kamendulis, David Ackley, Arthur W. Lington* and James E. Klaunig (2002) Comparative *in Vivo* Hepatic Effects of Di-Isononyl Phthalate (DINP) and Related C_7–C_{11} Dialkyl Phthalates on Gap Junctional Intercellular Communication (GJIC), Peroxisomal Beta-Oxidation (PBOX), and DNA Synthesis in Rat and Mouse Liver, *Toxicological Sciences* 54, 312-321

levels, with increased DNA damage in sperm, the authors noted that previous *in vitro* studies had found di-*n*-butyl phthalate (DBP) and di-isobutyl phthalate (DiBP) to be genotoxic in human epithelial cells of the upper aerodigestive tract as well as in mucosal cells and lymphocytes.

A very recent study (Ren-Shan Ge et al 2007) [8] concluded that contemporary epidemiological evidence indicates that boys born to women exposed to phthalates during pregnancy have an increased incidence of congenital genital malformations and spermatogenic dysfunction, signs of a condition referred to as testicular dysgenesis syndrome (TDS).

It has been shown that phthalates can be hormone disruptors,[9] immunotoxins,[10] cancer promoters and/or reproductive and developmental toxins.[11] DEHP has been classified as a "probable human carcinogen" by the USEPA.

Phthalates are detected in the blood and urine of both adults and children,[12] with the US National Toxicology Program (NTP) expressing concern over the adverse development of babies born to pregnant women who are exposed to DEHP, at current levels estimated for an adult.

Exposure to phthalates and their metabolites have been associated with a broad range of health effects in humans, including:

- asthma and other respiratory problems, rhinitis and eczema in children;
- deteriorated semen quality in men;
- DNA damage;
- adverse male genital development; and
- reduction in reproductive hormones.

In 2002, researchers[13] explored whether general levels of phthalates in the U.S. population were associated with altered semen quality and found suggestive evidence of an association between high mono-benzyl phthalate (MBzP) levels and low sperm counts and between high mono-methy phthalate (MMP) and poor sperm morphology. Mono-n-butyl phthalate (MBP), MBzP and MMP were associated with altered semen quality.

In a related study, in 2003[14] it was found that urinary monoethyl phthalate (MEP), at environmental levels, is associated with increased DNA damage in sperm. Rozati et al.

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[7] Susan M. Duty,1 Narendra P. Singh, Manori J. Silva, Dana B. Barr, John W. Brock, Louise Ryan,4 Robert F. Herrick, David C. Christiani, and Russ Hauser, (2003) The Relationship between Environmental Exposures to Phthalates and DNA Damage in Human Sperm Using the Neutral Comet Assay , *Environmental Health Perspectives* Vol 111 : 9

[8] Ren-Shan Ge, Guo-Rong Chen, Cigdem Tanrikut and Matthew P. Hardy, (2007) Phthalate ester toxicity in Leydig cells: Developmental timing and dosage considerations, *Reproductive Toxicology* Volume 23 : 3, 366-37

[9] Lovekamp TN, Davis BJ (2001) Mono-(2-ethylhexyl) phthalate suppresses aromatase transcript levels and estradiol in cultured rat granulose cells. *Toxicol Appl Pharmacol* 172(3):217-24

[10] Nencioni A, Wesselborg S, Brossart P (2003) Role of peroxisome proliferators-activiated receptor gamma & its ligands in the control of immune responses. *Crit Rev Immunol*; 23(1-2(1-13)

[11] Sharpe, RM and DS Irvine. (2004) How Strong is the Evidence of a Link Between Environmental Chemical and Adverse Effects on Human Reproductive Health? *British Medical Journal. 328(21 Feb):447-451.*

[12] Second National Report on Human Exposure to Environmental Chemicals (January 2003), Department of Health and Human Services, Centers for Disease Control and Prevention

[13] Duty, S., Silva, M., Barr, D., Brock, J., Ryan, L., Zuying, C., Herrick, R., Christiani, D., Hauser, R., (2002). Urinary phthalate monoesters at general populations exposure levels are associated with altered semen quality. *Epidemiology* July 2002, Volume 13 Number 4 Supplement

[14] Duty, S., Singh, N., Silva, M., Barr, D., Brock, J., Ryan, L., Herrick, R., Christiani, D., Hauser, R., (2003). The relationship between environmental exposures to phthalates and DNA damage in human sperm using the Neutral Comet Assay. *Environ. Health Perspect.* 111: 1164-1169.

(2002)[15] had found that the concentration of phthalate esters was significantly higher in infertile men compared with controls and concluded that they may be instrumental in the deterioration of semen quality in infertile men without an obvious etiology.

Impacts on women had been suggested in 2003 study [16], which linked environmental contamination with DEHP, through its metabolite MEHP, and the suppression of estradiol production in the ovary, leading to anovulation.

A 2004 study [17] demonstrated that the daily exposure to DEHP of 3–30 ug/kg body weight/day comes close to the TDI of 37 ug/kg body weight/day of the EU Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE). The study found that the RfD (reference dose) of the US Environmental Protection Agency (EPA) of 20 ug/kg body weight/day is even exceeded and the 3–30 ug/kg body weight/day may be increased by 2–3 orders of magnitude for infants undergoing intensive therapeutic interventions. Thus, the actual exposure to DEHP is higher than previously believed and the TDI can be exceeded within the general population considerably. In particular, it was shown that nursery school children aged 2–6 years are probably exposed to twice as much DEHP as adults. The authors argue that the available toxicity data and the limited, but suggestive human exposure data are cause for serious concern that DEHP exposure may be detrimental to human fertility and reproduction. In particular, since the blood-testis barrier forms just before puberty in humans, permeability of the blood-testis barrier is increased in children and particularly in newborns, whose testicles are still developing. As a consequence, male newborns are thought to be at the greatest potential risk.

A 2005 [18] study showed how the urinary concentrations of four phthalate metabolites [monoethyl phthalate (MEP), mono-n-butyl phthalate (MBP), monobenzyl phthalate (MBzP), and monoisobutyl phthalate (MiBP)] were inversely related to anogenital index (AGI). The authors note that the associations between male genital development and phthalate exposure seen are consistent with the phthalate-related syndrome of incomplete virilization that had been reported in prenatally exposed rodents. These data further supports the hypothesis that prenatal phthalate exposure at environmental levels can adversely affect male reproductive development in humans.

In 2005, the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) convened an expert panel to re-evaluate the reproductive and developmental toxicities of di(2-ethylhexyl)phthalate (DEHP). The expert panel expressed concern that DEHP exposure can adversely affect reproductive development in infants less than one year old. Where DEHP/MEHP exposure is high due to medical procedures in infants the expert panel had serious concern that such exposures may adversely affect male reproductive tract development and function.[19]

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[15] Rozati, R., Reddy, R., Reddanna, P., Mujtaba, R., (2002) Role of environmental estrogens in the deterioration of male factor fertility. *Fertility & Sterility* 78: 1187-1194

[16] *Tara Lovekamp-Swan and Barbara J. Davis (2003)* Mechanisms of Phthalate Ester Toxicity in the Female Reproductive System, *Environ Health Perspect* 111:139–145

[17] Latini, G., De Felice, C., Verrotti, A., (2004) Plasticizers, infant nutrition and reproductive health. *Reproductive Toxicology* Vol. 19:1, 27-33.

[18] Shanna H. Swan, Katharina M. Main, Fan Liu, Sara L. Stewart, Robin L. Kruse, Antonia M. Calafat, Catherine S. Mao, J. Bruce Redmon, Christine L. Ternand, Shannon Sullivan, J. Lynn Teague, and the Study for Future Families Research Team, (2005) Decrease in Anogenital Distance among Male Infants with Prenatal Phthalate Exposure, *Environmental Health Perspectives* Vol/ 113 : 8

[19] October 14, 2005 MEETING SUMMARY NATIONAL TOXICOLOGY PROGRAM CENTER FOR THE EVALUATION OF RISKS TO HUMAN REPRODUCTION EXPERT PANEL RE-EVALUATION OF DEHP OCTOBER 10–12, 2005

A 2006 study[20] supported these concerns concluding that data on reproductive hormone profiles and phthalate exposures in newborn boys are in accordance with rodent data and suggest that human Leydig cell development and function may also be vulnerable to perinatal exposure to some phthalates. Their study supported other recent human data showing incomplete virilization in infant boys exposed to phthalates prenatally and supports previous findings that DBP, DEHP and its metabolite mono-2-ethylhexyl phthalate (mEHP), and di-isononyl phthalate (DiNP) show antiandrogenic effects diminishing fetal testosterone production.

In January 2006, many of these concerns were acknowledged by the European Commission in their News Alert Issue No 7, (January 2006) 'Phthalates May Affect Baby Boys'. The alert reviewed further evidence from another 2006 study,[21] which demonstrated that exposure to phthalates through lactation can trigger the reduction of reproductive hormones in baby boys. The contamination by six phthalate monoesters was measured in 130 breast milk samples from Danish and Finnish mothers included in a cohort study conducted from 1997 to 2001. The blood samples of their 3 months old sons were analyzed for sex-hormones. The results of the study showed that 3-months old boys exposed to higher concentrations of phthalate monoesters in breast milk, showed slight, but significant, decrease in levels of reproductive hormones, including the main male sex-hormone - testosterone. *Importantly, the range of concentrations of phthalates in breast milk samples appeared to be below the estimates of the tolerable daily intake levels (TDI).* However, they note that a direct comparison to TDI values was not possible in this study since exposure through lactation is only one of the possible routes of exposure to phthalates in children.

The 2006 EU announcement quoted by the Vinyl Council was based on the 2003 EU Risk Assessments of DINP and DIDP. In assessing DINP, risk assessors noted their difficulty in assessing the level of consumer exposure to DINP, "as DINP is not chemically bound to PVC, it can be released during the entire cycle of life of end products that are used by consumers." These end products are building materials (cables, floor covering, paints, etc.), car undercoating, clothes, gloves, shoes and boots, toys and child care articles. [22]

In relation to di-isodecyl phthalate (DIDP) they note that the calculations are based on the assumption that it is not used in toys and "in case DIDP should be a substitute for other phthalates in toys in the future, margin of safety (MOS) of 18.8, derived from hepatic toxicity in dogs, would not be considered sufficient to protect infants." They conclude that owing to the uncertainty on the applicability of the NOAEL (no observable effect level of 16.5 mg/kg bw/d) for reduced offspring survival and the significance of the MOS (83 and 41, respectively without and with toys), no formal conclusion could be drawn."[23]

The 2003 EU Risk Assessments of DINP and DIDP fails to take into account the synergistic impacts of the many hundreds of man made chemicals present in umbilical cord blood, breast milk, adult fat and blood.

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[20] Katharina M. Main, Gerda K. Mortensen, Marko M. Kaleva, Kirsten A. Boisen, Ida N. Damgaard, Marla Chellakooty, Ida M. Schmidt, Anne-Maarit Suomi, Helena E. Virtanen,2 Jørgen H. Petersen, Anna-Maria Andersson, Jorma Toppari, and Niels E. Skakkebæk, (2006) Human Breast Milk Contamination with Phthalates and Alterations of Endogenous Reproductive Hormones in Infants Three Months of Age, Vol 14:2 2006 • *Environmental Health Perspectives*

[21] Main, M.K. et al. (2006) "Human Breast Milk Contamination with Phthalates and Alterations of Endogenous Reproductive Hormones in Infants Three Months of Age", *Environmental Health Perspectives* 114 (1).

[22] EUROPEAN COMMISSION JOINT RESEARCH CENTRE Institute for Health and Consumer Protection European Chemicals Bureau I-21020 Ispra (VA) Italy "1,2-BENZENEDICARBOXYLIC ACID, DI-C8-10-BRANCHED ALKYL ESTERS, C9-RICH and DI-"ISONONYL" PHTHALATE (DINP) CAS Nos: 68515-48-0 and 28553-12-0 EINECS Nos: 271-090-9 and 249-079-5 Summary Risk Assessment Report 2003 Special Publication I.03.101

[23] EUROPEAN COMMISSION JOINT RESEARCH CENTRE Institute for Health and Consumer Protection European Chemicals Bureau I-21020 Ispra (VA) Italy "1,2-BENZENEDICARBOXYLIC ACID, DI-C9-11-BRANCHED ALKYL ESTERS, C10-RICH and DI-"ISODECYL" PHTHALATE (DIDP) CAS Nos: 68515-49-1 and 26761-40-0 EINECS Nos: 271-091-4 and 247-977-1 Summary Risk Assessment Report 2003 Special Publication I.03.103

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