APERC Comments on 59th Report of the Interagency Testing Committee Docket ID Number EPA-HQ-OPPT-2006-0961 FR Vol. 72, No. 13, January 22, 2007

The 59th Report of the Interagency Testing Committee (ITC) to the EPA Administrator (FR Vol. 72, No. 13, January 22, 2007) states that Phenol, 4-(1,1-dimethylethyl) (CAS 98-54-4) also known as *para-tert*-butylphenol (*pt*BP) was removed from the TSCA Section 4(3) Priority Testing List (PTL) based on the submission of a reproductive effects study on this compound conducted in rats. The Report also states that Phenol, 4-nonyl-, branched (CAS 84852-15-3) also known as nonylphenol (NP) and Phenol, 4-(1,1,3,3-tetramethylbutyl) (CAS 140-66-9) also known as octylphenol (OP) will remain on the PTL to determine if existing fish reproductive effects data are sufficient to meet the ITC's data needs as well as to determine if these two compounds should be tested for avian reproductive effects. Additionally, the Report notes the ITC's interest in reviewing the Safer Detergent Stewardship Initiative, which has been proposed by the EPA Design for Environment Program. Following are the Alkylphenols & Ethoxylates Research Council's (APERC's) comments on the ITC's decisions and data interests regarding the above mentioned alkylphenol compounds.

I. Support Removal of Phenol, 4-(1,1-dimethylethyl) from the PTL

APERC supports the ITC's removal of Phenol, 4-(1,1-dimethylethyl), more commonly referred to as *para-tert*-butylphenol (*pt*BP), from the TSCA Section 4(3) Priority Testing List based on the submission of a reproductive effects study on this compound conducted in rats. The study was conducted according to Good Laboratory Practices using a protocol consistent with OECD Method 422, a two-generation rat study that measures reproductive endpoints, and the delisting of this compound is well founded. No adverse effects on reproduction were found in the absence of maternal toxicity in this study and the No Observed Effect Level (NOEL) for *pt*BP was determined to be 800 ppm (dietary).[1]

II. Existing Fish Reproductive Effects Studies Should Be Sufficient to Address ITC's Data Interests

EPA's Water Quality Criteria (WQC) for NP are based on a comprehensive review of the available literature related to the aquatic toxicity of this compound.[2] In addition, studies used in the development of WQC were reviewed to ensure that they meet data acceptability requirements outlined by EPA.[3] The chronic toxicity studies used in

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[1] Charles Rivers Laboratories, Edinburgh, Scotland, Final Report: p-tert-butylphenol Two Generation Reproduction Study in Rats. Study No. 493595. Report No. 24804. Unpublished Report sponsored by SASOL GmbH (Germany) and SI Group-Switzerland GmbH (Formerly Schenectady Pratteln GmbH, Switzerland), February 2006.

[2] US EPA. (2005, December). Final NP WQC document (EPA-822-R-05-055). http://www.epa.gov/waterscience/criteria/nonylphenol/.

[3] Stephen, C.E. *et al*. (1985). Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses. http://www.epa.gove/waterscience/criteria/85guidelines.pdf.

deriving the NP WQC included the assessment of effects on reproduction endpoints in fish and other aquatic organisms. Two life cycle studies on NP by Yokoto *et al.*, 2001[4] and Schwaiger *et al.*, 2002[5] are cited and considered in the NP WQC document. Also considered in the NP WQC are early life-stage studies with embryos and fry of rainbow trout (*Oncorhynchus mykiss*) by Brooke *et al*. (1993)[6] and fathead minnow (*Pimephales promelas*) by Ward and Boeri, 1991.[7] Also included in the WQC document is a one-year flow-through exposure during the embryonic, larval and juvenile stages in juvenile rainbow trout (*Oncorhynchus mykiss*) by Ackermann *et al.,* 2002[8] that measured endpoints of survival, hatch rate, weight and sex ratio and found no effects up to measured concentrations of 10.17 μg/L for any endpoint.

Staples *et al*., 2004[9] provides another useful weight of evidence review of the chronic effects of NP in aquatic species. As in the NP WQC document, these authors also found that reproductive effects in fish and aquatic species are not as sensitive as other chronic endpoints.

Van Miller and Staples[10] published a "Review of the Potential Environmental and Human Health-Related Hazards and Risks from Long-Term Exposure to p-tert-Octylphenol" in 2005, which included a comprehensive review of the chronic effects, including reproductive and developmental, for this compound in fish and other aquatic species.

These existing reviews and chronic and reproductive effects studies should be sufficient to address the ITC's interest in reproductive effects of NP and OP in fish.

III. Use and Exposure of NP and OP Do Not Warrant Avian Reproductive Effects Testing

NP and OP are not used in applications that would result in any significant exposure to birds; they are not used in pesticide or fertilizer products that are dispersed directly into the terrestrial or aquatic environment. Therefore avian reproductive effects testing does not seem to be warranted for these two compounds. Rattner *et al.* (2004) concluded that

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[4] Yokota, H., Seki, M., Maeda, M., Oshima, Y., Tadokoro, H., Honjo, T., and Kobayshi, K. (2001). Life-cycle Toxicity of 4-nonylphenol to Medaka (*Oryzias latipes*). Environ. Toxicol. Chem., 20, 2552-2560.
[5] Schwaiger, J., Mallow, U., Ferling, H., Knoerr, S., Braunbeck, T., Kalbfus, W., and Negele, R.D. (2002). How estrogenic is nonylphenol: A transgenerational studying using rainbow trout (Oncorhynchus mykiss) as a test organism. Aquat. Toxicol., 59, 177-189.
[6] Brooke, L.T. (1993a). Acute and chronic toxicity of nonylphenol to ten species of aquatic organisms. Report to US EPA for Work Assignment No. 02 of Contract No. 68-C1-0034. Lake Superior Research Institute, University of Wisconsin- Superior, Superior, WI. 30 pp. Amended 18 October 2005, 34 pp.
[7] Ward, T.J., and Boeri, R.L. (1991). Early life stage toxicity of nonylphenol to the fathead minnow, Pimephales promelas. Study Number 8979 CMA. EnviroSystems, Hampton, NH. 59 pp.
[8] Ackermann, G.E., Schwaiger, J., Negele, R.D., *et al.* (2002). Effects of long-term nonylphenol exposure on gonadal development and biomarkers of estrogenicity in juvenile rainbow trout (*Oncorhynchus mykiss*). Aquatic Toxicol, 60, 203-21.
[9] Staples, C., Mihaich, E., Carbone, J., Woodburn, K., and Klecka, G. (2004). A Weight of Evidence Analysis of the Chronic Exotoxicity of Nonylphenol Ethoxylates, Nonylphenol Ether Carboxylates and Nonylphenol, Human and Ecological Risk Assessments, 10, 999-1017.
[10] Van Miller, J., and Staples, C. (2005). Review of the Potential Environmental and Human Health-Related Hazards and Risks from Long-Term Exposure to p-tert-Octylphenol. Human and Ecological Risk Assessment, 15, 17.

findings of their study, which monitored contaminants in the eggs from oprey nests in Chesapeake Bay regions of concern, did not clearly and completely resolve the question of whether contaminants are affecting osprey reproduction.[11] NP and OP were among the numerous analytes tested. Since NP was detected in the eggs but with the exception of a few of the samples levels were not quantifiable, these compounds do not appear to warrant further concern regarding avian reproductive toxicity. Since OP was not detected in any of the egg samples in this study, it clearly does not warrant any additional avian testing.

IV. Amphibian Studies

The 59th ITC Report notes that there are two amphibian toxicity studies available for OP, which may be sufficient to meet the ITC's amphibian toxicity data needs for both NP and OP.Since APERC's last correspondence with the ITC, two additional amphibian studies have been identified.

An amphibian study on NP in bullfrog tadpoles (*Rana catesbetana*) was recently published by Christensen *et al.* (2005).[12] However, based on the authors' own cautions the study was determined to be not valid. The test substance did not dissolve homogeneously in the water column, even with the presence of methanol solvent and in some cases NP concentrations resulted in the formation of an oily residue on the surface of the water. This could result in varying degrees of exposure to the tadpoles and may have resulted in physical/chemical effects such as smothering the tadpoles. The author also cautioned that the highest tested concentration of NP, which affected tail resorption and the rate of metamorphosis, is generally greater than what is found in the environment. Also, the author cites his own unpublished data on NP that determined a 24 hour LC50 > 3.43 mg/L in Bullfrog tadpoles (*Rana catesbetana)* and for the Red-legged frog (*Rana aurora*) determined a 24 hour LC50 of 310 ug/L and a 48 hour LC50 of 250 µg/L, which indicate that the effect levels found in this study occurred at concentrations (936 µg/L) known to be in the lethal range.

Another recently published study by Hogan *et al.* (2006)[13] assessed the toxicity of OP using a 2 week LC50 assay in the Northern Leopard frog (*Ranid pipiens*) and the Wood frog (*Ranid sylvatica*). The LC50 for OP was reported as 1.36 - 1.42 µM in stage 26 tadpoles. The authors report that OP was detected in water at concentrations of up to 13 µg/L (~63 nM) in an estruary in the UK but note that concentrations of approximately 1-10 µg/L (~ 5-50 nM) are more common.

Results from a statistical analysis of OP concentrations in US surface waters, which included two large nationwide monitoring studies and 17 additional investigations

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[11] Rattner, B.A., McGowan P.C., Golden, N.H., Hatfield, J.S., Toschik, P.C., Lukei, R.F. Jr., Hale, C. Schmitz-Alfonzo, I., and Rice, C.P. (2004). Contaminant Exposure and Reproductive Success of Ospreys (*Pandion haliaetus*) Nesting in Chesapeake Bay Regions of Concern. Arch. Environ. Contam. Toxicol., 47, 126-140.
[12] Christensen, *et al.* (2005). Effects of Nonylphenol on Rates of Tail Respoption and Metamorphosis in Rana catesbeiana tadpoles. Journal of Toxicology and Environmental Health Part A-Current Issues, 68, 557-572.
[13] Hogan, N.S., Lean, D.R.S., and Trudeau, V.L. (2006). Exposures to estradiol, ethinylestradiol and octylphenol affects survival and growth of Rana pipiens and Rana sylvatica tadpoles. Journal of Toxicology and Environmental Health-Part A-Current Issues, 69, 1555-1569.

conducted between 1995 and 2005, are more relevant to the ITC's purposes. Based on the frequency of detection in surface waters, 67% of all alkylphenol related analytes were below their detection limits. In those samples were OP was detected, the average OP concentration was found to be 0.46 µg/L (~2.3 nM) and the maximum concentration for OP was 1.10µg/L (~ 5nM).[14]

V. EPA's Safer Detergent Stewardship Initiative Not Relevant to ITC Activities

The ITC is likely already aware that EPA's Design for Environment (DfE) office proposed a program called the Safer Detergent Stewardship Initiative (SDSI) that encourages companies to deselect nonylphenol ethoxylates (NPEs) as ingredients in detergents.[15] According to EPA, SDSI is intended to reduce the amount of NPE surfactants and NP in streams and "assist in attainment of the Aquatic Life Criteria for nonylphenol." Since concentrations of NP found in US surface waters are - with only a few exceptions - already below the final NP WQC,[14] APERC believes that a national program, even one that is voluntary, promoting deselection of NPEs is not warranted. Instead, APERC advocates that local risk management mechanisms should be used to manage the infrequent situations where exceedances might occur. Since SDSI is not based on scientific risk assessment, it should not influence the ITC's judgment regarding the need for additional studies.

[14] Klečka, G. *et al.* (2007). Exposure Analysis of C8- and C9-Alkylphenol, Alkylphenol Ethoxylates, and their Metabolites in Surface Water Systems within the United States. Water Environment Research. (In press)
[15] EPA Design for Environment Program. (2006). Safer Detergent Stewardship Initiative. http://www.epa.gov/dfe/pubs/projects/formulat/sdsi.htm.