

A P E R E S E A R C H C O U N C I L

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APERC Statement Commercial Nonylphenol Ethoxylates Are Not Estrogenic October 24, 2005

Scientists determine whether a compound is estrogenic by testing the substance in a system that is known to respond to estrogen in a specific way. Since the uterus is highly responsive to estrogenic compounds, an uterotrophic assay is often used. Several uterotrophic studies in the rat conducted with nonylphenol ethoxylates - "NPEs" - (specifically NPE4 and NPE9) show no estrogen-like activity up to maximum tolerable doses of these commercial surfactant products.^{1,2,3}

More recently, a study conducted in fish showed no estrogenic effect of the commercial products NPE4 and NPE9 based on measures of sex ratio and vitellogenin induction.⁴ The ratio of males to females in most fish populations is known to be influenced by estrogenic compounds. Vitellogenin induction, the production of a protein expected to occur primarily in female fish, is also known to be affected by estrogen.

The misperception that commercial NPEs are estrogenic is due in part because people confuse them with nonylphenol (NP), which is only weakly estrogenic. Also, often-cited studies^{5,6} conducted a decade ago, concluded that NPEs were estrogenic in fish. Uncertainties about the chemical purity of the test material in these studies called into question the results and, as a consequence, additional studies were conducted with commercially representative material, according to accepted methodologies for measuring estrogenicity in both fish and rats. These latter studies confirmed that the commercial NPEs are not estrogenic. The results from the older studies on the test material of unknown purity were never confirmed in other studies.

¹ Williams, J., Brady, A.M., Lewis, R.W., and Hughes, L. (1996). Assessment of alkylphenol derivatives for estrogenic activity in a rat uterotrophic model. Proceedings of the 4th World Surfactants Congress, 3, 34-41, Barcelona,

² Moffat, G.J. (1996). Screening of chemicals for effects on uterine growth in immature female rats: nonyl phenol, octyl phenol and nonylphenoxyacetic acid. ICI Report No. CTL/R/1249. Unpublished study prepared for the CMA Alkylphenols and Ethoxylates Panel.

³ MB Research. (1996). Uterine Weight Assay of p-Nonylphenol (NP) and p-Octylphenol Ethoxylate-5 (OPE-5) Administered Orally to Ovariectomized Sprague Dawley Rats. Unpublished Study prepared for the CMA Alkylphenols and Ethoxylates Panel.

⁴ Balch, G.C., Metcalfe, C.D., Mihaich, E., Foran, C.M., and Peterson, B.N. (2003). Endocrine Effects in Fish from Nonylphenol Ethoxylates and their Biodegradation Metabolites. Aquatic Toxicity Workshop, Ottawa, Canada. (Manuscript in press, [Chemosphere](#))

⁵ Jobling, S., and Sumpter, J.P. (1993). Detergent components in sewage effluent are weakly oestrogenic to fish: an in vitro study using rainbow trout (*Oncorhynchus mykiss*) hepatocytes. *Aquatic Toxicology*, 27, 361-372.

⁶ Jobling, S., Sheahan, D., Osborne, J.A., Matthiessen, P., and Sumpter, J.P. (1996). Inhibition of testicular growth in rainbow trout (*Oncorhynchus mykiss*) exposed to estrogenic alkylphenol chemicals. *Environmental Toxicology and Chemistry*, 15, 194-202.