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March 23, 2018

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Re. CS: Nonylphenol ethoxylates in “inerts”

These comments to the National Organic Standards Board (NOSB) on its Spring 2018 agenda are submitted on behalf of Beyond Pesticides. Founded in 1981 as a national, grassroots, membership organization that represents community-based organizations and a range of people seeking to bridge the interests of consumers, farmers, and farmworkers, Beyond Pesticides advances improved protections from pesticides and alternative pest management strategies that reduce or eliminate a reliance on pesticides. Our membership and network span the 50 states and the world.

The NOSB should not delay in evaluating NPEs.

In Spring 2016, the Crops Subcommittee committed to a discussion document for the next meeting on removing nonylphenol ethoxylates from pesticide products used in organic production. It is a year and a half after that promised date, and we see that that project is “on hold.” These comments are intended to support an expedited approach.

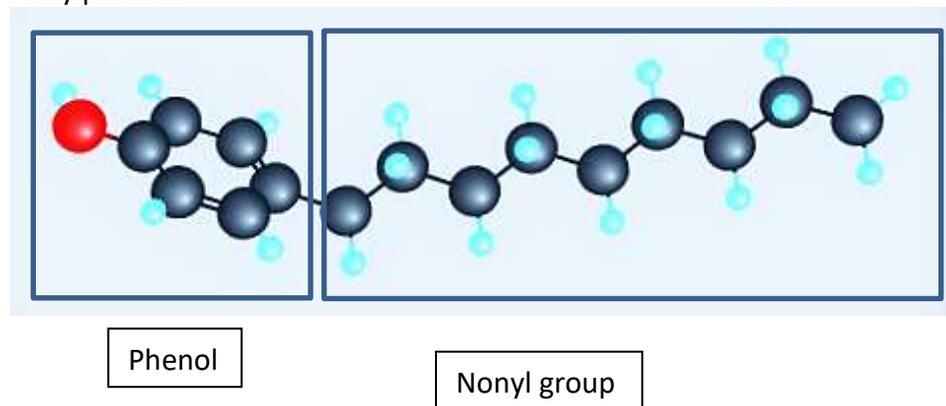
Nonylphenol was one of the first endocrine disrupting contaminants discovered. In the late 1980s, researchers in the UK discovered that effluents from sewage treatment plants were estrogenic, causing the production of vitellogenin –a hormone involved in egg production– in male fish. Results of this research were not published until 1994, but were rapidly followed by other research confirming the findings and identifying estrogenic components of sewage discharges, among them nonylphenol (NP).¹

¹ The original article was Purdom, C. E., Hardiman, P. A., Bye, V. V. J., Eno, N. C., Tyler, C. R., & Sumpter, J. P. (1994). Estrogenic effects of effluents from sewage treatment works. *Chemistry and Ecology*, 8(4), 275-285. The research that followed included (not a complete list): Sumpter, J. P., & Jobling, S. (1995). Vitellogenesis as a biomarker for estrogenic contamination of the aquatic environment. *Environmental health perspectives*, 103(Suppl 7), 173. Harries, J. E., Janbakhsh, A., Jobling, S., Matthiessen, P., Sumpter, J. P., & Tyler, C. R. (1999). Estrogenic potency of effluent from two sewage treatment works in the United Kingdom. *Environmental Toxicology and Chemistry*, 18(5), 932-937. Jobling, S., Nolan, M., Tyler, C. R., Brighty, G., & Sumpter, J. P. (1998). Widespread sexual disruption in wild fish. *Environmental science & technology*, 32(17), 2498-2506. Jobling, S., Sumpter, J. P., Sheahan, D., Osborne, J. A., & Matthiessen, P. (1996). Inhibition of testicular growth in rainbow trout (*Oncorhynchus mykiss*) exposed to estrogenic alkylphenolic chemicals. *Environmental toxicology and chemistry*, 15(2), 194-202. Desbrow, C. E. J. R.,

The major use of NP is as an intermediate in the production of nonylphenol ethoxylates (NPEs), and NP in the environment is mostly present as the major breakdown product of NPEs.² Therefore, it is fair to say that without NPEs, a major endocrine disrupting contaminant –NP– would not be present in the environment. Although the major use of NPEs has been in detergents, the use in pesticide products as a surfactant (which promotes higher penetration of the cuticle on the target insect or plant) involves direct release into the environment without the possibility of treatment to remove NPEs and NP.

What are NPEs?

Nonylphenol ethoxylates comprise a subclass of alkylphenol ethoxylates. Alkylphenol ethoxylates begin with an alkylphenol, which consists of phenol (a benzene ring with a hydroxyl group) that is bonded to an alkyl group. Alkyl groups are chains of carbon atoms (straight or branched) attached to hydrogen atoms. Alkylphenols are named according to the length of the alkyl chain –thus, nonylphenol contains a nonyl chain of nine carbons, and octylphenol contains an octyl chain of eight carbons.³ Alkylphenols are distinguished among themselves by the location of the alkyl group relative to the hydroxyl group. The molecule illustrated below is a 4-nonylphenol.



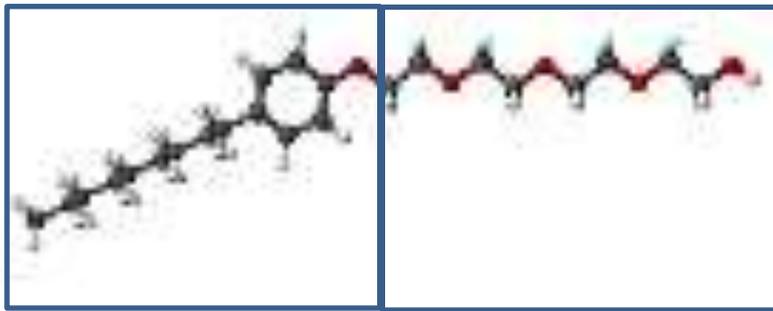
Nonylphenol is ethoxylated by inserting ethylene oxide. The degree of ethoxylation –the number of ethylene oxide molecules added– is indicated by a number, so NPE-4 might look like the following:⁴

Routledge, E. J., Brighty, G. C., Sumpter, J. P., & Waldock, M. (1998). Identification of estrogenic chemicals in STW effluent. 1. Chemical fractionation and in vitro biological screening. *Environmental science & technology*, 32(11), 1549-1558. White, R., Jobling, S., Hoare, S. A., Sumpter, J. P., & Parker, M. G. (1994). Environmentally persistent alkylphenolic compounds are estrogenic. *Endocrinology*, 135(1), 175-182.

² US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

³ Nonylphenol picture from <https://pubchem.ncbi.nlm.nih.gov/compound/4-nonylphenol#section=3D-Conformer>. Oxygen in red, carbon in black, hydrogen in light blue.

⁴ NPE-4 picture from http://www.mdpi.com/molecules/molecules-18-09441/article_deploy/html/images/molecules-18-09441-g001-1024.png. Oxygen in red, carbon in black, hydrogen in white.



Nonylphenol

Ethylene oxide X 4

However, the term NPE-4 also applies to branched molecules as well as straight chains, so there are actually many different chemicals with the same name.

NP and NPEs are toxic and estrogenic.

The term “nonylphenol ethoxylates” refers to a large group of chemicals that vary in chemical structure and toxicological effects. However, they all share common degradation products – nonylphenols and the short chain NPEs– that are more toxic and have similar effects. Since the less toxic NPEs have short biodegradation half-lives, and their metabolites are longer lived, consideration of toxicology and ecotoxicology focuses mostly on NP and the short-chain NPEs (NP-1 and NP-2), which are persistent, bioaccumulative, and extremely toxic to aquatic organisms.⁵ NP and other alkylphenols are potent xenoestrogens, causing hormonal responses at concentrations as low as 1 femtomole to 10 picomoles per liter (10^{-15} to 10^{-11} moles per liter), exceeding the potency of estradiol.⁶

The largest volume of use of NPEs has been as a surfactant in detergents, and EPA established water quality criteria for NP of 6.6 $\mu\text{g/L}$ for acute exposures and 1.7 $\mu\text{g/L}$ for chronic exposures. EPA’s Design for the Environment/Safer Choice program is actively promoting alternative surfactants in order to reduce discharges of NPEs and NP into surface water. However, significant quantities of direct discharges of NPEs also find their way into surface water from agricultural fields.⁷

Classification and Identification of NP and NPEs

NPEs vary in the location of the nonyl group, the branching of the nonyl group, and the degree of ethoxylation. These may all have an impact on the toxicity and other impacts of NPEs. In

⁵ US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

⁶ Kochukov, M. Y., Jeng, Y. J., & Watson, C. S. (2009). Alkylphenol Xenoestrogens with Varying Carbon Chain Lengths Differentially and Potently Activate Signaling and Functional Responses in $\text{GH}_3/\text{B}_6/\text{F}_{10}$ Somatomammotropes. *Environmental health perspectives*, 117(5), 723.

⁷ Zgoła-Grzeškowiak, A., Grzeškowiak, T., Rydlichowski, R., & Łukaszewski, Z. (2009). Determination of nonylphenol and short-chained nonylphenol ethoxylates in drain water from an agricultural area. *Chemosphere*, 75(4), 513-518.

addition, NPEs generally occur in mixtures of isomers, and are identified by the predominant isomer in the mixture.

NPEs are identified by their degree of ethoxylation, ranging from four (NPE-4) to 80 (NPE-80) ethoxylates per molecule in commercial use. NPE-9s are by far the most commonly manufactured NPEs. While some CAS numbers specific to certain levels of ethoxylation exist, all degrees of ethoxylation may be subsumed under the CAS number for polyethoxylates (CAS # 127087-87-0), as long as they are synthesized via polymerization reaction between NP and ethylene oxide.⁸ EPA explains further:⁹

Chemical Abstract Service registry names and numbers (CASRNs) routinely used to refer to nonylphenols or nonylphenol ethoxylates may not accurately reflect the identity of those substances. The nine carbon nonyl group may be branched or linear and bind at various locations around the phenol ring (“ortho”, “meta” or “para”). Many manufacturers incorrectly use the linear identity when referring to the branched nonylphenol. CASRN 84852-15-3 corresponds to the most widely produced nonylphenol, branched 4-nonylphenol (referred to herein as NP). Note that NP is not a single chemical structure. It is a complex mixture of highly branched nonylphenols, largely mono-substituted in the *para*- position, but with small amounts of *ortho*- and di-substituted nonylphenols. In addition it includes small amounts of branched C₈ and C₁₀ alkyl groups (Seidel 2004a). Much of the literature refers to the linear (or normal-) nonylphenol (CASRN 25152-52-3), often the specific *para*- regioisomer (i.e. 4-n-nonylphenol, CASRN 104-40-5). Many, but not all, references are inaccurate about the identity of the substances listed as nonylphenol. This is likely due to inaccurate identities in the source material. A supplier of nonylphenol may use CASRN 104-40-5, signifying 4-n-nonylphenol, while actually supplying branched 4-nonylphenol (CASRN 84852-15-3).

The mono- and di-ethoxy NPEs (NP1EO, NP2EO [NP-1, NP-2]) do not appear on the TSCA inventory, but are among the degradation products of the polymeric NPEs and may be present with NP in the environment in appreciable concentrations.

Toxicity and Estrogenicity of NPEs and NP

NPEs are generally considered to have low acute toxicity to humans, but NP is highly irritating and corrosive to the skin and eyes.¹⁰ Chronic toxicity manifests as decreased food

⁸ US EPA, 2012. DfE Alternatives Assessment for Nonylphenol Ethoxylates.

https://www.epa.gov/sites/production/files/2014-06/documents/npe_final.pdf.

⁹ US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

¹⁰ Danish Environmental Protection Agency. (1999). Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl, Phosphates and Benzoic Acid. <http://www.statensnet.dk/pligtarkiv/fremvis.pl?vaerkid=6944&reprid=0&filid=22&iarkiv=1%20-%20non8.1>.

utilization and body weight; increases in relative weights of kidney, liver, and testes; decreased ovary size; and significant changes in blood chemistry.¹¹

On the other hand, NP and NPEs are highly toxic to fish, aquatic invertebrates, and aquatic plants, with short chain NPEs being about half as toxic as NP. The bioconcentration factor for NP in fish is low, but in mussels ranges from low to moderate.¹²

The most important impacts of NP and NPEs are their effects on the endocrine and reproductive systems. As noted at the beginning, NP was among the first xenoestrogens identified in the environment. Xenoestrogens—synthetic chemicals that behave like the hormone estrogen—comprise one class of endocrine disrupting chemicals (EDCs). EPA points out the likely danger to children from exposure to NPEs.¹³

Experts in endocrinology have warned, citing the low dose effects of NP among other chemicals, that the regulation of EDCs should be based on the principles of endocrinology.¹⁴ This means that regulation of EDCs must take into account, among other things, the fact that hormones act at low doses, and that low doses sometimes have a greater effect—or the opposite effect—than higher doses. Hence, in regulating EDCs, the aim should be not to reduce exposure—which may merely change the impact of the chemical without reducing it—but to eliminate exposure.

NP and NPEs are part of a larger class of chemicals—APs and APEs—that share the same toxic features.

Nonylphenol belongs to a larger class—alkylphenols (APs)—all of which contain an alkyl group attached to phenol. The similarities are recognized by the adoption of alkylphenols as a category in EPA's High Production Volume (HPV) Challenge Program. The class includes propylphenol, butylphenol, amylphenol, heptylphenol, octylphenol, nonylphenol, dodecylphenol and others.¹⁵ Like nonylphenol, the others may also be ethoxylated to form alkylphenol ethoxylates (APEs). Just as NPEs are metabolized to NP and shorter chain NPEs,

¹¹ Danish Environmental Protection Agency. (1999). Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl, Phosphates and Benzoic Acid.

<http://www.statensnet.dk/pligtarkiv/fremvis.pl?vaerkid=6944&reprid=0&filid=22&iarkiv=1%20-%20non8.1>.

¹² US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

¹³ US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

¹⁴ Vandenberg, L. N., Colborn, T., Hayes, T. B., Heindel, J. J., Jacobs, D. R., Lee, D. H., ... & Welshons, W. V. (2013). Regulatory decisions on endocrine disrupting chemicals should be based on the principles of endocrinology. *Reproductive Toxicology*, 38, 1-15.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902067/pdf/nihms445411.pdf>.

¹⁵ Schenectady International, 2002. Alkylphenols Category: Section One, Development of Categories and Test Plans. Submitted to EPA for the HPV Challenge Program, Chemical Right-to-Know Initiative.

other APEs break down to APs and shorter chain APEs.¹⁶ A large body of research confirms that these metabolites are xenoestrogens.¹⁷ Besides their endocrine disrupting effect, APs and APEs have been identified as potential carcinogens, hepatotoxins, genotoxins, and modifiers of basic survival behaviors.¹⁸

The process of eliminating NP and NPEs from production and use is underway.

The problems associated with NP and NPEs are widely recognized. Regulatory agencies worldwide are responding to documented threats from exposure of humans and the environment to NP and NPEs.¹⁹ The response has been in the form of identifying alternative surfactants and encouraging their use. In the EU, legislation under the regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) limits the marketing and use of NP and NPEs for most uses, including cleaning products, teat dips, and pesticide co-formulants, to concentrations of less than 0.1%.²⁰ In the U.S., EPA has initiated an action plan under the Toxic Substances Control Act and through the agency's Design for the Environment/Safer Choice program to identify and encourage the use of substitutes for NP and NPEs, which has resulted the adoption of alternative surfactants in many cases.²¹

¹⁶ Ying, G. G., Williams, B., & Kookana, R. (2002). Environmental fate of alkylphenols and alkylphenol ethoxylates—a review. *Environment international*, 28(3), 215-226.

<http://iris.metis.upmc.fr/laborie/Recherches%20Th%C3%A8se/Alkylph%C3%A9nols/Environmental%20fate%20of%20alkylphenols%20and%20APE%20-%20A%20review.pdf>.

¹⁷ For example, Kochukov, M. Y., Jeng, Y. J., & Watson, C. S. (2009). Alkylphenol Xenoestrogens with Varying Carbon Chain Lengths Differentially and Potently Activate Signaling and Functional Responses in GH₃B₆/F₁₀ Somatomammotropes. *Environmental health perspectives*, 117(5), 723; White R, Jobling S, Hoare SA, Sumpter JP, Parker MG. 1994. Environmentally persistent alkylphenolic compounds are estrogenic. *Endocrinology* 135(1):175-182; Kovarova, J., Blahova, J., Divisova, L., & Svobodova, Z. (2013). Thiele, B., Günther, K., & Schwuger, M. J. (1997). Alkylphenol ethoxylates: trace analysis and environmental behavior. *Chemical reviews*, 97(8), 3247-3272. https://www.researchgate.net/profile/Bjoern_Thiele2/publication/11509044_Alkylphenol_Ethoxylates_Trace_Analysis_and_Environmental_Behavior/links/54ae2a020cf24aca1c6f752d.pdf.

¹⁸ Kovarova, J., Blahova, J., Divisova, L., & Svobodova, Z. (2013). Alkylphenol ethoxylates and alkylphenols—update information on occurrence, fate and toxicity in aquatic environment. *Polish journal of veterinary sciences*, 16(4), 762-771.

¹⁹ US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. U.S. Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf. Danish Environmental Protection Agency. (1999). Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl, Phosphates and Benzoic Acid.

<http://www.statensnet.dk/pligtarkiv/fremvis.pl?vaerkid=6944&reprid=0&filid=22&iarkiv=1%20-%20non8.1>.

European Chemicals Bureau (ECB). (2014). Background Document to RAC AND SEAC Opinions on Nonylphenol ethoxylate. <http://echa.europa.eu/documents/10162/8bdb40dc-1367-480e-8d81-b5d308bc5f81>.

²⁰ REACH factsheet on NP and NPEs. <http://eng.mst.dk/topics/chemicals/legislation-on-chemicals/fact-sheets/fact-sheet-nonylphenol-and-nonylphenol-ethoxylates/>.

²¹ US EPA. 2010. Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan [RIN 2070-ZA09]. US Environmental Protection Agency, August 2010. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf.

The NOSB and NOP should be among the leaders in eliminating NP and NPEs.

The Principles of Organic Production and Handling adopted by the National Organic Standards Board in 2001 begin with the statement, “Organic agriculture is an ecological production management system that promotes and enhances biodiversity, biological cycles, and soil biological activity.” The use of toxic and endocrine-disrupting materials like NP and NPE is clearly inconsistent with that requirement, as stated in the Technical Review of NPEs:

[T]he use of NPEs in organic agriculture is ultimately tied to the environmental contamination resulting from the industrial production of NPE adjuvants and associated waste streams from these processes.

NPEs do not exhibit the high levels of toxicity, estrogenic activity or environmental persistence associated with NP. However, release of NPEs to the environment from agricultural and consumer products ultimately leads to the introduction of more highly toxic and persistent NP residues. A lifecycle analysis of NPEs therefore highlights a conflict between use of these substances and the principles of organic agriculture, which seeks to avoid contamination of the environment with toxic and persistent substances.

However, the responsibility of organic regulators and practitioners goes beyond the compatibility with organic principles and compliance with organic standards. Organic production should be leading the way in environmental protection and regeneration. One of the purposes of the Organic Foods Production Act, as stated in the Senate version of the bill, is to “encourage environmental stewardship through the increased adoption of organic, sustainable farming methods.”²² With regard to NP and NPEs, the organic sector has fallen behind the industry. EPA has identified alternatives to NPEs, and it is time for the NOSB and National Organic Program to prohibit these harmful substances.

Thank you for your consideration of these comments.

Sincerely,



Terry Shistar, Ph.D.
Board of Directors

²² House Conference Report, Food and Agriculture Act of 1990.