January 17, 2019

Karl Palmer, Chief
Safer Products and Workplaces Program
Department of Toxic Substances Control
1001 I Street
Sacramento, CA 95814

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF NONYLPHENOL ETHOXYLATES (NPEs) IN LAUNDRY DETERGENT AS A PRIORITY PRODUCT

Dear Mr. Palmer:

This letter responds to the attached October 24, 2018 request for external scientific peer review for the subject noted above. The review process is described below. All steps were conducted in confidence. Reviewers' identities were not disclosed.

To begin the process for selecting reviewers, I contacted the University of California, Berkeley (University) and requested recommendations for candidates considered qualified to perform the assignment. The University was provided with the October 24, 2018 request letter to me and attachments. No additional material was asked for. This service by the University includes interviews of each promising candidate and is supported through an Interagency Agreement cosigned by CalEPA and the University.

Each candidate who was both qualified and available for the review period was asked to complete a Conflict of Interest (COI) Disclosure form and send it to me for review, with Curriculum Vitae. The cover letter for the COI form describes the context for COI concerns that must be taken into consideration when completing the form. "As noted, staff will use this information to evaluate whether a reasonable member of the public would have a serious concern about [the candidate's] ability to provide a neutral and objective review of the work product."

Later, I sent approved reviewers letters to initiate the review. These letters provided access instructions to a secure FTP site where all material to be reviewed was placed. Attachment 2 to the October 24, 2018 request memorandum was highlighted as the focus for the review. Each initiating letter identified specific conclusions which that reviewer committed to address. This commitment is detailed in the paragraph following "Attachment 2", appearing on page 2 of the letter. Thirty days were provided for the review. I also asked reviewers to direct enquiring third-parties to me after they have submitted their reviews.

With the same letter, I provided the attached October 2018 Supplement to the CalEPA Peer Review Guidelines, which, in part, serves two purposes: a) it provides guidance to ensure confidentiality through the course of the external review, and b) it notes reviewers are under no objection to discuss their comments with third-parties after reviews have been submitted. **We recommend they do not.** All outside parties are provided opportunities to address a proposed regulatory action through a well-defined rulemaking process.

Reviewers' names, affiliations, curriculum vitae, and reviews are being sent to you now with this letter. All attachments can be electronically accessed through the bookmark icon at the left of the screen.

Approved reviewers are as follows:

1. Michael J. Carvan, Ph.D.
Professor, School of Freshwater Sciences
University of Wisconsin - Milwaukee
600 E. Greenfield Avenue
Milwaukee, Wisconsin 53204
Phone: (414) 382-1706
Email: carvanmj@uwm.edu

2. Chis Metcalfe, Ph.D.
Professor, School of the Environment
Trent University
1600 West Bank Drive
Peterborough, Ontario, Canada K9L 0G2
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3. Heiko L. Schoenfuss, Ph.D.
Professor
Department of Biology, WSB-273
St. Cloud State University
St. Cloud Minnesota 56301
Phone: (320) 308-3130 (office)
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If you have any questions, or require clarification from the reviewers, please contact me directly.

Regards,

Gerald W. Bowes

Gerald W. Bowes, Ph.D.
Manager, Cal/EPA Scientific Peer Review Program
Office of Research, Planning and Performance
State Water Resources Control Board
1001 “I” Street, 16th Floor
Sacramento, California 95814
Telephone: (916) 341-5567
Email: gerald.bowes@waterboards.ca.gov

cc: Nancy Ostrom, Senior Environmental Scientist

Attachments:

(1) October 24, 2018 Request by Karl Palmer for Scientific Peer Review
(2) Letters to Reviewers Initiating the Review
  (a) Michael J. Carvan, Ph.D.
  (b) Chis Metcalfe, Ph.D.
  (c) Heiko L. Schoenfuss, Ph.D.
(3) October 22, 2018 Supplement to Cal/EPA Peer Review Guidelines
(4) Curriculum Vitae
  (a) Michael J. Carvan, Ph.D.
  (b) Chis Metcalfe, Ph.D.
  (c) Heiko L. Schoenfuss, Ph.D.
(5) Reviews
  (a) Michael J. Carvan, Ph.D.
  (b) Chis Metcalfe, Ph.D.
  (c) Heiko L. Schoenfuss, Ph.D.

ATTACHMENT 1

Department of Toxic Substances Control

Matthew Rodriquez
Secretary for
Environmental Protection

Barbara A. Lee, Director
1001 "I" Street
P.O. Box 806
Sacramento, California 95812-0806

Edmund G. Brown Jr.
Governor

M E M O R A N D U M

TO: Gerald Bowes, Ph.D.
Manager, CalEPA Scientific Peer Review Program
Office of Research, Planning and Performance
State Water Resources Control Board

FROM: Karl Palmer, Chief
Safer Products and Workplaces Program
Department of Toxic Substances Control

DATE: October 24, 2018

SUBJECT: REQUEST FOR EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF NONYLPHENOL ETHOXYLATES (NPES) IN LAUNDRY DETERGENT AS A PRIORITY PRODUCT

The subject of this review is a proposed regulation to adopt the following product-chemical combination as a Priority Product:

Nonylphenol Ethoxylates (NPEs) in Laundry Detergents

The California Safer Consumer Products (SCP) regulations[1] require the Department of Toxic Substances Control (DTSC) to identify product-chemical combinations that pose risks to people or the environment and to adopt them as Priority Products[2] in regulation. Once DTSC adopts a Priority Product in regulation, manufacturers must take one of the following actions to improve the safety of their products:

- remove or replace the Chemical(s) of Concern in the product,

[1] California Code of Regulations, Title 22, sections 69503 – 69503.7
[2] "Priority Products" are consumer products that a) contain chemicals included in DTSC's Candidate Chemicals List; b) may expose people or the environment to these chemical(s) through normal use; and c) have been adopted in regulation. Candidate Chemicals exhibit hazard traits or environmental or toxicological endpoints and are included on authoritative lists established by government agencies or scientific organizations (www.dtsc.ca.gov/SCP).

- remove the product from the California marketplace, or
- conduct an Alternatives Analysis (AA) to determine if safer alternatives exist.

In accordance with Health and Safety Code section 57004, DTSC requests external scientific peer review of the basis for proposing NPEs in Laundry Detergents as a Priority Product. As required by regulation, DTSC reviewed reliable scientific literature and concluded that this product-chemical combination meets the required regulatory criteria[3] for listing as a Priority Product based on the following conclusions:

1. NPEs are a class of chemicals that can be broken down to form degradation products, including nonylphenol, and enter the aquatic environment,
2. NPEs and their degradation products have hazard traits and can cause cumulative adverse impacts when organisms are exposed to the class of chemicals,
3. Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environment, and
4. Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organism due to the adverse impact and exposure considerations described in the product-chemical profile.

For this review, DTSC recommends that reviewers have expertise in the following areas, in order of importance:

- aquatic toxicology, especially for fish and invertebrates, associated with nonylphenol ethoxylates or Chemicals of Emerging Concern. This expertise is needed for Conclusions 2 and 4.
- aquatic exposure assessment, especially for sewage derived contamination. This expertise is needed for Conclusions 3 and 4.
- fate and transport of aquatic contaminants, especially for nonylphenol ethoxylates. This expertise is needed for Conclusions 1 and 3.

We estimate that three reviewers will be adequate to cover all of the necessary areas of expertise.

DTSC intends to initiate the formal rulemaking process by early 2019. The documents are ready for review at any time, and the preferred period of review is 30 days. The following attachments are enclosed:

- Attachment 1: Plain English Summary of the Proposal to Adopt NPEs in Laundry Detergents as a Priority Product

[3] Prior to proposing a product-chemical combination for adoption as a Priority Product, DTSC must ensure that the product-chemical combination meets both of the following criteria: 1) there must be potential public and/or environmental exposure to the chemical(s) in the product; and 2) there must be potential for one or more exposures to contribute to or cause significant or widespread adverse impacts (22CCR section 69503.2(a)).

- Attachment 2: Scientific Conclusions to Be Addressed by Peer Reviewers
- Attachment 3: List of Participants
    - Section A: DTSC Participants
    - Section B: External Participants
- Attachment 4: Reference Titles

Please direct inquiries regarding this request to Nancy Ostrom, of my staff, at nancy.ostrom@dtsc.ca.gov or 916-445-3077.

Attachment 1:

Plain English Summary of the Proposal to Adopt Laundry Detergents Containing Nonylphenol Ethoxylates (NPEs) as a Priority Product

A. Brief Statement of Conclusions[4]

DTSC identified laundry detergents containing nonylphenol ethoxylates (NPEs) as a proposed Priority Product. This determination was based on a consideration of available, reliable scientific and/or authoritative information regarding the potential for exposure to NPEs from laundry detergents and the potential for these exposures to contribute to or cause significant or widespread adverse impacts to aquatic organisms.

NPEs are a class of surfactants (compounds in detergents that increase cleaning efficiency) used for their cleaning properties in a variety of consumer products. NPEs are well-known aquatic toxicants that break down into nonylphenol and other degradation products that are more toxic than NPEs. Nonylphenol can persist in the environment and is the most characterized of these chemicals. NPEs and their degradation products can impact the growth, reproduction, and development of fish and aquatic invertebrates at low concentrations. Cumulative exposure to NPEs and their degradation products can affect aquatic wildlife populations.

DTSC determined that there is a potential for exposure related to the use of laundry detergents containing NPEs, and there is potential for these exposures to cause or contribute to significant or widespread adverse impacts to aquatic organisms. This determination is based on chronic exposure to NPEs and their degradation products in the aquatic environment and their respective hazard traits.

Laundry detergents are marketed to on-premises launderers like hotels and hospitals, which can discharge significant amounts of NPEs to wastewater treatment plants. An estimated 2 billion pounds of laundry are washed per year by on-premises launderers in California, and concentrations of NPEs in these laundry detergents can range from 5 to 50 percent. NPEs are continuously released to the aquatic environment through wastewater discharge (effluent).

Nonylphenol has been detected in California surface waters, sediments, and wastewater-related media, including influent, effluent, sludge, and biosolids. These detections can exceed aquatic guidelines, standards, or criteria established by various governments to protect aquatic organisms from adverse impacts. Detections in coastal organisms across multiple levels of the food chain illustrate that nonylphenol can transfer from the aquatic environment to these organisms. Since California's surface water environments provide habitat for hundreds of fish species (including several endangered or threatened species) and hundreds of freshwater invertebrate species, many important populations may be impacted by exposure to NP. These

[4] Excerpted from "*Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent.*" page 4.

high environmental concentrations and widespread detections in organisms demonstrate the potential for NPEs and their degradation products to contribute to significant or widespread adverse impacts to aquatic organisms.

B. Overview of the Safer Consumer Products Regulatory Program

The SCP program's primary goal is to ensure safer products and healthier lives by reducing and eliminating use of toxic chemicals in consumer products sold in California.

The SCP regulations, implemented on October 1, 2013, specify the process for identifying consumer products that contain hazardous chemicals, evaluating safer alternatives to those chemicals, and eliminating or reducing potential exposures to and adverse impacts from these products. The regulations intentionally use a narrative standard for identifying and prioritizing product-chemical combinations, rather than a traditional risk-assessment-driven decision-making standard. This approach provides DTSC with a flexible process that allows the SCP program make decisions based on a reasonable amount of reliable information and the potential for exposure and adverse impacts. The SCP regulations also use the hazard traits, toxicological and environmental endpoints, and other relevant data contained in Chapter 54 of the California Code of Regulations, Title 22.

To adopt a Priority Product listing, DTSC must follow the procedure described in the SCP regulations and adopt the listings through a rulemaking procedure. These regulations use the following prioritization factors[5] for listing Priority Products:

- There must be potential[6] public and/or aquatic, avian, or terrestrial animal or plant organism exposure[7] to the Candidate Chemical(s) in the product; and
- There must be the potential for one or more exposures to contribute to or cause significant or widespread adverse impacts.[8]

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[5] CCR §69503.2 *et seq*.
[6] "Potential" is defined as reasonably foreseeable, based on reliable information (CCR §69503.1(a)(51)).
[7] The potential for exposure is evaluated by considering one or more of the following factors: market presence of the product, the occurrence or potential occurrence of exposures to the Candidate Chemical in the product, the household and workplace presence of the product, potential exposure to the Candidate Chemical in the product during the product's lifecycle (CCR §69503.3(b)).
[8] 22 CCR §69503.2 and §69503.3. The potential to contribute to or cause adverse impacts is evaluated by considering reasonably available information about one or more of the following factors: hazard traits, endpoints, aggregate effects, cumulative effects, physicochemical properties, environmental fate, affected populations or organisms, potential for the Candidate Chemical(s) to degrade, form reaction products, or metabolize into another chemical that exhibits hazard traits or endpoints. DTSC shall give special consideration to the potential for adverse impacts to sensitive subpopulations, environmentally sensitive habitat, endangered and threatened species, and impaired environments. DTSC may also evaluate and consider adverse impacts associated with structurally or mechanistically similar chemicals with known toxicity profiles.

Once DTSC adopts a Priority Product listing, DTSC requires product manufacturers to submit a Priority Product notification[9] and conduct one of several types of Alternatives Analyses to determine if safer alternatives exist.[10] Alternatively, product manufacturers may instead elect to:

- remove or replace the chemical of concern in the product with a safer alternative, or
- remove the product from the California marketplace.

If the product manufacturers do not comply, DTSC is authorized to require importers, assemblers, and/or retailers to stop selling the product in California.

B. Overview of the Proposal to Adopt NPEs in Laundry Detergent as a Priority Product

The proposed regulation defines laundry detergent as any product intended to clean or remove soil or unwanted deposits from laundered clothes and textile products, such as sheets and tablecloths. This includes but is not limited to laundry detergents of any form, including granules, liquids, powders, tabs, crystals, or pods, that are used in washing machines, for hand washing, or as part of a laundry system. Detergents intended for use as a pre-soak or pre-spotter or with fabric or color protection properties are also included

As required by regulation, DTSC considered a number of factors including the hazard traits, toxicological and environmental endpoints, and environmental fate associated with NPEs as well as potential adverse impacts to aquatic organisms.

After reviewing the scientific literature and obtaining stakeholder input during public workshops, DTSC concluded that aquatic organisms are likely to be exposed to NPEs once laundry detergents containing this class of chemicals are discharged from drains and wastewater treatment plants. These exposures may contribute to or cause significant or widespread adverse impacts to those exposed due to the following hazard traits and toxicological and environmentals endpoints:

- Bioaccumulation of nonylphenol in some conditions
- Environmental persistence of nonylphenol in some conditions
- Immunotoxicity, including changes in circulating immune cell numbers,
- Wildlife developmental impairment, including malformations, adverse impacts on rate of development and metamorphosis in aquatic species,
- Wildlife growth impairment, including abnormalities in growth rates and body size in aquatic species,

[9] CCR §69503.7.
[10] CCR §69505.1 *et seq*.

- Wildlife reproductive impairment, including adverse changes in reproductive endocrine function, structure and function of reproductive organs, including intersex organs, secondary sex characteristics, and vitellogenin production,
- Wildlife survival impairment, including death and narcosis.

By concluding that exposures to NPEs through the use of laundry detergents have the potential to adversely affect the health of aquatic organisms, DTSC has met the regulatory requirements to adopt this 'product-chemical' combination as Priority Product in regulation. Once this regulation is adopted, DTSC will have the authority to require the manufacturers to determine if there are safer alternatives to these chemicals.

Attachment 2:

Scientific Conclusions to Be Addressed by Peer Reviewers Regarding DTSC's Proposal to Adopt NPEs in Laundry Detergents as a Priority Product

The statutory mandate for external scientific peer review (Health and Safety Code section 57004) states that the reviewer's responsibility is to determine whether the scientific portion of the proposed regulation is based on sound scientific knowledge, methods, and practices.

DTSC requests that you make this determination for each of the following conclusion statements that constitute the scientific portion of the proposed regulation. An explanatory statement is provided for each conclusion to focus this review.

The subject of this review is a proposed regulation to adopt NPEs in Laundry Detergents as a Priority Product under the Safer Consumer Products regulatory framework. This framework requires DTSC to ensure that all product-chemical combinations proposed as Priority Products meet the following criteria:

- There is potential for exposure to the Candidate Chemical(s) in the product, and
- Exposures may contribute to or cause significant or widespread adverse impacts to people or the environment.

Following a review of available scientific literature, DTSC concluded that the proposal to adopt NPEs in Laundry Detergents as a Priority Product meets the required regulatory criteria described above and requests that this review focus on the following conclusions:

1. NPEs are a class of chemicals that can be broken down to form degradation products, including nonylphenol, and enter the aquatic environment,
2. NPEs and their degradation products have hazard traits and can cause cumulative adverse impacts when organisms are exposed to the class of chemicals,
3. Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environment, and
4. Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organism due to the adverse impact and exposure considerations described in the product-chemical profile.

The results of DTSC's scientific literature review and research are presented in the report, "*Product-Chemical Profile for NPEs in Laundry Detergents*" completed in May 2018 and subsequently updated in September 2018. The framework regulations for the SCP program and the references listed in the specific sections of this report noted below will be provided on CD(s). DTSC will provide additional references from this report or the framework regulations upon request.

Conclusion #1

NPEs are a class of chemicals that can be broken down to form degradation products, including nonylphenol, in wastewater treatment plants or the aquatic environment.

NPEs released from laundry detergents to wastewater treatment plants (WWTPs) and the aquatic environment will break down into intermediate degradation products such as shorter chained NPEs, nonylphenol ethoxy carboxylates (NPECs), and NP. Degradation of NPEs is fastest in oxic (oxygen containing) environments such as surface waters and slowest in anoxic (oxygen poor) environments such as sediments. The resulting degradation products are less biodegradable than the parent compounds.

The breakdown of NPEs to intermediate degradation products is primarily attributed to biodegradation via shortening of the ethoxylate side chain to short-chain NPEs and oxidation to NPECs, which can be further degraded to nonylphenol (NP). Shorter-chained NPEs (e.g. NP1-3EO) and NP degrade more slowly than longer-chain NPEs. Once shorter-chained NPEs and NP are formed, the ultimate breakdown to carbon dioxide and water under anaerobic conditions is unlikely.

Incomplete removal of NPEs in wastewater treatment plants can lead to high concentrations of NPEs' degradation products (NPEDs) in wastewater effluent, sludge, and biosolids. While WWTPs effectively degrade higher-ethoxylated NPEs, the overall removal rate drops considerably when NPECs, shorter-chain NPEs, and NP are accounted for.

NPEs and their degradation products partition differentially across sediments and water according to their physicochemical properties. NP1-3EOs and NP preferentially partition to the organic matter found in sediments, particulates, and sludges, while the more water soluble, higher ethoxylated NPEs and NPECs are found more readily in water and effluent. While NP is not considered to be mobile in the aquatic environment, sediments that accumulate NP and NP1-2EOs may become resuspended and serve as a continued source of these compounds to the water column.

The presence of NPEs, NPDs, and NP in surface waterbodies and underlying sediments is a definitive indicator for the potential exposure of aquatic organisms to those compounds.

The sections of the product-chemical profile (noted above) that pertain to Conclusion 2 include:

- Summary, page 4,
- Section 2.1 – Physicochemical Properties, pages 9 – 10,
- Section 2.2 – Fate and Transport, pages 10 - 13

References included in these sections will be provided to the reviewers as part of this request.

Conclusion #2

NPEs and their degradation products have hazard traits and can cause cumulative adverse impacts when aquatic organisms are exposed to mixtures of the class of chemicals.

NPEs have the following hazard traits because they are acutely toxic to aquatic organisms (e.g., fish and aquatic invertebrates), and they break down to several degradation products that are more potent than NPEs. NP is the best characterized of these degradation products and are associated with the following environmental and toxicological hazard traits, as defined by the Green Chemistry Hazard Trait regulations:

- wildlife growth impairment,
- wildlife reproductive impairment,
- wildlife developmental impairment,
- wildlife survival impairment, and
- immunotoxicity.

These hazard traits are based on laboratory testing on aquatic organisms at concentrations less than 20 µg/L. Additionally, NP exhibits the following exposure potential hazard traits: environmental persistence, and bioaccumulation. Authoritative reports show human hazard traits associated with NPEs and their degradation products. However, that is not the basis of the proposed regulation, and therefore not required for the External Scientific Peer Review.

DTSC also recognizes that because NPEs and their degradation products each exhibit hazard traits, there are cumulative impacts associated with this group of chemicals. Some authoritative organizations have developed methods for quantifying these cumulative impacts. DTSC applied one of these methods (Canada's toxic equivalency factors) to environmental monitoring data as an example, which illustrated that the effective hazards of NPEs and their degradation products combined is higher than just considering NP alone in environmentally relevant samples.

There is a potential for exposures to pesticides combined with alkylphenols and alkylphenol ethoxylates (chemical classes that includes NP and NPEs) to produce a synergistic reproduction-related effect in whole fish. However, contrasting results in cell cultures suggest that the physiological pathways that trigger the effect in whole fish are complex and need further evaluation.

The sections of the product-chemical profile (noted above) that pertain to Conclusion 2 include:

- Summary, page 4,
- Section 2.3 – Hazard Traits, pages 14 – 17;
- Section 2.4.1 – Cumulative Effects With Other Chemicals, pages 19-21
- Section 5.1.4 – Additional Considerations, pages 49-51
- Appendix C – Summary of Hazard Traits Associated with NP

References included in these sections will be provided to the reviewers as part of this request.

Conclusion #3

Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environnment.

NPEs are surfactants used to increase cleaning efficiency in laundry detergents. While the use of these chemicals appears to be phased out in household and industrial laundry detergents, they are still used in detergents marketed to on-premises laundries (OPLs) such as hotels, hospitals, and nursing facilities. An online search of laundry detergents intended for OPLs found detergents containing NPEs available for sale from over 25 percent of manufacturers.

OPLs in California wash an estimated 2 billion pounds of laundry per year. Based on recommend usage rates and active ingredient concentrations of detergents containing NPEs, this equates to over 2 million pounds of NPEs used in California per year. Since the purpose of NPEs is to remain in the wash water, it is assumed that all of the NPEs in laundry detergents is released to wastewater treatment plants (WWTPs).

WWTPs in California discharge significant volumes of wastewater directly into the aquatic environment. Secondary wastewater-related sources of NPEs and NPEDs in the aquatic environment include WWTP effluent discharged to land, irrigation with recycled water, wastewater treated by septic tanks, and runoff from the land application of biosolids.

NPEs and their degradation products are detected in wastewater-related samples (i.e., effluent, influent, biosolids, and septic tank liquids and solids) and environmental media (surface water, sediment, and aquatic biota) in California.

The sections of the product-chemical profile (noted above) that pertain to Conclusion 3 include:

- Section 3.1.1- 3.1.2 – Presence and Use Patterns of the Product, pages 31 – 32,
- Section 3.3 – Exposures to the Candidate Chemical Throughout the Product Life Cycle, pages 35 – 42,
- Appendix E – Environmental monitoring data for NPEs and NPEDs, pages 92 – 106,

References included in these sections will be provided to the reviewers as part of this request.

__Conclusion 4__.

Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organism due to the adverse impact and exposure considerations in the product-chemical profile.

The previously listed conclusions, paraphrased below, demonstrate the potential for aquatic organisms to experience adverse impacts or exposure to NPEs and their degradation products:

- Conclusion 1: NPEs are a class of chemicals that can be broken down to form degradation products, including nonylphenol, in wastewater treatment plants or the aquatic environment,
- Conclusion 2: NPEs and their degradation products have hazard traits and can cause cumulative adverse impacts when organisms are exposed to the class of chemicals,
- Conclusion 3: Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environment.

There are additional factors in the Profile that build on these conclusions to support the determination that the exposure of aquatic organisms to NPEs and their degradation products have the potential to cause or contribute to *significant or widespread* adverse impacts, as summarized here:

- Recent detections of NPEs' degradation products in freshwater, marine water, and sediment can exceed guidelines, standards, or criteria (GSCs) established by authoritative organizations. GSCs are concentrations intended to be protective of aquatic organisms chronically exposed to nonylphenol or NPEs and their degradation products. The exceedances noted by DTSC may be due to exposure of nonylphenol alone, or mixtures of NPEs and their degradation products (*See* Sections 3.3.1 and 5.1.4, and Appendix E-3 and E-4).
- Detections of nonylphenol in California aquatic organisms are widespread (*See* Section 3.3.1 and Appendix E-6)
- California has hundreds of wastewater treatment plants that discharge into surface water that result in wastewater-impacted environments. These environments are habitat for early life stage aquatic organisms, which are particularly sensitive to the adverse effects of NPEs and their degradation products, and for threatened and endangered fish species. Wastewater discharge can result in chronic exposure of NPEs to aquatic organisms. In some of these environments, wastewater serves as the dominant water source resulting in exposure to higher concentrations of NPEs and their degradation products and for longer periods of time. California experiences long-term droughts which has the potential to exacerbate concentrations of contaminants such as NPEs (*See* Sections 2.5.1 3.3.1 3.3.3 and 2.5.2, and Appendix C).

The sections of the product-chemical profile (noted above) that pertain to Conclusion 4 include:

- Section 2.5 – Populations that may be harmed by the Candidate Chemical, pages 21-30
- Section 3.3.1 – Environmental detections of NPEs, and their exceedances of GSCs, pages 35 – 38,
- Section 3.3.3 – Exposures to the Candidate Chemical Throughout the Product Life Cycle, pages 42 – 43,
- Section 5.1.4 – Additional Considerations, pages 49 – 51,
- Appendix E – Environmental monitoring data for NPEs and NPEDs, pages 92 – 106.

References included in these sections will be provided to the reviewers as part of this request.

The Big Picture

Reviewers are not limited to addressing only the specific issues presented above, and are asked to contemplate the following questions.

(a) In reading the product-chemical profile and proposed implementation language, are there any additional scientific issues that are part of the scientific basis of the proposed regulation not described above? If so, please comment.

(b) Taken as a whole, is the scientific portion of the proposed regulation based upon sound scientific knowledge, methods, and practices?

Reviewers should also note that some proposed regulatory actions may rely significantly on professional judgment where available scientific data are not as extensive as desired to support the statutory requirement for absolute scientific rigor. In these situations, the proposed course of action is favored over no action.

Reviewers should recognize that DTSC has a legal obligation to consider and respond to all feedback on the scientific portions of the proposed regulation. Because of this obligation, reviewers are encouraged to focus feedback on the scientific issues that are relevant to the central regulatory elements being proposed.

Attachment 3:

List of Participants

Section A. California Department of Toxic Substances Control Personnel

Name	Title	Program	Location
André Algazi	Senior Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Anne Cooper Doherty	Senior Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Michael Ernst	Hazardous Substances Engineer	Safer Products and Workplaces Program	Sacramento, CA
Edward Fendick	Staff Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Lynn Goldman	Attorney	Office of Legal Affairs	Sacramento, CA
Valerie Hanley	Staff Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Andrew King*	Research Program Specialist II	Safer Products and Workplaces Program	Sacramento, CA
Patrick Kerzic	Staff Toxicologist	Human and Ecological Risk Office	Chatsworth, CA
Daphne Molin	Senior Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Lynn Nakayama Wong	Staff Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Karl Palmer	Environmental Program Manager I	Safer Products and Workplaces Program	Sacramento, CA
Nivashni Veerasamy	Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Meredith Williams	Deputy Director	Safer Products and Workplaces Program	Sacramento, CA

* No longer works for DTSC

Section B. External Participants.

Name	Title	Department / Program	Location
Gail Krowech	Retired Annuitant	Scientific Affairs Division, Office of Environmental Health Hazard Assessment	Oakland, CA
Gina Solomon*	Deputy Secretary for Science and Health	California Environmental Protection Agency	Sacramento, CA

* No longer works for the listed department

Attachment 4:

Reference Titles

Regulatory:
California Code of Regulations, Title 22, sections 69401 – 69407.2
California Code of Regulations, Title 22, sections 69503 – 69503.7
Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent
California Code of Regulations, Title 22, proposed sections 69511(b)(4) – 69511.4

Literature Relied upon:
ABC (2015) ABC Compounding Co. Inc., Safety Data Sheet - Sunbrite. In. http://aero.abccompounding.com/resources/sds/6389.pdf Accessed 4/5/2017
Ackerman D, Schiff K, Trim H, Mullin M (2003) Characterization of water quality in the Los Angeles River. Bulletin of the Southern California Academy of Sciences 2(1):17-25
Ackermann GE, Schwaiger J, Negele RD, Fent K (2002) Effects of long-term nonylphenol exposure on gonadal development and biomarkers of estrogenicity in juvenile rainbow trout *Oncorhynchus mykiss*. Aquat Toxicol 60(3-4):203-21
Ahel M, Giger W (1993) Aqueous solubility of alkylphenols and alkylphenol polyethoxylates. Chemosphere 26(8):1461-1470
Ahel M, Giger W, Koch M (1994a) Behaviour of alkylphenol polyethoxylate surfactants in the aquatic environment—I. Occurrence and transformation in sewage treatment. Water research 28(5):1131-1142 doi:http://dx.doi.org/10.1016/0043-1354(94)90200-3
Ahel M, Giger W, Schaffner C (1994b) Behaviour of alkylphenol polyethoxylate surfactants in the aquatic environment—II. Occurrence and transformation in rivers. Water research 28(5):1143-1152 doi:http://dx.doi.org/10.1016/0043-1354(94)90201-1
Ahel M, McEvoy J, Giger W (1993) Bioaccumulation of the lipophilic metabolites of nonionic surfactants in freshwater organisms. Environmental Pollution 79(3):243-248 doi:http://dx.doi.org/10.1016/0269-7491(93)90096-7
AHLA (2017) American Hotel and Lodging Association (AHLA). 2017 Lodging Industry by the Numbers: California. In. https://www.ahla.com/sites/default/files/2017-01/State_Facts_CA_2017_0.pdf Accessed 3/14/2018
Alliance for Water Efficiency (2016) Commercial Laundry Facilities Introduction. In. http://www.allianceforwaterefficiency.org/commercial_laundry.aspx Accessed 3/14/2018
APERC (2017) Alkylphenols & Ethoxylates Research Council (APERC). Comment letter - regarding DTSCs Background Document on Potential Aquatic Impacts and Continued Uses of Nonylphenol Ethoxylates and Triclosan. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=11771 Accessed 3/1/2017
Aquarium of the Pacific (2017) Unarmored Threespine Stickleback. In. http://www.aquariumofpacific.org/onlinelearningcenter/species/unarmored_threespine_stickleback Accessed 11/14/2017
Arslan OC, Parlak H (2007) Embryotoxic effects of nonylphenol and octylphenol in sea urchin *Arbacia lixula*. Ecotoxicology 16(6):439-44 doi:http://dx.doi.org/10.1007/s10646-007-0147-z
Arslan OC, Parlak H, Oral R, Katalay S (2007) The effects of nonylphenol and octylphenol on embryonic development of sea urchin (*Paracentrotus lividus*). Archives of environmental contamination and toxicology 53(2):214-9 doi:http://dx.doi.org/10.1007/s00244-006-0042-2

B&C Technologies (2014) Laundry Planning Handbook. In. https://bandctech.com/Manuals/commercial-laundry-planning-guide.pdf Accessed 4/10/2018

Balch G, Metcalfe C (2006) Developmental effects in Japanese medaka (*Oryzias latipes*) exposed to nonylphenol ethoxylates and their degradation products. Chemosphere 62(8):1214-23 doi:http://dx.doi.org/10.1016/j.chemosphere.2005.02.100

Barber LB, Loyo-Rosales JE, Rice CP, Minarik TA, Oskouie AK (2015) Endocrine disrupting alkylphenolic chemicals and other contaminants in wastewater treatment plant effluents, urban streams, and fish in the Great Lakes and Upper Mississippi River Regions. The Science of the total environment 517:195-206 doi:http://dx.doi.org/10.1016/j.scitotenv.2015.02.035

Baxter R, Breuer R, Brown L, et al. (2010) Interagency Ecological Program. 2010 Pelagic Organism Decline Work Plan and Synthesis of Results. In. https://www.water.ca.gov/LegacyFiles/iep/docs/FinalPOD2010Workplan12610.pdf Accessed 4/26/2018

Benotti MJ, Stanford BD, Snyder SA (2010) Impact of drought on wastewater contaminants in an urban water supply. Journal of Environmental Quality 39(4):1196-200

Billinghurst Z, Clare AS, Fileman T, Mcevoys J, Readman J, Depledge MH (1998) Inhibition of barnacle settlment by the environmental oestrogen 4-nonylphenol and the natural oestrogen 17b oestradiol. Marine Pollution Bulletin 36(10):833-839 doi:10.1016/S0025-326X(98)00074-5

Bradley PM, Barber LB, Kolpin DW, McMahon PB, Chapelle FH (2008) Potential for 4-n-nonylphenol biodegradation in stream sediments. Environmental toxicology and chemistry / SETAC 27(2):260-5 doi:http://dx.doi.org/10.1897/07-333R.1

Bradley PM, Journey CA, Romanok KM, et al. (2017) Expanded target-chemical analysis reveals extensive mixed-organic-contaminant exposure in U.S. streams. Environmental science & technology 51(9):4792-4802 doi:http://dx.doi.org/10.1021/acs.est.7b00012

British Columbia Ministry of Environment (2018) Fish & Habitats– White Sturgeon (*Acipenser transmontanus*) in British Columbia. In. http://www.env.gov.bc.ca/wld/fishhabitats/sturgeon/ Accessed 1/23/2018

Brown S, Devin-Clarke D, Doubrava M, O'Connor G (2009) Fate of 4-nonylphenol in a biosolids amended soil. Chemosphere 75(4):549-54 doi:http://dx.doi.org/10.1016/j.chemosphere.2008.12.001

Calafat AM, Kuklenyik Z, Reidy JA, Caudill SP, Ekong J, Needham LL (2005) Urinary concentrations of bisphenol A and 4-nonylphenol in a human reference population. Environmental health perspectives 113(4):391-5

CalFish (2017) California Fish Website: Green Sturgeon. In. http://www.calfish.org/FisheriesManagement/SpeciesPages/GreenSturgeon.aspx Accessed 10/19/2017

California Trout (2017) State of the Salmonids: Status of California's Emblematic Fishes, 2017. In. https://www.ucdavis.edu/news/nearly-half-californias-native-salmon-steelhead-and-trout-track-be-extinct-50-years/ Accessed 4/10/2018

CalRecycle (2015) Department of Resources Recycling and Recovery (CalRecycle). Organic Materials Management, Biosolids. In. http://www.calrecycle.ca.gov/organics/biosolids/ Accessed 4/10/2018

CCME (2002) Canadian Council of Ministers of the Environment (CCME). Canadian Water Quality Guidelines for the Protection of Aquatic Life: Nonylphenol and its Ethoxylates. In: Canadian Council of Ministers of the Environment. http://ceqg-rcqe.ccme.ca/download/en/198 Accessed 4/24/2018

CDFW (2015) California Department of Fish and Wildlife (CDFW). Unarmored Three Spine Stickleback Santa Clara River to Santa Francisquito Creek Rescue/Relocation - Update (June 2015). In. https://www.wildlife.ca.gov/Drought/projects/Stickleback Accessed 4/5/2018

CDFW (2017a) Fish Species of Special Concern. In. https://www.wildlife.ca.gov/Conservation/SSC/Fishes Accessed 10/19/2017

CDFW (2017b) State and Federally listed endangered & threatened animals of California. In. https://nrm.dfg.ca.gov/FileHandler.ashx?DocumentID=109405&inline Accessed 10/19/2017

Chang BV, Chiang F, Yuan SY (2005) Anaerobic degradation of nonylphenol in sludge. Chemosphere 59(10):1415-20 doi:http://dx.doi.org/10.1016/j.chemosphere.2004.12.055

Chang BV, Yu CH, Yuan SY (2004) Degradation of nonylphenol by anaerobic microorganisms from river sediment. Chemosphere 55(4):493-500 doi:http://dx.doi.org/10.1016/j.chemosphere.2004.01.004

City of Ventura, Stillwater Ecosystem WaRS, Carollo Engineers I (2010) Treatment wetlands feasibility study report. In. https://www.cityofventura.ca.gov/DocumentCenter/View/7071 Accessed 4/26/2018

Cox C, Surgan M (2006) Unidentified inert ingredients in pesticides: implications for human and environmental health. Environmental health perspectives 114(12):1803-6

Crauder J, Downing-Kunz MA, Hobbs JA, et al. (2016) Lower South Bay Nutrient Synthesis. San Francisco Estuary Institute & Aquatic Science Center. Contribution #732. In. http://sfbaynutrients.sfei.org/sites/default/files/2015_LSB_Synthesis_June%202015.b.pdf Accessed 4/26/2018

Danish Environmental Protection Agency (2006) Executive Order No. 1650 of 13 December 2006. In. https://www.retsinformation.dk/Forms/R0710.aspx?id=13056 Accessed 9/20/2018

David A, Fenet H, Gomez E (2009) Alkylphenols in marine environments: Distribution monitoring strategies and detection considerations. Marine Pollution Bulletin 58(7):953-960 doi:http://dx.doi.org/10.1016/j.marpolbul.2009.04.021

De Weert JP, Vinas M, Grotenhuis T, Rijnaarts HH, Langenhoff AA (2011) Degradation of 4-n-nonylphenol under nitrate reducing conditions. Biodegradation 22(1):175-87 doi:http://dx.doi.org/10.1007/s10532-010-9386-4

Di Corcia A, Costantino A, Crescenzi C, Marinoni E, Samperi R (1998) Characterization of recalcitrant intermediates from biotransformation of the branched alkyl side chain of nonylphenol ethoxylate surfactants. Environmental science & technology 32(16):2401-2409 doi:http://dx.doi.org/10.1021/es9801285

Diehl J, Johnson SE, Xia K, West A, Tomanek L (2012) The distribution of 4-nonylphenol in marine organisms of North American Pacific Coast estuaries. Chemosphere 87(5):490-7 doi:http://dx.doi.org/10.1016/j.chemosphere.2011.12.040

Dodder NG, Maruya KA, Lee Ferguson PL, et al. (2014) Occurrence of contaminants of emerging concern in mussels (*Mytilus spp.*) along the California coast and the influence of land use, storm water discharge, and treated wastewater effluent. Mar Pollut Bull 81(2):340-6 doi:http://dx.doi.org/10.1016/j.marpolbul.2013.06.041

Dow (2017a) Dow Answer Center: How is the logPOW calculated for Surfactants? In. https://dowac.custhelp.com/app/answers/detail/a_id/12859/~/surfactants-logpow%2Flogkow-statement Accessed 11/3/2017

EC (2018) Europrean Commmission (EC), Proposal for a Direction of the European Palaiament and the Council on the Quality of Water Intedned for Human Consumption. In. https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1519210589057&uri=CELEX:52017PC0753 Accessed 8/31/2018

ECHA (2012) European Chemicals Agency (ECHA). Member State Committee Support Document for Identification of 4-nonylphenol, branched and linear as Substances of Very High Concern Because Due to Their Endocrine Disrupting Properties They Cause Probably Serious Effects to the Environment Which Give Rise to an Equivalent Level of Concern to Those of CMRs and PBTs/vPvBs. In. https://echa.europa.eu/documents/10162/3024c102-20c9-4973-8f4e-7fc1dd361e7d Accessed 4/24/2018

ECHA (2013) Member State Committee Support Document for Identification of 4-Nonylphenol, Branched and Linear, Ethoxylated as Substances of Very High Concern Because, Due to Their Degradation to Substances of Very High Concern (4-Nonylphenol, Branched and Linear) with Endocrine Disrupting Properties, They Cause Probable Serious Effects to the Environment Which Give Rise to an Equivalent Level of Concern to Those of CMR and PBT/vPvB Substances. In. https://echa.europa.eu/documents/10162/9af34d5f-cd2f-4e63-859c-529bb39da7ae Accessed 4/24/2018

ECHA (2014a) Background Document to the Opinion on the Annex XV Dossier Proposing Restrictions on Nonylphenol and Nonylphenol Ethoxylates. In. https://echa.europa.eu/documents/10162/b94f33a1-6afb-4091-a3fa-b64303b88ed2 Accessed 4/24/2018

Ekelund R, Bergman Å, Granmo Å, Berggren M (1990) Bioaccumulation of 4-nonylphenol in marine animals— A re-evaluation. Environmental Pollution 64(2):107-120 doi:https://doi.org/10.1016/0269-7491(90)90108-O

Ekelund R, Granmo A, Magnusson K, Berggren M, Bergman A (1993) Biodegradation of 4-nonylphenol in seawater and sediment. Environ Pollut 79(1):59-61

Environment Canada (2002) Canadian Environmental Quality Guidelines for Nonylphenol and its Ethoxylates (Water, Sediment, and Soil). In. http://publications.gc.ca/collections/Collection/En1-34-4-2002E.pdf Accessed 4/24/2018

Environment Canada, Health Canada (2001) Priority Substances List Assessment Report: Nonylphenol and its Ethoxylates. In. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-1999-priority-substances-list-assessment-report-nonylphenol-ethoxylates.html Accessed 4/24/2018

European Chemicals Bureau (2002) European Union Risk Assessment Report 4-Nonylphenol (Branched) and Nonylphenol. In. https://oehha.ca.gov/media/downloads/crnr/eubisphenolareport325.pdf Accessed 4/26/2018

European Commision (2011) Common Implementation Strategy for the Water Framework Directive (2000/60/EC); Guidance Document 27; Technical Guidance for Deriving Environmental Quality Standards. In. https://circabc.europa.eu/sd/a/0cc3581b-5f65-4b6f-91c6-433a1e947838/TGD-EQS%20CIS-WFD%2027%20EC%202011.pdf Accessed 4/26/2018

European Union (2008) Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council. In. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32008L0105 Accessed 4/26/2018

Ferguson PL, Brownawell BJ (2003) Degradation of nonylphenol ethoxylates in estuarine sediment under aerobic and anaerobic conditions. Environmental toxicology and chemistry / SETAC 22(6):1189-99

Ferguson PL, Iden CR, Brownawell BJ (2001) Distribution and fate of neutral alkylphenol ethoxylate metabolites in a sewage-impacted urban estuary. Environmental science & technology 35(12):2428-2435 doi:http://dx.doi.org/10.1021/es001871b

Ferrara F, Ademollo N, Delise M, Fabietti F, Funari E (2008) Alkylphenols and their ethoxylates in seafood from the Tyrrhenian Sea. Chemosphere 72(9):1279-1285 doi:https://doi.org/10.1016/j.chemosphere.2008.04.060

Field JA, Reed RL (1996) Nonylphenol polyethoxy carboxylate metabolites of nonionic surfactants in U.S. paper mill effluents, municipal sewage treatment plant effluents, and river waters. Environmental science & technology 30(12):3544-3550 doi:http://dx.doi.org/10.1021/es960191z

Fong S, Louie S, Werner I, Davis J, Connon RE (2016) Contaminant Effects on California Bay-Delta Species and Human Health. San Francisco Estuary and Watershed Science 14(4) doi:http://dx.doi.org/10.15447/sfews.2016v14iss4art5

Giger W, Brunner PH, Schaffner C (1984) 4-nonylphenol in sewage sludge: accumulation of toxic metabolites from nonionic surfactants. Science 225:623

Giudice BD, Young TM (2011) Mobilization of endocrine-disrupting chemicals and estrogenic activity in simulated rainfall runoff from land-applied biosolids. Environmental toxicology and chemistry / SETAC 30(10):2220-8 doi:http://dx.doi.org/10.1002/etc.631

Gray JL, Borch T, Furlong ET, et al. (2017) Rainfall-runoff of anthropogenic waste indicators from agricultural fields applied with municipal biosolids. The Science of the total environment 580:83-89 doi:http://dx.doi.org/10.1016/j.scitotenv.2016.03.033

Hart CE, Lauth MJ, Hunter CS, Krasny BR, Hardy KM (2016) Effect of 4-nonylphenol on the immune response of the Pacific oyster *Crassostrea gigas* following bacterial infection with Vibrio campbellii. Fish Shellfish Immunol 58:449-461 doi:http://dx.doi.org/10.1016/j.fsi.2016.09.054

HD Chem (2015) Safety Data Sheet - Liquid Laundry Detergent. In. http://www.hdchem.net/DL%20-%20Liquid%20Laundry%20Detergent.pdf Accessed 4/10/2018

Hirano M, Ishibashi H, Kim JW, Matsumura N, Arizono K (2009) Effects of environmentally relevant concentrations of nonylphenol on growth and 20-hydroxyecdysone levels in mysid crustacean, *Americamysis bahia*. Comp Biochem Physiol C Toxicol Pharmacol 149(3):368-73 doi:http://dx.doi.org/10.1016/j.cbpc.2008.09.005

Howard J, Klausmeyer K, Fesenmyer K (2013) Below the Surface: California's Freshwater Biodiversity. In: The Nature Conservancy of California (ed). San Francisco, CA

Jobling S, Sheahan D, Osborne JA, Matthiessen P, Sumpter JP (1996) Inhibition of testicular growth in rainbow trout (*Oncorhynchus mykiss*) exposed to estrogenic alkylphenolic chemicals. Environmental Toxicology and Chemistry 15(2):194-202

KFF (2015a) Hospital Inpatient Days per 1,000 Population by Ownership Type, California, 2015. In. https://www.kff.org/other/state-indicator/inpatient-days-by-ownership/?currentTimeframe=0&selectedRows=%7B%22states%22:%7B%22california%22:%7B%7D%7D%7D&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D#notes Accessed 3/14/2018

KFF (2015b) Total Number of Residents in Certified Nursing Facilities, California, 2015. In. https://www.kff.org/other/state-indicator/number-of-nursing-facility-residents/?currentTimeframe=0&selectedRows=%7B%22states%22:%7B%22california%22:%7B%7D%7D%7D&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D Accessed 3/14/2018

Kinney CA, Furlong ET, Zaugg SD, et al. (2006) Survey of organic wastewater contaminants in biosolids destined for land application. Environmental science & technology 40(23):7207-7215 doi:http://dx.doi.org/10.1021/es0603406

Klečka G, Zabik J, Woodburn K, Naylor C, Staples C, Huntsman B (2007) Exposure analysis of C8- and C9-alkylphenols, alkylphenol ethoxylates, and their metabolites in surface water systems within the United States. Human and Ecological Risk Assessment: An International Journal 13(4):792-822 doi:http://dx.doi.org/10.1080/10807030701456726

Klečka GM, Naylor CG, Staples CA, Losey B (2010) Occurrence of nonylphenol ethoxylates and their metabolites in municipal wastewater treatment plants and receiving waters. Water Environ Res 82(5):447-54

Klosterhaus S, D. Y, Sedlak M, Wong A, Sutton R (2013a) Contaminants of Emerging Concern in San Francisco Bay: A Summary of Occurrence Data and Identification of Data Gaps. In: San Francisco Estuary Institute.

Klosterhaus SL, Grace R, Hamilton MC, Yee D (2013b) Method validation and reconnaissance of pharmaceuticals, personal care products, and alkylphenols in surface waters, sediments, and mussels in an urban estuary. Environ Int 54:92-9 doi:10.1016/j.envint.2013.01.009

Kroon FJ, Hook SE, Metcalfe S, Jones D (2015) Altered levels of endocrine biomarkers in juvenile barramundi (*Lates calcarifer*; Bloch) following exposure to commercial herbicide and surfactant formulations. Environmental toxicology and chemistry / SETAC 34(8):1881-90 doi:http://dx.doi.org/10.1002/etc.3011

La Guardia MJ, Hale RC, Harvey E, Mainor TM (2001) Alkylphenol ethoxylate degradation products in land-applied sewage sludge (biosolids). Environmental science & technology 35(24):4798-804

LACSD (2012) Los Angeles County Sanitation District (LACSD). Sanitation Districts of Los Angeles County Constituents of Emerging Concern Monitoring Summary 2007 to 2012. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=12740

LACSD (2014a) Constituents of Emerging Concern 2013 Monitoring Results and Trends from 2007 to 2013. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=12740

LACSD (2015) Constituents of Emerging Concern 2014 Monitoring Results and Trends from 2007 to 2014. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=12740

Lara-Martin PA (2017) Email to Anne Cooper Doherty RE: Data from 2014 Long Island Sound Study Paper.

Lara-Martin PA, Gonzalez-Mazo E, Petrovic M, Barcelo D, Brownawell BJ (2014) Occurrence, distribution and partitioning of nonionic surfactants and pharmaceuticals in the urbanized Long Island Sound Estuary (NY). Mar Pollut Bull 85(2):710-9 doi:http://dx.doi.org/10.1016/j.marpolbul.2014.01.022

Lavado R, Loyo-Rosales JE, Floyd E, et al. (2009) Site-specific profiles of estrogenic activity in agricultural areas of California's inland waters. Environmental science & technology 43(24):9110-6 doi:http://dx.doi.org/10.1021/es902583q

Lawrence Livermore National Laboratory, State Water Board (2006) California GAMA Program: Fate and Transport of Wastewater Indicators: Results from Ambient Groundwater and from Groundwater Directly Influenced by Wastewater.

Lesueur T, Boulange-Lecomte C, Xuereb B, et al. (2013) Development of a larval bioassay using the calanoid copepod, *Eurytemora affinis* to assess the toxicity of sediment-bound pollutants. Ecotoxicol Environ Saf 94:60-6 doi:http://dx.doi.org/10.1016/j.ecoenv.2013.04.025

Loyo-Rosales JE (2006) The fate and behavior of octyl- and nonylphenol ethoxylates and their derivatives in three american wastewater treatment plants and the Back River, Maryland. University of Maryland, College Park

Loyo-Rosales JE (2018) Email to Anne Cooper Doherty RE: Solids mass balance data.

Loyo-Rosales JE, Rice CP, Torrents A (2007a) Fate of octyl- and nonylphenol ethoxylates and some carboxylated derivatives in three American wastewater treatment plants. Environmental science & technology 41(19):6815-21

Loyo-Rosales JE, Rice CP, Torrents A (2010) Fate and distribution of the octyl- and nonylphenol ethoxylates and some carboxylated transformation products in the Back River, Maryland. J Environ Monit 12(3):614-21 doi:http://dx.doi.org/10.1039/b913229e

Lozano N, Rice CP, Pagano J, et al. (2012) Concentration of organic contaminants in fish and their biological effects in a wastewater-dominated urban stream. The Science of the total environment 420:191-201 doi:http://dx.doi.org/10.1016/j.scitotenv.2011.12.059

Lu Z, Gan J (2014) Analysis, toxicity, occurrence and biodegradation of nonylphenol isomers: A review. Environment International 73:334-345 doi:https://doi.org/10.1016/j.envint.2014.08.017

Lubliner B, Redding M, Ragsdale D (2010) Pharmaceuticals and Personal Care Products in Municipal Wastewater and Their Removal by Nutrient Treatment Technologies. In: Washington State Department of Ecology (ed). Olympia, WA.

Lyons R, Van de Bittner K, Morgan-Jones S (2014) Deposition patterns and transport mechanisms for the endocrine disruptor 4-nonylphenol across the Sierra Nevada Mountains, California. Environ Pollut 195:123-32 doi:http://dx.doi.org/10.1016/j.envpol.2014.08.006

Maruya KA, Dodder NG, Sengupta A, et al. (2016) Multimedia screening of contaminants of emerging concern (CECS) in coastal urban watersheds in southern California (USA). Environmental Toxicology and Chemistry 35(8):1986-1994 doi:http://dx.doi.org/10.1002/etc.3348

Maruya KA, Dodder NG, Tang CL, Lao W, Tsukada D (2015) Which coastal and marine environmental contaminants are truly emerging? Environmental science and pollution research international 22(3):1644-52 doi:http://dx.doi.org/10.1007/s11356-014-2856-1

Maruya KA, Dodder NG, Weisberg SB, et al. (2014) The Mussel Watch California pilot study on contaminants of emerging concern (CECs): synthesis and next steps. Mar Pollut Bull 81(2):355-63 doi:10.1016/j.marpolbul.2013.04.023

Maruya KA, Vidal-Dorsch DE, Bay SM, Kwon JW, Xia K, Armbrust KL (2012) Organic contaminants of emerging concern in sediments and flatfish collected near outfalls discharging treated wastewater effluent to the Southern California Bight. Environmental toxicology and chemistry / SETAC 31(12):2683-8 doi:http://dx.doi.org/10.1002/etc.2003

Meador JP, Yeh A, Young G, Gallagher EP (2016) Contaminants of emerging concern in a large temperate estuary. Environ Pollut 213:254-67 doi:http://dx.doi.org/10.1016/j.envpol.2016.01.088

Milieu Ltd, WRc, RPA (2010) Environmental, Economic and Social Impacts of the Use of Sewage Sludge on land. Part III: Project Interim Reports. Prepared for the European Commission, DG Environment. In. http://ec.europa.eu/environment/archives/waste/sludge/pdf/part_iii_report.pdf Accessed 4/26/2018

Miller DJ, Lea RN (1972) Guide to the Coastal Marine Fishes of California. State of California, The Resources Agency, Department of Fish and Game. Fish Bulletin 157

Minnesota Department of Health (2015) Fact Sheet: Nonylphenols and Drinking Water. In: Environmental Health Division (ed). Clean Water Land & Legacy Amendment, St. Paul, MN

Mitro SD, Dodson RE, Singla V, et al. (2016) Consumer product chemicals in indoor dust: A quantitative metaanalysis of U.S. studies. Environ Sci Technol, 50(19):10661-10672 doi:http://dx.doi.org/10.1021/acs.est.6b02023

Moyle PB, R. M. Quiñones, J. V. Katz, J. Weaver (2015) Fish Species of Special Concern in California, Third Edition. In. https://www.wildlife.ca.gov/Conservation/SSC/Fishes Accessed 4/10/2018

MPCA (2010) Minnesota Pollution Control Agency (MPCA). Aquatic Life Water Quality Standards Technical Support Document for Nonylphenol and Ethoxylates Triennial Water Quality Standard Amendments to Minn. R. chs. 7050 and 7052 Draft for External Review, October 2010. In. https://www.pca.state.mn.us/sites/default/files/wq-s6-16.pdf Accessed 10/13/2017

MPCA (2017) Comment on DTSCs Background Document for Potential Aquatic Impacts and Continued Uses of Nonylphenol Ethoxylates and Triclosan. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=11771&from=search Accessed 6/12/2017

Nagarnaik PM, Mills MA, Boulanger B (2010) Concentrations and mass loadings of hormones, alkylphenols, and alkylphenol ethoxylates in healthcare facility wastewaters. Chemosphere 78(8):1056-62 doi:http://dx.doi.org/10.1016/j.chemosphere.2009.11.019

National Drought Mitigation Center, USDA, National Oceanic and Atmospheric Administration (NOAA) (2018) United States Drought Monitor (USDM). In. http://droughtmonitor.unl.edu/Data/DataDownload/ComprehensiveStatistics.aspx Accessed 3/26/2018

National Park Service (2007) California Freshwater Shrimp Inventory at Golden Gate National Recreation Area and Point Reyes National Seashore. U.S. Department of the Interior. Pacific Coast Science and Learning Center In. http://www.sfnps.org/download_product/1159/0 Accessed 4/26/2018

National Research Council, Division on Earth and Life Studies, Commission on Geosciences, et al. (2000) Clean Coastal Waters: Understanding and Reducing the Effects of Nutrient Pollution. National Academies Press

Naylor CG (1996) The Environmental Fate and Safety of Nonylphenol Ethoxylates, vol 16. American Society for Testing and Materials

Nielsen E, Østergaard G, Thorup I, Ladefoged O, Erik Jelnes J (2000) Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl, Phosphates and Benzoic Acid,

NOAA (2018) National Oceanic and Atmospheric Administration (NOAA) US Seasonal Drought Outlook, March 15, 2018 through June 30, 2018 In. http://www.cpc.ncep.noaa.gov/products/expert_assessment/sdo_summary.php Accessed 3/30/2018

NOAA Fisheries (2016a) Black Abalone *(Haliotis cracherodii)*. In. http://www.nmfs.noaa.gov/pr/species/invertebrates/abalone/black-abalone.html Accessed 2/23/2018

NOAA Fisheries (2016b) Species in the Spotlight Priority Actions: 2016-2020 White Abalone *Haliotis sorenseni*. In. http://www.nmfs.noaa.gov/pr/species/Species%20in%20the%20Spotlight/white_abalone_spotlight_species_5-year_action_plan_final.pdf Accessed 4/25/2018

NOAA Fisheries (2016c) White Abalone *(Haliotis sorenseni)*. In. http://www.nmfs.noaa.gov/pr/species/invertebrates/abalone/white-abalone.html Accessed 2/23/2018

NOAA Fisheries (2018b) Critical Habitat for White Abalone. In. https://www.fisheries.noaa.gov/action/critical-habitat-white-abalone Accessed 9/13/2018

Noble Chemical Inc. (2013) Safety Data Sheet - Low Suds. In. https://www.webstaurantstore.com/documents/sds/147lowsuds_50.pdf Accessed 4/10/2018

Oates RP, Longley G, Hamlett P, Klein D (2017) Pharmaceutical and endocrine disruptor compounds in surface and wastewater in San Marcos, Texas. Water Environ Res 89(11):2021-2030 doi:http://dx.doi.org/10.2175/106143017X14902968254584

OEHHA (2009) Office of Environmental Health Hazard Assessment (OEHHA). Toxicological Profile for Nonylphenol. In. http://www.opc.ca.gov/webmaster/ftp/project_pages/MarineDebris_OEHHA_ToxProfiles/Nonylphenol%20Final.pdf Accessed 4/26/2018

OSPAR Commission (2009) Background Document on nonylphenol/nonylphenol ethoxylates. In. https://www.ospar.org/documents?v=7201 Accessed 4/24/2018

Proctor & Gamble (2005) Use of Nonylphenol and Nonylphenol Ethoxylates in P&G Products. In. http://wayback.archive.org/web/20060314005457/http:/www.pgperspectives.com/en_UK/productingredient/nonylphenolnonylphenolethoxylates_en.html Accessed 3/28/2018

Pryor SW, Hay AG, Walker LP (2002) Nonylphenol in anaerobically digested sewage sludge from New York State. Environmental science & technology 36(17):3678-82

Regents of the University of California (2017a) California Fish Website: Central Coast Coho Salmon. In. http://calfish.ucdavis.edu/species/?uid=25&ds=698 Accessed March 28, 2018

Regents of the University of California (2017b) California Fish Website: Unarmored threespine stickleback. In. http://calfish.ucdavis.edu/species/?uid=171&ds=698 Accessed 11/14/2017

Riesenberger J, Koeller J (2005) Potential Best Management Practices: Commercial Laundry Facilities. In. http://www.allianceforwaterefficiency.org/WorkArea/DownloadAsset.aspx?id=802 Accessed 4/19/2018

Rudel RA, Camann DE, Spengler JD, Korn LR, Brody JG (2003) Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. Environmental science & technology 37(20):4543-4553 doi:http://dx.doi.org/10.1021/es0264596

RWQCB Los Angeles (2017) Presentation to DTSC on CEC Monitoring Los Angeles Region 4. In. http://www.dtsc.ca.gov/SCP/upload/Michael-Lyons-RWQCB-Presentation.pdf 4/24/2018

RWQCB San Francisco (1995) Policy on the use of wastewater to create, restore, and/or enhance wetlands. In. https://www.waterboards.ca.gov/sanfranciscobay/board_decisions/adopted_orders/1994/R2-1994-0086.pdf Accessed 1/29/2018

Santos NR, Katz JVE, Moyle PB, Viers JH (2014) A programmable information system for management and analysis of aquatic species range data in California. Environmental Modelling & Software 53:13-26 doi:https://doi.org/10.1016/j.envsoft.2013.10.024

SCCWRP (2010) Southern California Coastal Water Research Project (SCCWRP): Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water, Recommendations of a Science Advisory Panel. In. https://www.waterboards.ca.gov/water_issues/programs/water_recycling_policy/docs/cec_monitoring_rpt.pdf Accessed 4/24/2018

SCCWRP (2012a) Management of Brine Discharges to Coastal Waters, Recommendations of a Science Advisory Panel. Technical Report 694. In. https://www.waterboards.ca.gov/water_issues/programs/ocean/desalination/docs/dpr051812.pdf Accessed 4/24/2018

SCCWRP (2017) Screening study for constituents of emerging concern (CECs) in selected freshwater rivers in the Los Angeles Region - Phase 3 - *in vitro* screening and targeted analysis of CECs in water and sediment. p 25

SCCWRP (2018) Pilot monitoring of constituents of emerging concern (CECs) in the Russian River watershed (Region 1). In. http://ftp.sccwrp.org/pub/download/DOCUMENTS/TechnicalReports/1020_PilotCECs.pdf Accessed SCCWRP Technical Report 1020

Schlenk D, Lavado R, Loyo-Rosales JE, et al. (2012) Reconstitution studies of pesticides and surfactants exploring the cause of estrogenic activity observed in surface waters of the San Francisco Bay Delta. Environmental science & technology 46(16):9106-11 doi:http://dx.doi.org/10.1021/es3016759

Schwaiger J, Mallow U, Ferling H, et al. (2002) How estrogenic is nonylphenol? A transgenerational study using rainbow trout (*Oncorhynchus mykiss*) as a test organism. Aquat Toxicol 59(3-4):177-89

Seki M, Yokota H, Maeda M, Tadokoro H, Kobayashi K (2003) Effects of 4-nonylphenol and 4-tert-octylphenol on sex differentiation and vitellogenin induction in medaka (Oryzias latipes). Environmental toxicology and chemistry / SETAC 22(7):1507-16

Sengupta A, Lyons JM, Smith DJ, et al. (2014) The occurrence and fate of chemicals of emerging concern in coastal urban rivers receiving discharge of treated municipal wastewater effluent. Environmental toxicology and chemistry / SETAC 33(2):350-8 doi:http://dx.doi.org/10.1002/etc.2457

Servos MR (1999) Review of the aquatic toxicity, estrogenic responses and bioaccumulation of alkylphenols and alkylphenol polyethoxylates. Water Qual Res J Canada 34(1)

SFEI (2017) San Francisco Estuary Institute (SFEI). The Pulse of the Bay: The 25th Anniversary of the RMP. SFEI Contribution #841. In. http://www.sfei.org/documents/pulse-bay-25th-anniversary-rmp Accessed 4/26/2018

SFEI (2018) San Francisco Estuary Institute Aquatic Science Center Comment Letter - regarding DTSC's announcement of the Product-Chemical Profile for NPEs in Laundry Detergent.

Shang DY, Macdonald RW, Ikonomou MG (1999) Persistence of nonylphenol ethoxylate surfactants and their primary degradation products in sediments from near a municipal outfall in the Strait of Georgia, British Columbia, Canada. Environmental science & technology 33(9):1366-1372 doi:http://dx.doi.org/10.1021/es980966z

Simoniz USA Inc. (2015) Safety Data Sheet - Liquid Laundry Detergent. In. https://www.webstaurantstore.com/documents/sds/147lowsuds_50.pdf Accessed 4/10/2018

Soares A, Guieysse B, Jefferson B, Cartmell E, Lester JN (2008) Nonylphenol in the environment: A critical review on occurance, fate, toxicity and treatment in wastewaters. Environment International 34:1033-1049 doi:10.1016/j.envint.2008.01.004

Staples C, Mihaich E, Carbone J, Woodburn K, Klecka G (2004) A weight of evidence analysis of the chronic ecotoxicity of nonylphenol ethoxylates, nonylphenol ether carboxylates, and nonylphenol. Human and Ecological Risk Assessment 10:999-1017 doi:http://dx.doi.org/10.1080/10807030490887122

Staples C, Weeks J, Hall JF, Naylor CG (1998) Evaluation of aquatic toxicity and bioaccumulation of C8- and C9-alkylphenol ethoxylates. Environmental Toxicology and Chemistry 17(12):2470-2480

Staples CA, Williams JB, Blessing RL, Varineau PT (1999) Measuring the biodegradability of nonylphenol ether carboxylates, octylphenol ether carboxylates, and nonylphenol. Chemosphere 38(9):2029-39

State Water Board (2008) Nonylphenol, total and nonylphenol ethoxylate, total analyzed in the Surface Water Ambient Monitoring Program (Region 1; FYs 2005-2006, 2006-2007, 2007-2008). California Environmental Data Exchange Network (CEDEN). In. http://ceden.waterboards.ca.gov/AdvancedQueryTool Accessed 7/10/2017

State Water Board (2011) Nonylphenol, total and nonylphenol ethoxylate, total analyzed in the Surface Water Ambient Monitoring Program (Region 9; 2011). CEDEN. In. http://ceden.waterboards.ca.gov/AdvancedQueryTool Accessed 7/10/2017

State Water Board (2013a) Nonylphenol, total and nonylphenol ethoxylate, total analyzed in the Surface Water Ambient Monitoring Program (Region 7; CY2013). CEDEN. In. http://ceden.waterboards.ca.gov/AdvancedQueryTool Accessed 7/10/2017

State Water Board (2013b) Policy for Water Quality Control for Recycled Water. In. https://www.waterboards.ca.gov/water_issues/programs/water_recycling_policy/docs/rwp_revtoc.pdf Accessed 4/25/2018

State Water Board (2016) Waste Discharge Requirements (WDRs) Program. In. https://www.waterboards.ca.gov/water_issues/programs/land_disposal/waste_discharge_requirements.shtml Accessed 3/23/2018

State Water Board (2017a) June 2015 - August 2017 Water Conservation Portal - Conservation Reporting. In. https://www.waterboards.ca.gov/water_issues/programs/conservation_portal/docs/2017mar/uw_presentation_030717.pdf Accessed 10/13/2017

State Water Board (2017b) Total Maximum Daily Load (TMDL) Program. In. https://www.waterboards.ca.gov/water_issues/programs/tmdl/ Accessed 3/13/2018

State Water Board (2018e) Storm Water Multiple Application and Report Tracking System (SMARTS). In. https://smarts.waterboards.ca.gov/smarts/faces/SwPublicUserMenu.xhtml Accessed 3/23/2018

Statista (2017) Sales of the leading liquid laundry detergent brands of the United States in 2017 (in million US Dollars). In. https://www.statista.com/statistics/188716/top-liquid-laundry-detergent-brands-in-the-united-states/ Accessed 10/13/2017

Stephen CE, Mount DI, Hanson DJ, Gentile JR, Chapman GA, Brungs WA (1985) Guidelines for Deriving Numerical National Water Quality Criteria for the Protection Of Aquatic Organisms and Their Uses. In: United States Environmental Protection Agency (ed). Corvallis, Oregon

Sunburst Chemicals (2017) Safety Data Sheet - Solid Golden Brite. In. http://19mpsc30gju7mackh6q4dgr7.wpengine.netdna-cdn.com/wp-content/uploads/2014/07/Solid-Goldenbrite-Rev-04.pdf Accessed 4/10/2018

Target (2018) Target's Sustainable Product Index Version 3.0. In. https://corporate.target.com/_media/TargetCorp/csr/pdf/Target-Sustainable-Product-Index_1.pdf Accessed 3/28/2018

Teneyck MC, Markee TP (2007) Toxicity of nonylphenol, nonylphenol monoethoxylate, and nonylphenol diethoxylate and mixtures of these compounds to *Pimephales promelas* (fathead minnow) and *Ceriodaphnia dubia*. Archives of environmental contamination and toxicology 53(4):599-606 doi:http://dx.doi.org/10.1007/s00244-006-0249-2

TRSA (2010) Textile Rental Services Association (TRSA). Commitment to Phase out Use of Industrial Laundry Detergents Containing Nonylphenol Ethoxylates ("NPE"). In. https://www.epa.gov/sites/production/files/2015-09/documents/trsa_npe_phase_out_commitment_letter.pdf Accessed 3/28/2018

U.S. Census Bureau (2017) Annual Estimates of the Resident Population: April 1, 2010 to July 1, 2017. In. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=PEP_2017_PEPANNRES&src=pt Accessed 3/14/2018

U.S. EPA (2005) U.S. Environmental Protection Agency (U.S. EPA) Office of Water and Office of Science and Technology. Aquatic Life Ambient Water Quality Criteria - Nonylphenol FINAL. In. https://bit.ly/2vQX565 Accessed 4/24/2018

U.S. EPA (2006) Action Memorandum: Subject Inert Reassessments: Four Exemptions from the Requirement of a Tolerance for Nonylphenol Ethoxylates. Office of Prevention, Pesticides, and Toxic Substances.

U.S. EPA (2007a) Draft Engineering Report of Nonylphenol (NP) and Nonylphenol Ethoxylate (NPEs) In Response to Section 21 Petition. Office of Pollution, Prevention and Toxics; Economics, Exposure and Technology Division; Chemical Engineering Branch.

U.S. EPA (2009) Occurrence of Contaminants of Emerging Concern in Wastewater From Nine Publicly Owned Treatment Works. In. https://19january2017snapshot.epa.gov/sites/production/files/2015-07/documents/2009_nine_potw_study.pdf Accessed 4/24/2018

U.S. EPA (2010a) Endangered Species Facts, California Freshwater Shrimp, *Syncaris pacifica*. In. https://www.epa.gov/sites/production/files/2013-08/documents/ca-fw-shrimp.pdf Accessed 4/24/2018

U.S. EPA (2010b) Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan. RIN 2070-ZA09. In. https://www.epa.gov/sites/production/files/2015-09/documents/rin2070-za09_np-npes_action_plan_final_2010-08-09.pdf 4/24/2018

U.S. EPA (2012a) Clean Watersheds Needs Survey. Detail Reports: Wastewater discharge method details for State of California. In. https://ofmpub.epa.gov/apex/cwns2012/f?p=CWNS2012:1 Accessed 1/29/2018

U.S. EPA (2014b) TSCA Work Plan for Chemical Assessments: 2014 Update. In. https://www.epa.gov/sites/production/files/2015-01/documents/tsca_work_plan_chemicals_2014_update-final.pdf Accessed 4/24/2018

U.S. EPA (2017) Comments on DTSC's Work Plan Implementation: Potential Aquatic Impacts and Continued Uses of Nonylphenol Ethoxylates and Triclosan (February 8, 2017). In. https://www.youtube.com/watch?v=MJpsQTwDfmw&feature=youtu.be Accessed 4/24/2018

U.S. FWS (2017) Recovery Plan for the Santa Ana sucker (*Catostomus santaanae*). In. https://ecos.fws.gov/docs/recovery_plan/20170228_Final%20SAS%20RP%20Signed.pdf Accessed 9/20/2018

US Chemical (2014) Safety Data Sheet - Nexus System Suds. In. http://www.uschemical.com/msdsdek/USCHEMICAL/NEXUS%20SYSTEM%20SUDS.pdf Accessed 4/10/2018

USDA (2003) United state Department of Agriculture (USDA). Human and Ecological Risk Assessment of Nonylphenol Polyethoxylate-based (NPE) Surfactants in Forest Service Herbicide Applications. USDA Forest Service,Pacific Southwest Region (Region 5). In. https://www.fs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb5346866.pdf Accessed 4/26/2018

USGS (2017) United States Geological Survey (USGS). Drought Impacts. In. https://ca.water.usgs.gov/data/drought/drought-impact.html Accessed 10/13/2017

Venkatesan AK, Halden RU (2013) National inventory of alkylphenol ethoxylate compounds in U.S. sewage sludges and chemical fate in outdoor soil mesocosms. Environ Pollut 174:189-93 doi:http://dx.doi.org/10.1016/j.envpol.2012.11.012

Wahba P (2016) Walmart Is Pushing Its Suppliers to Drop 8 Controversial Chemicals. In. http://fortune.com/2016/07/21/walmart-chemicals-formaldehyde/ Accessed 10/30/2017

Walters RA, Cheng RT, Conomos TJ (1985) Time scales of circulation and mixing processes of San Francisco Bay waters. Hydrobiologia 129(1):13-36 doi:http://dx.doi.org/10.1007/BF00048685

Wang Y, Na G, Zong H, et al. (2017) Applying adverse outcome pathways and species sensitivity-weighted distribution to predicted-no-effect concentration derivation and quantitative ecological risk assessment for bisphenol A and 4-nonylphenol in aquatic environments: A case study on Tianjin City, China. Environmental toxicology and chemistry / SETAC 37(2):551-562 doi:http://dx.doi.org/10.1002/etc.3994

Washington Department of Ecology (2017) Comment letter - regarding DTSCs Background Document on Potential Aquatic Impacts and Continued Uses of Nonylphenol Ethoxylates and Triclosan. In. https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=11771

WHO (2017) World Health Organziation (WHO), Support to the revision of Annex I Council Directive 98/83/EC on the Quality of Water Intended for Human Consumption. In. http://ec.europa.eu/environment/water/water-drink/pdf/WHO_parameter_report.pdf Accessed August 31, 2018

Writer JH, Ryan JN, Keefe SH, Barber LB (2012) Fate of 4-nonylphenol and 17beta-estradiol in the Redwood River of Minnesota. Environmental science & technology 46(2):860-8 doi:http://dx.doi.org/10.1021/es2031664

Xia K, Hundal LS, Kumar K, Armbrust K, Cox AE, Granato TC (2010) Triclocarban, triclosan, polybrominated diphenyl ethers, and 4-nonylphenol in biosolids and in soil receiving 33-year biosolids application. Environmental toxicology and chemistry / SETAC 29(3):597-605 doi:10.1002/etc.66

Xie L, Thrippleton K, Irwin MA, et al. (2005) Evaluation of estrogenic activities of aquatic herbicides and surfactants using an rainbow trout vitellogenin assay. Toxicological Sciences 87(2):391-8 doi:http://dx.doi.org/10.1093/toxsci/kfi249

Ying G-G (2006) Fate, behavior and effects of surfactants and their degradation products in the environment. Environment International 32(3):417-431 doi:http://dx.doi.org/10.1016/j.envint.2005.07.004

Ying G-G, Kookana RS (2003) Degradation of five selected endocrine-disrupting chemicals in seawater and marine sediment. Environmental science & technology 37(7):1256-1260 doi:http://dx.doi.org/10.1021/es0262232

Ying GGD, Williams B, Kookana R (2002) Environmental fate of alkylphenols and alkylphenol ethoxylates--a review. Environ Int 28(3):215-26

Yokota H, Seki M, Maeda M, et al. (2001) Life-cycle toxicity of 4-nonylphenol to medaka (*Oryzias latipes*). Environmental toxicology and chemistry / SETAC 20(11):2552-60

Yuan SY, Yu CH, Chang BV (2004) Biodegradation of nonylphenol in river sediment. Environ Pollut 127(3):425-30

Zep (2018) Safety Data Sheet - Zep PROLIFT 20GL. In. http://www.zep.com/zepsearch/default1.aspx?search=prolift&num=10&match=Exact&country=U Accessed 3/30/2018

Zha J, Sun L, Spear PA, Wang Z (2008) Comparison of ethinylestradiol and nonylphenol effects on reproduction of Chinese rare minnows (*Gobiocypris rarus*). Ecotoxicol Environ Saf 71(2):390-9 doi:10.1016/j.ecoenv.2007.11.017

REGULATIONS TEXT

DIVISION 4.5, TITLE 22, CALIFORNIA CODE OF REGULATIONS
CHAPTER 55. SAFER CONSUMER PRODUCTS
ARTICLE 11. PRIORITY PRODUCTS LIST

§ 69511. General.

(a) This article specifies product-chemical combinations listed as Priority Products pursuant to section 69503.5.

(b) The following product-chemical combinations are listed as Priority Products:

(1) Children's foam-padded sleeping products containing tris(1,3-dichloro-2-propyl) phosphate (TDCPP) or tris(2-chloroethyl) phosphate (TCEP);

(2) Spray polyurethane foam systems containing unreacted methylene diphenyl diisocyanates~~.~~; ~~and~~

(3) Paint or varnish strippers containing methylene chloride; and

(4) Laundry detergents containing nonylphenol ethoxylates (NPEs).

NOTE: Authority cited: Sections 25252, 25253, and 58012, Health and Safety Code. Reference: Sections 25252 and 25253, Health and Safety Code.

§ 69511.4. Laundry Detergents containing Nonylphenol Ethoxylates (NPEs).

(a) "Laundry detergent containing nonylphenol ethoxylates (NPEs)" means any product intended to clean or remove soil or unwanted deposits from laundered clothes and textile products, such as sheets and tablecloths. This includes but is not limited to laundry detergents of any form, including granules, liquids, powders, tabs, crystals, or pods, that are used in washing machines, for hand washing, or as part of a laundry system. Detergents intended for use as a pre-soak or pre-spotter or with fabric or color protection properties are also included.

(b) Candidate Chemical. For purposes of this chapter, the following Candidate Chemical is identified as the basis for the product defined in subsection (a) being listed as a Priority Product:

(1) NPEs, a class of chemicals meeting either of these definitions:"4-nonylphenol, branched and linear, ethoxylated: substances with a linear and/or branched alkyl chain with a carbon number of 9 covalently bound in position 4 to phenol, ethoxylated covering Unknown of Variable Composition, Complex Reaction Products and Biological Materials (UVCB) and well-defined substances, polymers and homologues, which include any of the individual isomers and/or combinations thereof" or "Nonylphenol

ethoxylates described with the formula C9H19-C6H4OH(CH2CH2O)n, where n = 2 - 50, normally between 6 and 12". Twelve Chemical Abstract Services Registry Numbers related to NPEs have been identified.

(2) NPEs also include the following degradation products: nonylphenol, nonylphenol carboxylates, and shorter chain NPEs (i.e., nonylphenol mono ethoxylate and nonylphenol diethoxylate) that have broken down from longer chain NPEs, as described in 69511.4(b)(1).

(c) Hazard traits associated with NPEs include:

(1) Bioaccumulation,
(2) Environmental Persistence,
(3) Immunotoxicity,
(4) Wildlife developmental impairment,
(5) Wildlife growth impairment,
(6) Wildlife reproductive impairment,
(7) Wildlife survival impairment.

(d) Environmental and toxicological endpoints associated with NPEs include:

(1) changes in circulating immune cell numbers,
(2) malformations, adverse impacts on rate of development and metamorphosis in aquatic species,
(3) abnormalities in growth rates and body size in aquatic species,
(4) adverse changes in reproductive endocrine function, structure and function of reproductive organs, including intersex organs, secondary sex characteristics, and vitellogenin production,
(5) death and narcosis.

(e) For purposes of this chapter, the Candidate Chemical identified in subsection (b) is designated as the Chemical of Concern for the product defined in subsection (a).

(f) The Preliminary Alternatives Analysis Report for this Priority Product shall be submitted within 180 days after the effective date of this regulation.

NOTE: Authority cited: Sections 25252, 25253, and 58012, Health and Safety Code. Reference: Sections 25252 and 25253, Health and Safety Code.

ATTACHMENT 2

December 4, 2018

Michael J. Carvan, Ph.D.
Professor, School of Freshwater Sciences
University of Wisconsin - Milwaukee
600 E. Greenfield Avenue
Milwaukee, WI 53204

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF NONYLPHENOL ETHOXYLATES (NPEs) IN LAUNDRY DETERGENT AS A PRIORITY PRODUCT

Dear: Professor Carvan:

The purpose of this letter is to initiate the external review.

The Department of Toxic Substances Control (DTSC) will receive reviewers' comments and curriculum vitae from me after the review has concluded, and not be a party to the process.

Documents for review are being provided through a secure FTP site. Sections I and II below give instructions for accessing the FTP site and list the documents on the site.

You can access this site through the one-month period of review. The URL, username and password are as follows:

https://ftp.waterboards.ca.gov/WebInterface/login.html

Username: gbowes-ftp1

Password: FFLtzV

1. **List of documents at FTP site:**
   A. **October 24, 2018 Memorandum signed by Karl Palmer "Request for External Peer Review for the Proposed Adoption of Nonylphenol Ethoxylates (NPEs) in Laundry Detergent as a Priority Product".**

      Attachment 1:

      Plain English Summary of the Proposal to Adopt NPEs in Laundry Detergents as a Priority Product.

Attachment 2:

Scientific Conclusions to be Addressed by Peer Reviewers.

These are the focus for the review. In your November 18, 2018 memo to me, you indicated you could review with confidence Conclusions 2 and 4. Please do so.

Attachment 3:

- List of Participants.
- Section A: DTSC Participants
- Section B: External Participants

Attachment 4:

Reference Titles

B. Regulatory References

Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent
California Code of Regulations, Title 22, sections 69401 – 69407.2
California Code of Regulations, Title 22, sections 69503 – 69503.7
California Code of Regulations, Title 22, proposed sections 69511(b)(4) – 69511.4

C. Copies of Literature Relied Upon

D. <u>October 22, 2018 Supplement to CalEPA External Scientific Peer Review Guidelines.</u>

This supplement provides guidance to ensure the review is kept confidential through its course. The Supplement notes reviewers are under no obligation to discuss their comments with third-parties after reviews have been submitted. We recommend they do not. All outside parties are provided opportunities to address a proposed regulatory action through a well-defined regulatory process. Please direct third parties to me.

Please send your reviews to me on January 14, 2019 to ensure I receive all on the same day.

Questions about the review should be for clarification, in writing –email is fine, and addressed to me. My responses will be in writing also. All this information will be posted at the State Water Board program website for this proposal. Your acceptance of this review assignment is most appreciated.

Sincerely,

Gerald W. Bowes

Gerald W. Bowes, Ph.D.
Manager, Cal/EPA Scientific Peer Review
Program Office of Research, Planning and
Performance State Water Resources Control Board
Sacramento, California 95814

Telephone: (916) 341-5567
Email: GBowes@waterboards.ca.gov

December 4, 2018

Chis Metcalfe, Ph.D.
Professor, School of the Environment
Trent University
1600 West Bank Drive
Peterborough, Ontario, Canada K9L 0G2

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF NONYLPHENOL ETHOXYLATES (NPEs) IN LAUNDRY DETERGENT AS A PRIORITY PRODUCT

Dear: Professor Metcalfe:

The purpose of this letter is to initiate the external review.

The Department of Toxic Substances Control (DTSC) will receive reviewers' comments and curriculum vitae from me after the review has concluded, and not be a party to the process.

Documents for review are being provided through a secure FTP site. Sections I and II below give instructions for accessing the FTP site and list the documents on the site.

You can access this site through the one-month period of review. The URL, username and password are as follows:

https://ftp.waterboards.ca.gov/WebInterface/login.html

Username: gbowes-ftp1

Password: FFLtzV

1. **List of documents at FTP site:**
   A. **October 24, 2018 Memorandum signed by Karl Palmer "Request for External Peer Review for the Proposed Adoption of Nonylphenol Ethoxylates (NPEs) in Laundry Detergent as a Priority Product".**

      Attachment 1:

      Plain English Summary of the Proposal to Adopt NPEs in Laundry Detergents as a Priority Product.

Attachment 2:

Scientific Conclusions to be Addressed by Peer Reviewers.

These are the focus for the review. In your November 6, 2018 memo to me, you indicated you could address all four conclusions. Please do so.

Attachment 3:

- List of Participants.
- Section A: DTSC Participants
- Section B: External Participants

Attachment 4:

Reference Titles

B. Regulatory References

Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent
California Code of Regulations, Title 22, sections 69401 – 69407.2
California Code of Regulations, Title 22, sections 69503 – 69503.7
California Code of Regulations, Title 22, proposed sections 69511(b)(4) – 69511.4

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Please send your reviews to me on January 14, 2019 to ensure I receive all on the same day.

Questions about the review should be for clarification, in writing –email is fine, and addressed to me. My responses will be in writing also. All this information will be posted at the State Water Board program website for this proposal. Your acceptance of this review assignment is most appreciated.

Sincerely,

Gerald W. Bowes

Gerald W. Bowes, Ph.D.
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December 4, 2018

Heiko L. Schoenfuss, Ph.D.
Professor
Department of Biology, WSB-273
St. Cloud State University
St. Cloud MN 56301

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF NONYLPHENOL ETHOXYLATES (NPEs) IN LAUNDRY DETERGENT AS A PRIORITY PRODUCT

Dear: Professor Schoenfuss:

The purpose of this letter is to initiate the external review.

The Department of Toxic Substances Control (DTSC) will receive reviewers' comments and curriculum vitae from me after the review has concluded, and not be a party to the process.

Documents for review are being provided through a secure FTP site. Sections I and II below give instructions for accessing the FTP site and list the documents on the site.

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Attachment 2:

Scientific Conclusions to be Addressed by Peer Reviewers.

These are the focus for the review. In your November 2, 2018 memo to me, you indicated you were confident in your ability to review Conclusions 2 and 4. Please do so.

Attachment 3:

- List of Participants.
- Section A: DTSC Participants
- Section B: External Participants

Attachment 4:

Reference Titles

B. Regulatory References

Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent
California Code of Regulations, Title 22, sections 69401 – 69407.2
California Code of Regulations, Title 22, sections 69503 – 69503.7
California Code of Regulations, Title 22, proposed sections 69511(b)(4) – 69511.4

C. Copies of Literature Relied Upon

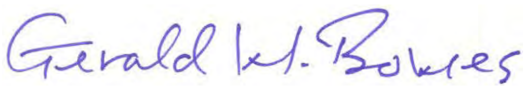
D. <u>October 22, 2018 Supplement to CalEPA External Scientific Peer Review Guidelines.</u>

This supplement provides guidance to ensure the review is kept confidential through its course. The Supplement notes reviewers are under no obligation to discuss their comments with third-parties after reviews have been submitted. We recommend they do not. All outside parties are provided opportunities to address a proposed regulatory action through a well-defined regulatory process. Please direct third parties to me.

Please send your reviews to me on January 14, 2019 to ensure I receive all on the same day.

Questions about the review should be for clarification, in writing –email is fine, and addressed to me. My responses will be in writing also. All this information will be posted at the State Water Board program website for this proposal. Your acceptance of this review assignment is most appreciated.

Sincerely,



Gerald W. Bowes, Ph.D.
Manager, Cal/EPA Scientific Peer Review
Program Office of Research, Planning and
Performance State Water Resources Control Board
Sacramento, California 95814

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ATTACHMENT 3

October 22, 2018

Supplement to Cal/EPA External Scientific Peer Review Guidelines – "Exhibit F" in Cal/EPA Interagency Agreement with University of California

Gerald W. Bowes, Ph.D.

1. **REVISIONS**. If changes are made in the final, signed request for review, and before the review has begun, a revised request must be discussed with, and submitted to the review manager. Normally, this is the CalEPA program manager for scientific peer review. The accepted revision must clearly describe changes, and at the time of review initiation, be sent to the reviewers by the program manager as the basis for the review. The original final request had been sent earlier to candidate reviewers and discussed with them during an interview. Candidates that were eventually approved as reviewers, must clearly understand parts of the request have been changed, and where.

   A revised cover letter must a) indicate in red text at the top right corner, **"Revised"** and date of revision**;** and b) be re-signed by the requesting party.

   The cover letter also must describe in red text the nature of the changes and where they occur, e.g. in Attachment 2. **"Revised"** and date of revision must be typed in red text at the top right corner on each page where a change has been made. Revised text also must be highlighted in red, and presented in strikeout/underline format.

2. **DOCUMENTS REQUIRING REVIEW.** All scientific underpinnings of a proposed science-based rule must be submitted for external peer review. The underpinnings include all publications, conference proceedings, reports, model descriptions, and raw data upon which the proposal is based. Data from proprietary models cannot be used to support a proposal.

3. **DOCUMENTS NOT REQUIRING PEER REVIEW.** The Cal/EPA External Peer Review Guidelines note that there are circumstances where external peer review of supporting scientific documents is not required. An example would be "A particular work product that has been peer reviewed with a known record by a recognized expert or expert body." This allowance should be treated with caution. The context of the work product must be taken into account, and considered with respect to relevance to the proposal to be reviewed. The reviewers' independence and objectivity for the prior review must be considered. A safe approach would be to provide such a document to the reviewers, and let them decide if their review is needed, or at least for parts of the work product.

4. **REVIEW OF IMPLEMENTATION STRATEGY.** Publications which have a solid peer review record, such as a US EPA Criteria document, do not always include an implementation strategy. The Cal/EPA Guidelines require that the implementation of the scientific components of a proposal, or other initiative, must be submitted for external review.

5. **CONFIDENTIALITY OF REVIEWER IDENTITIES, AND REVIEWS.** External reviewers must not know the identity of other reviewers. Their identities can only be known to the CalEPA program manager for peer review (who manages the reviews), or other person delegated to managing the review. After the reviews have been completed and submitted by the program manager to the organization which requested the review, the timing of release of the reviews and identities of reviewers and their curriculum vitae, is a decision to be made by the organization, including participating legal staff.

6. **REQUESTS FROM REVIEWERS FOR ADDITIONAL SPECIFIC SUPPORTING DOCUMENTS, OR CLARIFICATION.** This should be provided to the requesting reviewer, and to all other reviewers to ensure all reviewers have the same information.

7. **USE OF PANELS**. Formation of reviewer panels is not appropriate. Panels can take on the appearance of scientific advisory committees and the external reviewers identified through the Cal/EPA process are not to be used as scientific advisors.

8. **USE OF EXTERNAL EXPERTS TO ASSIST IN PREPARATION OF RESPONSES TO EXTERNAL REVIEWERS.** California Health and Safety Code Section 57004 directs external reviewers to critically analyze CalEPA staff-developed assumptions, findings, and conclusions as the basis for proposed science-based rules. These are derived from staff's review and interpretation of relevant scientific literature. They are described in the review request, Attachment 2.

   Normally, staff prepares responses to reviewers' comments, which are reviewed by the respective executive offices. On rare occasions, staff may solicit outside expert assistance in preparing these responses. Staff must be careful that rules of confidentiality are followed by assisting experts to protect reviewers' identities and nature of the reviews. Each review sent to such experts must be marked, "Highly Confidential – Not to be Shared". Communications must be directly between the staff person designated as the contact for the assisting experts, and the experts.

   Prior to this engagement, the CalEPA organization seeking outside assistance must ensure through a conflict of interest vetting process that the enlisted experts meet certain criteria. First, the experts must have no financial interest in the outcome of the review. Second, they have no working relationships with any private or public sector entity that would benefit by, or be restricted in some way by, the proposed regulation.

   If the outside assistance takes the form of experts brought together as a panel (not recommended) with a designated chair, assuring confidentiality becomes more of a challenge. Further, a panel report implies the expert reviews represent a consensus of panel members on the stated conclusions. This would be misleading. The panel expertise is identified as a critical mass which collectively could cover the range of conclusions described as the basis for the proposed rule. It would mirror the critical mass expertise originally identified and approved as reviewers of the proposal itself. The reviewers agree to address one or a few of the conclusions, based on expertise. Similarly, staff is best served by receiving independent and objective comments from individual advising experts on the reviews, based on expertise.

The path taken to solicit such assisting experts, and the path back for this assistance, must be described and approved before such steps are taken. This must include a description of measures designed to protect reviewers' identities and the substance of their reviews.

Guidance to Reviewers:

1. **Discussion of review.**

Reviewers are not allowed to discuss the proposal with individuals who participated in development of the proposal. These individuals are listed in Attachment 3 of the review request.

Discussions between staff and reviewers are not permitted.

Reviewers may request clarification of certain aspects of the review process or the documents sent to them. The requests and responses must be in writing These communications will become part of the administrative record.

The organization requesting independent review should be careful that organization-reviewer communications do not become collaboration, or are perceived by others to have become so. The reviewers are not technical advisors. As such, they would be considered participants in the development of the proposal, and would not be considered by the University of California as external reviewers for future revisions of this or related proposals. The statute requiring external review of science-based rules proposed by Cal/EPA organizations prohibits participants serving as peer reviewers.

2. **Disclosure of reviewer Identity and release of review comments.**

Confidentiality begins at the point a potential candidate is contacted by the University of California. Candidates who agree to complete the conflict of interest disclosure form should keep this matter confidential, and should not inform others about their possible role as reviewer.

Reviewer identities must be kept confidential until review comments are received by the organization that requested the review. After the comments are received, reviewer identity and comments must be made available to anyone requesting them, within a reasonable time period specified by legal staff.

Reviewers are under no obligation to disclose their identity to anyone enquiring. It is recommended reviewers keep their role confidential until after their reviews have been made public by requesting CalEPA organization.

3. **Requests to reviewers by third parties to discuss comments.**

After they have submitted their reviews, reviewers may be approached by third parties representing special interests, the press, or by colleagues. Reviewers are under no obligation to discuss their comments with them, and we recommend that they do not.

All outside parties are provided an opportunity to address a proposed regulatory action during the public comment period and at the Cal/EPA organization meeting where the proposal is considered for adoption. Discussions outside these provided avenues for comment could seriously impede the orderly process for vetting the proposal under consideration.

4. **Reviewer contact information.**

The reviewer's name, professional affiliation, and date should accompany each review. Home address and other personal contact information are considered confidential and should not be part of the comment submittal.

ATTACHMENT 4

NSF BIOGRAPHICAL SKETCH

NAME: Carvan, Michael

NSF ID:

POSITION TITLE & INSTITUTION: Shaw Associate Professor, University of Wisconsin-Milwaukee

A. PROFESSIONAL PREPARATION

INSTITUTION	LOCATION	MAJOR / AREA OF STUDY	DEGREE (if applicable)	YEAR YYYY
University of North Carolina-Wilmington		Marine Biology	BS	1985
University of Miami-RSMAS		Biological Oceanography	MS	1988
Texas A&M University		Veterinary Anatomy and Public Health/Toxicology	PHD	1993
Department of Environmental Health, University of Cincinnati Medical Center	Cincinnati, Ohio	Postdoctoral Fellow	NIH training grant	1993 - 1996

B. APPOINTMENTS

2015-	Shaw Associate Professor, University of Wisconsin-Milwaukee, School of Freshwater Sciences, Milwaukee, WI
2011 - 2015	Shaw Associate Professor, University of Wisconsin-Milwaukee, School of Freshwater Sciences, Milwaukee, WI
2011 -	Affiliate Professor, University of Wisconsin-Milwaukee, Zilber School of Public Health, Milwaukee, WI
2006 - 2011	Shaw Associate Scientist, University of Wisconsin-Milwaukee, Great Lakes WATER Institute, Milwaukee, WI
2001 -	Affiliate Assistant/Associate/Full Professor, University of Wisconsin-Milwaukee, Department of Biological Sciences, Milwaukee, WI
2000 -	Clinical Associate/Full Professor, University of Wisconsin-Milwaukee, College of Health Sciences, Milwaukee, WI
2000 - 2006	Shaw Assistant Scientist, University of Wisconsin-Milwaukee, Great Lakes WATER Institute, Milwaukee, WI
1997 - 1999	Research Assistant Professor, Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, OH
1996 - 1997	Research Associate, Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, OH

C. PRODUCTS

Products Most Closely Related to the Proposed Project

1. Mora-Zamorano FX, Klingler R, Basu N, Head J, Murphy CA, Binkowski FP, Larson JK, Carvan MJ 3rd. Developmental Methylmercury Exposure Affects Swimming Behavior and Foraging Efficiency of Yellow Perch (<i>Perca flavescens</i>) Larvae. ACS Omega. 2017 Aug 31;2(8):4870-4877. PubMed PMID: 28884165; PubMed Central PMCID: PMC5579541.
2. Carvan MJ 3rd, Kalluvila TA, Klingler RH, Larson JK, Pickens M, Mora-Zamorano FX, Connaughton VP, Sadler-Riggleman I, Beck D, Skinner MK. Mercury-induced epigenetic transgenerational inheritance of abnormal neurobehavior is correlated with sperm epimutations in zebrafish. PLoS One. 2017;12(5):e0176155. PubMed PMID: 28464002; PubMed Central PMCID: PMC5413066.
3. Mora-Zamorano FX, Svoboda KR, Carvan MJ 3rd. The Nicotine-Evoked Locomotor Response: A Behavioral Paradigm for Toxicity Screening in Zebrafish (Danio rerio) Embryos and Eleutheroembryos Exposed to Methylmercury. PLoS One. 2016;11(4):e0154570. PubMed PMID: 27123921; PubMed Central PMCID: PMC4849578.
4. Carvan III MJ, Di Guilio RT. Studies on Experimental Toxicology and Pharmacology. Roberts SM, Kehrer JP, Klotz L, editors. Switzerland: Springer; 2015. Oxidative Stress Responses in Aquatic and Marine Fishes; p.481-493. 498p.
5. Liu Q, Spitsbergen JM, Cariou R, Huang CY, Jiang N, Goetz G, Hutz RJ, Tonellato PJ, Carvan MJ 3rd. Histopathologic alterations associated with global gene expression due to chronic dietary TCDD exposure in juvenile zebrafish. PLoS One. 2014;9(7):e100910. PubMed PMID: 24988445; PubMed Central PMCID: PMC4079602.

Other Significant Products, Whether or Not Related to the Proposed Project

1. Watanabe KH, Andersen ME, Basu N, Carvan MJ 3rd, Crofton KM, King KA, Suñol C, Tiffany-Castiglioni E, Schultz IR. Defining and modeling known adverse outcome pathways: Domoic acid and neuronal signaling as a case study. Environ Toxicol Chem. 2011 Jan;30(1):9-21. PubMed PMID: 20963854.

2. Weber DN, Klingler RH, Carvan MJ. Current Topics in Neurotoxicity: Methylmercury and Neurotoxicity. Aschner M, Ceccatelli S, editors. New York: Springer; 2012. Zebrafish as a model for methylmercury neurotoxicity; p.335-355.
3. Delinger M, Carvan MJ, Klingler RH, McGraw JE, Ehlinger T. An Exploratory Analysis of Stream Teratogenicity and Human Health Using Zebrafish Whole-Sediment Toxicity Test. Challenges. 2014 February; 17(5):75-97.
4. Flentke GR, Klingler RH, Tanguay RL, Carvan MJ 3rd, Smith SM. An evolutionarily conserved mechanism of calcium-dependent neurotoxicity in a zebrafish model of fetal alcohol spectrum disorders. Alcohol Clin Exp Res. 2014 May;38(5):1255-65. PubMed PMID: 24512079; PubMed Central PMCID: PMC3999225.
5. Larson JK, Carvan MJ 3rd, Teeguarden JG, Watanabe G, Taya K, Krystofiak E, Hutz RJ. Low-dose gold nanoparticles exert subtle endocrine-modulating effects on the ovarian steroidogenic pathway ex vivo independent of oxidative stress. Nanotoxicology. 2014 Dec;8(8):856-66. PubMed PMID: 23992423; PubMed Central PMCID: PMC4340664.

D. SYNERGISTIC ACTIVITIES

1. UBM-Group: Integrated Undergraduate Research Experiences in Aquatic Biology and Mathematical Sciences at the University of Wisconsin Milwaukee (funded by NSF)
2. Participant, Great Lakes Native American Research Center for Health Summer Research Internship Program, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin.
3. Participant, Middle School Life Science-Education Partnership, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin.
4. Participant, National Science Foundation Research Experience for Undergraduates, University of Wisconsin-Milwaukee Great Lakes WATER Institute.
5. Participant, Milwaukee Lead to Succeed Program for Milwaukee Water Council Workforce Development.

E. COLLABORATORS & OTHER AFFILIATIONS

Collaborators and Co-editors

Nil Basu, McGill University; Matthew Cave, University of Louisville; Victoria Connaughton, American University; Richard DiGulio, Duke University; George Flentke, University of Wisconsin-Madison; Natalia Garcia-Reyero, Mississippi State University; Kimberley Gray, Northwestern University; Tiago Hori, Memorial University of St. John's; Sridhar Mani, Albert Einstein College of Medicine; Joseph McGraw, Concordia University; Cheryl Murphy, Michigan State University; Matthew Rise, Memorial University of St. John's; Michael Skinner, Washington State University; Susan Smith, University of Wisconsin-Madison.

Total Collaborators/Co-Editors: 14

Graduate Advisors and Postdoctoral Sponsors

David Busbee, Texas A&M University, retired; Daniel Nebert, University of Cincinnati, retired; Daniel Odell, University of Miami/Hubbs Sea World Research Institute, retired.

Total Advisors/Sponsors: 3

Thesis Advisor and Postgraduate-Scholar Sponsor

Abigail DeBofsky, (MS 2015) USEPA Region 5, Chicago, IL; Katie Gajeski, (MS 2011) Health Officer, City of Cudahy, WI; Jacob Jozefowski (MS 2018) City of Racine Department of Public Health; Thomas Kalluvila, (PhD 2015) Professor, Milwaukee Area Technical College; Rebekah Klingler, (Postdoc 2018) Alverno College, Milwaukee, WI; Jeremy Larson, (MS 2013) Research Associate, Medical College of Wisconsin, Milwaukee, WI; Qing Liu, (PhD 2012) Instructor, Stanford University; Susan Miller, (MS 2012) self-employed, Milwaukee, WI; Chad Mitchell (MS current) University of Wisconsin-Milwaukee, Milwaukee, WI; Francisco Mora, (PhD 2015) self-employed, Tijuana, Mexico; Matthew Pickens, (MS 2015) Veterinary School, Grenada; Emily Tolliver (MS current) University of Wisconsin-Milwaukee, Milwaukee, WI;

Total Advised/Sponsored: 9

Resume'

METCALFE, Christopher D.
Environmental and Resource Studies Program, Trent University
Peterborough, Ontario, K9J 7B8, Canada
PHONE: (705) 748-1011 x7272
E-Mail: CMETCALFE@TRENTU.CA

Education
B.Sc. (Hons.), University of Manitoba (1973), Zoology
M.Sc., University of New Brunswick (1976), Biology
Ph.D., McMaster University (1984), Biochemistry

Positions Held

2017	Erskine Visiting Fellow, University of Canterbury, Christchurch, NZ
2011 to present	Senior Advisor, UN University – Institute for Water Environment and Health, Hamilton, ON
2009 to present	Adjunct Professor, UN University – Institute for Water Environment and Health, Hamilton, ON
2013 to 2014	Acting Chair, Environmental & Resource Studies, Trent University
2006 to present	Director, Institute for Watershed Science, Trent University
2000 to 2004	Dean of Research and Graduate Studies, Trent University
1995 to present	Full Professor, Environmental & Resource Studies, Trent University
1999 to 2000	Interim Director, Watershed Ecosystems Graduate Program
1995 to 1998	Chair, Environmental & Resource Studies, Trent University
1989 to 1995	Assoc. Professor, Environmental & Resource Studies, Trent University
1988 to 1991	Director, Watershed Ecosystems Graduate Program
1984 to 1989	Assist. Professor, Environmental & Resource Studies, Trent University
1977 to 1980	Toxicological Chemist, Fisheries & Oceans, St. Andrews, N. B.

Teaching
Environmental Toxicology and Chemistry (ERSC 3701H); Environmental Health (ERSC-PSYC 3710H); Environmental Risk Assessment (ERSC 3702H); Environment and Development (ERSC/ST 3230H); Field Monitoring Techniques (ENLS 5041H).

Research Interests
I am interested in determining the environmental fate and toxic effects of contaminants in the environment. Currently, I am conducting research on endocrine disruption and other biological responses in fish, and the fate and effects of pharmaceuticals and personal care products, pesticides, and nanomaterials in the aquatic environment. I am also interested in research and capacity building in the area of watershed management; with a particular focus on community-based projects in First Nations communities in Canada, and in communities in developing countries.

Peer-reviewed Publications:
232 journal articles
20 book chapters
1 book (co-editor)

Relevant publications on alkylphenols and alkylphenol ethoxylates:

Metcalfe, C.D., T.L. Metcalfe, Y. Kiparissis, B.G. Koenig, C. Khan, R.J. Hughes, T.R. Croley, R.E. March and T. Potter. 2001. The estrogenic potency of chemicals in sewage treatment plant effluents as determined by *in vivo* assays with the Japanese medaka, *Oryzias latipes*. Environ. Toxicol. Chem. 20:297-308.

Gray, M.A., K.L. Teather and C.D. Metcalfe. 1999. Reproductive success and behaviour of Japanese medaka *(Oryzias latipes)* exposed to 4-*tert*-octylphenol. Environ. Toxicol. Chem. 18:2587-2594.

Hawrelak, M., E. Bennett and C. Metcalfe. 1999. The environmental fate of the primary degradation products of alkylphenol ethoxylate surfactants in recycled paper sludge. Chemosphere 39:745-752.

Gray, M.A., A.J. Niimi and C.D. Metcalfe. 1999. Factors affecting the development of testis-ova in medaka, *Oryzias latipes*, exposed to octylphenol. Environ. Toxicol. Chem. 18:1835-1842.

Bennett, E.R. and C.D. Metcalfe. 1998. The distribution of alkylphenol compounds in Great Lakes sediments, United States and Canada. Environ. Toxicol. Chem. 17:1230-1235.

Gray, M.A. and C.D. Metcalfe. 1997. Induction of testis-ova in Japanese medaka *(Oryzias latipes*) exposed to p-nonylphenol. Environ. Toxicol. Chem. 16:1082-1086.

Recent refereed journal publications (last 6 months)

Metcalfe CD, Sultana T, Martin JD, Newman K, Helm P, Kleywegt S, Shen L, Yargeau V. 2019. Silver near municipal wastewater discharges into western Lake Ontario, Canada, Environ. Monitor. Assess., In press.

Martin JD, Frost PC, Hintelmann H, Newman K, Paterson MJ, Hayhurst L, Rennie MD, Xenopoulos MA, Yargeau V, Metcalfe CD. 2019. Accumulation of silver in yellow perch (*Perca flavescens*) and northern pike (*Esox lucius*) from a lake dosed with nanosilver. Environ. Sci. Technol. 52:11114-11122.

Parrott J, Metcalfe CD. 2019. Assessing the effects of environmentally relevant concentrations of antidepressant mixtures to fathead minnows exposed over a full life cycle. Sci. Total Environ. 648:1227-1236.

Metcalfe CD, Helm PA, Paterson G, Kaltenecker G, Murray C, Nowierski M, Sultana T. 2019. Pesticides related to land use in the watersheds in the Great Lakes basin. Sci.Total Environ. 648:681-692.

Edwards QA, Sultana T, Kulikov SM, Garner-O'Neale LD, Metcalfe CD. 2018. Contaminants of emerging concern in wastewater in Barbados, West Indies. Bull. Environ. Contam. Toxicol. 101:1-6.

Maya N, Crispo C, McFarland V, Nasuhoglu D, Isazadeh S, Yargeau V, Metcalfe CD. 2018. Toxicity of extracts from municipal wastewater to early life stages of Japanese medaka (*Oryzias latipes*) to evaluate removals of micropollutants by wastewater treatment. Environ. Toxicol. Chem. 37:136-144.

CURRICULUM VITA
Heiko Lars Schoenfuss
Professor
Department of Biological Sciences,
720 Fourth Avenue South, WSB-273
St. Cloud State University, St. Cloud, MN 56301

hschoenfuss@stcloudstate.edu

a. Professional Preparation

Institution	Areas (s) of Study	Degree (Year)
University of Bayreuth, Germany	Biology	B.S. (1991)
Louisiana State University	Veterinary Anatomy	M.S. (1997)
Louisiana State University	Evolutionary Morphology	Ph.D. (1997)
University of Minnesota	Endocrine Toxicology	Postdoctoral (1998-2001)

b. Appointments

2008-present	Professor, St. Cloud State University, Biology
2005-2008	Associate Professor, St. Cloud State University
2001-2005	Assistant Professor, St. Cloud State University
1994-1997	Lecturer, Eastern Louisiana University, Hammond, LA

c. Publications

(i) Five publications most closely related to the project (of ~100 total)

Lozano N, Rice CP, Pagano J, Zintek L, Barber LB, Murphy EW, Nettesheim T, Minarik TA, **Schoenfuss** HL. 2012. Concentration of organic contaminants in fish and their biological effects in a wastewater-dominated urban stream. *Science of the Total Environment* 420:191-201.

Schoenfuss HL, Bartell SE, Bistodeau TB, Cediel RA, Grove KJ, Zintek L, Lee KE, Barber LB. 2008. Impairment of the reproductive potential of male fathead minnows by environmentally relevant exposures to 4-nonylphenol. *Aquatic Toxicology* 86:91-98.

Julius ML, Stepanek J, Tedrow O, Gamble C, **Schoenfuss** HL. 2007. Estrogen-receptor independent effects of two ubiquitous environmental estrogens on *Melosira varians* Agardh, a common component of the aquatic primary production community. *Aquatic Toxicology* 85:19-27.

Barber LB, Lee KE, Swackhamer D, **Schoenfuss** HL. 2007. Response of Male Fathead Minnows Exposed to Wastewater Treatment Plant Effluent, Effluent Treated with XAD8 Resin, and an Environmentally Relevant Mixture of Alkylphenol Compounds. *Aquatic Toxicology* 82:36-46.

Bistodeau TJ, Barber LB, Bartell SE, Cediel RA, Grove KJ, Klaustermeier J, Woodard JC, Lee KE. **Schoenfuss** HL. 2006. Larval exposure to environmentally relevant mixtures of alkylphenolethoxylates reduces reproductive competence in male fathead minnows. *Aquatic Toxicology* 79:268-277.

(ii) Five other significant publications (complete list: web.stcloudstate.edu/aquatictox)

Fairbairn DJ, Elliott SM, Kiesling RL, **Schoenfuss** HL, Ferrey ML, Westerhoff BM. 2018. Contaminants of emerging concern in urban stormwater: Spatiotemporal patterns and removal by iron-enhanced sand filters (IESFs). *Water Research* in press.

Westerhoff BM, Fairbairn DJ, Ferrey ML, Matilla A, Kunkel J, Elliott SM, Kiesling RL, Woodruff D, **Schoenfuss** HL. 2018. Effects of urban stormwater and iron-enhanced sand filtration on D. magna and Pimephales promelas. *Environmental Toxicology & Chemistry* in press.

Elliott SM, Brigham ME, Kiesling RL, **Schoenfuss** HL, Jorgenson ZG. 2018. Environmentally Relevant Chemical Mixtures of Concern in U.S. Tributaries to the Great Lakes. *Integrated Environmental Assessment and Management* DOI: 10.1002/ieam.4041.

Jorgenson ZG, Thomas L, Elliott SM, Cavallin JE, Randolph EC, Choy SJ, Alvarez DA, Banda JA, Gefell DJ, Lee KE, Furlong ET, **Schoenfuss** HL. 2018. Contaminants of Emerging Concern Presence and Adverse Effects in Fish: A Case Study in the Laurentian Great Lakes. *Environmental Pollution* 236:718-733. DOI: 10.1016/j.envpol.2018.01.070.

Guyader M, Warren L, Green E, Proudian A, Kiesling R, **Schoenfuss** HL, Higgins CP. 2018. Trace Organic Contaminant (TOrC) Mixtures in Minnesota Littoral Zones: Effects of On-Site Wastewater Treatment System (OWTS) Proximity and Biologic Impact. *Science of the Total Environment* 626:1157-1166. DOI: 10.1016/j.scitotenv.2018.01.123.

d. Synergistic Activities

- **(i)** Chair (2017-20) and Member (2014-20), Steering Committee of the SETAC Global Advisory Group on Endocrine Disrupter Testing and Risk Assessment (EDTRA).
- **(ii)** I have peer reviewed for over 20 journals in the past five years and reviewed proposals for the US EPA, Polish-, Swiss-, and Canadian Science Foundations. I was named one of the top 15 peer reviewers for the joural “environmental Toxicology & Chemistry in 2018
- **(iii)** I have served as principal advisor to 30 Master's students (27 have graduated, 3 are current students).
- **(iv)** Member, Program Committee, *Society for Environmental Toxicology & Chemistry*.
- **(i)** In the past 6 years, I have included over 40 undergraduate students, representing all continents (except Antarctica) in my research. Most of these students have presented at either the annual SSCU Research Colloquium (23) and/or at regional, national or international meetings (16).
- **(i)** I was appointed to the USGS Toxics Program Review Committee in 2014.
- **(ii)** I received the inaugural St. Cloud State “University Scholar” distinction.
- **(iii)** Member, MN Department of Health, Task Force on Criterion Development for Contaminants of Emerging Concern (2010-12).

ATTACHMENT 5

Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergents
Review prepared by Michael Carvan, University of Wisconsin-Milwaukee
14 January 2019

The purpose of this document is to review a proposed regulation to adopt nonylphenol ethoxylates (NPEs) in laundry detergents (mostly commercial and industrial) as a Priority Product under the Safer Consumer Products regulatory framework of the California Code of Regulations. This regulation is being sought because of adverse ecological impacts, which are well documented in the scientific literature and the Product-Chemical Profile. This Profile is exceptionally well-developed and provides a summary of all the relevant information supporting the hazardous nature of NPEs in the environment. My review will specifically focus on Conclusions 2 and 4, which are re-stated below. I will mention the sections of the product-chemical profile directly related to these conclusions, but the entire profile is helpful in adding context and creating a complete analysis of the problem.

> Conclusion 2 – NPEs and their degradation products have hazard traits and can cause cumulative adverse impacts when aquatic organisms are exposed to mixtures of the class of chemicals.
>
> Conclusion 4 – Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organisms due to the adverse impact and exposure considerations in the product-chemical profile.

In the opinion of this reviewer, the scientific issues that are part of the scientific basis of the proposed regulation have been very well stated and addressed with sufficient depth and breadth in the product-chemical profile and proposed implementation language. It is also my opinion that the scientific portion of the proposed regulation is based on sound scientific knowledge, methods, and practices and demonstrates a commitment to scientific rigor.

Conclusion 2
NPEs are toxic and their breakdown products (NPEDs, generally from the removal of ethoxylate groups) tend to be even more toxic. The most stable and well-studied NPED is nonylphenol (NP) which, along with NPEs, causes narcosis (decreased activity and reduced reaction to external stimuli), endocrine disruption (affecting growth, development, and reproduction), and surfactant effects (at higher concentrations). The product-chemical profile has an excellent summary of the hazard traits and environmental or toxicological endpoints (section 2.3, Appendix C) which includes both acute and subchronic exposures. Hazards from acute exposures are mostly related to the effects of narcosis. Environmental hazards from subchronic exposures are mostly related to interactions with cellular receptors resulting in endocrine disruption. NP and NPEs are environmentally persistent (they have long half-lives) and uptake is higher than excretion (results in bioaccumulation). The combination of persistence and bioaccumulation contributes significantly to the toxicity NPEs and NPEDs.

Because of their structural similarity, the toxicity of NPEs can be expressed relative to NP as toxic equivalency factors (NP=1, other NPEs are 0.5 and lower generally dependent on the number of ethoxylate groups). This is very well described and justified in section 2.4. Section 5.1.4 provides an excellent summary of the importance of considering both NP and NPEs when determining hazard potential for specific media. Exemplar studies of sediment and water samples are provide in which the NP-related toxicity (effective NP) was estimated to be 2 to 6 times higher than from NP alone.

It is also important to remember that while NPEs occur as a mixture in the environment, they also co-occur with a wide variety of toxicants that may act on similar pathways and result in an additive response. As shown in 5.1.4, many environmental chemicals can have synergistic effects on many endocrine pathways even if they are not closely related structurally. The example provided is an excellent study of pyrethroid pesticides and NPEs acting synergistically to induce vitellogenin production, which is mostly regulated by estrogen receptor activation. For this reason, the product-chemical profile suggests that there are sensitive species that may be at risk from mixtures of NPEs, NPEDs, and pesticides.

Overall the evidence is strong for NPEs and their degradation products having hazard traits and having the potential to cause cumulative adverse impacts when aquatic organisms are exposed to mixtures of this class of chemicals.

<u>Conclusion 4</u>
This product-chemical profile does an excellent job in section 2.5 discussing the fish and aquatic invertebrate populations that may be harmed by NPEs. Water quality guidelines, standards, and criteria (GSC) are discussed in relation to levels in specific California watersheds and the presence of threatened or endangered fish and aquatic invertebrate species. The co-location of these sensitive species and waste water treatment plants (WWTPs) suggests that hazardous exposures are likely to occur. The GSC that are presented (many of which are provisional) have come to a modest consensus (within an order of magnitude) on the criteria for freshwater systems based on the organisms they were designed to protect from chronic exposures to contaminated water and sediment. The State of California will establish its own guidelines based on the sensitivity of the species of concern, however, there is little doubt that NP and NPEs are hazardous to the environment. The coverage of existing GSC provides an excellent starting point.

Environmental distribution analysis of NP is much more common than for NPEs, and has been detected in sediments, surface waters, ground water, dust, effluent, sludge and biosolids, and biological samples from humans and wildlife. This is well covered in section 3.3.1 and Appendix E. Both of these sections also provides specific examples from California and demonstrate the widespread potential for exposure and adverse impact. As further clarified in 3.3.3, WWTPs provide a near-constant long-term source of NPEs into surface waters resulting in chronic exposures to aquatic organisms. Drought conditions and water conservation efforts increase the concentration of NPEs in surface waters, however, the overall discharge of NPEs year-to-year into the environment seems to be relatively consistent.

Overall the evidence is strong that laundry detergents containing NPEs have the potential for significant and widespread impacts to aquatic organisms due to the adverse impact and exposure considerations in the product-chemical profile.

External Peer Review for the Proposed Adoption of Nonylphenol Ethoxylates (NPEs) in Laundry Detergent as a Priority Product

Review Submitted by
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January 14, 2019

INTRODUCTION

The Department of Toxic Substance Control (DTSC) for the State of California identified laundry detergents containing nonylphenol ethoxylates (NPEs) as a proposed Priority Product, based upon evidence in the peer-reviewed literature and from other sources of information that there is potential for exposure to NPEs from laundry detergents and adverse impacts to aquatic organisms. Based upon this conclusion, a panel of experts, including myself were asked to review the "Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergent" and the literature cited in this profile, and to comment on the conclusions of the DTSC stemming from this report. The four conclusions are:

1) NPEs are a class of chemicals that can be broken down to degradation products, including nonylphenol, and can enter the aquatic environment.
2) NPEs and their degradation products have hazard traits and can cause cumulative adverse effects when organisms are exposed to this class of chemicals.
3) Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environment.
4) Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organisms due to the adverse impact and exposure considerations described in the product-chemical profile.

In addition, the Reviewers were asked to comment on:

i) Whether there are any additional scientific issues that are part of the scientific basis of the proposed regulation that were not described in the product-chemical profile or were not considered by the DTSC in arriving at the four conclusions.

ii) Whether the proposed regulation is based upon sound scientific knowledge, method and practices.

COMMENTS ON THE CONCLUSIONS OF THE DTSC:

<u>Conclusion 1:</u> **NPEs are a class of chemicals that can be broken down to degradation products, including nonylphenol, and can enter the aquatic environment.**

The peer-reviewed scientific literature clearly indicates that NPEs undergo a process of degradation which initially results in reductions in the length of the ethoxylate chain of these surfactants. These transformations occur under both aerobic and anaerobic conditions. The degradation processes ultimately result in the formation of nonylphenol (NP), as well as primarily NP1EO and NP2EO under anaerobic conditions and primarily NP1EC and NP2EC under aerobic conditions. These degradation processes occur within wastewater treatment plants (WWTPs), which are the primary point source of NPEs and NP, and the transformations continue to occur in aquatic environments when NPEs and degradation products are released from a point source. Because of its moderately hydrophobic properties, NP tends to partition into wastewater sludges and into sediments in the aquatic environment. NP deposited in sediments tends to be relatively immobile and is confined to the immediate area around point source discharges (Ferguson et al., 2001; Bennett and Metcalfe, 2000). The other transformation products mentioned above (i.e. NP1EO, NP2EO, NP1EC, NP2EC) are more hydrophilic and tend to partition into the aqueous phase, where they can be transported more widely.

Overall assessment: The available scientific evidence supports Conclusion 1.

<u>Conclusion 2:</u> NPEs and their degradation products have hazard traits and can cause cumulative adverse effects when organisms are exposed to this class of chemicals.

Evidence from *in vitro* and *in vivo* studies conducted in the laboratory that are described in the peer-reviewed literature show that NP is an estrogen agonist that binds to the estrogen receptor. NP can cause a range of effects in fish at environmentally relevant concentrations, including feminization, induction of inter-sex and reproductive impairment. There is also some evidence in the literature that NP can affect growth, moulting and larval settlement in freshwater and marine invertebrates. NP is moderately estrogenic in comparison to the much higher potencies of natural estrogens, such as estradiol and estrone, and synthetic estrogens, such as ethinylestradiol (Metcalfe et al., 2001). There is also evidence that NP1EO and NP2EO are estrogenic, but at potencies lower than the potency of NP (Metcalfe et al., 2001). NPECs do not appear to have estrogenic activity. However, since NP, NP1EO and NP2EO are typically present in environmental matrixes (e.g. water, sediments) at concentrations several orders of magnitude greater than the concentrations of natural and synthetic estrogens, the contribution of NPE degradation products to total estrogenicity can be significant. NP has also been shown to affect levels of insulin-like growth factor in salmonids (Arsenault et al. 2004) and has been implicated in the failure of Atlantic salmon to go through a "smoltification" stage of development (Fairchild et al., 1999).

The thresholds for the endocrine disrupting effects of NP in fish are in the low ppb (µg/L) range of concentrations. Therefore, various regulatory agencies have set water quality standards for NP that are in this range. Because NP1EO and NP2EO are typically present in water at orders of magnitude higher concentrations than the concentrations of NP, they can make a significant contribution to the overall estrogenic equivalents of NPEs in water, despite the lower potency of these NPEO compounds. The product-chemical profile documents cases where the cumulative toxic equivalent quantities of NP, NP1EO and NP2EO detected in water exceeded regulatory thresholds for NP. However, as acknowledged in the product-chemical profile, there are few recent data on the levels of these compounds in the aquatic environment in California. Therefore, the high toxic equivalents reviewed in the product-chemical profile generally reflect historical contamination before the ban on the use of NPEs in domestic products.

What is missing from the literature is definitive evidence that NP and its degradation products cause endocrine disruption in organisms exposed to these compounds *in situ*. This is primarily because NPEs co-occur in the environment with a range of other natural estrogens and xenoestrogens that are released from WWTPs and other point sources. Feminization and reproductive impairment of fish has been documented in several areas in the USA, Canada, the U.K. and Europe in areas impacted by discharges from WWTPs, but these effects cannot be specifically attributed to exposure to NP and other NPE degradation products. The total burden of estrogenic substances in the environment is responsible for these effects. The product-chemical profile documents that there are many watersheds in California where discharges from WWTPs comprise a high proportion of the total flows of surface waters; especially under drought conditions. Therefore, there is potential for aquatic organisms to be exposed to high concentrations of estrogenic substances discharged from the WWTPs, including NPEs. In addition, the product-chemical profile documents that the distribution of many species at risk in California overlaps with the watersheds impacted by WWTP discharges.

There is evidence from the literature that NP is moderately bioaccumulative. However, recent estimates of bioaccumulation factors between seawater and biota in the marine environment off California show that $BAF_{seawater}$ values can exceed 5,000 (Diehl et al., 2012). These values are lower than the bioaccumulation factors for more lipophilic compounds, such as PCBs and PBDEs, and there is no evidence of biomagnification of NP through food webs. The variations in bioaccumulation factors reported for NP are probably a function of species-specific differences in the capacity of organisms to metabolize and eliminate these compounds, their habitat (e.g. benthic vs pelagic), whether the organisms are sessile or mobile, and their feeding strategies (e.g. filter feeders, deposit feeders, herbivores, molluscivores, piscivores), and the tissues that were analyzed (e.g. liver, muscle).

Overall assessment: The available scientific evidence supports Conclusion 2.

<u>Conclusion 3:</u> Laundry detergents containing NPEs can serve as a source of NPEs and their degradation products to the aquatic environment.

There is ample evidence from the scientific literature that NPEs in laundry detergents are the primary source of these compounds and their degradation products in the aquatic environment. The product-chemical profile identifies some other potential sources of these compounds (e.g. surfactants in paints, pesticide formulations), but these are probably minor sources compared to the total amounts of NPEs used in laundry detergents that are carried in municipal sewage into WWTPs.

What is less clear is how much NPE is <u>currently</u> being released into WWTPs in California following the enforced or voluntary phase out of NPEs from domestic laundry detergents and cleaning products. The product-chemical profile states that the use of NPEs in California is now confined to products used in commercial laundries and in the hospitality sector (e.g. hotels). The total estimated amounts of NPEs in detergents used by these sectors in California appear to be substantial but are likely much less than the total amounts of NPEs released before the ban on their use in domestic detergents. This conclusion is supported by recent data on the levels of NP in profiles of marine sediments in California that indicate that NP concentrations were historically higher in subsurface sediments corresponding to deposition in in the 1970s relative to the levels in recently deposited surface sediments (Maruya et al., 2014). However, recent data on the concentrations in marine organisms off the coast of California indicate that NP is still a contaminant present in biota at elevated concentrations (Diehl et al., 2012).

Overall assessment: The available scientific evidence supports Conclusion 3.

<u>Conclusion 4:</u> Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organisms due to the adverse impact and exposure considerations described in the product-chemical profile.

The operative word in this conclusion is "potential", since there is no definitive evidence that organisms exposed *in situ* to NPEs are experiencing adverse impacts. As mentioned previously, definitive evidence of *in situ* impacts is difficult to find because of the presence of co-occurring contaminants with estrogenic and/or other toxic activities. However, using an ecological risk assessment approach, there is evidence that the measured environmental concentrations (MECs) for total estrogenic equivalents of NP, NP1EO and NP2EO in water are frequently in the same range as the concentrations at which estrogenic effects have been observed in fish exposed to NP in the laboratory, and are certainly greater than the predicted no effect concentration (PNEC) for NP. Therefore, laundry detergents that contain NPEs have the "potential" for adverse impacts.

Another important phrase in this conclusion is "significant or widespread impacts on aquatic organisms". There is strong experimental evidence that NP, NP1EO and NP2EO can induce gonadal intersex in exposed fish (Metcalfe et al., 2001; Gray and Metcalfe, 1997). Severe gonadal intersex in fish exposed i*n situ* to endocrine disrupting compounds discharged in the effluents from WWTPs has been associated with reduced reproductive capacity. Therefore, exposure to degradation products from NPEs could reduce recruitment in exposed fish populations. The product-chemical profile documents that WWTPs in several watersheds in California discharge into areas where there are aquatic species at risk, so there is potential for degradation products of NPEs discharged in WWTP effluents in California to contribute to the extirpation of endangered species, which would certainly be a "significant" impact.

California is a heavily populated (i.e. >37 million people) and according to the Water Education Foundation, there are over 900 WWTPs operating in the state that generate approximately 4 billion gallons per day of treated wastewater. Therefore, there is potential for "widespread" impacts in California from the discharge of degradation products of NPEs from the WWTPs distributed throughout the state. NP tends to be localized to sediments near the point-source discharges of wastewater (Bennett and Metcalfe, 2000), but NP1EO and NP2EO are more mobile in the aquatic environment and can be distributed more widely (Ferguson et al., 2001).

Overall assessment: The available scientific evidence supports Conclusion 4.

OTHER COMMENTS

i) Whether there are any additional scientific issues that are part of the scientific basis of the proposed regulation that were not described in the product-chemical profile or were not considered by the DTSC in arriving at the four conclusions.

In this review, I identified some additional relevant publications that were not included in product-chemical profile. These additional references support the four conclusions of the product-chemical profile. In my opinion, there are not any additional "scientific issues" that were omitted from the product-chemical profile.

ii) Whether the proposed regulation is based upon sound scientific knowledge, method and practices.

The proposed regulation is based upon "sound science" that is documented in the peer-reviewed literature and the conclusions drawn in the report are appropriate. However, as acknowledged in the product-chemical profile, there are few recent data on the levels of NPEs and their degradation products in surface waters and in the marine environment in California. Therefore, it is difficult to state whether current discharges of these compounds as a result of their continued use in commercial products are a significant threat to the aquatic environment. Having said this, any regulation that reduces the use of substances with estrogenic activity is good public policy and will contribute to protecting the environment.

References:

Arsenault JTM et al. 2004. Effects of water-borne 4-nonylphenol and 17ß-estradiol exposures during parr-smolt transformation on growth and plasma IGF-I of Atlantic salmon (*Salmo salar* L.) Aquatic Toxicol. 66: 255-265.

Bennett ER, Metcalfe CD 2000, Distribution of degradation products of alkylphenol ethoxylates near sewage treatment plants in the lower Great Lakes, North America. Environ. Toxicol. Chem. 19:784-792.

Diehl J et al. 2012. The distribution of 4-nonylphenol in marine organisms of North American Pacific Coast estuaries. Chemosphere 87:490-497.

Fairchild WL et al. 1999. Does an association between pesticide use and subsequent declines in catch of Atlantic salmon (*Salmo salar*) represent a case of endocrine disruption? Environ. Hlth. Persp. 107:349-358.

Ferguson PL et al. 2001. Distribution and fate of neutral alkylphenol ethoxylate metabolites in a sewage-impacted urban estuaries. Environ. Sci. Technol. 35: 2428-2435.

Fuzzena MLM et al. 2015. intersex is predictive of poor fertilization success in populations of rainbow darter (*Etheostoma caeruleum*). Aquatic Toxicol. 160:106-116.

Gray MA, Metcalfe CD. 1997. Induction of testis-ova in Japanese medaka *(Oryzias latipes*) exposed to p-nonylphenol. Environ. Toxicol. Chem. 16:1082-1086.

Maruya KA et al. 2016. Multimedia screening of contaminants of emerging concern (CECs) in coastal urban watersheds in southern California (USA). Environ. Toxicol. Chem. 35:1986-1994.

Metcalfe CD et al. 2001. Estrogenic potency of chemicals detected in sewage treatment plant effluents as determined by *in vivo* assays with Japanese medaka (*Oryzias latipes*). Environ. Toxicol. Chem. 20:297-308.

Water Education Foundation. Wastewater Treatment Process in California.
https://www.watereducation.org/aquapedia/wastewater-treatment-process-california;
accessed on January 13, 2019.

<u>External Peer Review</u> for the Proposed Adoption of Nonylphenol Ethoxylates (NPEs) in Laundry Detergent as a Priority Product

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January 14, 2019

Synopsis

As requested, this peer review assesses whether the scientific conclusions 2 and 4 as outlined in the document entitled "Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergents" (hereafter *product-chemical profile*) were derived using sound scientific knowledge, methods, and practices. Specifically, the review addresses whether "NPEs and their degradation products have hazard traits and cause cumulative adverse impacts when organisms are exposed to the class of chemicals," (Conclusion 2); and "Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organisms due to the adverse impact and exposure considerations described in the product-chemical profile." (Conclusion 4).

Conclusion 2

The *product-chemical profile* document provides an inclusive and accurate review of the available literature to support the conclusions that "NPEs and their degradation products have hazard traits and cause cumulative adverse impacts when organisms are exposed to the class of chemicals," (Conclusion 2). Comments to further strengthen and clarify this conclusion are provided below.

Section 2.3.1 Environmental hazard traits

- The reference Staples et al., 1998 was not provided to peer reviewers. However, after retrieving the publication from the journal's website, it was confirmed that the summary of the results from Staples et al., 1998 are accurately presented in the *product-chemical profile* document.
- It is surprising that the reference Talmage, 1994 (Talmage SS, 1994. Environmental and Human Safety of Major Surfactants. The Soap and Detergent Association) was not included in the literature review for the *product-chemical profile* document. Although slightly outdated and superseded by more recent literature, it was the first comprehensive assessment of occurrence and effects of NPEs in North America.
- The assertion that physical surfactant effects require aquatic NPE concentration sufficient to form micelles is not supported by the provided reference (Environment Canada 2002). Although this statement is found in the reference Environment Canada 2002, no data (or references) are presented to support this statement. Indeed, Servos et al., 2003 (An

Ecological Risk Assessment of Nonylphenol and its Ethoxylates in the Aquatic Environment. Human and Ecological Risk Assessment 9(2):569-587) states that "The longer-chain-length NPEs may have a physical surfactant effect." However, this statement is also not supported by additional data or references. It appears that there is no substantive information available to assess the NPE concentrations needed to produce physical surfactant effects in exposed aquatic organisms. As a consequence, it would be advisable to remove this statement from the document unless other, substantive information can be provided to support the statement.

- The second paragraph of 2.3.1 is misleading. It references the well-establish estrogenicity of NPEs and considers them "weakly estrogenic" in comparison with 17β-estradiol, which is accurate. However, the following sentence "Regardless of NP's low estrogenic potency," is misleading as it fails to indicate that NPE concentrations in the environment are frequently 1,000 to 10,000 times greater than 17β-estradiol, therefore, cancelling out the low potency of NPEs and making its estrogenic <u>effects</u> similar to those of 17β-estradiol. Removing "regardless of NP's low estrogenic potency," and adding a statement about its higher aquatic concentrations when compared to 17β-estradiol will make this paragraph more accurate. In addition, why does the potency refer to "NP's" and not "NPE's" – is this a typo or a deliberate limitation of the statement (especially in light of the last sentence of the paragraph which indicates that at least NP1-2EOs are endocrine active as well)?
- The summary of the NP-induced reproductive impairments observed in fish studies (fourth paragraph of 2.3.1) would benefit from a distinction between species and endpoints. Several of the observed effects can be misleading if placed in the common context of multiple fish species. For example, the statement "…occurrence of mixed secondary sex characteristics..." only applies to Japanese Medaka and only one of the cited studies (Balch and Metcalfe, 2006). This finding would unlikely to be reproduced in trout or minnows, which have a very different set of secondary sex characteristics. Indeed, NP exposure does not seem to alter secondary sex characteristics in male fathead minnows (Pimephales promelas) (Miles-Richardson et al., 1999. Environ Research 80(2):S122-S137). Similarly, Ackermann et al., 2002 indicate that NP did not induce intersex in male trout which may not be apparent from the current structure of the fourth paragraph of 2.3.1. In addition, "…increased gonadosomatic index (…) in females…" may not be interpreted as a "NP-induced reproductive impairment..." as greater relative ovarian size could also imply greater fecundity, which is not usually considered an impairment (although it may under specific circumstances). Lastly, "induction of vitellogenin in both males and females" is misleading as vitellogenin is naturally present in mature female fathead minnows. As such, there may be an increase in circulating plasma vitellogenin in NP-exposed female fish, but not an *a-priori* induction.
- The description of NPE effects in freshwater invertebrates falls short in representing the effects of NPE exposures across the diverse family of unionid freshwater mussels despite the fact that this taxon of aquatic invertebrates comprises the largest group of invertebrates listed under the Endangered Species Act. Milam et al., 2003 (Acute Toxicity of Six Freshwater Mussel Species (Glochidia) to Six Chemicals: Implications for Daphnids and

Utterbackia imbecillis as Surrogates for Protection of Freshwater Mussels (Unionidae) Arch Environ Toxicol Chem 48:166-173) founds 4-NP to be the most toxic of six compounds tested in a 24hr acute assay using glochidia of six species of freshwater mussels with LC50s as low as 0.49mg/L. These findings are particularly significant as they were conducted using only NP-laced water. As mussels are in direct contact with sediment, additional exposure routes may further enhance to toxicity of NP to freshwater mussels. In the same study, the aquatic invertebrates *Ceriodaphnia dubia* and *Daphnia magna* recorded LC50 values of 0.2 and 0.21 mg/L, respectively.

Section 2.3.2 Exposure potential hazard traits

- Environmental persistence: Although the *product-chemical profile* document cites Staples et al., 1999, a review by Servos et al., 2003 (An Ecological Risk Assessment of Nonylphenol and its Ethoxylates in the Aquatic Environment. Human and Ecological Risk Assessment 9(2):569-587) provides a broader discussion of the persistence of NP and lower ethoxylated NPEs. Much of this discussion is based on Heinis et al., 1999 (Persistence and distribution of 4-nonylphenol following repeated application to littoral enclosures. Environmental Toxicology and Chemistry 18:363-75). Based on these sources, it is very likely that NPEs and NPECs are persistent under anaerobic conditions.
- Environmental persistence: the discussion of environmental persistence (either in section 2.3.2 or in section 5.1) may benefit from inclusion of the concept of “pseudo-persistence” as defined by Daughton, 2002 (Environmental stewardship and drugs as pollutants. Lancet 360:1035–1036). The continuous release of NPEs from multiple sources (as outlined in the *product-chemical profile* document) results in a de-facto continuous presence of NPEs in aquatic environments independent of the rate of degradation.
- Bioaccumulation: This section of the *product-chemical profile* document mixes bioaccumulation (subtitle of paragraph) and bioconcentration (second major bullet). Although both measures suggest that NPEs may be higher in organismal matrices than in environmental matrices, maintaining a distinction between studies that measured bioaccumulation through food uptake and aqueous absorption and those that just assess bioconcentration from NPE-laced water is important.
- It should also be noted that BCFs for freshwater mussels have been calculated at approximately 1,000 L/kg (Riva et al., 2010. Evaluation of 4-nonylphenol in vivo exposure in *Dreissena polymorpha*. Comp Biochem Physiol C. 152:175-181) although the short duration of this study (seven days) required an extrapolation of BCFs. This finding somewhat contradicts Diehl et al., 2012.

Section 2.4.1 Cumulative effects with other chemicals

- The finding that NPEs may contribute to the adverse impacts of pesticides in exposed aquatic organisms (Schlenk et al., 2012) by improving their bioavailability likely extends beyond pesticides to other compounds with similar chemical characteristics. The lack of congruence between *in vivo* and *in vitro* results may not be related to alternative physiological pathways as suggested in the *product-chemical profile*, but rather highlights the critical role gill surfaces play in preventing contaminants from entering organisms (and the role NPEs may play in reducing this obstacle to other contaminants). For example, Tiehm et al., 1997 (Surfactant-Enhanced Mobilization and Biodegradation of Polycyclic Aromatic Hydrocarbons in Manufactured Gas Plant Soil, Environmental Science and Technology 31(9):2570-2576) demonstrated enhanced bioavailability of PAHs in the presence of APEs.

- Additional work assessing the combined effects of NP as an inert ingredient in pesticide formulations and the associated pesticides has strengthened the evidence for cumulative effects of these pollutant mixtures (for example, Aronzon et al., 2016. Synergy between Diazinon and Nonylphenol in toxicity during the early development of the *Rhinella arenarum* toad. Water, Air, and Soil 227:139).
- The term "synergistic" should be used with caution. Neither Schlenk et al. 2012 nor Xi et al., 2005 use the term to describe their results. Although it is used in Aronzon et al., 2016, it would be best to eliminate the term from this discussion.

Section 5.1.4 Cumulative and synergistic effects from exposure to chemical mixtures

- A few studies (for example Bistodeau et al., 2006. Larval exposure to environmentally relevant mixtures of alkylphenolethoxylates reduces reproductive competence in male fathead minnows. Aquatic Toxicology 79:268-277) have compared the effects of NP vs. an environmentally realistic mixture of NPEs and found effects congruent with a cumulative or additive scenario as described in this paragraph.
- See also my comments regarding section 2.4.1 relating to pesticides and NPEs.
- Last paragraph of 5.1.4. The section beginning with "The synergistic effects…" (Also note my comments regarding the use of "synergistic" in 2.4.1) is highly speculative and does not add meaningful content to the discussion. The complexity of the chemical, physical and biological landscape in which *Pelagic Organism Decline* is occurring does not lend itself as an example for the cumulative effects of NPEs and other compounds. Instead, the argument for cumulative effects of NPEs and other environmental contaminants in the *product-chemical profile* document would benefit from a review of the recent literature on mixture toxicity (for example Aronzon et al., 2016; Li et al., 2018 [Chemosphere 204:44-50]; Wang et al., 2018 Ecotoxicology and Environmental Safety 154:145-153]).

Conclusion 4

The *product-chemical profile* document provides an inclusive and accurate review of the available literature to support the conclusions that "Laundry detergents containing NPEs have the potential for significant or widespread impacts to aquatic organisms due to the adverse impact and exposure considerations described in the product-chemical profile." (Conclusion 4). Comments to further strengthen and clarify this conclusion are provided below.

Section 2.5 Populations that may be harmed by the candidate chemical

- The *product-chemical profile* document focuses on treated wastewater effluent as the route of exposure so aquatic environments. Although this may be the case in many instances, on-site septic systems may also serve as a more direct route of transport for NPEs to nearby aquatic environments – especially in sensitive ecological habitats that may serve a limited population (i.e. State Parks, National Parks etc.). Given the poor performance of most on-site septic systems when compared to WWTPs (Du et al., 2014. Comparison of contaminants of emerging concern removal, discharge, and water quality hazards among centralized and on-site wastewater treatment system effluents receiving common wastewater influent. Science of the Total Environment 466:976-984) this route of exposure can result in high local concentrations of contaminants of emerging concern in ecologically sensitive areas (see also Diehl et al., 2012 cited in this *product-chemical profile* document).
- It is surprising that this discussion does not mention any freshwater mussel species. The freshwater invertebrates are particularly susceptible to NP exposure (see my comments regarding section 2.3.1) and often represent endangered or threatened species (although none appears in CDFW 2017a). It is beyond the expertise of this reviewer to know whether freshwater mussels are found in the waterways discussed in section 2.5.1.
- It is worth noting that the higher concentrations of NP in the aquatic life criteria derived by the US EPA do not take into consideration the additive effect of NPEs as described in the approaches employed by Environment Canada and Minnesota AWQS.
- Green sturgeon: given the low BAF for NP in fish species (Staples et al., 1998), it is unlikely that the ingestion of NP contaminated sediment represents an important exposure route for fish species.
- Delta smelt: the discussion of greater pesticide bioavailability in the presence of NPEs (Schlenk et al., 2012) is relevant in the context of the decline of the Delta smelt.

Section 3.3.1 Indicators of potential exposure to candidate chemical from the product

- No concerns about this section.

Section 3.3.3 Frequency extend, level, and duration of potential exposure for each use and end-of-life scenario

- The chronic exposure scenario described in 3.3.3 is consistent with the concept of "pseudo-persistence" as defined by Daughton, 2002 (see my comments to section 2.3.2).
- The discussion about effluent discharge and its temporal and spatial variability, while important, lacks focus on the question at hand (NPE toxicity) and is not supported by the

two presented references. Ackerman et al., 2003 does not provide any data or direct evidence for spatial and temporal variability of effluent contribution to landscapes. Even the Crauder et al., 2016 reference only tangentially discusses effluent variability in a spatial and temporal sense. There is a wealth of publication on temporal and spatial variability in effluent contributions to aquatic ecosystems and, more importantly the spatial and temporal variability in NPE concentrations as a result of effluent discharge. This section should be re-written and supported with appropriate literature citations.

- Third paragraph: the impact of draught on effluent (and in extension NPE) concentrations is well established and an important consideration. In addition to prolonged draught, the intensity of precipitation events is also predicted to increase in the coming decades. As NPEs, and especially NP, often partition to biosolids (as accurately described in the *product-chemical profile* document), more intense precipitation events may also increase movement of NPEs into the aquatic environment from land-applied biosolids.

Section 5.1.4 Cumulative and synergistic effects from exposure to chemical mixtures

- A few studies (for example Bistodeau et al., 2006. Larval exposure to environmentally relevant mixtures of alkylphenolethoxylates reduces reproductive competence in male fathead minnows. Aquatic Toxicology 79:268-277) have compared the effects of NP vs. an environmentally realistic mixture of NPEs and found effects congruent with a cumulative or additive scenario as described in this paragraph.
- See also my comments regarding section 2.4.1 relating to pesticides and NPEs.
- Last paragraph of 5.1.4. The section beginning with “The synergistic effects…” (Also note my comments regarding the use of “synergistic” in 2.4.1) is highly speculative and does not add meaningful content to the discussion. The complexity of the chemical, physical and biological landscape in which *Pelagic Organism Decline* is occurring does not lend itself as an example for the cumulative effects of NPEs and other compounds. Instead, the argument for cumulative effects of NPEs and other environmental contaminants in the *product-chemical profile* document would benefit from a review of the recent literature on mixture toxicity (for example Aronzon et al., 2016; Li et al., 2018 [Chemosphere 204:44-50]; Wang et al., 2018 Ecotoxicology and Environmental Safety 154:145-153]).

5.2 Key Data Gaps

- While there may be a lack of data on NPE occurrence in effluent, biosolids and aquatic environments for California, there is an abundance of such data (for example, Elliott et al., 2017. Contaminants of emerging concern in tributaries to the Laurentian Great Lakes: I. Patterns of occurrence; PLOS One 12(9): e0182868) for the remainder of the US with little indication that California NPE occurrence data would differ substantially.
- 5.2.3 This is an accurate and very important point-of-note. Suspended solids are indeed likely major source of NPEs to particle feeders with unknow consequences.

- 5.3.1 The detection limit for 4-NP in Bradley et al., 2017 was inexplicitly high at 1.6μg/L. 4-NP was reported at concentrations of 200-1,000ng/L for California streams – well within the range in which adverse effects are likely to occur. This study illustrates the data gap identified in 5.2.2 (limitations of analytical approaches).

6 Discussion of Potential for Significant or Widespread Adverse Impacts

- Accurate summary of the evidence provided in sections 1-5

Conclusions

The *product-chemical profile* document follows sound scientific practices and accurately describes and interprets data derived from prior peer-reviewed studies and documents. The congruence of findings in the current document with several prior reviews of the toxicity of NPEs by authoritative organizations (European Chemical Bureau; Environment Canada; US EPA; Minnesota Pollution Control Agency) further strengthens the validity of Conclusions 2 and 4 derived in the *product-chemical profile* document. The Key Data Gaps mentioned in Section 5.2 of the *product-chemical profile* document underscore the likelihood that the full environmental impacts of NPEs are underestimated in the current document. The combined adverse environmental effects of NPE mixtures and the effects of NPE mixtures ***and*** other commonly found environmental contaminants are poorly understood and command a precautionary approach.