**CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY**
**OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT**

# SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 (PROPOSITION 65)

# NOTICE OF INTENT TO LIST: PERFLUOROOCTANOIC ACID (PFOA) and PERFLUOROOCTANE SULFONATE (PFOS)

**September 16, 2016**

The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) intends to list *perfluorooctanoic acid (PFOA)* and *perfluorooctane sulfonate (PFOS)* as known to the state to cause reproductive toxicity under the Safe Drinking Water and Toxic Enforcement Act of 1986[1]. This action is being proposed under the authoritative bodies listing mechanism[2].

| Chemical [CAS No.] | References | Chemical Use | Endpoints |
|---|---|---|---|
| Perfluorooctanoic acid [335-67-1] | US EPA (2016a,b) | PFOA and PFOS are surfactants that have been used in a variety of consumer products, including carpets, textiles, leather, non-stick cookware, and paper coatings used in food packaging, to confer stain, grease and water resistance. PFOA is used in the production of fluoropolymers. PFOA and PFOS are generated as degradation products of other perfluorinated compounds. | Developmental toxicity |
| Perfluorooctane sulfonate [1763-23-1] | US EPA (2016c,d) | | |

**Background on listing via the authoritative bodies mechanism:** A chemical must be listed under the Proposition 65 regulations when two conditions are met:

1) An authoritative body formally identifies the chemical as causing reproductive toxicity pursuant to Title 27, Cal. Code of Regs., section 25306(d)[3].
2) The evidence considered by the authoritative body meets the sufficiency criteria contained in section 25306(g).

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[1] Commonly known as Proposition 65, the Safe Drinking Water and Toxic Enforcement Act of 1986 is codified in Health and Safety Code section 25249.5 *et seq*.
[2] See Health and Safety Code section 25249.8(b) and Title 27, Cal. Code of Regs., section 25306.
[3] All further references are to sections of Title 27 of the Cal. Code of Regulations, unless otherwise stated.

However, the chemical is not listed if scientifically valid data which were not considered by the authoritative body clearly establish that the sufficiency of evidence criteria were not met (Section 25306(h)).

The US Environmental Protection Agency (US EPA) is one of several institutions designated as authoritative for the identification of chemicals as causing reproductive toxicity (Section 25306(l)). OEHHA is the lead agency for Proposition 65 implementation. After an authoritative body has made a determination about a chemical, OEHHA evaluates whether listing under Proposition 65 is required using the criteria contained in the regulations.

**OEHHA's determination:** *Perfluorooctanoic acid (PFOA)* and *perfluorooctane sulfonate (PFOS)* each meet the criteria for listing as known to the state to cause reproductive toxicity under Proposition 65, based on findings of the US EPA (2016a,b,c,d), as outlined below.

**Formal identification and sufficiency of evidence for *PFOA*:** In 2016, US EPA released the documents: *Drinking Water Health Advisory (HA) for Perfluorooctanoic Acid (PFOA)*(US EPA, 2016a) and *Health Effects Support Document for Perfluorooctanoic Acid* (US EPA, 2016b). In the former document, US EPA developed a lifetime drinking water HA for PFOA (US EPA, 2016a) based on a reference dose (RfD) derived from a developmental toxicity study in mice in which developmental toxicity was manifested as reduced ossification in proximal phalanges and accelerated puberty in males (US EPA, 2016b). Both documents contain conclusions about the developmental toxicity of PFOA, referencing studies in which developmental toxicity results entirely or predominantly from prenatal exposure to the chemical.

Section 25306(d)(1) provides three separate criteria, of which at least one must be met in order for the chemical to be formally identified. These reports and documents meet two of the formal identification criteria in Section 25306(d)(1) because PFOA "is the subject of a report which is published by the authoritative body and which concludes that the chemical causes…reproductive toxicity", *and* because PFOA "has otherwise been identified as causing … reproductive toxicity by the authoritative body in a document that indicates that such identification is a final action". The latter criterion is met by the development by US EPA of a lifetime drinking water HA for PFOA based on a reference dose (RfD) derived from developmental toxicity in mice. Further, Section 25306(d)(2) provides six additional criteria, of which at least one must be met in order for the chemical to be formally identified. In this case three criteria are met because the report or document has been "published by the authoritative body in a publication, such as, but not limited to, the federal register…" (US EPA, 2016a,b); *and* "reviewed by an advisory committee in a public meeting, if a public meeting is required" (US EPA, 2016a); *and* "made subject to public review and comment prior to its issuance" (US EPA, 2016a).

These reports and documents also meet the sufficiency of evidence criteria in Section 25306(g). Pertinent statements in the US EPA reports documenting the Agency's conclusions about developmental toxicity include the following:

In *Drinking Water Health Advisory for Perfluorooctanoic Acid* (US EPA, 2016a):

- "The US Environmental Protection Agency (EPA) is issuing a lifetime drinking water Health Advisory (HA) for PFOA of 0.07 micrograms per liter (µg/L) based on a reference dose (RfD) derived from a developmental toxicity study in mice; the critical effects included reduced ossification in proximal phalanges and accelerated puberty in male pups following exposure during gestation and lactation." (p. 9)
- "For PFOA, ...studies report developmental effects (survival, body weight changes, reduced ossification, delays in eye opening, altered puberty, and retarded mammary gland development) … Overall, the toxicity studies available for PFOA demonstrate that the developing fetus is particularly sensitive to PFOA-induced toxicity." (p. 9)
- "The effects that serve as the basis for the RfDs for both PFOA and PFOS are developmental endpoints (reduced ossification and accelerated puberty in males for PFOA and decreased pup weight for PFOS*)*." (p. 55)
- "The animal toxicology studies were used in the dose-response assessment for PFOA. These studies demonstrated dose-related effects on systemic and developmental endpoints in multiple species (monkeys, rats, mice) …" (p. 33)
- "There are extensive human data from epidemiological data from the general population as well as worker cohorts. The epidemiology data provide strong support for the identification of hazards observed following exposure to PFOA in the laboratory animal studies and human relevance." (p. 51)
- "Based on the consistency of the responses across the chronic studies and those for reproductive and developmental endpoints, and with recognition of the use of developmental toxicity as the most sensitive endpoint, 0.00002 mg/kg/day was selected as the RfD for PFOA. This value is based on the HED *[Human Equivalent Dose]* for developmental effects (reduced ossification in male and female pups and accelerated puberty in male pups) from the Lau et al. (2006) study." (p. 54)
- "The lifetime HA for PFOA is based on effects (reduced ossification in male and female pups and accelerated puberty in male pups) on the developing fetus resulting from exposures that occur during gestation and lactation. These developmental endpoints are the most protective for the population at large and are effects that can carry lifetime consequences for a less than lifetime exposure." (p. 55)
- "EPA's risk assessment guidelines reflect that, as a general matter, a single exposure to a developmental toxin at a critical time in development can produce an adverse effect (US EPA 1991). In addition, short-term exposure to PFASs *[perfluoroalkyl substances]* can result in a body burden that persists for years and can increase with additional exposures. Thus, EPA recommends that the lifetime HA for PFOA of 0.07 µg/L apply to both short-term (i.e., weeks to months)

scenarios during pregnancy and lactation, as well as to lifetime-exposure scenarios." (p. 10)

In *Health Effects Support Document for Perfluorooctanoic Acid* (US EPA, 2016b):

- "Developmental effects observed in animals include decreased survival, delayed eye opening and reduced ossification, skeletal defects, …" (p. ES-2)
- "Overall, the developmental and reproductive toxicity studies available for PFOA demonstrate that the developing fetus is particularly sensitive to PFOA-induced toxicity." (p. ES-3)

OEHHA has reviewed the studies or study descriptions cited by US EPA (2016a,b) in support of its formal identification of PFOA as causing reproductive toxicity (developmental endpoint) relative to the criteria in Section 25306(g). Based on the PFOA HA (US EPA, 2016a) and the supporting document (US EPA, 2016b), and the studies cited in those documents, OEHHA finds the criteria for listing PFOA through the authoritative bodies mechanism as causing reproductive toxicity (developmental endpoint) have been met.

**Formal identification and sufficiency of evidence for *PFOS*:** In 2016, US EPA released the documents: *Drinking Water Heath Advisory for Perfluorooctane Sulfonate (PFOS)* (US EPA, 2016c) and *Health Effects Support Document for Perfluorooctane Sulfonate* (US EPA, 2016d). In the former document US EPA developed a lifetime drinking water HA for PFOS (US EPA, 2016c) based on a reference dose (RfD) derived from a developmental toxicity study in rats in which developmental toxicity was manifested as reduced body weight of pups on lactation day 1 (US EPA, 2016d). Both documents make conclusions about the developmental toxicity of PFOS, referencing studies in which prenatal exposure to the chemical results in developmental toxicity.

Section 25306(d)(1) provides three separate criteria, of which at least one must be met in order for the chemical to be formally identified. These reports and documents meet two of the formal identification criteria in Section 25306(d)(1) because PFOS, "is the subject of a report which is published by the authoritative body and which concludes that the chemical causes…reproductive toxicity", *and* because PFOS "has otherwise been identified as causing … reproductive toxicity by the authoritative body in a document that indicates that such identification is a final action". The latter criterion is met by the development by US EPA of a lifetime drinking water HA for PFOS based on a reference dose (RfD) derived from developmental toxicity in rats. Further, Section 25306(d)(2) provides six additional criteria, of which at least one must be met in order for the chemical to be formally identified. In this case three criteria are met because the report or document has been "published by the authoritative body in a publication, such as, but not limited to, the federal register…" (US EPA, 2016c,d); *and* "reviewed by an advisory committee in a public meeting, if a public meeting is required" (US EPA, 2016c); *and* "made subject to public review and comment prior to its issuance" (US EPA, 2016c).

These reports and documents also meet the sufficiency of evidence criteria in Section 25306(g). Pertinent statements in the US EPA reports documenting the Agency's conclusions about developmental toxicity include the following:

In *Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS)* (US EPA, 2016c):

- "The US Environmental Protection Agency (EPA) is issuing a lifetime drinking water health advisory (HA) for PFOS of 0.07 micrograms per liter (µg/L) based on a reference dose (RfD) derived from a developmental toxicity study in rats; the critical effect was decreased pup body weight following exposure during gestation and lactation." (p. 10)
- "For PFOS, … studies report developmental effects (decreased body weight, survival, and increased serum glucose levels and insulin resistance in adult offspring) … Overall, the toxicity studies available for PFOS demonstrate that the developing fetus is particularly sensitive to PFOS induced toxicity." (p. 10)
- "Adverse effects observed following exposures to PFOA and PFOS are the same or similar, and include effects on lipids, birth weight, and antibodies in humans…The effects serving as the basis for the RfDs for both PFOA and PFOS are developmental endpoints (e.g., reduced ossification and accelerated puberty in males for PFOA and decreased birth weight for PFOS…)" (p.51)
- "EPA believes the uncertainty in the chosen POD *[point of departure]* and the reliance on studies with serum data is minimized because of the large and extensive database examining hazard, and the selection of pup body weight as the critical effect with lifetime implications at a NOAEL (0.1 mg/kg/day) from the low end of the range of values evaluated." (p. 51)
- "The RfD is based on the HED derived from serum levels at the NOAEL from a developmental study in rats (Luebker et al. 2005b). …The selected RfD is based on the most sensitive endpoint, developmental effects (e.g., decreased pup body weight), to provide protection to the general population and sensitive life stages." (p. 52)
- "EPA's risk assessment guidelines reflect that, as a general matter, a single exposure to a developmental toxin, at a critical time in development can produce an adverse effect (US EPA 1991). In addition, short-term exposure to PFASs *[perfluoroalkyl substances]* can result in a body burden that persists for years and can increase with additional exposures. Thus, EPA recommends that the lifetime HA for PFOS of 0.07 µg/L apply to both short-term (i.e., weeks to months) scenarios during pregnancy and lactation, as well as to lifetime-exposure scenarios." (p. 11)

In *Health Effects Support Document for Perfluorooctane Sulfonate (PFOS)* (US EPA, 2016d):

- "EPA derived a reference dose (RfD) for PFOS…based on decreased neonatal rat body weight from the two-generation study by Luebker et al. (2005b). …The HED for effects on pup body weight in the two generation study is supported by

comparable values derived from the lowest observed adverse effect level for the same effect in the one-generation study and the NOAEL for effects seen in a developmental neurotoxicity study." (p. ES-2)

- "At 3.2 mg/kg/day *[PFOS, oral dose in rats]*, there were significant decreases in gestation length and number of implantation sites, and reductions in litter size." (p. 3-63)
- "For pups only exposed prenatally, mortality was 9% compared to 1.1% for those exposed during lactation only. Reductions in pup body weights on LD 1 were observed in groups exposed both gestationally and lactationally and in those with gestational exposure only." (p. 3-64)
- "Based on the consistency of the response and of the use of the most sensitive endpoint, developmental toxicity, as the critical effect, the RfD of 0.00002 mg/kg/day from Luebker et al. (2005a) is selected as the RfD for PFOS. This RfD is derived from reduced pup body weight in the two-generation study in rats." (p. 4-16)

OEHHA has reviewed the studies or study descriptions cited by the US EPA (2016c,d) in support of its formal identification of PFOS as causing reproductive toxicity (developmental endpoint) relative to the criteria in Section 25306(g). Based on the PFOS HA (US EPA, 2016c) and the supporting document (US EPA, 2016d), and the studies cited in those documents, OEHHA finds the criteria for listing PFOS through the authoritative bodies mechanism as causing reproductive toxicity (developmental endpoint) have been met.

**Request for comments:** OEHHA is requesting comments as to whether PFOA and PFOS meet the criteria set forth in the Proposition 65 regulations for authoritative bodies listings. In order to be considered, **OEHHA must receive comments by 5:00 p.m. on October 17, 2016.** We encourage you to submit comments via e-mail, rather than in paper form. Comments transmitted by e-mail should be addressed to P65Public.Comments@oehha.ca.gov with "NOIL – PFOA and PFOS" in the subject line. Comments submitted in paper form may be mailed, faxed, or delivered in person to the addresses below:


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Comments received during the public comment period will be posted on the OEHHA web site after the close of the comment period. Electronic files submitted should not have any form of encryption.

If you have any questions, please contact Michelle Ramirez at Michelle.Ramirez@oehha.ca.gov or at (916) 445-6900.

**References**

US Environmental Protection Agency (US EPA, 2016a). Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA). EPA Document Number: 822-R-16-005. May, 2016. Available at: https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final-plain.pdf

US Environmental Protection Agency (US EPA, 2016b). Health Effects Support Document for Perfluorooctanoic Acid (PFOA). EPA Document Number: 822-R-16-003. May, 2016. Available at: https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_hesd_final-plain.pdf

US Environmental Protection Agency (US EPA, 2016c). Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS). EPA Document Number: 822-R-16-004. May, 2016. Available at: https://www.epa.gov/sites/production/files/2016-05/documents/pfos_health_advisory_final-plain.pdf

US Environmental Protection Agency (US EPA, 2016d). Health Effects Support Document for Perfluorooctane Sulfonate (PFOS). EPA Document Number: 822-R-16-002. May, 2016. Available at: https://www.epa.gov/sites/production/files/2016-05/documents/hesd_pfos_final-plain.pdf