Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Dodecylphenols

Evaluation statement

30 June 2022

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AICIS evaluation statement

Subject of the evaluation

Dodecylphenols

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Phenol, 4-isododecyl-	27459-10-5
Phenol, 4-dodecyl-	104-43-8

Reason for the evaluation

The Evaluation Selection Analysis indicated a potential risk to human health.

Parameters of evaluation

These chemicals are dodecylphenols listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified industrial uses of chemicals in this group. These chemicals have been assessed as a group as they are expected to have similar toxicity and bioavailability.

Summary of evaluation

Summary of introduction, use and end use

No specific Australian introduction, use and end use information has been identified for chemicals in this group.

Based on international information, chemicals in this group are predominantly used in the manufacture of oil and lubricant additives and fuel system cleaners. These chemicals may also be used as intermediates in the manufacture of resins used in paints, vanishes, inks and tyres. These chemicals may also be present in end use products as impurities.

Human health

Summary of health hazards

There is limited toxicological information for chemicals included in this Evaluation Statement. Available data for other dodecylphenols not listed on the Inventory, tetrapropenylphenol

(TPP) (CAS No. 74499-35-7) and branched dodecylphenol (CAS No. 121158-58-5) are used for read across to draw conclusions regarding the toxicity of chemicals covered by the evaluation.

Based on read across data, the critical health effects for risk characterisation are skin and eye corrosion and reproductive toxicity.

These chemicals are expected to cause skin and eye corrosion. Read across data from studies in rats shows evidence of severe skin irritation and corrosion in in vivo tests (effects across several studies include severe erythema, oedema, and necrosis). Skin corrosive chemicals are considered to cause serious eye damage. Mixed results were reported in eye irritation studies.

In repeated dose toxicity studies, reductions in food consumption and bodyweight were observed. The reproductive organs appear to be the target organs for systemic toxicity. Available data from in vivo studies in rats shows evidence of adverse effects for various reproductive parameters. Reported no observed adverse effect levels (NOAELs) were 5–15 mg/kg bodyweight (bw)/day. Effects on female fertility included reduced ovary weights with decreased corpora lutea and lengthened oestrous cycles with an increase in incidence of persistent dioestrus. Effects in male fertility included reduction in male reproductive organ weights with reduced sperm concentration. While reduced food consumption and lower bodyweights may have contributed to these findings, the reproductive effects, particularly in females, cannot be explained by this mechanism alone. Effects on animal development were considered secondary to maternal toxicity.

The effects on female rat reproductive organs and functional parameters are consistent with an oestrogenic mode of action. Mechanistic in vivo studies clearly indicate oestrogenicity, including increased uterus weight in uterotrophic assays and accelerated pubertal development in female pubertal assays. Anti-androgenic, as well as oestrogenic activity could lead to effects similar to those observed on certain reproductive parameters, and an overlap of both modes of action cannot be completely excluded. Direct androgen receptor antagonism is unlikely as there was no significant effect on anogenital distance in the 2-generation study and a Hershberger assay with 4-dodecylphenol was reported to be negative. However, there are insufficient data in the literature to determine how weak oestrogenic activity may disrupt fertility.

Studies on nonylphenol show indirect anti-androgenic effects via a reduction in testosterone (NICNAS 2019). No such data are available for dodecylphenols. Androgen binding assays are not relevant to this type of effect. While receptor binding assays mostly implicate oestrogen receptor agonism, there are no data to examine indirect anti-androgenic mechanisms, which are relevant for effects on male reproductive organs caused by phthalates (NICNAS 2010). A potential indirect anti-androgenic mode of action for the reproductive effects caused by dodecylphenols cannot be determined.

There are some indications for interaction of these chemicals with the thyroid hormone system. However, effects on the thyroid were not consistently observed in all studies in which thyroid histology was performed.

Based on the available data chemicals in this group are:

- expected to have low acute and dermal toxicity
- not expected to be sensitising to skin
- not expected to be genotoxic.

No data are available on carcinogenicity.

Hazard classifications relevant for worker health and safety

These chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This evaluation does not consider classification of physical hazards and environmental hazards.

Some of these recommended classifications are based on read across principles (see **Supporting Information – Grouping rationale section**). If empirical data become available for any member of this group indicating that a lower (or higher) classification is appropriate for a specific chemical, that data may be used to amend the default classification for that chemical.

Health hazards	Hazard category	Hazard statement
Corrosion/irritation	Skin Corr. 1	H314: Causes severe skin burns and eye damage
Eye Damage	Eye Dam. 1	H318: Causes serious eye damage.
Reproductive and developmental	Repr. 1B	H360F: May damage fertility

Summary of health risk

Public

Based on the available use information it is unlikely that the public will be widely exposed to these chemicals. Members of the public that undertake car maintenance activities may be exposed to these chemicals as impurities. Automotive products available to consumers are also expected to be available in the workplace and are subject to workplace labelling. Workplace labelling will identify the hazards of any products containing these chemicals. Therefore, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, dermal and ocular exposure might occur, particularly where manual or open processes are used. These processes could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the critical systemic long term and local health effects, these chemicals could pose a risk to workers.

Control measures to minimise dermal and ocular exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Proposed means for managing risk

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety.

Information relating to safe introduction and use

The information in this statement, including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risk arising from exposure to these chemicals include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with these chemicals.

Measures required to eliminate or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and how these chemicals are used.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to these chemicals, if valid techniques are available to monitor the effect on the worker's health.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare a safety data sheet and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The conclusions of this evaluation are based on the information described in this statement.

Considering the proposed means of managing risks, the Executive Director is satisfied that the identified risks can be managed within existing risk management frameworks. This is provided that all requirements are met under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory and the proposed means of managing the risks identified during this evaluation are implemented.

Note: Obligations to report additional information about hazards under *Section 100 of the Industrial Chemicals Act 2019* apply.

Supporting information

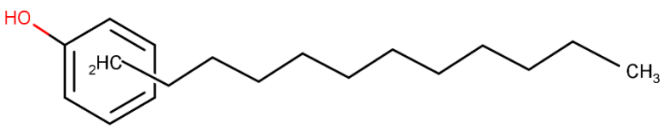
Grouping rationale

Chemicals in this group are dodecylphenols listed on the Australian Inventory of Industrial Chemicals (the Inventory). They are branched and linear dodecylphenols that are expected to have similar toxicity profiles. The term 'dodecylphenol' corresponds to various isomeric compounds, varying by the degree of branching of the dodecyl group and the substitution position on the phenol ring. C12 alkyl chains are predominantly present in the UVCB substance. Nevertheless, fractions of C7–C15 constituents can also be present, albeit in lower quantities compared to C12. The CAS No. 104-43-8 implies a well-defined substance that is a linear dodecylphenol. As is the case of nonylphenol, this identifier may be wrongly used to identify substances that contain a branched alkyl chain (ECHA 2021b).

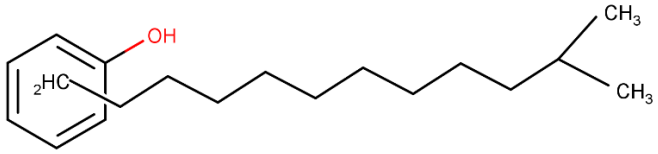
Limited data are available for these chemicals. Available data for other dodecylphenols not listed on the Inventory, TPP (CAS No. 74499-35-7) and branched dodecylphenol (CAS No. 121158-58-5) are used to draw conclusions regarding the systemic effects of chemicals in this group.

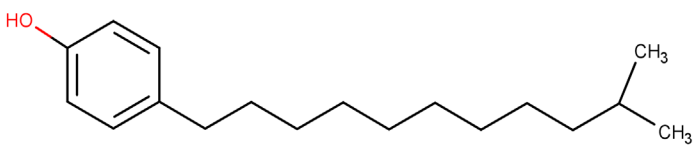
Chemicals included in this Evaluation Statement and chemicals used for read across have similar chemical structure and physico-chemical properties (ECHA 2021b). Where data were available for chemicals included in this Evaluation Statement, observed effects were consistent with those observed with TPP and branched dodecylphenol. Data has also been included for other alkylphenols, in particular nonylphenol.

Chemical identity

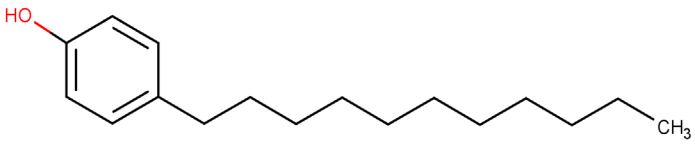
Chemical name	Phenol, dodecyl-
CAS No.	27193-86-8
Synonyms	Dodecylphenols, dodecylphenol (mixed isomers)
Structural formula	
Molecular formula	C18H30O
Molecular weight (g/mol)	262.434
SMILES	[*]['Rgp'].Oc1ccccc1
Chemical description	UVCB — composed of dodecylphenol isomers (varying by the degree of branching of the dodecyl group and the substitution position on the phenol ring)

Chemical name	Phenol, isododecyl-

CAS No.	11067-80-4
Synonyms	-
Structural formula	
Molecular formula	C18H30O
Molecular weight (g/mol)	262.434
SMILES	CC(C)CCCCCCCCCc1ccccc1O
Chemical description	Structure may vary by substitution position on the phenol ring and branching

Chemical name	Phenol, 4-isododecyl-
CAS No.	27459-10-5
Synonyms	4-(10-methylundecyl)phenol, p-isododecylphenol -
Structural formula	
Molecular formula	C18H30O
Molecular weight (g/mol)	262.434
SMILES	CC(C)CCCCCCCCCC1=CC=C(C=C1)O
Chemical description	-

Chemical name	Phenol, 4-dodecyl-
CAS No.	104-43-8
Synonyms	-

Structural formula	
Molecular formula	C18H30O
Molecular weight (g/mol)	262.434
SMILES	CCCCCCCCCCCCc1ccc(O)cc1
Chemical description	-

Relevant physical and chemical properties

There are limited available physical and chemical data for the members of this group. Two of the group members (CAS Nos.104-43-8 and 27193-86-8) have similar log P values (7.91 and 6.6, respectively) and water solubility (0.01 and 0.03 mg/L at 25 °C, respectively). These 2 chemicals have the same vapour pressure (2.30 x 10^{-6} mm Hg at 25 °C) (NLM; OECD 2006). Other members of the group are expected to have similar physical and chemical properties.

Introduction and use

Australia

No specific Australian introduction, use or end use information has been identified for chemicals in this group.

International

Limited specific data are available on the use of chemicals included in this evaluation.

These chemicals (CAS Nos. 27193-86-8 and 104-43-8) have the following reported uses in the Substances and Preparations in Nordic countries (SPIN) database:

- engine oils, including gear and hydraulic fluids and additives
- lubricants and additives.

However, it should be noted that SPIN does not distinguish between direct use of the chemical and use of the materials that are produced from chemical reactions involving the chemical.

These chemicals (CAS Nos. 104-43-8 and 27459-10-5) have identified use as commercial dispersants for asphaltenes (ECHA 2021a).

Based on information on dodecylphenols as a group or the read across chemicals TPP (CAS No. 74499-35-7) and branched dodecylphenol (CAS No. 121158-58-5) (Danish EPA 2013; ECHA 2015; ECHA 2021a; OECD 2006; UK EA 2007) these chemicals are predominantly used in the manufacture of oil and lubricant additives and fuel system cleaners. These include calcium phenates, aryl-based zinc dialkyldithiophosphates and dodecylphenol

ethoxylates (DPEO). These additives are mostly used in petrol (gasoline) and diesel powered road vehicles and marine diesel engines.

These additives are likely to contain these chemicals as impurities. Depending on the starting materials and the process conditions, different levels of unreacted dodecylphenols are found in additives with levels up to 11.7% reported, and concentration in end use products up to 2% (ECHA 2021a).

Dodecylphenols are also used as intermediates in the production of resins used in paints, varnishes and inks, and tyre manufacture. Typical impurity levels of 2.5–5% have been reported.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for these chemicals.

Public

Chemicals in this group are not listed in the *Poisons Standard–the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)* (TGA 2021).

Workers

These chemicals are not listed as hazardous on the Hazardous Chemicals Information System (HCIS) and no exposure standards are available for these chemicals in Australia (SWA).

International regulatory status

Exposure standards

No specific exposure standards were identified.

Canada

Dodecylphenol (CAS No. 27193-86-8) is listed on the Canadian 'Screening assessment substances identified as being of low concern using the ecological risk classification of organic substances and the threshold of toxicological concern (TTC)-based approach for certain substances' (Government of Canada 2018).

European Union

'Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP)' are listed as a substances of very high concern (SVHC) and are included in the Candidate List for Authorisation. These chemicals are included due to concerns related to reproductive toxicity and endocrine disruption (ECHA 2021b). In the European Union (EU), inclusion in the Candidate List brings immediate obligations for suppliers of the substance, such as:

- supplying a safety data sheet
- communicating on safe use
- responding to consumer requests within 45 days
- notifying ECHA if the article they produce contains an SVHC in quantities above one tonne per producer/importer per year and if the substance is present in those articles above a concentration of 0.1% (w/w).

The non-exhaustive list of group members includes 3 chemicals covered by this Evaluation Statement: phenol, dodecyl- (CAS No. 27193-86-8), p-dodecylphenol (CAS No. 104-43-8) phenol, 4-isododecyl- (CAS No. 27459-10-5). It also covers branched dodecylphenol (CAS No. 121158-58-5) and TPP (CAS No. 74499-35-7), the structural analogues from which data has been read across to other chemicals in this group (ECHA 2021b).

Health hazard information

Toxicokinetics

There are no toxicokinetic data available for the specific chemicals in this group. There are some data for the analogue TPP which can be read across to the dodecylphenol chemicals in this group.

Systemic availability of TTP is dependent on its ability to be absorbed across various tissues. Factors that affect absorption include its water solubility (1.54 mg/L), lipophilicity (characterised by the log of the partition coefficient, log Kow), degree of ionization (the dissociation constant, pKa), and molecular size. TTP is an oily liquid at 20 ºC and 101.3 Kpa. The compound is very lipophilic, with an estimated log Kow of 7.14.

The high lipophilicity and low water solubility of TPP suggest the chemical will be readily absorbed via cell membranes, retained in various tissues of the body and widely distributed (ECHA 2021a; OECD 2006).

Various rat studies using oral administration confirm that TTP is distributed to various tissues as effects have been observed in the liver and reproductive organs in both males and females. Changes in the liver of rats orally administered TPP at low doses have also been observed, suggesting that some degree of metabolism of the chemical may occur in this organ. The liver is expected to be the primary organ for metabolism, making the chemical more soluble via oxidation and conjugation. The chemical is expected to be eliminated via the bile, in the gastrointestinal tract (REACH).

There are conflicting data regarding the dermal absorption of TPP. Based on its molecular weight (<500 g/mole) and its lipophilicity, the chemical is expected to penetrate the skin and distribute throughout the body. This notion is supported by high dose dermal exposure studies in rabbits which showed macroscopic adverse effects in the lungs, liver, spleen, kidneys, gall bladder, and the gastrointestinal tract. Effects in these organs were found to be completely reversible by the end of the study, which suggests TPP was eliminated over the study's observation period (REACH). However, there are some conflicting data regarding the absorption of TPP. In an in vivo rat study conducted according to OECD TG 427, dermal absorption was found to be low. Dermal absorption and subsequent bioavailability following exposure to TPP in humans has also been reported to be low. A study showed that ~3% of dermally applied radiolabelled TPP was absorbed. The rate was not significantly affected by concentration (0.001 to 1%) or duration of exposure (up to 72 hours). The absorption of TPP is expected to be affected by other components in products containing the chemical (ECHA 2013a).

The chemical TPP exists as a liquid at atmospheric conditions. It is not expected to be aerosolised during industrial uses. Information indicates it has low vapour pressure. Therefore inhalation of the chemical is unlikely (REACH).

Acute toxicity

Oral

Based on the available data, chemicals in this group have low acute oral toxicity. No hazard classification is warranted.

In an acute oral toxicity study conducted similar to OECD TG 401, Sprague Dawley (SD) rats [5 (mix of males and females)/dose] were treated with a single dose of dodecylphenol, mixed isomers at 0, 1260, 1580, 2000, 2510, 3160 or 3980 mg/kg bodyweight (bw). Mortality rates for these doses were 0/5, 1/5, 2/5, 2/5, 4/5, 4/5 and 4/5, respectively. Clinical signs included weight loss, increasing weakness, diarrhoea, collapse and mortality. Necropsy showed haemorrhagic lesions in the lungs, discolouration of liver and gastrointestinal inflammation.

A medial lethal dose (LD50) of 2100 mg/kg bw was determined (OECD 2006; REACH).

In 3 other non-guideline oral acute toxicity studies, isododecylphenol (CAS No. 11067-80-4) was found to have oral LD50 values of: 2200 mg/kg bw in male and female rats of unspecified strain; >500 mg/kg bw in male SD rats; and <5000 mg/kg bw in SD rats of both sexes. Sub-lethal clinical signs observed included: ruffled fur, diarrhoea, diuresis, bloodstained nose, deep red eyes, impaired motion, slight to medium sedation, ataxia and abnormal posturing in the first study; abnormal bowel movements and bloody urine in animals in the second study; and ruffled, oily coats and mild diarrhoea in the third study (OECD 2006; REACH).

Dermal

Limited data are available for these chemicals. The data for this endpoint includes read across from analogues.

Based on the available data, these chemicals have low acute dermal toxicity. No hazard classification is warranted.

In a non-guideline dermal acute toxicity study, New Zealand White (NZW) rabbits (2/sex/dose) were topically administered a single dose of dodecylphenol, mixed isomers at 0, 1260, 2000, 3160, 5010 or 7940 mg/kg bw. Animals were exposed for a period of 24 hours under semi-occlusive conditions. Sub-lethal clinical signs included weight loss, increasing weakness and collapse. The dermal LD50 was estimated to be >2000 mg/kg bw and no mortalities were reported (OECD 2006; REACH).

In a dermal acute toxicity study conducted similar to OECD TG 402, NZW rabbits (6/sex/dose) were topically administered a single dose of the branched dodecylphenol at 0, 5 or 15 g/kg bw. Animals were exposed for a period of 24 hours under occlusive conditions. Animals were observed for 14 days. Mortality rates were 0/6, 0/6 and 3/6 for the 0, 5 and 15 g/kg bw dose groups. The dermal LD50 was determined to be 15 g/kg bw. Reported sub-lethal signs of toxicity included skin irritation. No gross pathology was observed in any surviving animals euthanised at 14 days (OECD 2006; REACH).

Inhalation

No data are available for chemicals in this group.

Corrosion/Irritation

Skin irritation

The limited data available for specific chemicals in this group indicate that these chemicals are corrosive or severely irritating to skin. The analogue chemicals TPP and branched dodecylphenol were reported to cause skin corrosion in animal studies. Branched dodecylphenol and TPP have harmonised classifications of 'Skin Corrosion – Category 1C (H314); Causes severe skin burns and eye damage' (ECHA 2013a). The related chemical nonylphenol also causes corrosive effects (NICNAS 2019). In the absence of further data on these chemicals, classification is warranted for chemicals included in this evaluation. Data are insufficient to sub-categorise classification for skin irritation/corrosion as the available studies do not include all relevant exposure time points.

In a study reported to be in accordance with OECD TG 404, 6 rabbits (White Russian, sex unspecified) were treated with 0.5 mL of isododecylphenol for 4 hours. Reddish brown colouration and necrosis with thickening of the skin was observed 24 hours after patch removal. Corrugated incrustations were formed with eschar. Due to considerable necrosis, the study was terminated on day 6 post dosing (OECD 2006).

In a non-guideline study, dodecylphenol, mixed isomers were applied under semi-occlusive dressings to the clipped, intact and abraded skin of 6 NZW male and female rabbits for 24 hours. The chemical was reported to be severely irritating with a primary irritation score of 8 (OECD 2006).

In a skin irritation study conducted similar to OECD TG 404, female NZW rabbits (6) were treated with 0.5 mL of TPP for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48, 72 hours and then 7 and 14 days after patch removal. The following mean scores for the 6 animals were reported for observations at 24, 48 and 72 hours: 4, 4 and 4 for erythema and 4, 3.4, 2.6 for oedema, respectively (maximum score of 4). A primary irritation score of 6.2 was reported. Severe erythema was observed at 24 hours and was irreversible in some cases during the observation period; oedema was present through to day 7. Cracking was observed on one animal at 72 hours. Necrotic skin was still present at 14 days. Treatment related microscopic findings included acanthosis, hyperkeratosis and subacute inflammation at all sites. Epidermal exudate was also observed (OECD 2006; REACH).

In a non-guideline study, TPP (dose not specified) was applied to the skin of 6 rabbits (strain and sex not specified) for an exposure period of 24 hours under occlusive conditions. The chemical produced severe irritation characterised by erythema and oedema, neither of which were reversible within 72 hours. After 7 days, skin at the application site had become necrotic and was lifting. A primary irritation score of 6 was reported. Limited study details are available (OECD 2006; REACH).

Branched dodecylphenol has been assessed for its potential to produce skin irritation in several non-guideline studies. The chemical produced: severe irreversible skin irritation in NZW rabbits (24 hour exposure, semi-occlusive conditions, 7 day observation), severe irreversible skin irritation including necrosis in rabbits (strain not specified) (4 hour exposure, 6 day observation), severe irreversible skin irritation including necrosis in rabbits (strain not

specified) (3 minute exposure, 5 day observation), severe irreversible skin irritation resulting in scar formation in rabbits (strain not specified) (3 minute exposure, 17 day observation). Of note, the results of the latter 3 studies were considered unreliable due to ineffective skin washing. Due to its low water solubility, the chemical is unlikely to be effectively removed from the skin using water alone (OECD 2006; REACH).

Eye irritation

Limited data are available for these chemicals. Mixed results were reported in eye irritation studies conducted. In one study with isododecylphenol, one animal showed signs of irritation that persisted for 21 days although in another study with the analogue TPP, effects had cleared in 10 days. The related chemical nonylphenol caused irreversible damage to the eyes (NICNAS 2019). Skin corrosive chemicals are considered to cause serious eye damage. The analogue chemicals, branched dodecylphenol and TPP have harmonised classifications of 'Eye Damage – Category 1 (H318); Causes serious eye damage'. In the absence of further data on these chemicals, classification is warranted for chemicals in this evaluation.

In a non-guideline eye irritation study, 0.1 mL of dodecylphenol, mixed isomers was instilled into 1 eye each of 6 male and 6 female NZW rabbits. Observations were made at unspecified intervals up to 7 days following administration. The chemical was moderately irritating to the eye with a reported irritation score of 33.3/110. Very few experimental details were available (OECD 2006; REACH).

In a non-guideline eye irritation study, 0.1 mL of isododecylphenol (CAS No. 11067-80-4) was instilled into one eye each of 6 rabbits (sex and strain unspecified). Animals were observed at 24, 48, 72 hours and up to 21 days following treatment. All animals showed slight to severe conjunctival irritation that was reversed by 72 hours. Five out of the 6 animals showed corneal opacity and iritis; one of these animals still showed signs of irritation at day 8. One animal showed signs of irritation that lasted for 21 days. Few experimental details were available (OECD 2006; REACH).

In an eye irritation study conducted similar to OECD TG 405, TPP was instilled into one eye each of 9 NZW rabbits (6 unwashed/3 washed) of unspecified sex. The eyes of 3 animals were washed out after 30 seconds. Animals were observed at 1, 24, 48, 72 hours and 7 and 14 days following treatment. No corneal opacity or iritis was observed in any animal at any time point. Conjunctival irritation persisted to day 7, and all eyes were clear of irritation by day 10. Washed and unwashed eyes showed comparable severity and persistence of irritation. (OECD 2006; REACH).

In an eye irritation study, 0.1 mL of TPP was instilled into one eye each of 6 male NZW rabbits. Observations were made at 24, 48, and 72 hours after administration. Severe conjunctivitis was observed in all rabbits and iritis and corneal opacity were observed in 3 animals (OECD 2006; REACH).

Sensitisation

Skin sensitisation

No data are available for chemicals in this group. The data for this endpoint are read across from analogue chemicals.

An in vivo skin sensitisation study was conducted to assess TPP, using 19 Hartley guinea pigs of both sexes. The study was conducted in accordance with OECD TG 406 (Buehler test). Animals were induced with 2.5% concentration of the chemical in mineral oil. The animals were challenged and rechallenged with 1% TPP in mineral oil. There was no increased incidence of positive reactions in any of the test chemical animals compared with negative control groups. The chemical was reported to be non-sensitising in this study (REACH).

In an in vivo skin sensitisation study conducted in accordance with OECD TG 406 (Buehler test), 15 Hartley guinea pigs of both sexes were induced with 5–10% concentration TPP in mineral oil. The animals were challenged with 5% TPP in mineral oil. No sensitisation reactions were observed in the 15 animals induced and challenged with the test material. Based on this study, the chemical was non-sensitising (OECD 2006; REACH).

Repeat dose toxicity

Oral

Limited data are available for these chemicals. The data for this endpoint include read across. Repeated exposure to these chemicals caused reductions in food consumption and bodyweights. The reproductive organs appear to be the target organs for systemic toxicity. Classification for repeat dose effects is not warranted.

In a 28 day study conducted similar to OECD TG 407, SD rats (10/sex/dose) were administered dodecylphenol, mixed isomers in feed at 0, 500, 2500 or 5000 ppm (approximately 0, 25, 125, and 250 mg/kg bw/day), 7 days per week, for 28 days. The study report indicated that some clinical pathological changes occurred in the 2500 and 5000 ppm dose groups, including decreases in reticulocytes. This was not expected to be specifically related to the test chemical. Treatment related macroscopic observations included small prostate glands, seminal vesicles and testes and abnormally soft consistency of testes in the highest dose males. Theses gross changes occurred in 8 out of 10 high dose males with supporting microscopic changes observed in 7 of 8 of these animals. Treatment related microscopic changes were observed in the testes, epididymides, prostate glands, seminal vesicles, bone marrow and spleens in the highest dose males, and in the bone marrow and spleens of the highest dose females. Microscopic changes included hypoplasia and/or decreased sperm content or absence of sperm in epididymides of some highest dose males. Abnormal secretion in the prostates of some highest dose males was observed. Splenic congestion and bone marrow hypoplasia was also observed in some highest dose animals of both sexes. This study did not report effects in female reproductive organs. It is not clear if these organs were examined. The study Director reported a no observed effect level (NOEL) of 500 ppm for both sexes (ECHA 2013a; OECD 2006; REACH). Based on these findings, a NOAEL of 2500 ppm may be considered appropriate.

In a 28 day repeat dose toxicity study conducted in accordance with OECD TG 407, Crl:CD rats of both sexes (5/sex/dose) were administered TPP via oral gavage at 0, 5, 20, 60, 180 or 300 mg/kg body weight (bw)/day (in corn oil), 7 days a week for 28 days. The study report indicated that half the test group animals were necropsied at the end of the exposure period. No treatment related deaths occurred during the study. There was evidence of excessive salivation in males and females in the 180 and 300 mg/kg bw/day groups during the dosing period. Animals in 60, 180 and 300 mg/kg bw/day groups showed urogenital staining during the dosing period. There were decreases in cumulative body weight gain for males (significant) and females in the 2 highest dose groups. Moderate changes in blood chemistry (haemoglobin and haematocrit levels) were observed in the 2 highest dose group females. Changes to lymphocyte and reticulocyte numbers were also observed in females in the 2

highest dose groups. Small testes (15–42% weight reduction), prostate (56–78% weight reduction), seminal vesicles (67–79% weight reduction), epididymides (28–58% weight reduction) and coagulating glands were notes in the 180 and 300 mg/kg bw/day males at necropsy. Treatment related microscopic findings were observed in all dose groups. Findings in the 180 and 300 mg/kg bw/day groups included decreased secretion in the seminal vesicles, prostate and coagulating glands, depletion of germ cells and interstitial cell atrophy in the testes, luminal cellular debris and/or hypospermia in the epididymides. Decreased ovary weights were observed at the 2 highest doses (76% and 72% of control, respectively). This was accompanied by decreased corpora lutea. Increased liver weights were observed at the highest dose in both males and females. Centrilobular hepatocellular hypertrophy and hepatocellular vacuolisation in the liver were observed at 60 mg/kg bw/day and above. Microscopic changes in reproductive organs persisted until the end of the recovery period in the highest dose group. Based on changes to organ weights and microscopic findings in reproductive organs, the NOAEL was determined to be 60 mg/kg bw/day for males and females (REACH).

In a 90 day study conducted in accordance with OECD TG 408, SD rats of both sexes (10/sex/dose) were administered TPP in feed daily at 0, 50, 100, 150 or 200 mg/kg bw/day, for 90 days. There were no reported treatment related clinical signs and no deaths at any dose level during the study. Animals showed dose dependent reduced body weight gain and reduced feed intake. Clinical pathological changes consisted of lower erythrocyte count and haemoglobin in males from the highest dose group. There were also reduced white blood cell counts in males and females in the highest dose group, as well as lower mean alanine aminotransferase in males from the 2 highest dose groups and lower mean cholesterol in females from the 100, 150 and 200 mg/kg bw/day groups. Macroscopic evaluation revealed small coagulating glands, prostate and seminal vesicles in males from the 2 highest dose groups and small epididymides and testes in males in the highest dose group. Males in the 100, 150 and 200 mg/kg bw/day groups had higher adrenal weights and lower prostate and seminal vesicle weights. Females in the 100, 150 and 200 mg/kg bw groups had lower ovary weights and females in the 2 highest dose groups had lower uterus weights. Histological findings consisted of adrenal hypertrophy, renal tube mineralisation, atrophy of the coagulating glands and prostates in highest dose males; periportal hepatocellular vacuolation in males and females in the 2 highest dose groups; decreased secretion in seminal vesicles in males in the 2 highest does groups, as well as decreased corpora lutea in the ovaries of females in the 2 highest dose groups. The histological effects observed at 150 and 200 mg/kg bw/day were direct and potentially adverse effects of TPP; therefore, the NOAEL was determined to be 100 mg/kg bw/day (ECHA 2013a; REACH).

In a 90 day non-guideline study, FDRL albino rats of both sexes (20/sex/dose) were administered dodecylphenol, mixed isomers at 0, 0.05, 0.2 or 0.4% in the diet (approximately equivalent to 27, 106 and 217 mg/kg bw/day, respectively). The study indicated that there were no reported treatment related deaths at any dose level. Females in the middle dose group had decreased growth. Investigators indicated this effect may not be adverse nor treatment related, as food consumption was also decreased. Animals of both sexes showed decreased growth in the middle and highest dose groups. No treatment related changes to haematological, clinical chemical or urinalysis parameters were observed. Highest dose animals of both sexes had significant increases in mean liver weights. Highest dose males had a significant reduction in the mean testes weight. The only significant histopathological finding was testicular hypospermia in 30% males in the highest dose group. Based on these findings, the NOAEL was 0.05% (equivalent to 27 mg/kg bw/day); however, the effects in females at 0.2% may not have been truly adverse findings (ECHA 2013a; OECD 2006; REACH).

In a study of similar design in beagle dogs (sex unspecified) no treatment related effects were observed in the clinical signs, body weight, food consumption, haematology, clinical chemistry, or urinalysis data of treated animals. Organ weight, macroscopic observations at necropsy, and microscopic evaluation of selected tissues (including testes and ovaries) were unremarkable (ECHA 2013a; OECD 2006).

Dermal

No data are available for chemicals in this group.

Inhalation

No data are available for chemicals in this group.

Genotoxicity

In vitro

Limited data are available for these chemicals. Data for this endpoint included read across data from analogues. Based on the negative results from in vitro and in vivo studies these chemicals are not expected to be genotoxic.

In vitro

The following results from in vitro genotoxicity assays were reported for dodecylphenol, mixed isomers (OECD 2006):

- Negative results were reported in a bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* TA 1535, TA 1537, TA 98 and TA 100 with and without metabolic activation at concentrations up to 1000 µg/plate.
- Negative results were reported in a bacterial reverse mutation assay (OECD TG 471) in *S, typhimurium* TA98, TA100, TA1535, and TA1537 with and without metabolic activation at concentrations up to 10.0 mg/plate.
- Negative results were reported in a mammalian gene mutation assay (OECD TG 476) in the hypoxanthine-guanine phosphoribosyl transferase (Hprt) locus in Chinese hamster ovary (CHO) cells with and without metabolic activation at concentrations up to 10 µg/mL.

The following results from in vitro genotoxicity assays were reported for the analogue chemicals branched dodecylphenol and TPP (OECD 2006; REACH):

- Negative results were reported for TPP in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100 with and without metabolic activation at concentrations up to 1000 µg/plate.
- Negative results were reported for branched dodecylphenol in a bacterial reverse mutation assay conducted similar to OECD TG 471, in *S. typhimurium* TA 1538, TA 1535, TA 1537, TA 98 and TA 100 with and without metabolic activation at concentrations up to 5000 µg/plate.

Negative results were reported for TPP in a mammalian gene mutation assay (OECD TG 476) in the hypoxanthine-guanine phosphoribosyl transferase (Hprt) locus in Chinese hamster ovary (CHO) cells with and without metabolic activation at concentrations up to 10 µg/mL.

In vivo

In a mammalian erythrocyte micronucleus test conducted similar to OECD TG 474, rats (strain not specified) (6/sex/dose) were treated with a single dose of dodecylphenol, mixed isomers at 0, 500, 1500 or 5000 mg/kg bw. The method of administration was not specified. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (OECD 2006; REACH).

Carcinogenicity

No data are available for chemicals in this group.

Reproductive and development toxicity

Limited data are available for these chemicals. Based on available data including read across information from the branched dodecylphenol and TPP, these chemicals are expected to cause specific adverse effects on fertility, warranting classification. Effects on female fertility included reduced ovary weights with decreased corpora lutea and lengthened oestrous cycles with increase in the incidence of persistent diestrus. Effects in male fertility include reduction in male reproductive organ weights with reduced sperm concentration. While reduced food consumption and lower bodyweights may have contributed to these findings the reproductive effects particularly in females cannot only be explained by this mechanism. Effects on developmental toxicity were considered secondary to maternal toxicity (ECHA 2013a). The analogue chemicals have a harmonised classification of 'Reproductive toxicity – Category 1B (H360F); May damage fertility'.

Branched dodecylphenol was assessed in a 2 generation reproductive toxicity assay conducted according to OECD TG 416. Three groups of male and female Crl:CD(SD) rats (30/sex/group) were exposed to the test substance in diet for at least 70 consecutive days prior to mating, at 1.5, 15 or 75 mg/kg/day for P0 and F1 generations. The test substance was administered daily to males and females. P0 animals were dosed during growth, mating, during the resulting pregnancies and through the weaning of their first generation offspring. F1 animals were administered the chemical during their growth into adulthood, mating and production of the second generation (F2). P0 animals were administered the chemical for 129 –134 consecutive days, and F1 animals were administered the chemical for 210–227 consecutive days. Due to reduced fertility in all groups (including control) in the F1 animals, F1 animals were re-bred to produce two second generation (F2) litters, the F2 and the F2a litters. Parental toxicity was observed as lower mean body weights and slowed body weight gain in the P0 and F1 highest dose animals. Highest dose males from both the P0 and F1 generations were reported to have lower reproductive organ weights (cauda epididymides, epididymides, prostate, and seminal vesicles/coagulating glands) and higher pituitary weights. Highest dose F1 males had lower testes weights. Highest dose P0 and F1 females had lower ovary weights. Highest dose F1 females had higher adrenal weights. Histopathologic changes were observed in P0 males at the highest dose, and in F1 males at 15 and 75 mg/kg bw/day (renal mineralisation). P0 and F1 females had decreased corpora lutea at the highest dose. Based on these effects, the NOAEL for parental toxicity in P0 and F1 generations was 15 and 1.5 mg/kg/day, respectively. Highest dose P0 females had decreased implantation sites. Highest dose P0 and F1 females had increased oestrous cycle lengths and increased number of females in persistent dioestrus. Highest dose P0 males had a reduction in mean epididymal sperm concentration. Based on these effects, the NOAEL for male and female reproductive toxicity was 15 mg/kg bw/day. There were reported reductions in highest dose F2 and F2a postnatal survival. There were lower F1, F2, and F2a offspring body weights and body weight gains, as well as accelerated onset of vaginal patency in F1 females at the highest dose. There was no effect on anogenital distance (AGD) and

anogenital distance index (AGDi) in F2 offspring on PND1 (not investigated in F1 and F2a). Based on these effects, the NOAEL for neonatal toxicity was 15 mg/kg/day (ECHA 2013b; OECD 2006; REACH).

In a one-generation reproduction toxicity study conducted in accordance with OECD TG 415, Crl:CD (SD) rats in the P0 generation (30/sex/group) were administered TPP by gavage once daily at 5, 25 or 125 mg/kg bw/day, daily for 73 days prior to mating. P0 males were administered the chemical throughout mating up until completion of parturition (the day prior to euthanasia) (number of days not specified). P0 females were administered the chemical throughout mating, gestation, lactation and until weaning on day 21. Treatment related parental systemic toxicity was observed as decreased body weights, body weight gain in the middle and highest dose group males and in the highest dose group females. Treatment related changes to organ weights were observed from the 25 mg/kg bw/day dose group and higher in P0 males (kidneys, adrenal and liver), and in the 125 mg/kg bw/day group in females (kidneys). Treatment related effects on P0 reproductive parameters were reported to occur at all dose levels. A marked reduction in fertility was only observed at the highest dose; only 4 P0 females at this dose conceived litters which were unusually small and higher rates of mortality. P0 males showed decreased seminal vesicle/coagulating gland weights and decreased cauda epididymis weights at 25 and 125 mg/kg bw/day. Decreased prostate, epididymis and testes weights were reported in the highest dose group. Sperm concentrations were lower in 25 and 125 mg/kg bw/day P0 males. P0 females had decreased ovary and oviduct weights in the middle and highest group, and increased uterus weights in the highest dose group. Ovarian cysts, decreased corpora lutea and endometrial gland cysts were observed in P0 females in the highest dose. There were corresponding decreases in the numbers of implantation sites in this group of females. Increased oestrous cycle length was noted in females in the 2 highest doses. At 25 mg/kg bw/day, decreased P0 offspring mean body weights and/or body weight gains were noted throughout the pre-weaning and weaning period. A mortality occurred in the 25 mg/kg bw/day F1 group post weaning. This was attributed to P0 chemical administration. Based on study results, the chemical was reported to adversely effect reproductive parameters at ≥25 mg/kg bw/day. At the same dose levels, significant systemic parental toxicity was observed. The NOAEL for reproductive and developmental toxicity was 5 mg/kg bw/day (ECHA 2013b; OECD 2006; REACH).

In a prenatal developmental toxicity study conducted in accordance with OECD TG 414, pregnant SD rats (24/dose) were administered dodecylphenol, mixed isomers by gavage once daily at 0, 20, 100 or 300 mg/kg bw/day on gestational days (GD) 6–15. No mortality was recorded in any rats at any dose level tested. At 20 and 100 mg/kg bw/day, no evidence of maternal toxicity, embryotoxicity, foetotoxicity or teratogenicity was observed. At 300 mg/kg bw/day, there was an increase in the rate of foetal malformations (various ossification variation and retardation) and lower foetal body weight. However, these effects also coincided with evidence of maternal toxicity at the same dose level. Evidence of maternal toxicity consisted of reductions in weight gain and food consumption, as well as evidence of gastrointestinal dysfunction. Based on these effects, the NOAEL for both maternal toxicity and foetotoxicity was 100 mg/kg bw/day (REACH).

Effects on reproductive organs consistent with those observed in the one and 2 generation studies were reported in repeated dose toxicity studies with dodecylphenol, mixed isomers (see **Repeat dose toxicity** section).

Endocrine effects

In vitro data indicate that these chemicals may interact with oestrogen receptors (ER) and androgen receptors (AR). Mechanistic in vivo studies clearly indicate oestrogenicity but no anti-oestrogenic, androgenic, or anti-androgenic activity. Observed effects include:

- increased uterus weight in uterotrophic assays
- accelerated pubertal development in female pubertal assays.

Effects in the thyroid hormone system were also observed in vitro and in vivo.

Endocrine studies on chemicals in the group

Several studies on endocrine effects were available for 4-dodecylphenol, mixture of isomers and 4-dodecylphenol (ECHA 2021a; ECHA 2021b).

Toxcast models for these chemicals predict oestrogenic and antiandrogenic activity.

In a competitive binding assay using cytosolic rat uterine (ER) preparation, it was reported that the branched dodecylphenol was found to compete with ligand binding with a half maximal inhibitory concentration (IC50) of 4.85 µM corresponding to an RBA of 0.019 % when compared to the positive control. The IC50 value was in the same range as 4-nonylphenol and 4-tert-octylphenol.

In a binding assay using recombinant human ERα (hERα) competitive binding of 4-dodecylphenol to the ligand biding domain of hERα with an RBA of 0.24 % when compared to the positive control E2 (no IC50 values were reported).

In an AR binding study, weak competitive binding of 4-dodecylphenol to AR with an IC50 of 20 µM and an RBA of 0.015 % compared to the positive control was reported.

Two immature rat uterotrophic assay conducted according to OECD TG 440 (uterotrophic bioassay in rodents) were available for 4-dodecylphenol. In both studies the chemical was administered subcutaneously to immature female Crj:CD (SD) rats, both with and without 17α-ethinylestradiol (EE2) (examining the anti-oestrogenic effect). In both studies the chemical was reported to have induced a significant increase in uterine weight at ≥ 40 mg/kg bw/d. No anti-oestrogenic effect was observed when rats where co-exposed to EE2.

In a Hershberger assay 4 dodecylphenol was administered by gavage to castrated male rats (6 per dose). The dosage was 10, 30, 100 mg/kg bw/d 4-DP (examining the androgenic effect) or 10, 30, 100 mg/kg bw/d 4-DP and 0.2 mg/kg bw/d testosterone propionate (examining the antiandrogenic effect). In the androgenic part of the assay, a decrease in the weight of the bulbocavernosus/levator ani muscle (BC/LA) at a dose of 100 mg/kg bw/d was observed. However, since there was no dose response, no effects on other androgen-sensitive organ weights and no effects in the anti-androgenic part of the test indicated, the Hershberger assay was reported to be negative.

Chemicals, 4-Dodecylphenol (mixture of isomers) and 4-dodecylphenol were tested in vitro for inhibition of deiodinases 1, 2, 3 (DIO 1, 2, 3) using high throughput assays investigating effects on the thyroid hormone system. Both substances were positively identified as inhibitors of all three DIOs. These chemicals were also tested for inhibition of iodotyrosine deiodinase (IYD) in another high throughput screening assay. Both chemicals were identified as inhibitors of IYD.

Endocrine studies on analogue chemicals TPP and branched dodecylphenol

Branched dodecylphenol has been assessed in androgen binding assays. In a competitive binding assay using rat prostate AR, the chemical was reported to be a weak binder. It was only reported to be an effective inhibitor when present at 60,000 times the concentration of the reference androgen (Thomas et al. 2012a).

In a competitive binding assay using rat uterine oestrogen receptor, branched dodecylphenol was found to compete with ligand binding. Competitive inhibition began at a concentration of approximately 10^{-7} M. Complete inhibition was observed at a concentration of 10^{-5} M. The chemical was reported as having weak to moderate competitive binding with an IC50 of 1.1 µM and an RBA of 0.11 % compared to the positive control (Thomas et al. 2012b).

In two separate uterotrophic assays conducted according to OECD TG 440 (uterotrophic bioassay in rodents), TPP was administered to ovariectomised female SD rats (six animals/group) at doses of 0, 75, 125, 250 or 500 mg/kg bw/day, for three consecutive days, by oral gavage. A positive control group received an oestrogenic positive control substance (17α-ethynylestradiol) and a vehicle control group received the vehicle only. Reductions in body weight gain and significant increases in the mean uterine weight were observed in all treatment groups except the vehicle control group in both studies. Both studies suggested that the chemical 'demonstrated or mimicked biological activities consistent with agonism of natural oestrogens' (ECHA 2013b)

Four female pubertal assays were conducted in immature female SD rats (15 animals/group) by administering TPP or derivatives of TPP, once daily for 20 consecutive days (post-natal days 22–41) via gavage. Two studies were conducted with TPP at doses of 10, 50, 200 or 800 mg/kg bw/day, one study at 5, 20 or 60 mg/kg bw/day and another study at 60, 250 or 1000 mg/kg bw/day. The control groups in each study received the vehicle using a comparable regimen. The observations from these studies indicated that some oestrogenic effects of the chemical were observed at doses of 20 mg/kg bw/day and above, including: early attainment of vaginal patency; oestrous cycle disturbances; reduced weights of the uterus; thymus and ovaries/oviducts. Morphological changes including absence of corpora lutea, oocyte degeneration and necrosis of follicular cells in the ovaries were also observed. Systemic toxicity was observed at 200 mg/kg bw/day (reduced body weight) and 800 mg/kg bw/day (mortality). Some effects in the thyroid were also reported in some studies including increased incidence of thyroid hypertrophy. No differences in T4 levels were observed. TSH levels were significantly increased at 800 mg/kg bw/d in one out of 3 pubertal assays which measured this parameter (ECHA 2013b).

References

Chemwatch (n.d.) *Galleria Chemica*, Chemwatch website, accessed January 2022.

Danish EPA (Environmental Protection Agency) (2013) Survey of alkylphenols and alkylphenol ethoxylates Danish EPA website, accessed March 2022.

EC (European Commission) (n.d.) *CosIng*, EC website, accessed January 2022.

ECHA (European Chemicals Agency) (2013a) *CLH Report - Proposal for Harmonised Classification and Labelling for Phenol, dodecyl-, branched*, ECHA, accessed February 2022.

ECHA (European Chemicals Agency) (2013b) *Committee for Risk Assessment (RAC) Opinion - proposing harmonised classification and labelling at EU level of Phenol, dodecyl-, branched [1]; Phenol, 2-dodecyl-, branched; Phenol, 3-dodecyl-, branched; Phenol, 4-dodecyl-, branched; Phenol, (tetrapropenyl) derivatives [2*, ECHA, accessed February 2022.

ECHA (European Chemicals Agency) (2021a) *Annex XV Report - Proposal for Identification of Substances of Very High Concern (SVHC) on the Basis of the Criteria Set Out in Reach Article 57*, ECHA, accessed January 2022.

ECHA (European Chemicals Agency) (2021b) *Substances of Very High Concern (SVHC) support document - Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/or combinations,* ECHA, accessed February 2022.

ECHA (European Chemicals Agency) (n.d.) *Substance Infocard for EC No. 799-972-3*, ECHA website, accessed January 2022.

EWG (Environmental Working Group) (n.d.) *EWG's Skin Deep*, EWG website, accessed January 2022.

Government of Canada (2018) *Screening assessment substances identified as being of low concern using the ecological risk classification of organic substances and the threshold of toxicological concern (TTC)-based approach for certain substances*, Government of Canada, accessed January 2022.

OECD (Organisation for Economic Co-operation and Development) (2006), *SIDS Initial Assessment Profile for Phenol, (tetrapropenyl) derivatives, Tetrapropenyl phenol, Phenol, dodecyl-, branched*, OECD. Accessed February 2022.

Personal Care Products Council (n.d.) *Cosmetic Ingredient Identification Database*, Personal Care Products Council website, accessed January 2022.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for CAS No. 121158-58-5*, European Chemicals Agency website, accessed January 2022.

NLM (National Library of Medicine) (n.d.) *ChemIDplus Advanced Database*, NLM website, accessed February 2022.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2010) *Priority Existing Chemical (PEC) Assessment Report – Diethylhexyl Phthalate (DEHP): Human health assessment*, NICNAS, accessed February 2022.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2019) *IMAP Group Assessment Report – Nonylphenols: Human health tier II assessment*, NICNAS, accessed February 2022.

Thomas J et al. (2012a). In Vitro Rat Prostate Androgen Receptor Competitive Binding Assay with Tetrapropenyl Phenol. WIL Research Laboratories, Study number WIL-187133. Conducted for Chevron Energy Technology Company.

Thomas J et al. (2012b). In Vitro Rat Uterine Estrogen Receptor Competitive Binding Assay with Tetrapropenyl Phenol. WIL Research Laboratories, Study number WIL-187137. Conducted for Chevron Energy Technology Company.

UK EA (Environment Agency) (2007) *Environmental risk evaluation report: para-C12-alkylphenols (dodecylphenol and tetrapropenylphenol)*, accessed March 2022.