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RISKS TO PUBLIC HEALTH FROM EMERGING ORGANIC CONTAMINANTS IN THE NEW ZEALAND AQUATIC ENVIRONMENT

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EXECUTIVE SUMMARY

With improvements in the sensitivity and scope of analytical techniques, many chemicals that enter the environment through wastewater are now beginning to be quantified in riverine, estuarine, and marine systems. These chemicals include substances originating in the domestic residential environment, including over the counter and prescription pharmaceuticals, musks and fragrances, surfactants and disinfectants, and a range of other miscellaneous chemicals.

These substances are collectively termed Emerging Organic Contaminants (EOCs). EOCs are receiving significant research focus because of concerns as to how they enter and affect environments. There is potential for these substance to become concentrated (bioaccumulate) in aquatic species, resulting in long-term impacts on population viability.

EOCs have been defined as:

> "Any synthetic or naturally occurring chemical or any microorganism that is not commonly monitored in the environment but has the potential to enter the environment and cause known or suspected adverse ecological and (or) human health effects"

A relative unknown is the extent to which these chemicals may constitute a risk for humans using the environment for recreational purposes or harvesting biota from the environment for food.

Little information is available on EOCs in wastewater discharges or the receiving environment in New Zealand. However, the available information suggests that most classes of EOCs are potentially present in these media.

Highly conservative human health risk assessments were carried out for exposure scenarios of; swimming in an affected receiving environment, and eating shellfish from an affected receiving environment. For the swimming scenario, exposure was only considered due to ingestion of water. Inhalation of water is likely to be negligible in comparison to ingestion and suitable data for the estimation of dermal absorption of EOCs from water were not found.

Estimates of risk, either in the form of comparisons to health-based guidance values or margins of exposure to toxicological points of departure, suggest that the risks to human health from the discharge of EOCs into the environment is currently very low. However, no New Zealand specific concentration data were available for several classes of EOCs, and concentrations in shellfish were unavailable for most classes of EOCs.

Estimates of human exposure to EOCs from environmental contact were generally low in comparison to estimates of exposure from other sources (e.g. diet, dust), where available.

1. INTRODUCTION

With improvements in the sensitivity and scope of analytical techniques many chemicals that enter the environment through wastewater are now beginning to be quantified in riverine, estuarine and marine systems. These chemicals include substances originating in the domestic residential environment, including over-the-counter and prescription pharmaceuticals, musks and fragrances, surfactants and disinfectants, and a range of other miscellaneous chemicals.

These substances are collectively termed Emerging Organic Contaminants (EOCs). EOCs are receiving significant research focus because of concerns as to how they enter and affect environments. There is potential for these substances to become concentrated (bioaccumulate) in aquatic species, resulting in long-term impacts on population viability.

EOCs have been defined as:

> "Any synthetic or naturally occurring chemical or any microorganism that is not commonly monitored in the environment but has the potential to enter the environment and cause known or suspected adverse ecological and (or) human health effects"[1]

Wastewater treatment plants (WWTPs) were not designed to remove these substances and, in some cases, are ineffective in removing them from waste streams. The extent to which these chemicals can accumulate in the environment, including recreational waters and aquatic food species, and represent a hazard to people coming in contact with the environment is currently poorly understood.

1.1 CURRENT PROJECT

The current project has objectives to:

- Obtain and consolidate New Zealand data (regional council and other) on EOCs in wastewater and the receiving environment.
- Provide a qualitative or quantitative assessment of the risks to public health from EOCs in wastewater and the receiving environment, with reference to possible routes of human exposure.

1.2 SCOPE OF THE CURRENT PROJECT

1.2.1 EOCs considered

An enormous range of chemicals could potentially be classified as EOCs. The categories of EOCs recently proposed for environmental monitoring in New Zealand (Stewart *et al.*, 2016) are summarised in Table 1 and were assessed to cover the major categories considered internationally. Adoption of these categories would aid alignment of different EOC interests and efforts in New Zealand. However, further clarification is required with respect to some categories of EOCs.

Pesticides have been widely studied and monitored for several decades. It does not appear to be appropriate to consider pesticides to be 'emerging' contaminants. Emerging pesticide issues may occasionally arise, such as the detection of pesticide residues in environmental compartments not previously considered. For the current project, consideration of pesticides will be guided by the marker EOCs proposed by Stewart et al. (2016). Specifically:

[1] https://toxics.usgs.gov/investigations/cec/index.php Accessed 10 May 2017

- Glyphosate, due to widespread industrial and domestic use
- Neonicotinoid insecticides, due to current environmental concerns related to the use of these substances; and
- Synthetic pyrethroids, due to the increasing use of these pesticides to replace organophosphorus and carbamate pesticides

Table 1. EOC classes and marker EOCs proposed by Stewart et al. (2016)

Chemical class	Representative compound(s)	CAS number
Flame retardants	BDE47 BDE99 BDE209 Tris[2-chloro-1-(chloromethyl)ethyl] phosphate Triphenylphosphate Tris (1-chloro-2-propyl) phosphate	5436-43-1 60348-60-9 1163-19-5 13674-87-8 115-86-6 13674-84-5
Plasticisers	Bis(2-ethylhexyl)phthalate Benzyl butyl phthalate Bisphenol A	117-81-7 85-68-7 80-05-7
Surfactants	Nonylphenol Linear alkylbenzene sulphonate	84852-15-3 25155-30-0
Perfluorinated compounds	Perfluorooctanesulfonic acid, perfluorooctanoic acid	1763-23-1/335-67-1
Musk fragrances	Galaxolide Tonalide	1222-05-5 21145-77-7
Pesticides Neonicotinoid insecticides Pyrethroid insecticides Pyrethroid insecticides	Glyphosate Imidacloprid Bifenthrin Permethrin	1071-83-6 138261-41-3 82657-04-3 52645-53-1
Pharmaceuticals	Acetaminophen Diclofenac Ibuprofen Carbamazepine	103-90-2 15307-86-5 15687-27-1 298-46-4
Steroid estrogens	Estrone	53-16-7
Personal Care Products	Triclosan Methyltriclosan	3380-34-5 4640-01-1
Preservatives	Methylparaben	99-76-73
Corrosion inhibitors	Benzotriazole	95-14-7
Antifouling agents	Diuron Isoproturon	330-54-1 34123-59-6
UV-Filter	Benzophenone-3	131-57-7

BDE: brominated diphenyl ether

1.3 HUMAN HEALTH RISK ASESSMENT

The current study is primarily concerned with risks to human health resulting from the discharge of EOCs into the aquatic environment.

1.3.1 Potential routes of human exposure

EOCs primarily enter the environment as a component of human waste or as a consequence of other human activities. The majority of human waste discharges in New Zealand are to aquatic environments. Subsequent human contact with EOCs following discharge to the aquatic environment may occur through:

- Contact recreation
- Consumption of edible biota from the receiving environment

For the current study, it has been assumed that volatilisation of EOCs from the receiving environment and subsequent inhalation is a negligible route of exposure.

During contact recreation, water may be ingested, aerosolised and inhaled, or absorbed through the skin. It is generally considered that inhalation of water is negligible compared to

ingestion and will not be considered as an exposure route in the current study. Dermal absorption of chemicals is usually low in comparison with absorption from the gastrointestinal tract.

1.3.2 Information considered

The current project is primarily interested in New Zealand-specific information on EOCs in environmental media, including edible biota.

Regional councils were queried through the SWIM network (Tim Davie, SWIM Co-ordinator, personal communication). It was confirmed that there was no ongoing monitoring of EOCs being carried out and information available to regional councils was derived from a number of isolated studies, some of which were funded by regional councils.

In addition to project reports from studies carried out in New Zealand, the current project considered the scientific literature (via searches in PubMed, Web of Science) and the grey literature (via search on Google) for evidence of the occurrence of EOCs in the New Zealand environment. Due to the paucity of New Zealand data, information from Antarctica and Australia was also considered. However, the literature considered to date suggests that concentrations of individual EOCs detected in the environment can differ markedly between different countries and risk assessment activities were based solely on New Zealand-specific data.

Key New Zealand studies

Information on EOCs in New Zealand wastewater and the receiving environment was mostly contained in reports of five key studies (Emnet, 2013; Stewart *et al.*, 2014; Stewart, 2016; Tremblay *et al.*, 2013; Tremblay and Northcott, 2013). While these studies constitute an invaluable resource, in most cases sample numbers are quite small. Table 2 summarises some aspects of these studies.

Table 2. Aspects of key New Zealand studies on EOCs

Parameter	Tremblay *et al.* (2013)	Tremblay and Northcott (2013)	Emnet (2013)	Stewart *et al.* (2014)	Stewart (2016)
Matrices included (number of samples)	WWTP influent (13)	Waikato river water (8)	WWTP effluent (33) Seawater (53) Marine sediments (28) Mussels (9)	Marine sediments (13)	WWTP effluent (2)
Sample type	Grab (13 sites, 1 occasion)	Grab (8 sites, 1 occasion)	Grab (effluent – 3 sites, 11 occasions over 1 year, seawater – 14 sites on 4 seasonal occasions, sediments – 14 sites on 2 seasonal occasions) Mussels – 4-5 sites on 2 seasonal occasions, composite of eight shellfish	Composite of two replicate grab samples (1 occasion)	24-hour composite, (2 consecutive days)
Analytical method	GC-MS	GC-MS	GC-MS	GC-MS, LC-MS/MS, ELISA	MS/MS (not further specified)
Analytes (LOD, ng/L for liquid samples or μg/kg wet weight for solid samples)	Pr-PB (NS)[b] TCS (NS) BPA (NS)	E1 (0.01) E2 (0.01) α-E2 (0.01) E3 (0.01) EE2 (0.05) NP (0.01) OP (0.01) BPA (0.05) Me-PB (1.0) Et-PB (0.01) Pr-PB (0.01) Bt-PB (1.0) TCS (1.0) Me-TCS (0.01)	E1 (7.0, 0.7, 1.4, 3.5)[c] E2 (0.4, 0.7, 0.1, 0.2) E3 (2.1, 0.7, 0.4, 1.0) EE2 (1.4, 0.7, 0.3, 0.7) NP (0.4, 1.7, 0.1, 0.2) OP (0.2, 1.5, 0.04, 0.1) BPA (1.3, 0.3, 0.3, 0.6) Me-PB (0.8, 0.7, 0.2, 0.4) Et-PB (0.4, 0.7, 0.1, 0.2) Pr-PB (0.8, 1.3, 0.2, 0.4) Bt-PB (0.5, 1.3, 0.1, 0.2) TCS (0.5, 1.5, 0.1, 0.3) Me-TCS (0.2, 1.5, 0.04, 0.1) BP-3 (2.6, 0.3, 0.5, 1.3)	PBDEs (NS)[d] DEHP (550-1700) BBP (280-800) NP (100) OP (100) BPA (50) E1 (0.6) E2 (0.4) EE2 (1.8) Glyphosate (40) TCS (100) Pesticides (4-40) Pharmaceuticals (0.02-3.4)	PBDEs (BDE-47, -99, -209) (NS) PFRs (NS) TCS (NS) Me-TCS (NS) Me-PB (NS) Et-PB (NS) Bt-PB (NS) E1 (NS) E2 (NS) EE2 (NS) NP (NS) BPA (NS) DEHP (NS) BBP (NS) Galaxolide (NS) Tonalide (NS) Diclofenac (NS) Ibuprofen (NS) Acetaminophen (NS) Bifenthrin (NS) Permethrin (NS)

WWTP: wastewater treatment plant, GC-MS: gas chromatography-mass spectrometry, LC-MS/MS: liquid chromatography-tandem mass spectrometry, ELISA: enzyme-linked immunosorbent assay, LOD: limit of detection, NS: not stated, Me-PB: methyl paraben, Et-PB: ethyl paraben, Pr-PB: propyl paraben, Bt-PB: butyl paraben, TCS: triclosan, Me-TCS: methyl triclosan, BPA: bisphenol-A, E1: estrone, E2: 17β-estradiol, α-E2: 17α-estradiol, E3: estriol, EE2: 17α-ethynylestradiol, NP: nonylphenol, OP: octylphenol, BP-3: benzophenone-3, PBDEs: polybrominated diphenyl ethers, DEHP: di(ethylhexyl)phthalate, BBP: butylbenzylphthalate, PFRs: Phosphate flame retardants

[a] Only analytes included in the current report are listed

[b] While specific LODs for analytes were not stated, it was reported that LODs were in the range 0.5-20 ng/L

[c] The study report defines the analytical limits as limits of quantification, but the definition given indicates they are LODs. LODs (in order) are for seawater, effluent, sediment, biota)

[d] Values are expressed on a dry weight basis

1.3.3 Hazard identification

Evidence for the ability of the selected EOCs to cause adverse health effects in humans was initially based on conclusions reached by national and international assessment organisations, such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the European Food Safety Authority (EFSA), when such assessments were available.

In the absence of previous assessments, evidence was collated primarily from human epidemiological studies, with greater emphasis given to studies of strong design (e.g. case-control studies). Animal toxicology data were considered to be secondary or supporting evidence of the potential for EOCs to cause adverse health effects in humans.

For many of the EOCs considered in this report, there is little or no evidence for causation of adverse effects in humans. In these cases, adverse effects from laboratory animal studies have been identified.

1.3.4 Dose-response

Information on the relationship between the exposure dose and adverse health effects for EOCs was also predominantly taken from international toxicological assessments. Dose-response information for non-cancer health effects are usually expressed in terms of health-based guidance values (HBGVs), such as acceptable or tolerable daily intakes (ADI or TDI), or as a toxicological point of departure (POD), such as a benchmark dose (BMD) or no observed adverse effect level (NOAEL); an exposure dose equating to a specified level of response, usually in laboratory animal studies.

HBGVs or PODs are generally based on the critical toxicological effect seen in animal studies. The critical effect is usually the adverse effect that occurs at the lowest dose in the most sensitive species.

1.3.5 Screening human exposure assessment

While New Zealand-specific information on EOCs is quite sparse, available information was used to conduct screening level risk assessments for two possible routes of exposure; primary contact recreation (swimming) in affected waters and consumption of shellfish from the affected environment. However, while New Zealand data were available to conduct screening risk assessments for swimming for many of the EOCs considered, data for EOCs in New Zealand shellfish were only available for two EOCs; methyl paraben and benzophenone-3. Where no New Zealand specific information on concentrations of EOCs in wastewater discharges or the receiving environment was available, no exposure or risk assessment was attempted.

The approach taken in the screening human exposure assessment is analogous to that used in New Zealand for assessment of human health impacts of wastewater discharges by quantitative microbiological risk assessment (QMRA) (McBride, 2014; McBride and Hudson, 2016). QMRA usually considers ingestion of water during swimming and shellfish consumption as the two main routes of human exposure to microbial pathogens discharged to the aquatic environment.

Swimming exposure assessment

Exposure to EOCs due to ingestion of water during swimming was calculated from:

$$E_{Swim} = \frac{IR \times ID \times C_{EOC}}{BW \times 1000} \quad (1)$$

Where:
IR = water ingestion rate (mL/hour)
ID = duration of ingestion (duration of swimming event) (hour)
C_{EOC} = concentration of EOC in recreational water (ng/L)
BW = body weight (kg)

The factor of 1000 converts water ingestion in mL to water ingestion in L. The exposure is expressed as ng/kg bw/day.

Assessments of risks due to ingestion of water during swimming are usually conducted for children, due to (1) their greater rate of ingestion of water during swimming, (2) their longer duration of swimming, and (3) their lower body weight. Deterministic exposure assessments were carried out for a 3-6 year old child (mean body weight 20 kg) (Cressey and Horn, 2016), as it was assumed that this was the youngest age group for which swimming events wouldn't be under strict parental control. A mean water ingestion rate of 23.9 mL/hr was used, based on a large US swimming pool study (Dufour *et al.*, 2017), while a mean duration of swimming of 1.1 hours was used, based on a Dutch estimate for duration of swimming in seawater (Schets *et al.*, 2011).

For the concentration of EOCs in the receiving environment, the highest concentration reported from any New Zealand study was used. In the absence of EOC concentration data for receiving waters, the highest concentration reported for any wastewater discharge was used, based on a scenario of a swimmer swimming in proximity to the point of wastewater discharge, with minimal dilution of the wastewater.

While non-pool swimming is usually a seasonal and non-daily activity, the exposure to EOCs from a swimming event was assumed to be a daily exposure for the purpose of the current screening risk assessment. To place this conservative assumption in perspective, a survey of 17,000 New Zealand children found that 4.7-14.8% (depending on age and gender) had not swum during the survey year, 46.4-63.4% had swum 'a few times' during the year and 21.8-48.2% had swum one or more times a week (Sport New Zealand, 2012).

Information on dermal absorption, to support an assessment of dermal exposure to EOCs, was considered on a chemical-by-chemical basis. It should be noted that information on dermal absorption is usually of the form of percentage absorption of an applied dose over an extended contact period (6-24 hours). This type of information is not suitable for assessment of dermal absorption during a swimming event, as the dose the skin surface is exposed to is not appreciably depleted and the period of exposure is much shorter (~1 hour). To support exposure assessment under a swimming scenario, information on the rate of dermal absorption is required.

Shellfish consumption human exposure assessment

Exposure to EOCs from consumption of shellfish was calculated from:

$$E_{SF} = \frac{CR_{SF}}{BW} \times C_{EOC} \qquad (2)$$

Where:
CR_{SF} = the consumption rate for shellfish (g/day)
C_{EOC} = concentration of EOC in shellfish (μg/kg)
BW = body weight (kg)

The exposure is expressed as ng/kg bw/day.

Shellfish are rarely consumed by children, so the risk assessment was carried out for a low body weight (10th percentile, 60 kg) adult (Cressey and Horn, 2016). A population mean daily consumption of shellfish of 1.2 g/person/day was used (Cressey, 2013). The EOC concentration value was taken as the highest measured concentration determined in New Zealand shellfish. It should be noted that data on concentrations of EOCs in New Zealand shellfish were only available for two classes of EOCs.

1.3.6 Risk characterisation

Where an ADI, TDI or other HBGV[2] was available for the EOC, risk was characterised as a risk index (RI), calculated as the estimated exposure as a percentage of the HBGV. The HBGV is a level of exposure that can be experienced for a lifetime without significant risk of adverse effects. Exposure estimates below the HBGV are considered to be acceptable and the further they are below the HBGV, the lower the risk.

$$RI = \frac{(E \times 100)}{HBGV} \quad (3)$$

Where:

E = E_{Swim} or E_{SF} from equations (1) and (2)

When no HBGV was available, a margin of exposure (MOE) approach was adopted. The MOE is the ratio between a toxicological point of departure (POD), such as a no observed adverse effect level (NOAEL) or a benchmark dose (BMD), and the estimate of human exposure. MOEs greater than 100-1000 are generally considered to represent a negligible level of risk for compounds that are not genotoxic carcinogens. The greater the MOE the lower the level of risk.

$$MOE = \frac{POD\ (BMD\ or\ NOAEL)}{E} \quad (4)$$

Where:

E = E_{Swim} or E_{SF} from equations (1) and (2)

To provide additional context for the risk estimates derived in the current study, New Zealand or overseas exposure estimates for various exposure route were also presented and compared to the exposure estimates from the current study.

1.3.7 Concentration units used

Concentrations of EOCs are reported in a range of formats. Concentration of trace contaminants in liquid media, such as water or wastewater are often expressed in ng/L and in this report most concentrations are expressed in these units. Occasional high contaminant concentrations have been expressed in μg/L or even mg/L. To convert between these units:

1 mg/L = 1000 μg/L

1 μg/L = 1000 ng/L

1 mg/L = 1,000,000 ng/L

Similarly, concentrations of EOCs in biota have usually been expressed in units of μg/kg or occasionally mg/kg. To convert:

1 mg/kg = 1000 μg/kg

Exposure estimates from screening risk assessments have been expressed in ng/kg bw/day. HBGVs are often expressed in μg/kg bw/day or mg/kg bw/day. The same thousand-fold conversion factors apply when converting between these units.

[2] HBGV is a collective term for health-based exposure guidelines such as acceptable daily intakes, tolerable daily intakes, reference doses, etc.

2. FLAME RETARDANTS

2.1 BROMINATED FLAME RETARDANTS

Brominated flame retardants (BFRs) are chemicals added to commercial items that contain foams, fabrics and plastics to reduce the likelihood of fires. A major class of BFRs, polybrominated diphenyl ethers (PBDEs), have emerged, over the past fifteen years, as persistent environmental contaminants of health concern. PBDEs are now commonly included in biomonitoring studies worldwide, including New Zealand ('t Mannetje *et al.*, 2013). These compounds occur globally in the environment due to the production of three commercial products; pentabromodiphenyl ether (pentaBDE), octabromodiphenyl ether (octaBDE), and decabromodiphenyl ether (decaBDE). The pentaBDE and octaBDE products have been either banned or restricted in use, leaving only the decaBDE formulation being actively produced in some areas. The three commercial products are mixtures of PBDE congeners that are commonly found in biological and environmental matrices. Of the 209 theoretical congeners possible, the congeners most commonly encountered in environmental or human sampling include BDE-28, BDE-47, BDE-99, BDE-100, BDE-138, BDE-153, BDE-154, BDE-183, and BDE-209 (EFSA, 2011a). These congeners have the same core diphenyl ether structure, but differ in the degree of bromination, ranging from the tribrominated BDE-28 to the decabrominated BDE-209. The increasing congener numbers correspond to increasing bromination, with BDE-99 and -100 both pentabrominated and BDE-153 and -154 both hexabrominated, but differing in the sites of bromination.

2.1.1 Hazard identification

PBDEs have been assessed by JECFA (2006), EFSA (2011a), Food Standards Australia New Zealand (FSANZ) (2007), and the United States Environmental Protection Agency (USEPA) (2017).

JECFA concluded that the available studies in humans were not adequate to evaluate whether exposure to PBDEs, at the levels studied, is associated with adverse health effects. FSANZ carried out an independent review of the epidemiological data assessed by JECFA and concurred with JECFA's conclusions.

EFSA reviewed available epidemiological studies considering associations between PBDE exposure and hyperthyroidism, neurodevelopmental effects, cancer, diabetes and metabolic syndrome, and effects on fertility or offspring (EFSA, 2011a). EFSA noted that while a number of studies had suggested an association between PBDE exposure and clinical or subclinical hyperthyroidism, two studies had shown associations with hypothyroidism. Similar inconsistency was seen with studies of other adverse effects.

Studies in rats and mice have shown that PBDEs cause neurotoxicity, developmental neurotoxicity, reproductive toxicity, thyroid toxicity, immunotoxicity, liver toxicity, pancreas effects (diabetes) and cancer (pentaBDE and decaBDE) (EFSA, 2011a; USEPA, 2017).

2.1.2 Hazard characterisation (dose-response)

JECFA concluded that the available data on PBDEs were not adequate to derive a TDI or other HBGV. EFSA also concluded that deficiencies in the toxicological database meant that it was inappropriate to derive a HBGV.

EFSA derived $BMDL_{10}$ (lower 95th percentile confidence limit for a 10% change in the selected benchmark effect) estimates for four congeners (EFSA, 2011a). Because of differences in the half-life of the congeners between rodents and humans (except BDE-209), the $BMDL_{10}$s were equated to a body burden that was then equated to a human chronic dietary exposure, used as an exposure benchmark. For BDE-47, -99, -153 and -209 the

associated $BMDL_{10}$s were 172, 4.2, 9.6 and 1,700,000 ng/kg bw/day, respectively. The critical toxicological effect used to derive these values was decreased total activity[3] in rodents.

USEPA has derived chronic oral reference doses (RfDs) for BDE-47, -99, -153 and -209 of 100, 100, 200 and 7000 ng/kg bw/day (USEPA, 2017). The RfDs were based on benchmark doses for neurobehavioural effects in mice, with the benchmark response being a one standard deviation difference in the response variable compared to controls. An uncertainty factor of 3000 was applied.

2.1.3 Exposure assessment

Occurrence - New Zealand

PBDEs have been detected in marine sediments from the Auckland region, with total PBDE concentrations in the range 0.6-573 μg/kg (dry weight basis) (Stewart *et al.*, 2014). The predominant congener was the decabrominated BDE-209, accounting for approximately 93% of total PBDEs.

PBDEs were analysed in two consecutive 24-hour composite wastewater discharge samples from the Omaha WWTP, north of Auckland (Stewart, 2016). Three marker PBDEs were detected in the wastewater; BDE-209 (0.23 ng/L), BDE-99 (0.016 ng/L) and BDE-47 (0.027 ng/L).

Exposure assessment

Two sets of New Zealand data on concentrations of PBDEs are available (Stewart *et al.*, 2014; Stewart, 2016). The data on PBDEs in marine sediments are difficult to interpret in terms of human health as there is no obvious mechanism for humans ingesting marine sediments. With respect to the data relating to the Omaha wastewater discharge, a highly conservative exposure assessment can be carried out assuming swimming at the point of discharge, with minimal dilution of the discharged wastewater. That is, the concentration of PBDEs in recreational water is assumed to be the same as the concentration in discharged wastewater.

No information is available on dermal absorption of PBDEs in humans and little information is available from animal studies (JECFA, 2006; USEPA, 2008a; b; d). The limited information suggests that dermal absorption is considerably less than gastrointestinal absorption and decreases with increasing congener bromination. Due to this paucity of data and indications of negligible dermal absorption of PBDEs, the current exposure assessment considered only oral ingestion.

Exposure to PBDEs from ingestion of water during swimming was assessed as outlined in section 1.3.5. No New Zealand data were available on PBDEs in shellfish; to provide a basis for exposure assessment.

Table 3 summarises the exposure assessment for the three detected PBDEs for a child swimming at the point of effluent discharge. It should be noted that these three compounds were the PBDEs detected at the highest mean concentrations in the serum of a representative cohort of New Zealanders ('t Mannetje *et al.*, 2013).

[3] The authors of the toxicological studies define total activity as all types of vibration within the cage, including those caused by mouse movements, shaking (tremors) and grooming

Table 3. Estimated exposure to BDE-47, -99 and -209 for a child swimming adjacent to a wastewater discharge

	BDE-47	BDE-99	BDE-209
Concentration of PBDE (ng/L)	0.027	0.016	0.23
Child mean water ingestion rate (mL/hr)	23.9		
Child mean swim duration (hrs)	1.1		
Child mean body weight (kg)	20		
Estimated exposure (ng/kg bw/event)	**3.5×10^{-5}**	**2.1×10^{-5}**	**3.0×10^{-4}**

PBDE: polybrominated diphenyl ether

2.1.4 Risk characterisation

Table 4 summarises the MOE risk characterisation and comparison of exposure estimates to the USEPA RfDs for the three detected PBDEs for a child swimming at the point of effluent discharge.

Table 4. Risk characterisation for BDE-47, -99 and -209 for a child swimming adjacent to a wastewater discharge

	BDE-47	BDE-99	BDE-209
Estimated exposure (ng/kg bw/event)	3.5×10^{-5}	2.1×10^{-5}	3.0×10^{-4}
Risk characterisation			
POD (BMD, ng/kg bw/day)	172	4.2	1,700,000
MOE (BMD/estimated exposure)	**4.9×10^{6}**	**2.0×10^{5}**	**5.7×10^{9}**
HBGV (RfD, ng/kg bw/day)	100	100	7000
RI (Estimated exposure as %RfD)	**3.5×10^{-5}**	**2.1×10^{-5}**	**4.3×10^{-6}**

POD: point of departure, BMD: benchmark dose, MOE: margin of exposure, Health-based guidance value, RfD: reference dose, RI: risk index

For non-genotoxic effects, such as those use to derive the benchmark doses for PBDEs, a MOE of greater than 100-1000 is usually considered to indicate a negligible level of risk. The very high MOEs (10^5-10^9) derived in Table 4 for exposure of a child to PBDEs during swimming in discharge wastewater-affected water and the very conservative assumptions made concerning PBDE concentrations in recreational waters suggests that PBDEs in discharged wastewater in New Zealand are unlikely to represent a human health risk. The comparison of exposure estimates to RfDs similarly indicates a very low level of risk with exposures representing <0.0001% of the respective RfDs.

JECFA and EFSA used a MOE approach to assess estimates of human dietary exposure against rodent benchmark doses (EFSA, 2011a; JECFA, 2007). Of the congeners considered, EFSA concluded that only exposure to BDE-99 represented a potential health concern. JECFA concluded that “there appeared to be a large margin of exposure (MOE) for a non-genotoxic compound, which, despite the inadequacy of the data on toxicity and intake, gave reassurance that intakes of PBDEs are not likely to be a significant health concern”.

FSANZ have assessed dietary exposure to PBDEs for the Australian population (FSANZ, 2007). Dietary exposure was estimated for the sum of PBDE congeners, although BDE-47, -99 and -209 were the predominant congeners detected in foods analysed in the FSANZ study. Mean estimates of dietary exposure for 2-5 years children (the closest group to the population group used for the current study) were in the range 60-2900 ng/day or 3-145 ng/kg bw/day for a 20 kg child. The low end of this exposure range is approximately 10,000-fold higher than the sum of the exposures estimated in the current study, suggesting that exposure to PBDEs from environmental contact is likely to be negligible compared to dietary exposure.

2.2 PHOSPHORUS FLAME RETARDANTS

Since the phasing out of BFRs, phosphorus flame retardants (PFRs) have been proposed as alternatives (van der Veen and de Boer, 2012). Three main groups of PFRs have been produced; organic (organophosphate esters, phosphonates and phosphinates), inorganic (mainly red phosphorus and ammonium polyphosphate) and halogen-containing. PFRs may also enter the environment due to their use as plasticisers.

Three PFRs have been proposed as part of environmental monitoring for EOCs in New Zealand; tris[2-chloro-1-(chloromethyl)ethyl]phosphate (TDCPP), triphenylphosphate (TPhP) and tris(1-chloro-2-propyl)phosphate (TCPP) (Stewart *et al.*, 2016). TPhP is an organophosphate ester, while the other two PFRs are classified as halogen-containing PFRs. However, analytical work carried out to date in New Zealand has considered a different range of PFRs; tributylphosphate (TBP), tris(isobutyl)phosphate (TiBP) and tris(2-ethylhexyl)phosphate (TEHP).

2.2.1 Hazard identification

Summary toxicological documents for some PFRs have been produced by USEPA and under the Environmental Health Criteria (EHC) and the Organisation for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) programmes (IPCS, 1990; 1991; 1998; 2000; UNEP, 1998; 2000; 2004; 2006; USEPA, 1985).

With respect to human health, these various assessments have noted:

- Skin, eye and respiratory irritation effects, although not reported for all studies (IPCS, 2000; UNEP, 2006; USEPA, 1985)
- Workers in a TDCPP manufacturing plant “had a 2-fold increase in the prevalence of "abnormal" electrocardiograms, but fewer exposed workers had a history of heart disease. There were no significant differences in any of the clinical chemistry parameters investigated. The prevalence of minor respiratory disease was slightly increased in exposed workers. The results of the study did not reveal any significantly increased morbidity in workers exposed to TDCPP” (IPCS, 1998)

There has been speculation concerning the neurotoxicity of PFRs, due to their structural similarities to organophosphate insecticides, however, animal studies have found no evidence of delayed neurotoxicity (IPCS, 1998; UNEP, 2000; 2006) or changes in cholinesterase activity (IPCS, 2000).

A review of the toxicity of various PFRs concluded there was some evidence of greater toxicity associated with halogen-containing PFRs (e.g. TCPP, TCEP and TDCPP), with some animal studies reporting neurotoxicity, mutagenicity, carcinogenicity and reproductive effects (van der Veen and de Boer, 2012). However, findings of different studies are by no means consistent.

2.2.2 Hazard characterisation (dose-response)

Most assessments carried out have not derived HBGVs for PFRs, individually or collectively.

The US Agency for Toxic Substances and Disease Registry (ATSDR) assessed PFRs and derived oral minimal risk levels (MRLs) for some PFRs (ATSDR, 2012). For PFRs detected in New Zealand, these included:

- TBP; acute duration (14 days or less) 1.1 mg/kg bw/day, intermediate duration (15-364 days) and chronic duration (365 days or more) 0.08 mg/kg bw/day. The MRLs were based on; reduced body weight gain in pregnant rats for acute and urinary bladder lesions in male rats for intermediate and chronic.
- TiBP; no MRLs set due to insufficient information

- TEHP; not considered

2.2.3 Exposure assessment

Occurrence - New Zealand

Assessment of EOCs in effluent from the Omaha WWTP, north of Auckland, included analyses for three organic PFRs; TiBP, TBP and TEHP (Stewart, 2016). These three compounds were detected in Omaha WWTP effluent at mean concentrations of 0.028, 0.039 and <0.0002 μg/L (28, 39 and <0.2 ng/L), respectively. Concentrations of TiBP and TBP were more than two orders of magnitude greater than the concentration of the most abundant PBDE (BDE-209), detected in the same effluent.

Occurrence - Australia

A halogen-containing PFR (tris(2-chloroethyl)phosphate; TCEP) was detected in effluent from WWTPs in Victoria (Allinson *et al.*, 2012). A wider range of PFRs were detected in WWTP influent to 11 plants across Australia (O'Brien *et al.*, 2015). The highest concentrations were detected for the organic PFR, tris(2-butoxyethyl)phosphate (TBEP), with a range of 0.4-6.6 μg/L (median 4.4 μg/L), followed by TCPP (range 0.5-4.1, median 2.5 μg/L) and TBP (range 1.1-1.6, median 1.4 μg/L). TCEP and TDCPP were detected at concentrations below 1 μg/L.

Five PFRs; TBP, TCEP, TCPP, TPhP and TDCPP, were detected in water from chlorinated indoor swimming pools at concentrations in the range 0.005-0.027, 0.007-0.29, 0.06-1.2, 0.008-0.13 and 0.01-0.67 μg/L, respectively (Teo *et al.*, 2016). Analysis of source waters suggested that they were not the source of the PFRs.

Exposure assessment

TBP is the only PFR detected in the New Zealand environment for which a HBGV could be identified. It was also the PFR present at the highest concentration in Omaha WWTP wastewater discharge. A highly conservative exposure assessment was carried out based on a scenario of swimming at the point of wastewater discharge and an associated assumption of minimal dilution of PFRs at the swimming location.

Very little information is available on dermal absorption of PFRs (ATSDR, 2012). While a rat study indicated that about half of an applied dose of radiolabelled TBP remained associated with the rat body, studies with minipigs suggest that the majority of the retained dose was associated with the dosing site. No information was available on the rate of PFR dermal absorption and the current exposure assessment considered only oral ingestion.

Exposure to TBP from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 5 summarises the exposure assessment for TBP for a child swimming at the point of effluent discharge.

No New Zealand data were available on PFRs in shellfish; to provide a basis for exposure assessment.

Table 5. Estimated exposure to TBP for a child swimming adjacent to a wastewater discharge

	TBP
Concentration of TBP (ng/L)	39
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**0.051**

TBP: tri-n-butyl phosphate

2.2.4 Risk characterisation

Table 6 summarises the risk characterisation for TBP for a child swimming at the point of effluent discharge.

Table 6. Risk characterisation for TBP for a child swimming adjacent to a wastewater discharge

	TBP
Estimated exposure (ng/kg bw/event)	0.051
Risk characterisation	
HBGV (MRL, ng/kg bw/day)	80,000
RI (Estimated exposure as %MRL)	**6.4×10^{-5}**

TBP: tri-n-butyl phosphate, HBGV: health-based guidance value, MRL: minimal risk level, RI: risk index

The very low proportion of the MRL (<0.0001%) represented by the estimated exposure to TBP for a child swimming in discharged wastewater-affect water and the very conservative assumptions made concerning TBP concentrations in recreational waters suggests that TBP in discharged wastewater in New Zealand is unlikely to represent a human health risk.

A human exposure assessment to PFRs from ingestion of indoor dust was reported in the scientific literature, but the study only included estimates for TPhP and diphenylphosphate (DPhP), but not TBP (Björnsdotter *et al.*, 2018).

3. PLASTICISERS

3.1 PHTHALATES

Phthalates are chemicals which are added to plastics to impart or improve flexibility to the polymer matrix. They are frequently added to polyvinyl chloride (PVC) plastics. As an additive to PVC plastics, phthalates are found in many everyday household objects, including recreational items and children's toys (ATSDR, 2002). Phthalates are not chemically bound into the polymer of the plastic in which they are additives and they can be released from the matrix into the surrounding environment by a number of physical and chemical mechanisms, throughout the life of the object.

3.1.1 Hazard identification

Phthalates have usually been assessed individually. At least some of the phthalates have been assessed in a food context by JECFA (JECFA, 1989) and EFSA (EFSA, 2005a; b; c; d; e). Other organisations to assess phthalates include ATSDR (ATSDR, 1997; 2001; 2002), the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNAS, 2010; 2012; 2013; 2015), the US National Toxicology Program Center for the Evaluation of Risks to Human Reproduction (CERHR) (NTP-CERHR, 2003a; b; 2006), the European Chemical Bureau (European Chemical Bureau, 2003b; c; 2004; 2007; 2008a), the US Consumer Product Safety Commission (CPSC) Chronic Hazard Advisory Panel (CHAP) (2014) and the US Food And Drug Administration (USFDA) (2000).

The most recent of these assessments concluded that the epidemiological evidence "suggests that phthalate exposure during gestation may contribute to reduced AGD[4] and neurobehavioral effects in male infants or children. Other limited studies suggest that adult phthalate exposure may be associated with poor sperm quality. The AGD effects are consistent with the phthalate syndrome in rats. However, it is important to note that the phthalates for which associations were reported were not always consistent and differed across publications. In some cases, adverse effects in humans were associated with diethyl phthalate exposure, although diethyl phthalate does not cause the phthalate syndrome in rats. None of these studies was designed to provide information on the specific sources of phthalate exposure or on the proportional contribution of exposure sources to body burden" (CHAP, 2014).

Available epidemiological studies could probably be described as being of moderate strength. Studies were either cross-sectional or prospective birth cohort studies, with cohort sizes ranging from about 30 to more than 600. While most of the studies defined phthalate exposure in terms of a single urinary analysis, the studies were generally consistent in their findings with respect to male reproductive tract development or neurobehavioural outcomes.

3.1.2 Hazard characterisation (dose-response)

CHAP arrived at consensus NOAELs for each phthalate, which were used as the basis for MOE calculations (CHAP, 2014). For the phthalates included in environmental analyses in New Zealand the NOAELs were 50 mg/kg bw/day (BBP; butylbenzylphthalate) and 5 mg/kg bw/day (DEHP; di(2-ethylhexyl)phthalate). Both NOAELs were based on developmental effects in male laboratory animals. The effects were decreased anogenital distance and increased nipple retention for BBP and reproductive tract malformation and decrease spermatocytes and spermatids for DEHP.

[4] Anogenital distance

3.1.3 Exposure assessment

Occurrence - New Zealand

A survey of EOCs in marine estuarine sediments in the Auckland region included analyses for seven phthalates (Stewart *et al.*, 2014). Two phthalates; DEHP and BBP were detected in sediment samples from 4/14 and 2/14 sites, respectively. Concentrations were in the range 2100-11,500 μg/kg dry weight and 560-1600 μg/kg dry weight, respectively.

DEHP and BBP were not detected in wastewater discharged from the Omaha WWTP, north of Auckland (Stewart, 2016), however, this may have been due to high limits of detection (LODs) for these analyses (50 and 1 ng/L, respectively).

Exposure assessment

Two sets of New Zealand data on concentrations of phthalates are available (Stewart *et al.*, 2014; Stewart, 2016). The data on phthalates in marine sediments are difficult to interpret in terms of human health as there is no obvious mechanism for humans ingesting marine sediments. Phthalates were not detected in Omaha wastewater discharge, however, limits of detection can be used to define upper bound concentrations for phthalates and allow a highly conservative risk assessment to be conducted, based on a scenario of swimming at the point of discharge and an associated assumption of minimal dilution of wastewater in the swimming environment.

Dermal absorption of phthalates has been reported to be substantially lower than gastrointestinal absorption, with dermal absorption increasing with increasing side-chain length (NICNAS, 2008). A single study was found that reported a dermal absorption rate for DEHP (Deisinger *et al.*, 1998). However, the absorbed dose included material that remained at the application site. The current exposure assessment only considered oral ingestion of phthalates.

Exposure to phthalates from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 7 summarises the exposure assessment for BBP and DEHP for a child swimming at the point of effluent discharge.

No New Zealand data were available on phthalates in shellfish; to provide a basis for exposure assessment.

Table 7. Estimated exposure to BBP and DEHP for a child swimming adjacent to a wastewater discharge

	BBP	DEHP
Concentration of phthalate (ng/L)[a]	1	50
Child mean water ingestion rate (mL/hr)	23.9	
Child mean swim duration (hrs)	1.1	
Child mean body weight (kg)	20	
Estimated exposure (ng/kg bw/event)	**1.3×10^{-3}**	**0.065**

BBP: benzylbutyl phthalate, DEHP: di(ethylhexyl) phthalate

[a] Concentration values are the limits of detection for Omaha WWTP effluent

3.1.4 Risk characterisation

Table 8 summarises the MOE risk characterisation for BBP and DEHP for a child swimming at the point of effluent discharge.

Table 8. Risk characterisation for BBP and DEHP for a child swimming adjacent to a wastewater discharge

	BBP	DEHP
Estimated exposure (ng/kg bw/event)	1.3×10^{-3}	0.065
Risk characterisation		
POD (NOAEL, ng/kg bw/day)	50,000,000	5,000,000
MOE (NOAEL/estimated exposure)	**3.8×10^{10}**	**7.6×10^{7}**

BBP: benzylbutyl phthalate, DEHP: di(ethylhexyl) phthalate, POD: point of departure, NOAEL: No observed adverse effect level, MOE: margin of exposure

For non-genotoxic effects, such as those use to derive the NOAELs for phthalates, a MOE of greater than 100-1000 is usually considered to indicate a negligible level of risk. The very high MOEs (10^7-10^{10}) derived in Table 8 for a child's exposure to phthalates during swimming in discharged wastewater-affected water and the very conservative assumptions made concerning phthalate concentrations in recreational waters suggests that phthalates in discharged wastewater in New Zealand are unlikely to represent a human health risk.

In a study carried out in Norway, exposure was estimated for phthalates from a range of exposure routes, but not swimming (Giovanoulis *et al.*, 2018). Mean total exposure to BBP and DEHP was estimated to be 0.16 and 0.84 μg/kg bw/day (160 and 840 ng/kg bw/day), respectively. Exposure was predominantly from dietary sources. The exposures estimated in the current study are at least 10,000-fold lower than the total exposure estimates in the Norwegian study.

3.2 BISPHENOL A

Bisphenol A (BPA) can enter the food chain from its use in lacquers of food cans and in polycarbonate food containers. BPA is also used in the manufacture of plastics, in particular polycarbonates used in contact with foods. Polycarbonates are used to make baby feeding bottles, water jugs, jugs, beakers and microwave ovenware.

BPA is classed as an endocrine disrupting chemical (EDC) due to its structural similarity to 17β-estradiol and its ability to activate the estrogen receptor.

3.2.1 Hazard identification

BPA has been assessed by regulatory bodies on a number of occasions (AIST, 2007; ANSES, 2011; EFSA, 2006; 2008a; 2010; 2015a; European Chemical Bureau, 2003a; 2008b; Health Canada, 2008; 2012; NTP-CERHR, 2008; SCF, 2002; USFDA, 2008). The EFSA (2015a) assessment is the most recent and considered potentially health effects of BPA in relation to:

- General toxicity
- Reproductive and developmental effects
- Neurological, neurodevelopmental and neuroendocrine effects
- Immune effects
- Cardiovascular effects
- Metabolic effects
- Mutagenicity
- Carcinogenicity
- Proliferative and morphological changes potentially related to carcinogenesis
- Mechanistic studies with BPA including epigenetic effects

EFSA adopted a weight of evidence approach, considering both human and animal studies and available mechanistic information. The weight of evidence for a causal relationship between BPA exposure and these various toxicological endpoints was considered to be 'less than likely' for all endpoints except general toxicological effects on the liver and kidneys and proliferative changes in the mammary gland.

3.2.2 Hazard characterisation (dose-response)

Based on general toxicological effects on the kidney in a two-generation mouse study, EFSA established a temporary tolerable daily intake (*t*-TDI) of 4 μg/kg bw/day.

EFSA also considered evidence for claims that BPA may exhibit a non-monotonic dose-response relationship for some endpoints. That is, a greater response at a low dose than at a higher dose, resulting in an inflection in the dose-response relationship (non-monotonic). EFSA concluded that there was no evidence of non-monotonic dose-response relationships for the endpoints where a causal relationship was considered likely.

A large chronic (2-year) rat study is currently nearing completion under the US National Toxicology Program (NTP), which is expected to provide further clarification on aspects of BPA toxicity.

3.2.3 Exposure assessment

Occurrence - New Zealand

In a study carried out in Whakaraupo (Lyttelton) Harbour, Canterbury, BPA was detected in effluent discharged into the harbour (32/33 samples, 3.7-165 ng/L), harbour seawater (33/57 samples, <1.3-5.2 ng/L), and marine sediments (13/28 samples, <0.4-9.9 μg/kg dry weight) (Emnet, 2013). While green-lipped mussels (*Perna canaliculus*) samples were collected and analysed, matrix effects precluded determination of BPA.

BPA was detected in all water samples from the Waikato river (8/8 samples, 0.8-4.3 ng/L) (Tremblay and Northcott, 2013).

Analyses of influents to 13 New Zealand WWTPs detected BPA at a mean concentration of 41 ng/L (maximum 199 ng/L) (Tremblay *et al.*, 2013). BPA was also detected in effluent from the Omaha WWTP, north of Auckland, at a mean concentration of 3.6 ng/L (Stewart, 2016).

A study of marine sediments in the Auckland region detected BPA in 3/13 sediments at concentrations in the range 50-145 μg/kg dry weight (Stewart *et al.*, 2014).

A study of the coastal environment of Antarctica associated with two research bases, including the New Zealand base (Scott Base), detected BPA in effluent from wastewater treatment plants and coastal water and sea ice (Emnet *et al.*, 2015).

Exposure assessment

Unlike many of the other EOCs considered in this report, data are available on the concentrations of BPA in the receiving environment (Whakaraupo harbour and the Waikato river). The highest concentration of BPA detected in these two studies was 5.2 ng/L in Whakaraupo harbour (Emnet, 2013). This concentration was used to conduct a conservative exposure assessment, based on a scenario of swimming in a receiving environment containing this level of BPA (Table 9).

EFSA considered dermal exposure to BPA due to handling thermal paper or through the application of cosmetics (EFSA, 2015a). These situations differ from that during swimming, as the EFSA scenarios dealt with a fixed and depletable BPA dose, while the swimming scenario involves exposure to an essentially non-depleting concentration of BPA. The EFSA scenarios further assume that the BPA-containing medium remains on the skin for 24 hours. This assumption is clearly not appropriate for a swimming scenario. While there is

insufficient information to assess exposure to BPA from swimming in contaminated water, studies that have considered both oral and dermal exposure to BPA have concluded that dermal exposure is negligible (Demierre *et al.*, 2012) or minor (EFSA, 2015a) compared to oral exposure.

Exposure to BPA from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 9 summarises the exposure assessment for a child swimming in a BPA-affected receiving environment.

No New Zealand data were available on BPA in shellfish; to provide a basis for exposure assessment.

Table 9. Estimated exposure to BPA for a child swimming in an affected receiving environment

	BPA
Concentration of BPA (ng/L)	5.2
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**6.8×10^{-3}**

BPA: bisphenol A

3.2.4 Risk characterisation

Table 10 summarises risk characterisation for a child swimming in a BPA-affected receiving environment. Exposure estimates were compared to the EFSA *t*-TDI of 4 μg/kg bw/day (4000 ng/kg bw/day).

Table 10. Risk characterisation for BPA for a child swimming in an affected receiving environment

	BPA
Estimated exposure (ng/kg bw/event)	6.8×10^{-3}
Risk characterisation	
HBGV (*t*-TDI, ng/kg bw/day)	4,000
RI (Estimated exposure as % of *t*-TDI)	**1.7×10^{-4}**

BPA: bisphenol A, HBGV: health-based guidance value, *t*-TDI: temporary tolerable daily intake, RI: risk index

The estimated exposure to BPA during swimming represents a very small proportion (~0.0002%) of the tolerable daily intake. This suggests that BPA in discharged wastewater are unlikely to represent a human health risk in New Zealand. It should also be noted that the *t*-TDI is a lifelong tolerable daily level of exposure, while the estimate for exposure during swimming is event-based. It is extremely unlikely that any individual would swim in a receiving environment every day for their entire life. Application of an averaging time to account for the non-daily occurrence of swimming would further reduce the already low estimate of risk.

EFSA estimated dietary exposure to BPA for infants (6-12 months), toddlers (12-36 months) and other children (3-10 years) (EFSA, 2015a). Estimates were in the range 290-375 ng/kg bw/day or approximately 50,000-fold higher than the estimates of exposure from swimming in BPA-affected water. A US study estimated total BPA exposure (inhalation, dietary and indirect ingestion) for children to be 1700-2700 ng/day (85-135 ng/kg bw/day for a 20 kg child) (Wilson *et al.*, 2007). The vast majority of exposure was due to dietary ingestion.

4. SURFACTANTS

4.1 NONYLPHENOL

Nonylphenol (NP) is mainly used in the manufacture of nonylphenol ethoxylates (NPEs) and both NP and NPEs are produced in large volumes. NPEs are nonionic surfactants used in a wide range of industrial and consumer products, such as laundry detergents, sanitisers, dust-control agents and deicers. Many uses of NPEs lead to widespread release to the aquatic environment.

NP has been shown to exhibit estrogenic properties in *in vitro* and *in vivo* assays. NP persists in the aquatic environment, bioaccumulates, and is extremely toxic to aquatic organisms, causing a range of adverse effects, such as cell respiratory toxicity and altered calcium transport, in addition to endocrine effects (feminisation of aquatic organisms, decrease in male fertility and reduced survival of juveniles at concentrations as low as 8.2 µg/l) (Soares *et al.*, 2008).

NPEs, though less toxic and persistent than NP, are also highly toxic to aquatic organisms. NPEs are degraded to NP in the environment.[5]

While the following section will primarily focus on NP, where information is available on the related alkylphenol surfactant, octylphenol (OP), this has also been reported. NP and OP may be present in the same product or may be used as alternative compounds for the same purpose.

4.1.1 Hazard identification

Toxicological concerns related to NP and OP are associated with structural similarities to the female sex hormone 17β-estradiol (estrogen). The toxicity of NP was assessed by the California Environmental Protection Agency (CEPA), which concluded that there was sufficient evidence to show that NP causes reproductive effects in laboratory animals, but limited human information was available on possible reproductive effects (CEPA, 2009). There was some evidence for immune system and nervous system effects in laboratory animals, but no evidence of carcinogenicity.

Several recent epidemiological studies have added some additional information on potential human health impacts of NP. However, the ubiquitous nature of NP in the environment means that adequately controlling for confounding exposures in such studies is challenging.

A case-control study of Taiwanese children with attention deficit-hyperactivity disorder (ADHD; *n* = 97) and matched controls (*n* = 110) found no significant difference in urinary NP between the two groups (Yu *et al.*, 2016).

NP was found to be present at higher concentrations in urine of women (*n* = 49) with uterine leiomyoma (benign smooth muscle tumours) than in a control group of women (*n* = 29) (Shen *et al.*, 2013). These differences only applied when considering women with two or less pregnancies. When all women were considered, urinary NP concentrations were higher in the control group (Zhou *et al.*, 2013). No differences in plasma concentrations of NP were seen between the two groups.

Urinary NP was compared between couples who had experienced spontaneous abortion (*n* = 70) and control couples (*n* = 180) with no history of spontaneous abortion (Chen *et al.*,

[5] https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/nonylphenol-and-nonylphenol-ethoxylates Accessed 20 December 2016

2013b). A higher, but non-significant odds ratio was seen for women who had experienced spontaneous abortion and had high urinary NP, compared to those with low NP. For total alkylphenols, the odds ratio was statistically significant. No differences in abortion risk were seen between low and high urinary NP male partners.

No significant difference was seen in plasma NP in children experiencing precocious puberty (early onset of puberty) compared to controls (normal onset of puberty) (Yum *et al.*, 2013).

Urinary NP was compared between men with idiopathic infertility (*n* = 877) and fertile controls (*n* = 713) (Chen *et al.*, 2013a). Cases with low sperm concentrations or low numbers of sperm per ejaculate were significantly more likely to have high urinary NP. No significant differences were seen for semen volume.

4.1.2 Hazard characterisation (dose-response)

NP and NPEs were assessed by the Danish Veterinary and Food Administration (Nielsen *et al.*, 2000). A TDI of 5 μg/kg bw/day was derived for NP, based on a lowest observed adverse effect level (LOAEL) of 15 mg/kg bw/day for reproductive and developmental effects in a three-generation rat study. A TDI of 13 μg/kg bw/day was also derived for NPEs, based on a LOAEL of 40 mg/kg bw/day for cardiotoxicity in dogs. It should be noted that these TDIs include an extra safety factor of 30 due to use of a LOAEL, rather than a NOAEL.

4.1.3 Exposure assessment

Occurrence - New Zealand

In a study carried out in Whakaraupo (Lyttelton) Harbour, Canterbury, OP, but not NP, was detected in wastewater discharged into the harbour (30/33 samples, 3.0-206 ng/L), harbour seawater (8/57 samples, <0.2-0.8 ng/L), and marine sediments (14/28 samples, 0.2-2.5 μg/kg dry weight) (Emnet, 2013). Similarly, OP, but not NP, was detected in green-lipped mussels (*Perna canaliculus*) samples (7/9 samples, 0.5-1.9 μg/kg wet weight).

Similarly, OP (1/8 sample, 0.11 ng/L), but not NP, was detected in water samples from the Waikato river (Tremblay and Northcott, 2013).

A study of marine sediments in the Auckland region detected NP in 11/13 sediments at concentrations in the range 110-32,000 μg/kg dry weight (Stewart *et al.*, 2014). The very high NP concentrations were found at the Puketutu Island site. This was an open estuarine site and was the previous location of decommissioned and remediated oxidation ponds of Auckland's major WWTP. NPEs were also detected at 7/13 sites (concentration range 100-1600 μg/kg). NP was also detected in effluent from the Omaha WWTP, north of Auckland, at a mean concentration of 0.28 μg/L (Stewart, 2016).

A study of the coastal environment of Antarctica associated with two research bases, including the New Zealand base (Scott Base), did not detect NP in effluent from wastewater treatment plants, coastal water or sea ice (Emnet *et al.*, 2015). NP was not reported from analyses of marine biota (clams, urchins and fish). However, the study reported some matrix issues with biota analyses and it is unclear whether this compromised the ability to detect NP. It should be noted that the related surfactant, OP, was detected in effluent, seawater, sea ice and fish.

Exposure assessment

Several New Zealand studies have failed to detect NP in discharged wastewater or the receiving environment. Analysis of wastewater discharged from the Omaha WWTP detected NP at a concentration of 0.28 μg/L (280 ng/L). A highly conservative exposure assessment was carried out based on a scenario of swimming at the point of wastewater discharge.

No information is available on dermal absorption of NP in humans and little information is available from *in vitro* studies (Moody *et al.*, 2010; Nielsen *et al.*, 2000). Due to this paucity of data, the current exposure assessment considered only oral ingestion.

Exposure to NP from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 11 summarises the exposure assessment for NP for a child swimming at the point of wastewater discharge.

No New Zealand data were available on NP in shellfish; to provide a basis for exposure assessment.

Table 11. Estimated exposure to NP for a child swimming adjacent to a wastewater discharge

	NP
Concentration of NP (ng/L)	280
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**0.37**

NP: nonylphenol

4.1.4 Risk characterisation

Table 12 summarises the risk characterisation for NP for a child swimming at the point of wastewater discharge. Exposure estimates were compared to the DEPA TDI of 5 μg/kg bw/day (5000 ng/kg bw/day).

Table 12. Risk characterisation for NP for a child swimming adjacent to a wastewater discharge

	NP
Estimated exposure (ng/kg bw/event)	0.37
Risk characterisation	
HBGV (TDI, ng/kg bw/day)	5000
RI (Estimated exposure as % of TDI)	**0.007**

NP: nonylphenol, HBGV: health-based guidance value, TDI: tolerable daily intake, RI: risk index

The very low proportion of the TDI (<0.01%) represented by the estimated exposure for a child swimming in discharged wastewater-affected water and the very conservative assumptions made concerning NP concentrations in recreational waters suggests that NP in discharged wastewater is unlikely to represent a human health risk in New Zealand.

A summary of dietary exposures to NP reported exposures in the range 43-520 ng/kg bw/day (Niu *et al.*, 2015). These estimates are approximately 100-1400-fold higher than the estimated exposure to NP from swimming, derived in the current study.

4.2 LINEAR ALKYLBENZENE SULPHONATE (LAS)

LASs are common anionic surfactants in commercial detergents (Sáez *et al.*, 2000). LASs occur with differing alkyl chain lengths (IPCS, 1996).

4.2.1 Hazard identification

The toxicity of LAS has been reviewed, but not recently (IPCS, 1996).

Acute oral toxicity of LAS is low, with LD_{50}s in the range 400-3400 mg/kg bw (IPCS, 1996). Minimal effects on the liver were seen in subchronic rodent studies following oral administration. Reproductive effects were seen following both oral and dermal administration, but these generally occurred at dose levels where maternal toxicity was also seen (IPCS, 1996). LAS are mild skin irritants in humans.

4.2.2 Hazard characterisation (dose-response)

No HBGVs have been derived for LAS.

4.2.3 Exposure assessment

Occurrence - New Zealand

No information was found on concentrations of LAS in wastewater discharges or the receiving environment in New Zealand.

Exposure assessment

No New Zealand data on LAS in wastewater or the receiving environment are available as a basis for exposure assessment.

4.2.4 Risk characterisation

In addition to the lack of data on which to base an exposure assessment, no HBGVs have been derived for LAS, to allow characterisation of risks.

5. PERFLUORINATED COMPOUNDS

Perfluorinated or perfluoroalkylated substances (PFASs) are highly fluorinated aliphatic compounds with high thermal and chemical stability, as well as high surface activity. PFASs are used in a range of industrial and chemical applications, including textiles, paper, packaging materials, paints and varnishes, and fire-extinguishing liquids (EFSA, 2012). Several PFASs are recognised as environmentally persistent organic pollutants. The diet, including drinking water, is considered the main source of exposure to PFASs. Primary international interest has focussed on perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA).

5.1 HAZARD IDENTIFICATION

Lipid and thyroid hormone effects have been reported in studies of humans occupationally exposed to PFOS (EFSA, 2008b). However, thyroid hormone (T_3) levels increased in humans occupationally exposed to PFOS, while in laboratory animal studies (Cynomolgus monkeys) T_3 levels decreased. There is some evidence of an increased risk of bladder cancer in workers occupationally exposure to PFOS, although the study reporting a significantly increased risk was based on only three bladder cancer cases. The study was further complicated as workers were also exposed to other chemicals.

Subsequent epidemiological studies have focussed on cancer, reproductive and neurobehavioural (e.g. attention deficit hyperactivity disorder) endpoints. Reproductive and neurobehavioural studies have generally not shown significant associations between PFOS body burden and the selected endpoints. Studies of cancer incidence and/or mortality have only been carried out in occupationally exposed cohorts. While some studies have found significant associations between PFOS or PFOA exposure and cancer endpoints, reassessment of several studies demonstrated that exposure was not well defined and reanalysis of the data did not result in significant associations.

ATSDR have reviewed information related to PFAS and concluded that there are consistent findings for associations of serum PFOA and PFOS with increases in serum lipid levels, decreases in birth weight, increases in uric acid levels, and alterations in biomarkers of liver damage (ATSDR, 2015). Evidence for an association with cancer endpoints was considered to be equivocal.

The German Bundesinstitut für Risikobewertung (BfR) considered the health risks from PFOS and PFOA in foods and concluded that “based on the latest scientific findings available, a health risk from the dietary intake of PFOS and PFOA is unlikely in conjunction with the levels in foods detected up to now” (BfR, 2008).

5.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

The Australian Department of Health have developed HBGVs for PFAS, to facilitate assessment of contamination incidents.[6] The HBGVs developed included TDIs of 0.02 μg/kg bw/day for PFOS and perfluorohexane sulfonate (PFHxS) and 0.16 μg/kg bw/day for PFOA. Additionally, drinking-water guideline levels of 0.07 and 0.56 μg/L (70 and 560 ng/L) were developed for PFOS/PFHxS and PFOA respectively and recreational water guidelines of 0.7 and 5.6 μg/L (700 and 5600 ng/L), respectively. The drinking-water guideline concentrations have been adopted as interim maximum acceptable values by the New Zealand Ministry of

[6] http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-pfas-hbgv.htm Accessed 9 February 2018

Health.[7] The TDI for PFOS was based on the NOAEL for decreased parental and offspring body weights in a reproductive toxicity study in rats, while the TDI for PFOA was based the NOAEL for foetal toxicity in a developmental and reproductive toxicity study in mice.

PFOS and PFOA have been considered by EFSA (EFSA, 2008b). A TDI of 0.15 μg/kg bw/day was established for PFOS. The TDI was derived from the NOAEL in a subchronic study in Cynomolgus monkeys, with lipid (HDL) and thyroid hormone effects seen at doses above the NOAEL.

EFSA derived a TDI of 1.5 μg/kg bw/day for PFOA, based on the NOAEL for a subchronic study in rats, with hepatocellular hypertrophy and increased liver weight seen at doses above the NOAEL. As for PFOS, the epidemiological evidence for adverse effects in humans due to exposure to PFOA are neither strong nor consistent.

ATSDR concluded that it was not possible to derive MRLs for PFAS from human epidemiological data (ATSDR, 2015). ATSDR derived intermediate duration (14-365 days) MRLs for PFOS and PFOA of 0.03 and 0.02 μg/kg bw/day, respectively. For both compounds, the MRL was based on increases in liver weight in animal studies.

5.3 EXPOSURE ASSESSMENT

5.3.1 Occurrence - New Zealand

No information was found on PFAS in New Zealand wastewater or the receiving environment.

PFAS have been detected in New Zealand groundwater, at the Ohakea and Woodbourne air bases.[8] PFAS were detected in 41 of 93 (44%) groundwater samples, with 7 of 93 (8%) containing concentrations above the interim drinking-water guidelines (0.07 and 0.56 μg/L for PFOS/PFHxS and PFOA, respectively). However, these contamination incidents appear to be due to the particular issue of use of PFAS-containing firefighting materials at these locations. The concentrations observed in these groundwater samples were not considered suitable for an assessment of human exposure to PFAS from the general receiving environment.

5.3.2 Exposure assessment

No information is available on PFAS in wastewater or the receiving environment in New Zealand.

5.4 RISK CHARACTERISATION

In the absence of New Zealand-specific information to enable assessment of exposure, it is not possible to characterise the risks to New Zealanders from environmental contact with PFAS.

[7] http://www.health.govt.nz/news-media/news-items/health-working-defence-legacy-fire-fighting-foam-chemicals Accessed 9 February 2018

[8] http://www.mfe.govt.nz/more/hazards/hazardous-substances/pfas/pfospfoa-nz Accessed 13 March 2018

6. MUSK FRAGRANCES

Musk fragrances (MFs) are polycyclic compounds used as a component of the fragrances in detergents, fabric softeners, cleaning agents, and cosmetic products such as soaps, shampoo and perfumes (Duedahl-Olesen *et al.*, 2005). In Europe, one compound accounts for about three-quarters of the total market; 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl-cyclopenta(c)-2-benzopyran abbreviated as HHCB and commercially known as galaxolide. Another compound, 6-acetyl-1,1,2,4,4,7-hexamethyl-tetralin abbreviated as AHTN (tonalide) is also a common component of fragrances.

6.1 HAZARD IDENTIFICATION

The MFs have not been assessed by EFSA or JECFA. The only assessments found were conducted by the European Chemicals Agency (ECHA). ECHA has carried out risk assessments for HHCB (ECHA, 2008a) and AHTN (ECHA, 2008b). The risk assessment documents summarised *in vitro*, animal and human information on adverse effects. With respect to human acute toxicity, dermal irritation and photoirritation, eye irritation, sensitisation and photosensitisation, repeated dose toxicity, carcinogenicity, and reproductive and developmental toxicity, there was either no information or the available information suggested no toxicity.

For HHCB, no consistent dose-related adverse effects were seen in 90-day repeated dose study in rats. In a developmental toxicity study, skeletal malformations were observed in foetuses, but only at dose levels above those at which maternal toxicity was observed.

A similar 90-day study carried out on AHTN showed dose-related haemotoxicity in the two highest dose groups.

6.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

For HHCB, ECHA identified a 90-day oral rat study as the pivotal study. This study reported no adverse effects at the highest dose administered and ECHA proposed this dose as a NOAEL of 150 mg/kg bw/day.

For AHTN, ECHA identified a lowest NOAEL, for a 90-day rat study, of 5 mg/kg bw/day. The effects seen at the LOAEL (15 mg/kg bw/day) were described as marginal. The effects included changes in blood biochemistry (increased prothrombin time and albumin/globulin ratio, decreased cholesterol, triglycerides and glucose) and haematology (decreased red blood cell count and total protein, increased packed cell volume and mean cell haemoglobin)

Trabalón *et al.* (2015) used these NOAELs and an uncertainty factor of 100 to derive provisional TDIs for HHCB and AHTN of 1500 and 50 μg/kg bw/day.

6.3 EXPOSURE ASSESSMENT

6.3.1 Occurrence - New Zealand

Analysis of the wastewater discharge from the Omaha WWTP, north of Auckland, detected HHCB and AHTN at mean concentrations of 60 and 1 ng/L, respectively (Stewart, 2016).

6.3.2 Occurrence - Australia

Analysis of effluent at a water recycling plant in Sydney found HHCB and AHTN to be the MFs present at the highest concentrations (2545 and 301 ng/L, respectively) (Wang and Khan, 2014). Other MFs were detected, but at considerably lower concentrations. Only HHCB and AHTN were detected in treated effluent, at concentrations of 21 and 2 ng/L, respectively.

In a study near Adelaide, a wetland area was used to remediate stormwater prior to using the water to recharge an aquifer (Page *et al.*, 2014). HHCB was detected using passive sampling at the aquifer injection sites, but not in water abstracted from the aquifer.

6.3.3 Exposure assessment

Only a single set of New Zealand data on concentrations of MFs is available (Stewart, 2016). MF concentrations in Omaha wastewater discharge were used to conduct a conservative exposure assessment, based on a scenario of swimming at the point of wastewater discharge, with an associated assumption of minimal dilution in the swimming environment.

While it has been suggested that dermal absorption of MFs, from use of personal care products, is the major human route of exposure (Lampard *et al.*, 2010), trials on human volunteers, conducted under good laboratory practice (GLP), indicated negligible dermal absorption of MFs (ECHA, 2008a; b). Based on these observations, the current exposure assessment only considered oral ingestion.

Exposure to MFs from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 13 summarises the exposure assessment for HHCB and AHTN for a child swimming at the point of wastewater discharge.

No New Zealand data were available on MFs in shellfish; to provide a basis for exposure assessment.

Table 13. Estimated exposure to HHCB and AHTN for a child swimming adjacent to a wastewater discharge

	HHCB	AHTN
Concentration of musk fragrance (ng/L)	60	1
Child mean water ingestion rate (mL/hr)	23.9	
Child mean swim duration (hrs)	1.1	
Child mean body weight (kg)	20	
Estimated exposure (ng/kg bw/event)	**0.079**	**0.0013**

HHCB: 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl- cyclopenta(c)-2-benzopyran (galaxolide), AHTN: 6-acetyl-1,1,2,4,4,7-hexamethyl-tetralin (tonalide)

6.4 RISK CHARACTERISATION

Table 14 summarises the risk characterisation for HHCB and AHTN for a child swimming at the point of wastewater discharge. The provisional TDIs derived by Trabalón *et al.* (2015) were used as the relevant HBGVs.

Table 14. Risk characterisation for HHCB and AHTN for a child swimming adjacent to a wastewater discharge

	HHCB	AHTN
Estimated exposure (ng/kg bw/event)	0.079	0.0013
Risk characterisation		
HBGV (Provisional TDI, ng/kg bw/day)	1,500,000	50,000
RI (Estimated exposure as % of TDI)	**5.3×10^{-6}**	**2.6×10^{-6}**

HHCB: 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl- cyclopenta(c)-2-benzopyran (galaxolide), AHTN: 6-acetyl-1,1,2,4,4,7-hexamethyl-tetralin (tonalide), HBGV: Health-based guidance value, TDI: tolerable daily intake, RI: risk index

The very low estimates of exposure relative to the provisional TDIs (<0.00001%) and the very conservative assumptions made concerning MF concentrations in recreational waters suggests that MFs in discharged wastewater are unlikely to represent a human health risk in New Zealand.

A Spanish study estimated dietary exposure to HHCB and AHTN from consumption of seafood (Trabalón *et al.*, 2015). Mean estimated dietary exposures were 20 and 3.7 ng/kg bw/day, respectively. These dietary estimates are approximately 250 and 2800-fold higher than exposure estimates due to swimming, derived from the current study.

A more recent Europe-wide study of dietary exposure to musk fragrances from seafood consumption derived lower estimates of dietary exposure to HHCB and AHTN than the Spanish study, of 3.4 and 1.9 ng/kg bw/day (Cunha *et al.*, 2018).

7. PESTICIDES

Trends in pesticide usage in the last 20-30 years have seen a move to active substances with lower environmental persistence. Organochlorine and organophosphorus insecticides have been displaced by synthetic pyrethroid and neonicotinamide insecticides. This period has also seen the near ubiquitous adoption of herbicides based on the active ingredient glyphosate. The following sections are mainly concerned with these 'newer' pesticides, rather than the older 'legacy' pesticides. In particular, information is presented on the marker pesticides proposed by Stewart *et al.* (2016); glyphosate, imidacloprid (neonicotinamide), bifenthrin and permethrin (synthetic pyrethroids)

Some pesticides are also used as antifouling agents (e.g. diuron, isoproturon) and these substances are addressed separately in section 13 of this report.

7.1 HAZARD IDENTIFICATION

The synthetic pyrethroid and neonicotinamide insecticides and the herbicide, glyphosate, have all been assessed by a range of expert bodies. Due to the very different modes of action, they need to be considered separately with respect to their toxicity.

7.1.1 Synthetic pyrethroids

Pyrethroids can be structurally divided either on the basis of age or the presence of an α-cyano group (USEPA, 2011). Older pyrethroids were based on chrysanthemic acid and characterised by a cyclopropane ring, bonded to a carboxylic acid moiety and a variety of halogenated and non-halogenated substituents. More recent pyrethroids do not have the cyclopropane ring structure. Pyrethroids without a α-cyano group are usually referred to as Type I pyrethroids, while those with the α-cyano group are referred to as Type II pyrethroids. The pyrethroids proposed for monitoring in the New Zealand environment (Stewart *et al.*, 2016), permethrin and bifenthrin, are both older type I pyrethroids.

USEPA considered the modes of action of the various pyrethroids and pyrethrins and concluded that they all share a common mode of action; interaction with voltage-gated sodium channels (VGSCs) in nerve tissues (USEPA, 2011). Pyrethroids delay the inactivation of affected VGSCs, allowing for an increase in sodium ion influx and resulting in delayed repolarisation. The delay is greater due to Type II pyrethroids (>>200 ms) than for the Type I pyrethroids (~20 ms). Mixed-Type pyrethroids (e.g. esfenvalerate and fenpropathrin) produce delays intermediate between the Type I and Type II pyrethroids.

Synthetic pyrethroid poisoning in humans is not uncommonly, but general relates to individuals involved in pesticides application (Osimitz *et al.*, 2009). Gastrointestinal, ocular, dermal and neurological symptoms were most commonly reported in these cases.

7.1.2 Neonicotinamides – imidacloprid

Imidacloprid has been assessed by EFSA (EFSA, 2013) and JMPR (JMPR, 2001). USEPA are in the process of carrying out registration review of imidacloprid and the human health risk assessment was due for completion in March 2017.[9] However, at 15 February 2018, an

[9] https://www.regulations.gov/contentStreamer?documentId=EPA-HQ-OPP-2008-0844-1089&contentType=pdf Accessed 21 April 2017

ecological risk assessment for imidacloprid, but not a human health risk assessment was available for public comment, with the comment period closing on 21 April 2018.[10]

In vitro studies suggest that imidacloprid may adversely affect developing mammalian nervous systems, through excitation and/or desensitisation of nicotinic acetylcholine receptors (EFSA, 2013). The available evidence was reviewed by EFSA. It was concluded that while imidacloprid may affect neuronal development, considerable uncertainties remain.

Reduced body weight gain was the most sensitive adverse effect seen in long-term rat studies, while effects on the liver and thyroid were also seen (JMPR, 2001). Developmental effects were noted in studies in rats (increased incidence of wavy ribs) and rabbits (retarded ossification), but only at maternally toxic doses.

7.1.3 Glyphosate

Adverse human health effects have been reported following accidental or intentional ingestion of concentrated glyphosate formulations (Lake, 2014). In such cases, symptoms have included gastrointestinal, cardiovascular, pulmonary and renal effects, sometimes resulting in death. It has been suggested that many of the adverse effects seen with ingestion of glyphosate formulations may be due to the surfactants present in these formulations.

Reviews of epidemiological studies examining associations between glyphosate exposure and a wide range of cancer and non-cancer endpoints found no evidence of a consistent pattern of positive associations indicative of a causal relationship (Mink *et al.*, 2011; Mink *et al.*, 2012).

In animal studies, hypertrophy and cytoplasmic alterations of the salivary glands was a common and sensitive effect seen (JMPR, 2006). Developmental toxicity was seen, but only at doses eliciting maternal toxicity.

There is currently contrasting scientific opinions on the carcinogenic potential of glyphosate.

The International Agency for Research on Cancer (IARC) assessed glyphosate and glyphosate formulations and concluded that glyphosate was 'probably carcinogenic to humans' (Group 2A) (Guyton *et al.*, 2015).

This assessment was reviewed by EFSA, which concluded that "glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential" (EFSA, 2015b). The toxicology of glyphosate was also recently reviewed by four expert panels, convened by Intertek Scientific and Regulatory Consultancy (Intertek, Mississauga, Ontario, Canada) and commissioned by the Monsanto Company. With respect to genetic toxicology, it was concluded that:

"The overall weight of evidence from the genetic toxicology data supports a conclusion that glyphosate (including GBFs and AMPA[11]) does not pose a genotoxic hazard and therefore, should not be considered support for the classification of glyphosate as a genotoxic carcinogen. The assessment of the epidemiological data found that the data do not support a causal relationship between glyphosate exposure and non-Hodgkin's lymphoma while the data were judged to be too sparse to assess a potential relationship between glyphosate exposure and multiple myeloma. As a result, following the review of the totality of the evidence, the Panels concluded that the data do not support IARC's conclusion

[10] https://www.epa.gov/pesticides/epa-extends-comment-period-neonicotinoid-risk-assessments Accessed 19 April 2018

[11] GBFs are glyphosate-based formulation and AMPA is aminomethylphosphonic acid, the major degradation product of glyphosate

that glyphosate is a “probable human carcinogen” and, consistent with previous regulatory assessments, further concluded that glyphosate is unlikely to pose a carcinogenic risk to humans” (Williams *et al.*, 2016).

The evidence for the carcinogenicity of glyphosate was also reviewed for the New Zealand Environmental Protection Authority, in light of the IARC assessment (Temple, 2016). The review concluded that “based on a weight of evidence approach, taking into account the quality and reliability of the available data – glyphosate is unlikely to be genotoxic or carcinogenic to humans and does not require classification under HSNO as a carcinogen or mutagen”.

7.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

7.2.1 Synthetic pyrethroids

USEPA derived oral relative potency factors (RPFs) for a range of pyrethroids, relative to deltamethrin. The potency of bifenthrin was determined to be near identical to that of deltamethrin (1.01), while the potency of permethrin is only about 10% that of deltamethrin (0.09). USEPA derived an index POD for deltamethrin of 11 mg/kg bw/day for acute neurotoxicity due to alterations of the VGSC, with a target MOE of 300 for young children and 100 for the balance of the population. The POD, target MOE and RPFs suggest ADIs for bifenthrin of 0.1 mg/kg bw/day for adults and 0.04 mg/kg bw/day for children. For permethrin, the implied ADIs are 1.2 and 0.4 mg/kg bw/day for adults and children, respectively.

The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) assessed bifenthrin most recently in 2009 and derived an ADI of 0-0.01 mg/kg bw and an acute reference dose (ARfD) of 0.01 mg/kg bw, based on developmental and neurological effects in rats (JMPR, 2011). Permethrin has been assessed a number of times, most recently in 2002, when an ADI of 0-0.05 mg/kg bw was confirmed and an ARfD of 1.5 mg/kg bw was derived (Inchem, 2006).

EFSA assessed bifenthrin in 2011 and derived an ADI of 0.015 mg/kg bw/day, based on neurotoxicity in a 1-year dog study, and an ARfD of 0.03 mg/kg bw, based on neurotoxicity in a 90-day rat study (EFSA, 2011b). EFSA have assessed permethrin separately as a pesticide and as a veterinary medicine, leading to the derivation of two different ADIs; 0.05 and 0.01 mg/kg bw/day, respectively (EFSA, 2016). These ADIs are derived from the same toxicological study, but with application of different uncertainty factors. No ARfD was set for permethrin by EFSA.

7.2.2 Neonicotinamides – imidacloprid

JMPR derived an ADI of 0-0.06 mg/kg bw, based on the NOAEL for reduced weight gain and liver and thyroid effects in a 2-year rat study (JMPR, 2001). An ARfD of 0.4 mg/kg bw was derived, based on acute neurotoxicity in rats. EFSA derived the same ADI for imidacloprid of 0.06 mg/kg bw/day, based on thyroid effects in a chronic rat study (EFSA, 2013). Developmental neurotoxicological effects were also seen with similar NOAELs in sub-chronic dog studies. Based on these studies an ARfD was set at the same value as the ADI.

7.2.3 Glyphosate

Glyphosate was last assessed by JMPR in 2004 (JMPR, 2006). An ADI of 0-1.0 mg/kg bw was set, based on the NOAEL for salivary gland alterations in a long-term study of toxicity and carcinogenicity in rats. Setting an ARfD was considered to be unnecessary.

EFSA set a slightly lower ADI of 0.5 mg/kg bw/day, based on the NOAEL for maternal and developmental toxicity in rabbits (EFSA, 2015b). The same NOAEL was used to derive an ARfD with the same value.

7.3 EXPOSURE ASSESSMENT

7.3.1 Occurrence - New Zealand

Analysis of marine sediments from the Auckland region did not detect residues of any of the 109 pesticides analysed for (Stewart *et al.*, 2014).

Analysis of the wastewater discharge from the Omaha WWTP, north of Auckland, did not detect the pesticides, chlorpyriphos, bifenthrin and permethrin (Stewart, 2016). However, the LODs (1-5 μg/L) for these analyses, while appropriate for analysis of food commodities, were not sufficiently sensitive for analysis of water/wastewater samples.

7.3.2 Exposure assessment

No concentration data on the selected pesticides in the New Zealand receiving environment or in discharged wastewater were available on which to base an exposure assessment. Given the high LODs for analyses carried out at the Omaha WWTP, it was considered inappropriate to carry out an upper bound estimate of exposure based on these LODs.

7.4 RISK CHARACTERISATION

Due to the inability to estimate exposure to any of the target pesticide from contact with the receiving environment, no risk characterisation was possible.

8. PHARMACEUTICAL RESIDUES

Human pharmaceuticals may enter the environment in discharges from manufacturing facilities, due to disposal of expired or unwanted prescriptions or due to excretion by individuals receiving medication. Common human pharmaceuticals include, amongst others, antibiotics, anti-depressants, analgesics/anti-inflammatories particularly non-steroidal anti-inflammatory drugs (NSAIDS), anti-epilepsy medication and anti-hypertensive drugs.

8.1 HAZARD IDENTIFICATION

While all substances are toxic at some level, the pharmaceutical compounds considered in this section have primarily been developed for administration to human subjects. The very small amounts of pharmaceutical compounds that will be ingested during environmental contact is likely to be very much lower than the amounts ingested during medication. For example, the maximum recommended dose for ibuprofen for pain relief is 3200 mg/day. A study carried out in China detected ibuprofen in carp at a concentration of 48 μg/kg dry weight (Xie *et al.*, 2015). Assuming carp contains about 20% moisture and assuming a daily fish intake of 100 g/day, the daily intake of ibuprofen from fish consumption would be about 1 μg/day or less than one millionth of the dose used for pain relief.

However, pharmacological doses apply to situations of intended ingestion, whereas the presence of pharmaceuticals in the receiving environment may result in unintended ingestion. In such circumstance there is unlikely to be any benefits associated with human exposure, while the low levels of risk associated with these compounds must still be considered.

8.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

Studies of risks due to the presence of pharmaceuticals in drinking-water have derived HBGVs, either from minimum inhibitory concentrations (MICs) of antimicrobials against gut microflora, lowest therapeutic doses, or NOAELs from animal studies (Bruce *et al.*, 2010; de Jesus Gaffney *et al.*, 2015; Khan and Nicell, 2015; Leung *et al.*, 2013; Schriks *et al.*, 2010; Schwab *et al.*, 2005; Sorell, 2016). Table 15 lists literature HBGVs and the basis for the HBGV for pharmaceuticals detected in the New Zealand receiving environment (Gielen, 2007; Stewart, 2016).

Table 15. Derived HBGVs for pharmaceuticals detected in the New Zealand receiving environment

Pharmaceutical	HBGV (μg/kg bw/day)	Basis for HBGV	Reference
Acetominophen	50	Acceptable daily intake, based on pharmacological lowest observed effect level for reduction in pyrexia (fever) in human infants (5 mg/kg bw, UF = 100)	(Khan and Nicell, 2015)
Amitriptyline	0.1	Occupational exposure limit	(Khan and Nicell, 2015)
Caffeine	150	Developmental effects in rats (cleft palate) exposed during gestation	(Leung *et al.*, 2013)
Carbamazepine	0.3	Carcinogenicity (hepatocellular tumours in	(Bruce *et al.*, 2010)

Pharmaceutical	HBGV (μg/kg bw/day)	Basis for HBGV	Reference
		females and benign testicular tumours in males) in rats (maximum tolerated dose = 250 mg/kg bw/day, UF = 740,000)	
Diclofenac	67	No observable effects in gestationally-exposed mice (NOAEL = 20 mg/kg bw/day, UF = 300)	(Bruce *et al.*, 2010)
Diltiazem	14	Lowest therapeutic dose (30 mg, UF = 30, BW = 70 kg)	(Schwab *et al.*, 2005)
Ibuprofen	110	Lowest therapeutic dose (200 mg, UF = 27, BW = 70 kg)	(Schwab *et al.*, 2005)
Naproxen	46	Reproductive/developmental effects in rats	(de Jesus Gaffney *et al.*, 2015)

UF: uncertainty factor, BW: body weight

The approach of Khan and Nicell (2015) of using occupational exposure limits (acute concentrations) to derive chronic exposure limits appears somewhat questionable and for amitriptyline further data were sought on which to base exposure limits.

Amitriptyline. The European Medicines Agency (EMA) assessment of amitriptyline reported that teratogenic effects were not observed in mice, rats, or rabbits when amitriptyline was given orally at doses of 2-40 mg/kg bw/day. However, studies in the literature have shown amitriptyline to be teratogenic in mice and hamsters when given by various routes of administration at doses of 28-100 mg/kg bw/day, producing multiple malformations. A rat study reported that an oral dose of 25 mg/kg bw/day produced delays in ossification of foetal vertebral bodies without other signs of embryotoxicity. In rabbits, an oral dose of 60 mg/kg/day was reported to cause incomplete ossification of the cranial bones (EMA, 2017). Considering 25 mg/kg bw/day as the LOAEL for teratogenic effects, uncertainty factors were applied including; extrapolation from LOAEL to NOAEL (x3), inter-species extrapolation (x10), intra-species variability (x10) and an additional factor, as the quality of the referenced studies is unknown (x10). The resulting ADI would be 8 μg/kg bw/day.

8.3 EXPOSURE ASSESSMENT

8.3.1 Occurrence - New Zealand

Analysis of wastewater from the Rotorua WWTP detected a range of pharmaceuticals, including (in decreasing concentration order) naproxen (analgesic), carbamazepine (nervous system), diltiazem (cardiovascular), ibuprofen (analgesic), amitriptyline (anti-depressant) (Gielen, 2007). Caffeine and 17α-ethinylestradiol (EE2) were also detected. However, EE2 is considered separately, in the section on steroid estrogens (section 9). The mean concentrations of these compounds in wastewater ranged from 30 ng/L (amitriptyline) to 990 ng/L (naproxen). Chlorpromazine, thioridazine and salicylic acid were analysed for, but were not detected.

A somewhat different profile of pharmaceuticals was found in marine sediments in the Auckland region (Stewart *et al.*, 2014). The analgesics, acetaminophen and naproxen were detected at mean concentrations of 7.5 and 5.5 μg/kg, respectively. All other pharmaceuticals were present at mean concentrations of 2 μg/kg or less, with those

detected, in descending concentration order, including metoprolol (cardiovascular), diclofenac (analgesic), fenofibrate (cardiovascular), clarithromycin (antibiotic), roxythromycin (antibiotic), ranitidine (alimentary tract), cimetidine (alimentary tract), and sotalol (coronary).

Analyses of EOCs in effluent from the Omaha WWTP, north of Auckland, only considered three analgesics (Stewart, 2016). These were detected at concentrations of 145 (ibuprofen), 51 (diclofenac) and 6 (acetaminophen) ng/L.

8.3.2 Exposure assessment

No information is available on concentrations of pharmaceuticals in the New Zealand receiving environment. However, information is available on pharmaceuticals in wastewater discharges and a highly conservative risk assessment can be carried out by assuming swimming at the point of wastewater discharge, with no dilution. This allows wastewater concentrations to be used as a proxy for concentrations in the receiving environment (Gielen, 2007; Stewart, 2016). Useable concentration data and a HBGV are available for all pharmaceuticals detected in wastewater in New Zealand.

No information was found on dermal absorption for detected pharmaceuticals and the exposure assessment was only carried out for oral ingestion during swimming.

Exposure to pharmaceuticals from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 16 summarises the exposure assessment for pharmaceuticals for a child swimming at the point of effluent discharge.

No New Zealand data were available on pharmaceuticals in shellfish; to provide a basis for exposure assessment.

Table 16. Estimated exposure to pharmaceuticals for a child swimming adjacent to a wastewater discharge

	Acetominophen	**Amitriptyline**	**Caffeine**	**Carbamazepine**	**Diclofenac**	**Diltiazem**	**Ibuprofen**	**Naproxen**
Concentration of pharmaceutical (ng/L)	6	29.5	109	709	51	133	145	987
Child mean water ingestion rate (mL/hr)	23.9							
Child mean swim duration (hrs)	1.1							
Child mean body weight (kg)	20							
Estimated exposure (ng/kg bw/event)	**7.9×10^{-3}**	**0.039**	**0.14**	**0.93**	**0.067**	**0.17**	**0.19**	**1.3**

8.4 RISK CHARACTERISATION

Table 17 summarises the risk characterisation for pharmaceuticals for a child swimming at the point of effluent discharge.

Table 17. Risk characterisation for pharmaceuticals for a child swimming adjacent to a wastewater discharge

	Acetominophen	Amitriptyline	Caffeine	Carbamazepine	Diclofenac	Diltiazem	Ibuprofen	Naproxen
Estimated exposure (ng/kg bw/event)	7.9×10^{-3}	0.039	0.14	0.93	0.067	0.17	0.19	1.3
Risk characterisation								
HBGV (ng/kg bw/day)	50,000	8000	150,000	300	67,000	14,000	110,000	46,000
RI (Estimated exposure as %HBGV)	**1.6×10^{-5}**	**4.9×10^{-4}**	**9.3×10^{-5}**	**0.31**	**1.0×10^{-4}**	**1.2×10^{-3}**	**1.7×10^{-4}**	**2.8×10^{-3}**

HBGV: health-based guidance value, RI: risk index

Estimates of exposure to selected pharmaceuticals discharged into the New Zealand environment are well below HBGVs. Given the conservative assumptions included in the exposure estimates and the fact that swimming is highly unlikely to be a daily event, pharmaceuticals in the New Zealand receiving environment are unlikely to represent a risk to human health.

9. STEROID ESTROGENS

Steroid estrogens are biologically active compounds produced and excreted by humans and animals. Domestic and livestock waste are therefore the main sources of steroid hormones to the environment. The main steroid estrogens are estrone (E1), 17β-estradiol (E2), estriol (E3), and the synthetic birth control ingredient 17α-ethinylestradiol (EE2). E1 has been proposed as an appropriate marker estrogenic compound for environmental monitoring (Stewart *et al.*, 2016).

9.1 HAZARD IDENTIFICATION

Steroid estrogens are important components of the human endocrine system, affecting developmental and physiological processes. Levels of steroid estrogens are under homeostatic control and, to a certain extent, the human body can manage exposure to endogenous sources of steroid estrogens (WHO, 2013). However, it has been suggested that exposure to exogenous sources of steroid estrogens (or other chemicals with estrogenic activity) may interfere with normal hormonal processes, leading to adverse health effects. Such chemicals are collectively known as endocrine disrupting chemicals (EDCs). In the context of the current report, steroid estrogens should be considered as potential EDCs.

The potential for estrogenic chemicals to cause adverse effects in humans was demonstrated in the case of diethylstilbestrol (DES), a powerful synthetic estrogen used during 1940-1970 to prevent miscarriage and other pregnancy complications (WHO, 2013). Maternal DES exposure was shown to result in a rare form of vaginal cancer in a small proportion of female offspring and more frequent occurrence of other reproductive problems in females exposed *in utero*, such as reproductive tract malformations and dysfunction, miscarriage, preterm delivery, low birth weight, ectopic pregnancies, and premature labour and births. However, it should be noted that the estrogenic doses received in the case of DES were huge compared to environmental exposures.

Exposure to the estrogenic EDCs has been implicated in effects on female and male reproductive organ development and reproductive performance, hormone-related cancers (e.g. breast, ovary, prostate), metabolic disorders (e.g. diabetes) and effects on the immune system (WHO, 2013).

The WHO ‘state of the science’ report (WHO, 2013) concluded *inter alia* that:

- There is limited and conflicting evidence for a role for EDC in female and male reproductive tract disorders
- There is evidence of gender ratio imbalances (less male offspring produced) due to EDCs in humans and animals
- While a role for environmental estrogens in causation of hormone-related cancers is plausible, currently the evidence of associations is weak and complicated by the fact that most studies have been retrospective, with the associated problems of defining exposure to estrogenic compounds at the time the cancers were initiated
- There is limited and insufficient evidence for a role for environmental estrogens in causation of metabolic disorders
- There is good epidemiological evidence linking some EDCs (e.g. PCBs) to immune system disorders.

9.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

E2 was assessed as a veterinary drug at the fifty-second meeting of JECFA (JECFA, 2000). An ADI of 0-50 ng/kg bw was established on the basis of changes in several hormone-dependent parameters in post-menopausal women.

9.3 EXPOSURE ASSESSMENT

It should be noted that a large number of studies reviewed considered estrogenicity, measured in receptor-based bioassays, rather than the concentration of individual steroid estrogens. As bioassays of estrogenicity will also include contributions from xenobiotic compounds with estrogenic activity, such as alkylphenols, the results of such studies have not been presented here.

9.3.1 Occurrence - New Zealand

In a study of effluent discharged into Whakaraupo (Lyttelton) Harbour, E1 was the most commonly detected steroid estrogen (27/33 samples), with concentrations in the range 2.1-114 ng/L (Emnet, 2013). E2, E3 and EE2 were detected in 4, 7, and 1 sample(s), respectively, with concentrations not exceeding 19 ng/L for any compound. E1 was less frequently detected in seawater and marine sediments and only at concentrations below the limit of quantification (LOQ). E2 and E3 were occasionally detected, while EE2 was not detected in any seawater or sediment samples. While E2, E3 and EE2 could be satisfactorily analysed in green-lipped mussels, they were not detected.

Analyses of dairy shed effluent in New Zealand included the same range of steroids plus 17α-estradiol (αE2), the dominant form excreted by cattle, and several metabolites of the steroids (Gadd *et al.*, 2010). The steroid αE2 was detected at the highest concentrations (maximum 11,000 ng/L), followed by E1 (maximum 580 ng/L) and E2 (maximum 310).

Another New Zealand study also determined steroid estrogens in farm effluent, including dairy farm effluent (Sarmah *et al.*, 2006). The dominant steroid found in this study was E1 (maximum 3100 ng/L), followed by αE2 (maximum 1028 ng/L) and E2 (330 ng/L). Three municipal WWTP effluents were also analysed, with substantially lower concentrations of E1 (maximum 85 ng/L), E2 (maximum 15 ng/L) and αE2 (maximum 10 ng/L) detected.

Analysis of marine sediments from sites around Auckland did not detect the birth control steroid, EE2, at any site (Stewart *et al.*, 2014). E1 and E2 were detected in about half of the sediment samples analysed, with concentrations in the range 0.7-2.2 μg/kg dry weight and 0.5-1.0 μg/kg dry weight, respectively.

None of the steroid estrogens found in other New Zealand studies (E1, E2, E3, EE2, αE2) were detected in Waikato river water (Tremblay and Northcott, 2013). The analytical limits of detection (LODs) for the study appear to be acceptably low (0.01 or 0.05 ng/L).

As part of the same study, these steroid estrogens were analysed in WWTP effluent from Antarctic research stations (Emnet *et al.*, 2015). The results were similar to those from Whakaraupo Harbour, with E1 the most frequently detected steroid (12/15 samples, 3.1-330 ng/L). E2 and E3 were not detected in any sample, but the birth control steroid, EE2, was detected in one of two sampling seasons, with concentrations in the range 11.5-78 ng/L. Very low levels of steroids were occasionally detected in Antarctic seawater and sea ice. Of the biota analysed (clams, urchins, fish), only E2 and EE2 were detected in clams (0.8-2.0 μg/kg wet weight and 1.5-4.3 μg/kg wet weight, respectively).

9.3.2 Occurrence - Australia

Biosolids were collected from 14 sites across Australia and analysed for a range of personal care products and estrogenic compounds (Langdon *et al.*, 2011). E2, E3 and EE2 were not detected in any sample, while E1 was detected in 6/14 samples at concentrations in the range 0.06-0.28 mg/kg (60-280 μg/kg).

Analysis of influent and intermediate processed effluent from a WWTP in south-east Queensland detected E1 (<LOD-37.5 ng/L) and E2 (<LOD-12.2 ng/L) in raw influent (Tan *et al.*, 2008). Solids or sludge from aerobic, anaerobic or anoxic processing resulted in concentrations of E1 and E2 in the range <LOD-4.5 and <LOD-3.6 μg/kg, respectively.

EE2 was analysed for in effluent from three WWTPs in south-east Queensland and at points up and downstream from the point of discharge into receiving waters (King *et al.*, 2016). Effluents contained EE2 at concentrations in the range 1.5-2.0 ng/L. Surface water sites downstream contained EE2 at concentration of approximately 0.2-0.3 ng/L, while upstream sites still contained detectable concentrations of EE2 (approximately 0.1 ng/L).

Concentrations of E1, E2 and EE2 were determined in influent, effluent and intermediate stages of treatment at three WWTPs (Bain *et al.*, 2014). E1 was the dominant steroid estrogen at all plants, with influent concentrations in the range 70-360 ng/L, while associated effluents contained approximately 2-40 ng/L. E2 and EE2 concentrations were uniformly low, with concentrations not exceeding 20 ng/L at any stage in any WWTP.

Effluents from 45 WWTPs in Victoria were examined for E1, E2 and EE2 (Allinson *et al.*, 2010). The highest concentrations of the three estrogenic species were 18.4, 18.5 and 0.6 ng/L, respectively.

Effluent discharged from 12 WWTPs in Victoria contained E2, with concentrations in the range 1.3-18 ng/L (Mispagel *et al.*, 2009).

Steroid estrogens (E1, E2, αE2, E3, EE2) were determined in river waters (n = 285) from sites around Australia (Scott *et al.*, 2014). E2 and E3 were not detected in any water samples, irrespective of the land use of the land adjoining the river. The bovine steroid, αE2 was detected in a single river water sample from an agricultural environment (4 ng/L). E1 was detected in 78/285 (27%) samples. E1 was most frequently detected in river water samples taken adjacent to WWTPs and residential areas (32% of each sample type), with maximum concentrations of 22 and 57 ng/L, respectively. EE2 was detected in 28/285 (10%) samples, with highest detection rates in rivers adjacent to agricultural land, industrial land and WWTPs (10-12.5% of samples). Concentrations of EE2 in river water were uniformly low (<0.2 ng/L).

9.3.3 Exposure assessment

Two studies have determined steroid estrogens in New Zealand receiving waters. No steroid estrogens were detected in Waikato river water (Tremblay and Northcott, 2013). E1, E2 and E3, but not EE2 were occasionally detected in Whakaraupo harbour water, although at concentrations below the LOQ (Emnet, 2013). For a screening level risk assessment, it was assumed that E1, E2 and E3 were present in recreational waters at concentrations equal to the LOQs in the study of Emnet (2013) (7, 0.4 and 2.1 ng/L, respectively). Using relative estrogenic potencies of 0.1, 1.0 and 0.038 (Chen *et al.*, 2014) for E1, E2 and E3 a composite concentration of 1.2 ng/L E2 equivalents can be derived. A conservative risk assessment, based on a scenario of swimming in a receiving environment containing this concentration of E2 was conducted.

Information on dermal absorption of steroid estrogens was not found. Consequently, the current exposure assessment only considered oral exposure.

Exposure to steroid estrogens from ingestion of water during swimming was assessed as outlined in section 1.3.5. Table 18 summarises the exposure assessment for E2 equivalents for a child swimming in an affected receiving environment.

No New Zealand data were available on steroid estrogens in shellfish; to provide a basis for exposure assessment.

Table 18. Estimated exposure to E2 equivalents for a child swimming in an affected receiving environment

	E2 equivalents
Concentration of E2 equivalents (ng/L)	1.2
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**0.0016**

E2: 17β-estradiol

9.4 RISK CHARACTERISATION

Table 19 summarises the risk characterisation for E2 equivalents for a child swimming in an affected receiving environment. The ADI for E2 was used as the HBGV.

Table 19. Risk characterisation for E2 equivalents for a child swimming in an affected receiving environment

	E2 equivalents
Estimated exposure (ng/kg bw/event)	0.0016
Risk characterisation	
HBGV (Provisional TDI, ng/kg bw/day)	50
RI (Estimated exposure as % of TDI)	**0.003**

E2: 17β-estradiol, HBGV: health-based guidance value, TDI: tolerable daily intake, RI: risk index

The very low estimates of exposure relative to the ADI (0.003%) and the very conservative assumptions made concerning steroid estrogen concentrations in recreational waters suggests that steroid estrogens in discharged wastewater are unlikely to represent a human health risk in New Zealand.

An estimate of dietary exposure to xenoestrogens[12] for New Zealand children reported a cumulative exposure across a range of compounds of 1.2 μg/day of E2 equivalents or 60 ng/kg bw/day for a 20 kg child (Cressey *et al.*, 2001). It should be noted that this estimate did not include contributions from E1, E2 and E3 that may be present in foods of animal origin. The estimate of dietary exposure to E2 equivalents is about 37,500-fold higher than the estimate of exposure to E2 equivalents from swimming, derived in the current study.

[12] Xenoestrogens is a term referring to a range of natural and synthetic substances that exhibit estrogenic activity, although generally at considerably lower potency than 17β-estradiol

10. TRICLOSAN AND METHYL TRICLOSAN

Triclosan (TCS) is an antibacterial and antifungal agent found in consumer products, including toothpaste, soaps, detergents and toys, and in surgical cleaning treatments. TCS may be partially transformed to methyl-triclosan (Me-TCS) during wastewater treatment.

10.1 HAZARD IDENTIFICATION

TCS has been assessed by USEPA as part of the Reregistration Eligibility Decision (RED) (USEPA, 2008c). No evidence from human studies or case reports was included in the assessment.

A small case-control study of subfertile Belgian males (*n* = 40 cases, *n* = 80 controls) found no association between reduced fertility parameters and serum TCS (Den Hond *et al.*, 2015). TCS was significantly associated with a 1.2% increase in levels of luteinising hormone and a 1.4% decrease in levels of inhibin B.

A systematic review of epidemiological studies on TCS concluded that "the current body of epidemiologic literature does not allow a meaningful WOE (weight of evidence) assessment due to methodological limitations of individual studies and lack of inter-study consistency" (Goodman *et al.*, 2018).

In animal studies, gastrointestinal, liver and haematological effects were reported (USEPA, 2008c). An increased incidence of hepatocellular adenoma and carcinoma was seen in a long-term mouse study. This was considered to be due to activation of the peroxisome proliferator (PP) receptor, rather than a mutagenic or cytotoxic mode of action. The PP receptor mechanism is not considered to be relevant to humans and TCS was classified as not likely to be carcinogenic to humans. Developmental effects were only seen at maternally toxic doses.

10.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

TCS and/or Me-TCS have not been assessed by JECFA or JMPR. EFSA have assessed TCS as a food contact material (EFSA, 2004b). TCS was assessed as a List 3 substance (Substances for which an ADI or a TDI could not be established, but where the present use could be accepted).

TCS has been assessed by USEPA as part of the Reregistration Eligibility Decision (RED) (USEPA, 2008c). The pivotal study for both acute and chronic effects was judged to be a chronic (one year) toxicity study in baboons. At 100 and 300 mg/kg bw/day dose levels, test animals were observed with signs of vomiting, failure to eat, and diarrhoea, which occurred 4-6 hours after dosing or during the night. At necropsy, an effect on the lining of the stomach was observed at the high dose. The systemic NOAEL was determined to be 30 mg/kg bw/day. An uncertainty factor of 100 was applied to derive a reference dose (RfD) (and an identical ARfD) of 300 μg/kg bw/day.

It should be noted that, although TCS is considered to have endocrine disrupting potential, the critical toxicological study does not appear to be related to this mode of action.

10.3 EXPOSURE ASSESSMENT

10.3.1 Occurrence - New Zealand

In a study carried out in Whakaraupo (Lyttelton) Harbour, Canterbury, TCS was detected in effluent discharged into the harbour (33/33 samples, 14-122 ng/L), but not in harbour seawater or marine sediments (Emnet, 2013). Me-TCS was also detected in effluent (25/33

samples, 2.7-35 ng/L) only. While green-lipped mussels (*Perna canaliculus*) samples were collected and analysed, matrix effects precluded determination of TCS or Me-TCS.

Analysis of marine sediments in the vicinity of Auckland city did not detect TCS at concentrations above the LOQ (100 μg/kg dry weight) (Stewart *et al.*, 2014). However, it was noted that the LOQ needed to be reduced to detect levels of TCS determined in overseas studies. It should be noted that the study of Emnet (2013) also did not detect TCS in marine sediments from Whakaraupo harbour, with a LOD of 0.1 μg/kg wet weight (0.15 μg/kg dry weight).

TCS, but not Me-TCS, was detected in treated wastewater from the Omaha WWTP, north of Auckland, at a concentration of 4 ng/L (Stewart, 2016).

However, in water samples from the Waikato river, Me-TCS (5/8 samples, 0.2-0.5 ng/L), but not TCS, was detected (Tremblay and Northcott, 2013).

Analyses of influents to 13 New Zealand WWTPs detected TCS at a mean concentration of 61 ng/L (maximum 100 ng/L) (Tremblay *et al.*, 2013).

TCS and Me-TCS were frequently detected in effluent from New Zealand's Antarctic research site, Scott Base, with concentrations up to 807 and 43 ng/L, respectively (Emnet *et al.*, 2015). TCS was also less frequently detected in Antarctic seawater at concentrations up to 1.7 ng/L, but was not detected in sea ice.

10.3.2 Occurrence - Australia

TCS was determined in influent and effluent from Australia's largest inland WWTP, near Canberra (Roberts *et al.*, 2016). While TCS concentrations in influent were high (mean 1850 or 3540 ng/L, depending on the season), the WWTP removed 99.8% of the influent TCS. Concentrations of TCS in effluent were approximately 4-5 ng/L. An earlier study reported much higher TCS concentrations in WWTP effluents (23-434 ng/L) and lower removal rates (72-93%) (Kookana *et al.*, 2011).

Mussels (*Mytilus galloprovincialis*) were deployed in cages in the Gulf St Vincent, South Australia at varying distances from two WWTPs (Kookana *et al.*, 2013). After 70 days, mean concentrations in mussels from the various sites fell within quite a narrow range (8.3-11.6 μg/kg for TCS and 4.6-10.2 μg/kg for Me-TCS).

10.3.3 Exposure assessment

Unlike many of the other EOCs considered in this report, analyses have been carried out for TCS and Me-TCS in the receiving environment (Whakaraupo harbour, Waikato river and Antarctic seawater). However, results are inconsistent, with only TCS detected in Antarctic seawater, while only Me-TCS was detected in Waikato river water and neither were detected in Whakaraupo harbour water.

In order to carry out a screening level exposure assessment the following assumptions were made:

- TCS and Me-TCS are of equal human toxicity
- There is potential for humans to be exposed to concentrations of TCS and Me-TCS determined in discharge wastewater
- The maximum concentration of TCS in discharge wastewater to Whakaraupo harbour is equal to the sum of the maximum concentrations of TCS and Me-TCS (157 ng/L)

This concentration was used to conduct a conservative exposure assessment, based on a scenario of swimming in a receiving environment containing the level of TCS equivalents

derived above (Table 20). Exposure to TCS equivalents from ingestion of water during swimming was assessed as outlined in section 1.3.5.

There is sparse and inconsistent evidence concerning the dermal absorption of TCS. Estimates of 9% (Lu *et al.*, 2018) and 48% (USEPA, 2008c) absorption of an applied dose have been reported. However, this information is not applicable to dermal absorption during a swimming event, as the rate at which TCS is absorbed was not reported. Consequently, the current exposure assessment has only considered oral ingestion.

No New Zealand data were available on TCS or Me-TCS in shellfish; to provide a basis for exposure assessment.

Table 20. Estimated exposure to TCS equivalents for a child swimming adjacent to a wastewater discharge

	TCS equivalents
Concentration of TCS (ng/L)	157
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**0.21**

TCS equivalents: The sum of triclosan and methyl triclosan

10.4 RISK CHARACTERISATION

Table 21 summarises risk characterisation for exposure to TCS equivalents for a child from swimming adjacent to a wastewater discharge. Exposure estimates were compared to the USEPA RfD of 300 μg/kg bw/day.

Table 21. Risk characterisation for TCS equivalents for a child swimming adjacent to a wastewater discharge

	TCS equivalents
Estimated exposure (ng/kg bw/event)	0.21
Risk characterisation	
HBGV (RfD, ng/kg bw/day)	300,000
RI (Estimated exposure as % of RfD)	**7.0×10^{-5}**

TCS equivalents: The sum of triclosan and methyl triclosan, HBGV: health-based guidance value, RfD: Reference dose, RI: risk index

The estimated exposure to TCS during swimming represents a very small proportion of the RfD (<0.0001%). This suggests that TCS equivalents in discharged wastewater are unlikely to represent a human health risk in New Zealand. It should also be noted that the RfD is a lifelong tolerable daily level of exposure, while the estimate for exposure during swimming is event-based. It is extremely unlikely that any individual would swim in a receiving environment every day for their entire life. Application of an averaging time to account for the non-daily occurrence of swimming would further reduce the already low estimate of risk.

A Chinese study determined exposure to TCS from swimming in an outdoor swimming pool, including consideration of ingestion and dermal absorption (Lu *et al.*, 2017). Exposure to TCS was estimated to be 0.008 ng/kg bw/event. While this exposure estimate is substantially lower than the current estimate, details of the exposure model were not elaborated in the Chinese study.

A more comparable study assessed exposure to TCS from recreational activities and fish consumption in Minnesota lakes and rivers (Yost *et al.*, 2017). Estimated exposure for a child (<6 years) from surface water ingestion was 0.01 ng/kg bw/day or about 5% of the

current New Zealand estimate. This appears reasonable, considering the highly conservative assumptions adopted in the current study.

A Belgian study estimated that the median exposure to TCS for toddlers from ingestion of household dust was in the range 11-44 ng/day (0.55-2.2 ng/kg bw/day for a 20 kg child) (Geens *et al.*, 2009).

11. PRESERVATIVES - PARABENS

Parabens are a class of preservatives widely used in cosmetic and pharmaceutical products. They are a series of parahydroxybenzoates or esters of parahydroxybenzoic acid (also known as 4-hydroxybenzoic acid). Parabens and their salts are used primarily for their bactericidal and fungicidal properties. They are used in shampoos, moisturisers, shaving gels, personal lubricants, topical/parenteral pharmaceuticals, spray tanning solutions, makeup and toothpaste. They are also used as food additives.

11.1 HAZARD IDENTIFICATION

The EU Scientific Committee on Consumer Products (SCCP) have examined links between paraben use in underarm deodorants and breast cancer (SCCP, 2005). SCCP concluded that "viewing the current knowledge, there is no evidence of demonstrable risk for the development of breast cancer caused by the use of underarm cosmetics"**.**

Epidemiological studies have focused on potential endocrine-disrupting effects of parabens.

Analysis of maternal urinary paraben concentrations and infant birth parameters was carried out for a birth cohort of 1006 mother-infant pairs in Wuhan city, People's Republic of China (Wu *et al.*, 2017). No significant associations were found with respect to birth weight or birth length.

A case-control study of male child urogenital malformations (cryptorchidism and hypospadias) and placental paraben concentrations was nested within a prospective birth cohort of 668 mother-child pairs in southern Spain (Fernández *et al.*, 2016). Mean concentrations of parabens in placental tissue were higher in cases than controls for methyl paraben (Me-PB), ethyl paraben (Et-PB), propyl paraben (Pr-PB) and butyl paraben (Bt-PB). However, a significantly elevated odds ratio for urogenital malformation was only found for Pr-PB at the highest tertile of placental Pr-PB concentration (adjusted OR 6.4, 95th percentile confidence interval 1.2-35.5). It should be noted that this study was quite small (28 cases and 51 controls).

Associations between urinary paraben concentrations and markers of ovarian reserve were examined in a prospective cohort (*n* = 192) of women seeking fertility treatment in Boston, USA (Smith *et al.*, 2013). Reduced fertility is associated with decreases in ovarian reserve, as happens naturally with age. A significant trend in decreasing antral follicle count with increasing urinary Pr-PB concentration was found, but no significant associations were found with 3-day follicle-stimulating hormone levels or ovarian volume. No significant associations were found with urinary Me-PB or Pr-PB.

The same study group examined associations between male urinary paraben concentrations and markers of male fertility (Meeker *et al.*, 2011). While detection rates of parabens were high (100% for Me-PB, 92% for Pr-PB and 32% for Bt-PB), no statistically significant associations were found between Me-PB or Pr-PB and the outcome measures. Categories of urinary Bt-PB concentration were not associated with hormone levels or conventional semen quality parameters, but they were positively associated with sperm DNA damage.

A JECFA evaluation noted a number of human studies, including administration of up to 2 g of paraben for up to 50 days without adverse effects (JECFA, 1974).

11.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

Me-PB, Et-PB and Pr-PB were assessed by JECFA at the 17th Meeting in 1973 (JECFA, 1974). A group ADI of 0-10 mg/kg bw was estimated for the three compounds, based on a

NOAEL of 1000 mg/kg bw/day for reduced growth rate during the early stages of a 96-week study in rats. The initial study was conducted with Me-PB, then confirmed with Et-PB and Pr-PB. Bt-PB was considered at the same meeting, but the absence of any long term toxicological study meant no evaluation could be made.

The 67th Meeting of JECFA reviewed additional information on Pr-PB and concluded that Pr-PB should be excluded from the group ADI due to effects on the tissues of male rat reproductive organs at doses as low as 10 mg/kg bw/day (JECFA, 2007).

EFSA reviewed the available information and reached similar conclusions to JECFA; supporting a group ADI for Me-PB and Et-PB, but concluding that no ADI could be derived for Pr-PB (EFSA, 2004a).

11.3 EXPOSURE ASSESSMENT

11.3.1 Occurrence - New Zealand

Me-PB, but not Et-PB or Bt-PB, was detected in effluent discharged from the Omaha WWTP, situated north of Auckland (Stewart, 2016). Me-PB was present at a concentration of 12 ng/L.

In a study carried out in Whakaraupo (Lyttelton) Harbour, Canterbury, Me-PB was detected in effluent discharged into the harbour (8/33 samples, 0.9-21 ng/L), harbour seawater (51/57 samples, <0.8-9.4 ng/L), and marine sediments (13/28 samples, <0.2-1.7 μg/kg dry weight) (Emnet, 2013). Other parabens were less frequently detected. Et-PB (3/33 samples, 4.0-6.8 ng/L), Pr-PB (1/33 samples, 49 ng/L) and Bt-PB (2/33 samples, 5.9-7.8 ng/L) were detected in effluent samples. However, none of these parabens were detected in marine sediments, while Pr-PB (5/57 sample, <0.8-2.2 ng/L) and Bt-PB (3/57 samples, <0.5-0.9 ng/L) were infrequently detected in seawater and Et-PB was not detected in seawater. Green-lipped mussel (*Perna canaliculus*) samples were collected and analysed, but matrix effects precluded determination of parabens other than Me-PB (9/9 samples, 0.9-4.1 μg/kg wet weight).

Me-PB (5/8 sample, 0.2-0.5 ng/L), Pr-PB (5/8 samples, 0.1-0.3 ng/L) and Bt-PB (2/8 samples, 0.5-0.6 ng/L), but not Et-PB or benzyl paraben, were detected in water samples from the Waikato river (Tremblay and Northcott, 2013).

Analyses of influents to 13 New Zealand WWTPs detected Pr-PB at a mean concentration of 328 ng/L (maximum 696 ng/L) (Tremblay *et al.*, 2013). Other PBs were not considered in this project.

Analysis of effluent from the New Zealand Antarctic research base, Scott Base, infrequently detected Me-PB (23-36 ng/L) and Bt-PB (10-11 ng/L), but not Et-PB and Pr-PB (Emnet *et al.*, 2015). Me-PB was also the paraben most frequently detected in Antarctic seawater (44/58 sample, <0.8-37 ng/L). Bt-PB (7/58, <0.5-2.3 ng/L) and Pr-PB (4/58), <0.8-3.0 ng/L) were detected less frequently, while Et-PB was not detected. No parabens were detected in Antarctic sea ice. Me-PB was also detected in Antarctic marine biota, including clams (<0.4-1.0 μg/kg wet weight), urchins (0.6 μg/kg wet weight) and fish (1.0-6.1 μg/kg wet weight). Pr-PB was detected in clams (0.4-1.9 μg/kg wet weight).

11.3.2 Occurrence - Australia

A study of urban river water and storm water found higher levels of Me-PB in storm water than urban rivers, while the highest peak paraben concentrations were associated with Et-PB (Evans *et al.*, 2016).

11.3.3 Exposure assessment

Unlike most other EOCs considered in this report, New Zealand data are available on parabens to allow consideration of two potential routes of exposure:

- From water ingestion during swimming, and
- From consumption of shellfish

The highest concentration of Me-PB detected in New Zealand receiving waters was 9.4 ng/L (Whakaraupo harbour). While Pr-PB and Bt-PB were also detected in receiving waters, no HBGVs are available to characterise risks. The maximum concentration of Me-PB detected in green-lipped mussels was 4.1 μg/kg.

Dermal absorption of parabens (Bt-PB) has been demonstrated following whole body topical application of a cream to human volunteers (Janjua *et al.*, 2008). On average, 0.32% of the applied Bt-PB was recovered in urine. While this study does demonstrate dermal absorption of Bt-PB, the fact that only urinary excretion was determined means that total absorption and absorption rate cannot be determined. *In vitro* studies suggest substantially higher absorption of Me-PB (Pazourekova *et al.*, 2013). However, these studies are inadequate to estimate dermal absorption of parabens during a swimming event and the current exposure assessment only considered oral ingestion.

Table 22 summarises conservative exposure assessments for two routes of exposure; swimming and consumption of shellfish. While children are most at risk of ingestion of contaminants during swimming, children tend not to be consumers of shellfish and the shellfish route of exposure has been examined for an adult consumer. Exposure to Me-PB from ingestion of water during swimming and consumption of shellfish was assessed as outlined in section 1.3.5.

Table 22. Estimated exposure to Me-PB for a child swimming in an affected receiving environment and for an adult consuming shellfish from an affected receiving environment

	Me-PB
Exposure assessment - swimming	
Concentration of Me-PB, seawater (ng/L)	9.4
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	0.012
Exposure assessment – shellfish consumption	
Concentration of Me-PB, shellfish (μg/kg)	4.1
Adult, population mean consumption (g/day)	1.2
Adult body weight (kg)	60
Estimated exposure (ng/kg bw/day)	0.082

Me-PB: methyl paraben

11.4 RISK CHARACTERISATION

Table 23 summarises risk characterisation for Me-PB for two routes of exposure; swimming and consumption of shellfish.

Table 23. Risk characterisation for Me-PB for a child swimming in an affected receiving environment and for an adult consuming shellfish from an affected receiving environment

	Me-PB
Estimated exposure (ng/kg bw/event)	0.012
Risk characterisation - swimming	
HBGV (ADI, ng/kg bw/day)	10,000,000
RI (Estimated exposure as % of ADI)	**1.2×10^{-7}**
Estimated exposure (ng/kg bw/day)	0.082
Risk characterisation – shellfish consumption	
HBGV (ADI, ng/kg bw/day)	10,000,000
RI (Estimated exposure as % of ADI)	**8.2×10^{-7}**

Me-PB: methyl paraben, HBGV: health-based guidance value, ADI: Acceptable daily intake, RI: risk index

The estimated exposure to Me-PB during swimming or from consumption of contaminated shellfish represents a very small proportion of the ADI (<0.000001%). This suggests that Me-PB in discharged wastewater is unlikely to represent a human health risk in New Zealand. It should also be noted that the ADI is a lifelong acceptable daily level of exposure, while the estimate for exposure during swimming is event-based. It is extremely unlikely that any individual would swim in a receiving environment every day for their entire life. Application of an averaging time to account for the non-daily occurrence of swimming would further reduce the already low estimate of risk.

A Chinese study determined exposure to Me-PB from swimming in an outdoor swimming pool, including consideration of ingestion and dermal absorption (Lu *et al.*, 2017). Exposure to Me-PB was estimated to be 0.069 ng/kg bw/event, very similar to the estimate from the current study. Ingestion accounted for approximately 95% of exposure. Details of the exposure model were not elaborated in the Chinese study.

A Vietnamese study estimated exposure to total parabens (Me-PB, Et-PB, Pr-PB and Bt-PB) from ingestion of dust by children to be 0.29 ng/kg bw/day (Tran *et al.*, 2016). Me-PB accounted for about 60% of total parabens in most dust samples. This level of exposure is approximately 20-fold higher than the exposure estimated from swimming and 4-fold higher than the exposure estimated from shellfish consumption, derived in the current study.

A French study estimated mean dietary exposure to total parabens for individuals aged 13-36 months of 0.35 mg/kg bw/day (350,000 ng/kg bw/day) (Mancini *et al.*, 2015). Based on these results, exposure to parabens from dietary sources is higher the exposure from swimming in paraben-affected water by a factor of approximately 30 million.

12. CORROSION INHIBITORS - BENZOTRIAZOLE

Benzotriazole (BT) is an effective corrosion inhibitor for copper and its alloys, acting by preventing undesirable surface reactions. It is known that a passive layer, consisting of a complex between copper and BT, is formed when copper is immersed in a solution containing BT. BT can also be found in dishwashing detergents, metal-cutting fluids, antifreeze products, such as aircraft de-icers, cooling and hydraulic fluids, and brake fluids (Loi *et al.*, 2013). BT is only partly removed in WWTPs and a substantial fraction reaches surface water such as rivers and lakes.

12.1 HAZARD IDENTIFICATION

Human data on the toxicity of BT is extremely scarce (Beltoft *et al.*, 2013; ECHA, 2017). While isolated cases of allergic-type reactions (contact dermatitis) have been reported (Ducombs *et al.*, 1980), testing of car mechanics and metal workers (n = 145) with contact dermatitis did not elicit any reactions to BT in 48-hour covered patch tests (de Boer *et al.*, 1989; Meding *et al.*, 1994).

In repeated dose animal studies, effects on a number of organ systems have been noted (Beltoft *et al.*, 2013). However, the effects were not consistent between different studies and in many cases occurred at higher prevalence in low dose groups than high dose groups. Acute toxicity appeared to be due to effects on the central nervous system.

12.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

ECHA have established a derived no effect level (DNEL) for oral exposure for the general population of 0.54 mg/kg bw/day (ECHA, 2017). The critical endpoint was reduced body weight gain in long-term rat and mouse studies. An uncertainty factor of 600 was applied.

The Danish Environmental Protection Agency derived a TDI for BT based on the same study as that identified by ECHA (Beltoft *et al.*, 2013). A TDI of 0.0067 mg/kg bw/day was derived after applying an uncertainty factor of 50,000 to the LOAEL of 335 mg/kg bw. The uncertainty factor included factors for inter-species extrapolation (x10) and intra-species variability (x10). An extra uncertainty factor was included (x500), to account for the use of a LOAEL, rather than a NOAEL, and because it could not be clearly evaluated whether BT is genotoxic and carcinogenic.

A combined Dutch and Nordic Expert Group reviewed essentially the same information considered by the Danish EPA, but did not derive a TDI (Stouten *et al.*, 2000).

An earlier USEPA report added no further context (USEPA, 1977).

12.3 EXPOSURE ASSESSMENT

12.3.1 Occurrence - New Zealand

No information was found on BT in New Zealand wastewater discharges or in the New Zealand aquatic environment.

12.3.2 Occurrence - Australia

BT was detected in secondary treated wastewater, from a predominantly urban WWTP, at a concentration of 3.3 μg/L (Loi *et al.*, 2013). BT was determined in influent and at various stages through the Bolivar WWTP in Adelaide (Liu *et al.*, 2012). Mean influent concentrations of BT were 5.7 μg/L, while effluent concentrations were up to 2.4 μg/L.

Groundwater from the same WWTP contained BT at a concentration of 0.28 μg/L (Liu *et al.*, 2011).

12.3.3 Exposure assessment

At present no exposure assessment for BT was possible, due the lack of any information on this EOC in the New Zealand environment.

12.4 RISK CHARACTERISATION

Risk characterisation for BT was not possible due to lack of data to derive an exposure estimate.

13. ANTIFOULING AGENTS – DIURON AND ISOPROTURON

Antifouling agents are applied to surfaces in contact with water, to prevent biofouling; the accumulation of microorganisms, plants, algae, or animals on wetted surfaces. With the phasing out of organotin compounds, algicidal pesticides such as diuron and isoproturon have been used as antifouling agents. Diuron is also used as a terrestrial herbicide and can enter the aquatic environment through land runoff.

13.1 HAZARD IDENTIFICATION

Diuron has been assessed by the USEPA under the Registration Eligibility Decision (RED) programme and by EFSA (EFSA, 2005f; USEPA, 2003).

No human epidemiological studies on diuron were reported in the two assessments or found in the more recent scientific literature.

The main effects seen in short- and long-term animal studies were effects on the blood system; haemolytic anaemia (EFSA, 2005f). Long-term studies also showed effects on the urothelial system, including hyperplastic and neoplastic changes. No reproductive or developmental toxicity or neurotoxicity has been reported.

Isoproturon has been assessed by EFSA (EFSA, 2015c). A three-year human study in occupationally exposed workers was reported, which failed to show any pathological abnormalities in the peripheral blood count or any indication of haemolytic anaemia (WHO, 2003).

Like diuron, isoproturon also induces haemolytic anaemia in a range of animal species (EFSA, 2015c). Effects on the liver, including hepatic tumours have been reported. However, the relevance of the mechanism for formation of liver tumours to humans is uncertain. Isoproturon reduced male fertility in reproductive toxicity studies. No evidence of developmental toxicity or neurotoxicity has been reported.

13.2 HAZARD IDENTIFICATION (DOSE-RESPONSE)

Diuron has been assessed by the USEPA under the Registration Eligibility Decision (RED) programme (USEPA, 2003). A chronic RfD of 0.003 mg/kg bw/day was derived, based on effect on the haemopoietic system in a long-term rat study. No ARfD was derived. EFSA have also assessed diuron and derived a higher ADI of 0.007 mg/kg bw/day, based on the same rat study as used by USEPA (EFSA, 2005f). No NOAEL was found in this study and LOAELs for female and male rats were 1.7 and 1.0 mg/kg bw/day, respectively. The USEPA RfD was based on the lower (male) LOAEL, with an uncertainty factor of 300, while the EFSA ADI was based on the higher (female) LOAEL, with an uncertainty factor of 250.

An ADI of 0.015 mg/kg bw/day was derived for isoproturon by EFSA, based on the NOAEL for liver tumour occurrence in a long-term rat study (EFSA, 2015c). An ARfD of 0.1 mg/kg bw/day was derived, based on haematological effects in a short-term study in dogs.

13.3 EXPOSURE ASSESSMENT

13.3.1 Occurrence - New Zealand

Following the grounding of the MV Rena on Astrolabe Reef, Bay of Plenty, extensive monitoring of the marine environment, including edible biota, was carried out for a range of contaminants, including diuron and isoproturon (Ross *et al.*, 2016). Diuron, but not

isoproturon, was detected in marine sediments from Astrolabe Reef (mean 460 μg/kg, maximum 7000 μg/kg), but not in sediments from reference sites. Neither substance was detected in any of the marine biota species examined (sea urchins, rock lobster, gastropods, fish). However, organotin compounds (mainly tributyl tin), older antifouling agents no longer approved for use in New Zealand, were detected in a proportion of marine biota examined.

13.3.2 Occurrence - Australia

Analysis of intertidal and subtidal sediments from the Queensland coast and the Great Barrier Reef detected diuron at concentrations in the range 0.2-10.1 μg/kg dry weight (Haynes *et al.*, 2000). Diuron was also detected in intertidal seagrasses (0.6-1.7 μg/kg dry weight). Analyses of water from the Great Barrier Reef and from the mouths of rivers on the Queensland coast found diuron at concentrations in the range 0.2-1.6 ng/L (Shaw and Müller, 2005).

13.3.3 Exposure assessment

No New Zealand data on concentrations of diuron or isoproturon in wastewater or the receiving environment are available and no exposure assessment can be performed.

In the recently conducted New Zealand total diet survey, isoproturon was not detected at all, while diuron was only detected in one sample of shrimps/prawns, which were imported into New Zealand (MPI, 2017).

13.4 RISK CHARACTERISATION

No risk characterisation was carried out due to the lack of data for estimation of exposure.

14. UV FILTERS – BENZOPHENONE-3

Ultra violet (UV) filters are chemicals added mainly to personal care products to absorb UV radiation and mitigate the effects of this radiation on human skin. UV filters are also used to stabilise inks and surface coatings used on food packaging. While UV filters may belong to a number of different chemical classes, the benzophenones have attracted the most attention as environmental contaminants.

The use of cosmetics containing UV filters is considered to be the major source of overall exposure (Kim *et al.*, 2016). Kim *et al*. (2016) determined urinary concentrations of benzophenones (BPs) and correlated these with self-reported food consumption information. Frozen stored foods, instant foods and instant coffee consumption frequencies were correlated to urinary levels of one or more BP. The authors of the study noted that these findings were consistent with information on migration of BPs from food packaging materials into foodstuffs. Aquatic foods were not considered in the analysis.

Supporting the recommendation of Stewart *et al.* (2016), that BP-3[13] is the most appropriate UV filter for monitoring in the New Zealand environment, BP-3 was the UV filter present at the highest mean concentration in the urine of Koreans (Kim *et al.*, 2016).

14.1 HAZARD IDENTIFICATION

Available toxicity data was reviewed by the EU Scientific Committee on Consumer Products (SCCP, 2008). SCCP concluded that BP-3 is of low acute toxicity. Effects found in chronic studies (rats, mice) were non-specific signs of systemic toxicity (decreased weight gain, decreased food intake) and effects on the kidneys and liver. The most sensitive endpoint was an increase in liver weight, however, this was without associated histopathological changes and SCCP concluded that it was probably an adaptive response.

No information on adverse human health effects from BP-3 was found.

14.2 HAZARD CHARACTERISATION (DOSE-RESPONSE)

An oral NOAEL of 411 mg/kg bw/day was found for chronic toxicity (SCCP, 2008). A NOAEL of 200 mg/kg bw/day was found for maternal and developmental toxicity (skeletal aberrations) in a developmental toxicity study.

More recent concerns have related to potential for endocrine disruption by BP-3 (Kim and Choi, 2014). BP-3 is structurally analogous to the female sex hormone, E2, and has been shown to be weakly estrogenic in bioassays. The estrogenic potential of BP-3 has been estimated to be about 1/45,000 of the activity of E2, while its metabolite BP-1 has higher activity; about 1/5000 the activity of E2 (Kim and Choi, 2014). Effects on reproductive indices have been observed in studies on aquatic species.

[13] The commonly-used nomenclature for substituted benzophenone UV filters is the international nomenclature for cosmetic ingredients (INCI) as elaborated by the Committee de Liaison des Associations Europeans de L'industrie de la Perfumerie, de Produits Cosmetics et de Toilette (COLIPA). All of these compounds are derivatives of 2-hydroxybenzophenone. However, the nomenclature is not systematic. The benzophenones mentioned in this report are; BP-1 is 2,4-dihydroxybenzophenone, BP-2 is 2,2',4,4'-tetrahydroxybenzophenone, BP-3 is 2-hydroxy-4-methoxybenzophenone, BP-4 is 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid.

BP-3 and other UV filters were also assessed by the Danish Environmental Protection Agency (DEPA, 2015). However, no new toxicity data on BP-3 was presented other than that reviewed by SCCP. The DEPA report only considered human exposure from use of sunscreens and other cosmetic products.

14.3 EXPOSURE ASSESSMENT

14.3.1 Occurrence - New Zealand

BP-3 was detected in 33/33 effluent samples discharged into Whakaraupo (Lyttelton) Harbour, with concentrations in the range 11-210 ng/L (Emnet, 2013). BP-1 was also detected in all 33 samples analysed (range 3.6-150 ng/L). BP-3 was detected in 48/57 seawater samples from the harbour (range <2.6-7.3 ng/L) and marine sediments (12/28; <0.8-1.6 μg/kg). BP-1 was less frequently detected and was detected at lower concentrations. BP-3 was detected in 1/9 green-lipped mussel samples at a concentration of 3.7 μg/kg wet weight.

Similar results were reported from analysis of effluent from Antarctic research stations, with 15/15 effluent samples containing BP-1 and BP-3 (Emnet *et al.*, 2015). While BP-3 concentrations were similar to those seen in Whakaraupo Harbour (maximum 195 ng/L), very high concentrations of BP-1 were reported in some samples (maximum 6800 ng/L). BP-3 was more frequently detected in Antarctic seawater (52/58; <2.6-88 ng/L) than BP-1 (7/58; <0.8-10 ng/L). BP-1 was not detected in sea ice, while BP-3 was detected in 5/5 samples (<2.6-3.8 ng/L). BP-3 was also detected in marine biota, including clams (1.4-23 μg/kg wet weight), urchins (composite, 0.9 μg/kg wet weight), fish muscle (<1.3-3.0 μg/kg wet weight) and fish liver (9.6 μg/kg wet weight).

14.3.2 Occurrence - Australia

BP-3 and non-benzophenone UV filters were determined in influent and effluent from the Bolivar WWTP in South Australia (Liu *et al.*, 2012). Influent concentrations of BP3 were 1060 (April) and 3100 (October) ng/L, the difference presumably reflecting greater use of sunscreens in Spring than Autumn. In the final effluent, BP-3 concentrations had been reduced to 3 and 9% of influent concentrations for April and October, respectively. An earlier study by the same group did not detect BP-3 in groundwater from the same WWTP (Liu *et al.*, 2011).

14.3.3 Exposure assessment

Unlike most other EOCs considered in this report, New Zealand data are available on BP-3 to allow consideration of two potential routes of exposure:

- From water ingestion during swimming, and
- From consumption of shellfish

The highest concentration of BP-3 detected in New Zealand receiving waters was 7.3 ng/L. The maximum concentration of BP-3 detected in green-lipped mussels was 3.7 μg/kg.

Dermal absorption of BP-3 from sunscreen has been determined in a pig ear model (SCCP, 2008). Absorption of BP-3 was reported to be negligible during the first 0.5-1.0 hours, with 3-4% of the applied dose absorbed during 24 hours. Given the negligible absorption of BP-3 during a typical period for swimming (0.5-1.0 hours), the current exposure assessment only considered oral ingestion.

Table 24 summarises conservative exposure assessments for two routes of exposure; swimming and consumption of shellfish. While children are most at risk of ingestion of contaminants during swimming, children tend not to be consumers of shellfish and the shellfish route of exposure has been examined for an adult consumer. Exposure to BP-3

from ingestion of water during swimming and consumption of shellfish was assessed as outlined in section 1.3.5.

Table 24. Estimated exposure to BP-3 for a child swimming in an affected receiving environment and for an adult consuming shellfish from an affected receiving environment

	BP-3
Exposure assessment - swimming	
Concentration of BP-3, seawater (ng/L)	7.3
Child mean water ingestion rate (mL/hr)	23.9
Child mean swim duration (hrs)	1.1
Child mean body weight (kg)	20
Estimated exposure (ng/kg bw/event)	**9.6×10^{-3}**
Exposure assessment – shellfish consumption	
Concentration of BP-3, shellfish (μg/kg)	3.7
Adult, population mean consumption (g/day)	1.2
Adult body weight (kg)	60
Estimated exposure (ng/kg bw/day)	**0.074**

BP-3: Benzophenone-3

14.4 RISK CHARACTERISATION

Table 25 summarises risk characterisation for the two potential routes of exposure for BP-3. Risk was expressed in terms of MOE against the lowest NOAEL from the SCCP assessment (200 mg/kg bw/day).

Table 25. Risk characterisation for BP-3 for a child swimming in an affected receiving environment and for an adult consuming shellfish from an affected receiving environment

	BP-3
Estimated exposure - swimming (ng/kg bw/event)	9.6×10^{-3}
Risk characterisation - swimming	
POD (NOAEL, ng/kg bw/day)	200,000,000
MOE (POD/estimated exposure)	**2.1×10^{10}**
Estimated exposure – shellfish consumption (ng/kg bw/day)	0.074
Risk characterisation – shellfish consumption	
POD (NOAEL, ng/kg bw/day)	200,000,000
MOE (POD/estimated exposure)	**2.7×10^{9}**

BP-3: Benzophenone-3, POD: point of departure, NOAEL: No observed adverse effect level, MOE: margin of exposure

For non-genotoxic effects, such as those use to derive the NOAEL for BP-3, a MOE of greater than 100-1000 is usually considered to indicate a negligible level of risk. The estimated exposure to BP-3 during swimming or from consumption of contaminated shellfish equate to an extremely high MOEs (>10^9). This suggests that BP-3 in discharged wastewater are unlikely to represent a human health risk in Zealand.

An Europe-wide study of dietary exposure to UV filters from seafood consumption derived an estimate for BP-3 of 2.3 ng/kg bw/day (Cunha *et al.*, 2018). This estimate is about 30-fold higher than the combined exposure estimates for swimming and shellfish consumption from the current study.

Exposure to BP-3 for adult women from the use of personal care products was estimated for China and the USA (Liao and Kannan, 2014). Geometric mean estimates of exposure for the two countries were 0.98 and 24.4 μg/day, respectively. For a 60 kg women, these exposures

equate to 16 and 410 ng/kg bw/day, respectively; about 200- and 5000-fold higher than the combined exposure estimates for the current study.

15. CONCLUSIONS

Little information is available on EOCs in wastewater discharges or the receiving environment in New Zealand. The available information suggests that most classes of EOCs are potentially present in the New Zealand environment. Information from the previous sections is summarised in Table 26. This table lists the highest concentration of the EOCs detected in various environmental media types, the lowest human exposure limits and associated risk characterisation estimates.

Highly conservative human health risk assessments were carried out for exposure scenarios of; swimming in an affected receiving environment, and eating shellfish from an affected receiving environment. For the swimming scenario, exposure was only considered due to ingestion of water. Inhalation of water is likely to be negligible in comparison to ingestion and suitable data for the estimation of dermal absorption of EOCs from water were not found.

Estimates of risk, either in the form of comparisons to a HBGV or MOEs to a toxicological POD, suggest that the risks to humans from the discharge of EOCs into the environment is currently very low. However, no New Zealand specific concentration data were available for several classes of EOCs, and concentrations in shellfish were unavailable for most classes of EOCs.

The screening exposure assessments carried out in the current study are potentially affected by a number of limitations, including:

- The paucity of relevant New Zealand-specific concentration data on EOCs in the receiving environment, and
- The lack of suitable information to assess exposure through dermal absorption.

However, the exposure estimates made are highly conservative, as they assume that:

- Swimming will be a year-round daily activity, and
- EOCs will always be present at the highest concentration observed in the New Zealand receiving environment or will be present in the receiving environment at the highest concentration determined in wastewater discharges.

Exposure assessments were also conservative in considering only the population group likely to have the highest exposure.

On balance, the exposure and risk assessments derived in the current study are likely to be over-estimates. The very large margins between the estimates of exposure and exposure levels at which adverse health effects may occur suggests that, on the basis of current knowledge, environmental exposures to EOCs in New Zealand are not likely to result in adverse human health effects. However, it should be noted that for many of these classes of chemicals, swimming or shellfish consumption will not be the primary route of exposure and exposure from these sources is likely to be additional to a higher level of exposure from the diet.

Table 26. Summary of information on emerging organic contaminants (EOCs) in New Zealand discharge wastewater and the receiving environment (water and sediment) and associated human health risk characteristics

EOC	Highest New Zealand relevant concentration (ng/L for water and wastewater, µg/kg dry weight for sediments, µg/kg wet weight for shellfish)				HBGV or POD, ng/kg bw/day (type)	Risk characteristics	
	Receiving water	Wastewater	Sediment	Shellfish		Swimming	Consuming shellfish
Flame retardants							
BDE47		0.027	1.4		172 (BMD) 100 (RfD)	4.9×10^{6} (MOE) 3.5×10^{-5} (%HBGV)	
BDE99		0.016	2.2		4.2 (BMD) 100 (RfD)	2.0×10^{5} (MOE) 2.1×10^{-5} (%HBGV)	
BDE209		0.23	570		1,700,000 (BMD) 7000 (RfD)	5.7×10^{9} (MOE) 4.3×10^{-6} (%HBGV)	
Tris(isobutyl)phosphate		28					
Tributylphosphate		39			80,000 (MRL)	6.4×10^{-5} (%HBGV)	
Tris(2-ethylhexyl)phosphate		<0.2					
Plasticisers							
Bis(2-ethylhexyl)phthalate		<50	11,500		5,000,000 (NOAEL)	$>7.6 \times 10^{7}$ (MOE)	
Benzyl butyl phthalate		<1	1600		50,000,000 (NOAEL)	$>3.8 \times 10^{10}$ (MOE)	
Bisphenol A	5.2	199	145		4000 (*t*-TDI)	1.7×10^{-4} (%HBGV)	
Surfactants							
Nonylphenol		280	32,000		5,000 (TDI)	0.007 (%HBGV)	
Linear alkylbenzene sulphonate							
Perfluorinated compounds							
PFOS					20 (TDI)		
PFOA					160 (TDI)		
Musk fragrance							
Galaxolide		60			1,500,000 (p-TDI)	5.3×10^{-6} (%HBGV)	
Tonalide		1			50,000 (p-TDI)	2.6×10^{-6} (%HBGV)	
Pesticides							
Glyphosate			950		500,000 (ADI)		
Imidacloprid					60,000 (ADI)		
Bifenthrin					10,000 (ADI)		
Permethrin					50,000 (ADI)		
Pharmaceuticals							
Acetaminophen		6	7.5		50,000 (ADI)	1.6×10^{-5} (%HBGV)	
Amitriptyline		29.5			8,000 (ADI)	4.9×10^{-4} (%HBGV)	
Caffeine		109			150,000 (ADI)	9.3×10^{-5} (%HBGV)	
Carbamazepine		709	1.0		300 (ADI)	0.31 (%HBGV)	
Diclofenac		51	2.0		67,000 (ADI)	1.0×10^{-4} (%HBGV)	

EOC	Highest New Zealand relevant concentration (ng/L for water and wastewater, μg/kg dry weight for sediments, μg/kg wet weight for shellfish)				HBGV or POD, ng/kg bw/day (type)	Risk characteristics	
	Receiving water	Wastewater	Sediment	Shellfish		Swimming	Consuming shellfish
Diltiazem		133			14,000	1.2×10^{-3} (%HBGV)	
Ibuprofen		145			110,000 (ADI)	1.7×10^{-4} (%HBGV)	
Naproxen		987			46,000 (ADI)	2.8×10^{-3} (%HBGV)	
Steroid estrogens							
Estrone (E1)	<7	3,100	2.2				
17β-estradiol (E2)	<0.4	330	1.0				
Estriol (E3)	<2.1	11	0.6				
17α-ethinylestradiol (EE2)		78					
17α-estradiol		11,000					
E2 equivalents	<1.2				50 (TDI)	0.003 (%HBGV)	
Personal care products							
Triclosan		122	<100				
Methyl-triclosan	0.5	35					
Triclosan equivalents		157			300,000 (RfD)	7.0×10^{-5} (%HBGV)	
Preservatives							
Methylparaben	9.4	21	1.7	4.1	10,000,000 (ADI)	1.2×10^{-7} (%HBGV)	8.2×10^{-7} (%HBGV)
Corrosion inhibitors							
Benzotriazole					6700 (TDI)		
Antifouling agents							
Diuron			7000		3000 (RfD)		
Isoproturon					15,000 (ADI)		
UV-filter							
Benzophenone-3	7.3	210	1.6	3.7	200,000,000 (NOAEL)	2.1×10^{10} (MOE)	2.7×10^{9} (MOE)

EOC: Emerging organic contaminant, HBGV: health-based guidance value, BMD: Benchmark dose, TDI: tolerable daily intake, *t*-TDI: temporary TDI, p-TDI: provisional TDI, ADI: acceptable daily intake, NOAEL: No observed adverse effect level, RfD: reference dose, MOE: Margin of exposure

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