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Complete List of Authors:	Scott, Phil Bartkow, Michael Blockwell, Stephen Coleman, Heather Khan, Stuart Lim, Richard McDonald, James Nice, Helen Nugegoda, Dayanthi Pettigrove, Vincent Tremblay, Louis Warne, Michael Leusch, Frederic; Griffith University, School of Environment
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A national survey of trace organic contaminants in Australian rivers

Philip D. Scott[a], Michael Bartkow[b], Stephen J. Blockwell[c], Heather M. Coleman[d], Stuart J. Khan[d], Richard Lim[e], James A. McDonald[d], Helen Nice[f], Dayanthi Nugegoda[g], Vincent Pettigrove[h], Louis A. Tremblay[i,j], Michael St.J. Warne[k], and Frederic D.L. Leusch[a,*]

[a] School of Environment, Griffith University, Southport, Queensland, 4222, Australia

[b] Seqwater, PO Box 16146, Brisbane City East, Queensland, 4002, Australia

[c] Sydney Water Corporation, PO Box 399, Parramatta, New South Wales, 2124, Australia

[d] School of Civil & Environmental Engineering, University of New South Wales, New South Wales, 2052, Australia

[e] School of the Environment, University of Technology Sydney, PO Box 123, Broadway, New South Wales, 2007, Australia

[f] Water Science Branch, Department of Water, Government of Western Australia, PO Box K822, Perth, Western Australia, 6842, Australia

[g] School of Applied Sciences, Royal Melbourne Institute of Technology, PO Box 71, Bundoora, Victoria, 3083, Australia

[h] Melbourne Water, PO Box 4342, Melbourne, Victoria, 3001, Australia

[i] Cawthron Institute, 98 Halifax Street East, Nelson, 7042, New Zealand

[j] School of Biological Sciences, University of Auckland, PO Box 92019, Auckland, 1142, New Zealand

[k] Water Quality and Investigations, Department of Science, Information, Technology, Innovation and the Arts, Queensland Government, GPO Box 5078, Brisbane, Queensland, 4001, Australia

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* Corresponding Author.
e: f.leusch@griffith.edu.au
p: +61 7 5552 7832
Mailing address:
Dr Frederic Leusch
Smart Water Research Centre (G51)
Griffith University, Gold Coast Campus
Southport, Queensland, 4222
Australia

List of abbreviations

APCI	Atmospheric Pressure Chemical Ionization
DEET	N,N-Diethyl-*meta*-toluamide
ESI	Electrospray Ionization
EU	European Union
HPLC	High Performance Liquid Chromatography
HQ	Hazard Quotient
LC-MS/MS	Liquid Chromatography Tandem Mass Spectrometry
LOQ	Limit of Quantification
MRM	Multiple Reaction Monitoring
NOEC	No Observable Effect Concentration

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NSW	New South Wales (state of Australia)
NT	Northern Territory (territory of Australia)
PCP	Personal Care Product
PNEC	Predicted No Effect Concentration
PPCP	Pharmaceutical and Personal Care Product
QLD	Queensland (state of Australia)
SA	South Australia (state of Australia)
SEM	Standard Error of the Mean
SPE	Solid Phase Extraction
TCEP	*tris*(2-Chloroethyl) Phosphate
TrOC	Trace Organic Contaminant
US	United States
VIC	Victoria (state of Australia)
WA	Western Australia (state of Australia)
WWTP	Wastewater Treatment Plant

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Abstract

Trace organic contaminant (TrOC) studies in Australia have focused on wastewater effluents, leaving a knowledge gap of their occurrence and risk in freshwater environments. This study

measured 42 TrOCs including industrial compounds, pesticides, pharmaceuticals and personal care products (PPCPs) by liquid chromatography tandem mass spectrometry at 73 river sites across Australia quarterly for one year. TrOCs were found in 92% of samples, with a median of three compounds detected per sample (maximum 18). The five most commonly detected TrOCs were the pharmaceuticals salicylic acid (82%; max = 1,530 ng/L), paracetamol (also known as acetaminophen; 45%; max = 7,150 ng/L) and carbamazepine (27%; max = 682 ng/L), caffeine (65%; max = 3,770 ng/L), and the flame retardant *tris*(2-chloroethyl) phosphate (TCEP; 44%; max = 184 ng/L). Pesticides were detected in 28% of the samples. To determine the risk posed by the detected TrOCs to the aquatic environment, hazard quotients were calculated by dividing the maximum concentration detected for each compound by Predicted No Effect Concentrations (PNEC). Three of the 42 compounds monitored (the pharmaceuticals carbamazepine and sulfamethoxazole and the herbicide simazine) had a hazard quotient >1 suggesting that they may be causing adverse effects at the most polluted sites. A further 10 compounds had hazard quotients >0.1 indicating a potential risk; these included four pharmaceuticals, three personal care products and three pesticides. Most compounds had hazard quotients significantly <0.1. The number of TrOCs measured in this study was limited and further investigations are required to fully assess the risk posed by complex mixtures of TrOCs on exposed biota.

Keywords

Hazard quotient; micropollutant; surface water; TrOC; water quality.

1. Introduction

With the human population surpassing seven billion, freshwater demand for municipal, agricultural and industrial use has never been higher. There are over 100,000 registered

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chemicals in the European Union (EU) alone (Schwarzenbach et al. 2006) and recent improvements in analytical chemistry methodologies have enabled the study of trace organic contaminants (TrOCs) in freshwater at relevant environmental concentrations. There are over 4,000 pharmaceutical and personal care products (PPCPs) on the market (Boxall et al. 2012) and studies on their fate in the environment are lacking, along with an understanding of the nature and toxicity of their environmental transformation products (Brausch and Rand 2011, Fent et al. 2006). This is particularly the case in Australia (reviewed in Santos et al. 2010). A 2002 study detected 76 out of 95 wastewater-associated TrOCs monitored in 139 streams across the United States (US; Kolpin et al. 2002). A follow up study targeted 74 groundwater and surface water sources of drinking water for 100 TrOCs and found at least one TrOC at 92% of the sites (Focazio et al. 2008). These two nation-wide studies established TrOC concentration patterns across US impacted waterways. The first EU-wide assessment of TrOCs covered 122 surface water sites across 27 countries where 90% of the samples had a detection of at least one of the target TrOCs (Loos et al. 2009).

Australian research on TrOCs has predominantly focused on wastewater treatment plant (WWTP) processes and effluent rather than the receiving environment (Braga et al. 2005a, b, Chapman 2003, Coleman et al. 2008, Leusch et al. 2006, Mispagel et al. 2009, Williams et al. 2007, Ying et al. 2009). Khan and Ongerth (2004) used fugacity models to predict WWTP effluent concentrations of at least 50 pharmaceuticals and prioritised subsequent efforts for analytical investigation. A recent study of 39 Victorian WWTP effluents confirmed the presence of various TrOCs including PPCPs, pesticides, food additives and alkylphenols (Allinson et al. 2012). Concentrations were typically in the 1-1000 ng/L range but some compounds like carbamazepine were found above this range. Another study detected antibiotics in WWTP effluents at concentrations up to 3,400 ng/L, while rivers typically had low ng/L concentrations (but a maximum of 2,000 ng/L) (Watkinson et al. 2009).

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For this study, 285 grab water samples were collected from 73 river sites across Australia every quarter over a one-year period. Samples were concentrated using solid phase extraction (SPE) and specific TrOCs analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The objective was to assess the risk of TrOCs to the environment by determining their concentrations in impacted freshwater environments to better understand the relationship between land-use activities and aquatic contamination.

2. Experimental section

2.1. Site selection

Sites were selected after extensive consultation with academics, regulators and water industry partners. Sample locations consisted of 19 sites each in New South Wales (NSW), Queensland (QLD), and Victoria (VIC), 10 sites in Western Australia (WA), and three sites each in the Northern Territory (NT) and South Australia (SA) (Fig. 1). Sampling locations (Fig. 1) reflect the fact that most Australians live in close proximity to the coast and the center of the continent receives little rain. Sites were categorized based on the primary land-use activity upstream in the catchment. Sites were rarely influenced by just one land-use and so the dominant land-use dictated site categorization. Detailed catchment information can be found in SI Table S1. Freshwater aquatic environments in catchments with agricultural, industrial, residential and WWTP activities were selected, along with sites in catchments with less anthropogenic influences (*i.e.*, "undeveloped" or "reference" sites) from each state/territory (Table 1). QLD consisted of five undeveloped sites, while NSW and VIC both had three. NT, SA and WA had only one undeveloped site per territory/state. Other land-uses had to be prioritized due to a smaller number of sampling locations.

[INSERT FIG 1 HERE]

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139 *[INSERT TABLE 1 HERE]*

140

141 *2.2. Water sampling*

142 Grab river water sampling started at the project commencement and samples were obtained
143 every three months, in Autumn (May 2011), Winter (August 2011), Spring (November 2011)
144 and Summer (February 2012) from each site (with the exception of NT sites, which were
145 only sampled twice, due to in-kind service personnel relocation) (Table 1). Two solvent-
146 rinsed 1 L amber glass bottles were submerged to approximately 20-30 cm depth in fast
147 flowing water as far towards the centre of the channel as possible from the water's edge in
148 order to collect 2 L grab water samples. To prevent biological degradation, 1.5 mL of 12 M
149 HCl (Merck, Victoria, Australia) was added to each bottle to lower the pH to approximately
150 2. Samples were packaged with ice blocks and sent by overnight courier to the laboratory for
151 solid-phase extraction (SPE). Geographic location and budgetary constraints made field
152 blanks unfeasible; however, one laboratory blank was generated for each sampling event.

153

154 *2.3. General water quality parameters*

155 Basic water chemistry (dissolved oxygen, electrical conductivity, pH, temperature) was
156 measured in the field for each sample prior to acidification (SI Table S2). To minimize risk of
157 contamination, a small volume of water from each sample was decanted into a small vial for
158 determination of nitrate and nitrite concentrations with Hach AquaChek Nitrate Nitrite strips
159 (Notting Hill, Australia). Total chlorine, free chlorine, total hardness, total alkalinity and pH
160 were then measured using Hach AquaChek 5-in-1 strips (Notting Hill, Australia) following
161 the manufacturer's instructions (SI Table S2), and the decanted sample was discarded.

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Stream flow data were not available at the time of sampling; however, rainfall (and atmospheric temperature) data were obtained for one week prior to sampling (SI Table S2).

2.4. Solid-phase extraction (SPE)

Upon arrival in the laboratory, water samples were adjusted to precisely pH 2 using 12 M HCl and extracted within 24 h. Samples were vacuum filtered through 2 µm glass fibre filters (47 mm diameter; Millipore, Kilsyth, Australia). One L of sample was passed through a preconditioned SPE cartridge (Oasis HLB SPE cartridges; 500 mg sorbent, 6 cc; Waters, Rydalmere, Australia) at 10 mL/min. Cartridges were pre-conditioned with 2× 5 mL of acetone: hexane (1: 1) (analytical reagent grade; Merck, Victoria, Australia) followed by 2× 5 mL methanol (analytical reagent grade; Labscan, Thailand) and finally 2× 5 mL distilled water. After passing the full water sample, the SPE cartridges were dried under vacuum at 20 mmHg for 2 h (or until dry). Dried cartridges were wrapped in aluminium foil and stored at 4ºC until elution (up to two weeks). A polar fraction was eluted with 2× 5 mL methanol and a non-polar fraction was eluted with 2× 5 mL acetone: hexane (1: 1). This was repeated for the second 1 L bottle. Fractions from both cartridges were combined and evaporated under nitrogen until dry and immediately reconstituted into 1 mL methanol for chemical analysis. One laboratory blank was generated for each sampling event.

2.5. Liquid chromatography

TrOCs were selected for monitoring based on their occurrence in WWTP effluents and environmental waters, availability of deuterated standards and previously established methods. Analytes were separated using an Agilent (Palo Alto, CA, USA) 1200 series high performance liquid chromatography (HPLC) system equipped with a 150 × 4.6 mm, 5 µm particle size, Luna C18(2) column (Phenomenex, Torrence CA, USA). A binary gradient

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consisting of 5 mM ammonium acetate in water (A) and 100% methanol (B) at a flow rate of 800 µL/min was used. For ESI positive analyses, the gradient was as follows: 10% B held for 0.50 min, stepped to 50% B at 0.51 min and increased linearly to 100% B at 8 min, then held at 100% B for 2 min. For ESI negative analyses, the gradient was as follows: 10% B held for 0.50 min, stepped to 60% B at 0.51 min and increased linearly to 100% B at 8 min, then held at 100% B for 3 min. A 5 min equilibration step at 10% B was used at the beginning of each run. For APCI analysis the eluents consisted of milli-Q grade water (A) and 0.1% v/v formic acid in methanol with the following ramp at a flow rate of 700 µL/min: 60% B held for 5 min, increased linearly to 100% B at 20 min, then held at 100% B for 3 min. A 3 min equilibrium step preceded injection. An injection volume of 10 µL was used for all methods. Analytical methods using electrospray ionization (ESI) were based on Vanderford and Snyder (2006).

2.6. *Mass spectrometry*

Mass spectrometry was performed using an API 4000 triple quadrupole mass spectrometer (Applied Biosystems, Foster City, CA, USA) equipped with a turbo-V ion source employed in both positive and negative electro-spray modes. Using multiple reaction monitoring (MRM), two mass transitions for all but three of the analytes were monitored for unequivocal confirmation. One mass transition for the labeled internal standard was monitored. Only the first transition was used for quantification. Relative retention times of the analyte and isotopically labeled internal standard were also monitored to ensure correct identification. A table of transitions can be found in the Supplementary Information (SI Tables S3 and S4).

2.7. Calibration and limits of quantification

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Standard solutions of all analytes were prepared at 1, 5, 10, 50, 100, 500 and 1000 ng/mL. A relative response ratio of analyte/ internal standard over a 1–1000 ng concentration range was generated enabling quantitation with correction for losses due to ion suppression. All calibration curves had a correlation coefficient of 0.99 or better. The limits of quantification (LOQs) were determined as an s/n ratio greater than 10.

2.8. Statistical analysis

When required, statistical analysis was performed using the Kruskal-Wallis nonparametric test, followed by Dunn's multiple comparison test, on Prism 5 software (GraphPad Software, California, USA).

3. Results and discussion

3.1. Chemical analysis

The monitored TrOCs were found in 92% of samples, with a median of three compounds detected per sample (maximum of 18). In contrast, Kolpin et al. (2002) reported a median of seven chemical detects per sample and a maximum of 38 (out of 95) in a study that investigated many overlapping chemical classes. Focazio et al. (2008) indicated that a median of four chemicals detected per sample, with a maximum of 31 (out of 100) in surface water and groundwater. These studies used LC-MS with detections typically between 10-500 ng/L. The most chemically diverse sample had 45% of the targeted compounds compared to 40% found in a US study (Kolpin et al. 2002). However, a subsequent US-based surface water and groundwater study reported 63% of targeted TrOCs present in the most chemically complex sample (Focazio et al. 2008). Overall, the six most frequently detected compounds in this study were salicylic acid (82%), caffeine (65%; not analyzed in Spring sampling),

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paracetamol (also known as acetaminophen; 45%; not analyzed in Spring sampling), TCEP (44%), carbamazepine (27%) and triclosan (25%). Four compounds were detected at least once at concentrations in excess of 1,000 ng/L: paracetamol (7,200 ng/L), simazine (3,900 ng/L), caffeine (3,800 ng/L) and salicylic acid (1,500 ng/L).

[INSERT FIG 2 HERE]

[INSERT TABLE 2 HERE]

[INSERT TABLE 3 HERE]

3.1.1. Land-use

The analytical methods were initially developed for wastewater contaminants such as pharmaceuticals and personal care products (PPCPs). Of the five land-uses targeted, samples collected downstream of WWTPs (n=50 out of 285) had the highest median number of detections with 7 chemicals per sample (average = 6.5) although this was not significantly different (Kruskal-Wallis test; $p>0.05$) from industrial, residential, or agricultural samples. Industrial (n=28), residential (n=74) and agricultural (n=80) samples had medians of 6, 4 and 2 TrOCs per sample, respectively (averages of 6.2, 4.3 and 2.6 TrOCs respectively). Finally, undeveloped sites had the lowest number of TrOCs with an average of 1.5 per sample (median = 1); this value was significantly different (Kruskal-Wallis test; $p<0.05$) from other land-uses. These results indicate that TrOCs are widespread across land-uses and not simply in rivers receiving WWTP discharges. This may be due to the presence of septic tank systems, leaking sewer lines, the result of combined sewer overflows into waterways

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following intense wet weather events, or some other unknown source. There is clearly a need for further research investigating TrOCs from other land-uses activities.

Fig. 2 (top) indicates that the top five most frequently detected compounds did not vary greatly across the different land-uses. The most frequently detected TrOCs were: salicylic acid, caffeine, paracetamol, TCEP, carbamazepine, triclosan, 2-phenylphenol and propylparaben (Tables 2 and 3). Of those, salicylic acid (64-100%) and caffeine (34-90%) were in the top five compounds for all land-use categories (Fig. 2, top). Caffeine is a common wastewater contaminant and has occasionally been used as a marker compound for human wastewater (Metcalfe et al. 2003). The prevalence of caffeine and PPCPs suggests widespread (but low) wastewater pollution, from an unknown source(s), possibly septic tank leakage, or sewage overflow during heavy rainfall, which was common in the sampling period (SI Table S2).

3.1.2. Location

Geographic location (Fig. 1, SI Table S2) was used to sort number of TrOCs per sample by Australian state or territory. Samples from NT (n=6) had the highest average number of detections per sample (6.5 compounds per sample). NSW (n=76) had 4.4, WA (n=40) had 4.3, SA (n=12) had 4.2, and VIC (n=76) had 4.1 detections per sample. QLD samples (n=75) had the lowest national average with 2.7 compounds detected per sample.

Salicylic acid was the most frequently detected compound in each state (Fig. 2, bottom) and detection frequencies varied from 61% in QLD to 100% in SA. It was interesting to see that salicylic acid was one of the most commonly detected compounds despite its relatively high LOQ.

3.1.3. Seasonal and land-use trends

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Qualitative assessment of the dataset indicated that most analytes had similar frequencies of detection throughout all four sampling events with a few exceptions (Table 2). Primidone was detected more frequently in Autumn (May-2011) and Spring (Nov-2011), compared to Winter (Aug-2011) and Summer (Feb-2012). Phenytoin was found consistently in Autumn, Winter and Spring (11, 15 and 13 times, respectively), but not once in Summer. Propylparaben was detected 23 times in Spring, but not as often in other sampling events (0 times in Autumn; 3 times in Winter; 8 times in Summer). The biocide 2-phenylphenol was only identified twice each in Autumn and Winter, seven times Spring, and 27 times in the Summer. Australia, a continent the size of Europe, experiences vast climatic and seasonal differences between states/territories and even between sites within states/territories. Temperature can significantly influence WWTP removal efficiencies of TrOCs (Ternes et al. 1999), and rainfall can impact their dilution in receiving environments (Ternes 1998). Analysis of chemical data sub-divided by land-use did not indicate any trends. Sites were categorized based on the most influential point (*e.g.* WWTP) or non-point sources (*e.g.* agricultural, industrial, or residential) and many had influence from multiple land-use categories. The data suggest that the water quality does not necessarily reflect the dominant proximal land-use influence.

3.1.4. Pharmaceuticals.

Six pharmaceuticals were detected in more than 10% of samples: salicylic acid (82%), paracetamol (45%), carbamazepine (27%), primidone (14%), phenytoin (14%) and gemfibrozil (11%). Nine pharmaceuticals were never detected (Table 2) and paracetamol and salicylic acid were detected at concentrations above 1,000 ng/L.

Salicylic acid, the most frequently detected compound, is an important metabolite of acetylsalicylic acid (aspirin), but is also a plant hormone and can be found in many species,

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most notably in willow tree bark (Krantz et al. 2010, National Center for Biotechnology Information 1999). Willows are a pest species in many Australian waterways and may partly explain the broad presence of salicylic acid in this study. Salicylic acid is relatively non-toxic to aquatic wildlife with a predicted no effect concentration (PNEC) usually ranging from 60,000 - 170,000 ng/L (Schowanek and Webb 2002, Wang et al. 2010), and the concentrations reported here represent a negligible risk. Many metabolites and degradation products exhibit toxicological effects (Lambropoulou and Nollet, 2014), so further research into these chemical products is required.

Paracetamol was detected in 45% of the samples, with a maximum of 7,150 ng/L (the highest concentration in this entire study). In two USA studies, maximum concentrations ranged from 160-10,000 ng/L (Focazio et al. 2008, Kolpin et al. 2002). With a PNEC of 9,200 ng/L (Schowanek and Webb 2002), our data suggests that paracetamol represents a low risk in Australian rivers, although it should be highlighted that the highest concentration detected provided only a narrow margin of safety (Table 3).

The next most common pharmaceutical was carbamazepine, an anticonvulsant, with a frequency of 27% and a maximum of 682 ng/L (Table 3). In a USA surface water and groundwater study, the frequency of detection was 22% and the maximum concentration was 200 ng/L (Focazio et al. 2008). However, in an EU-wide study of surface waters, carbamazepine was detected more frequently (95%) with a maximum concentration ~20× higher (Loos et al. 2009). Carbamazepine was one of five most frequently detected compounds in each land-use category, except for undeveloped. It was found most commonly in NSW and VIC. The PNEC for carbamazepine is 500 ng/L (Agerstrand and Ruden 2010), suggesting that while there is little cause for concern in most situations, carbamazepine may pose a risk to the receiving environment at some sites (carbamazepine was above 500 ng/L in five out of 285 measurements, *i.e.*, 1.7% of samples). Phenytoin (an antiepileptic also known

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as dilantin) and primidone (an anticonvulsant) had maximum concentrations of 145 and 259 ng/L, respectively (Table 3). In four USA streams, concentrations of phenytoin ranged from 3.7–391 ng/L (Snyder et al. 2007), while the maximum concentration in Japanese river water was 51 ng/L (Komori et al. 2013). Primidone was found in 10 German rivers at concentrations ranging from 10–594 ng/L, but typical concentrations were >300 ng/L (Hummel et al. 2006). In Japan, primidone was detected with a maximum concentration of 38 ng/L (Komori et al. 2013). Both phenytoin and primidone are relatively non-toxic to aquatic organisms with PNECs of >100,000 ng/L (Komori et al. 2013), suggesting that the concentrations found in this study are unlikely to be of environmental concern.

Gemfibrozil (an antiepileptic; LOQ = 5 ng/L) had a maximum concentration of 213 ng/L and a detection frequency of 11% (Table 3). In comparison, it was detected 3.5% of the time in one US-wide study (with a maximum concentration of 790 ng/L; LOQ = 15 ng/L) (Kolpin et al. 2002), and not at all in a follow-up study (LOQ = 15 ng/L; Focazio et al. 2008). However, gemfibrozil was found more frequently in a European study (35%; LOQ = 1 ng/L), which also reported a higher maximum concentration of 900 ng/L (Loos et al. 2009). While the maximum concentration is less than in other studies, the detection frequency is in a similar range. With a PNEC of 1,000 ng/L (Wang et al. 2010), the concentrations detected here represent negligible risk.

Sulfamethoxazole, an antibiotic often used in combination with trimethoprim (another antibiotic), was detected in nine percent of samples, with a maximum concentration of 67 ng/L (Table 3). Four samples had concentrations that exceeded the PNEC of 26.8 ng/L (Agerstrand and Ruden 2010), while two additional samples were close. Further effects monitoring at the most polluted sites would help assess the environmental risk of sulfamethoxazole.

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Although trimethoprim was only detected in 5% of samples, it was present at the sixth overall highest concentration (657 ng/L; Table 3). It was detected more frequently (12.5%) and had a higher maximum concentration of 710 ng/L in a US study (Kolpin et al. 2002). However, another US study had a much lower maximum concentration (20 ng/L) (Focazio et al. 2008). With a comparatively high PNEC of 180,000 ng/L (Halling-Sorensen et al. 2000), the concentrations of trimethoprim detected here are unlikely to cause direct environmental effects, however indirect antibiotic resistance could be a potential problem.

3.1.5. Personal care products (PCPs)

Caffeine was the most commonly detected PCP, occurring in 65% of samples, followed by triclosan (25%) and propylparaben (12%). Caffeine was the second most common TrOC in this study (median = 19 ng/L) and had the third highest reported concentration overall (3,770 ng/L; Table 3). The maximum concentration was measured in a NSW industrial sample. There were seven other samples with caffeine concentrations above 1,000 ng/L; four residential, three industrial and one WWTP samples. The maximum concentration of caffeine falls between that reported in Focazio et al. (2008) (270 ng/L) and Kolpin et al. (2002) (6,000 ng/L). All three mentioned maximums fall significantly short of 39,813 ng/L reported in a European surface water sample (Loos et al. 2009). The frequency of detection for caffeine corresponded closely with that reported in Kolpin et al (2002) (71%). With a PNEC for caffeine of 5,200 ng/L (Komori et al. 2013), caffeine generally poses a low risk, although it should be noted that some of the data points above 1,000 ng/L only leave a slim margin of safety.

Triclosan, a widely used broad spectrum antibacterial compound, was the second most commonly detected PCP (25%), with a maximum concentration of 87 ng/L. Kolpin et al. (2002) detected triclosan in 57% of samples with a maximum concentration of 2,300 ng/L

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and a median concentration of 140 ng/L. Triclosan was also found in wild fish in WWTP effluent receiving environments in Sweden at concentrations up to 0.90 mg/kg fresh weight of bile (Adolfsson-Erici et al. 2002). New evidence suggests that the risk from exposure to triclosan could be underestimated and as such, the PNEC of 500 ng/L (Perez et al. 2013) may not be adequate. For instance, triclosan was found to negatively affect larval fathead minnow (*Pimephales promelas*) swimming performance at 151 ng/L, an exposure concentration less than twice the maximum concentration reported herein (87 ng/L; Table 3; Cherednichenko et al. 2012). Drury et al. (2013) reported that sediment triclosan concentrations (a maximum concentration of 107 ± 18 ng/g) were directly proportional to the relative abundance of resistant bacteria. In light of this information, some triclosan concentrations in Australian rivers may pose considerable risk to aquatic organisms.

Propylparaben which is both a natural substance and a PCP, was the third most commonly detected PCP (12%) with a maximum concentration of 218 ng/L (Table 3). The maximum concentration reported is much less than that found in Spanish surface waters (32,000 ng/L) (Regueiro et al. 2009), while another Spanish study did not detect propylparaben in surface waters (<5 ng/L) (Pedrouzo et al. 2009). A UK study reported a maximum concentration of 11 ng/L in surface waters (Kasprzyk-Hordern et al. 2008). With a PNEC of approximately 20,000 ng/L (Yamamoto et al. 2011), the risk of propylparaben to the Australian aquatic environment appears negligible.

Triclocarban, used as an anti-bacterial and anti-fungal disinfectant in soaps and other household products, was detected in one percent of the samples, with a maximum concentration of 58 ng/L. A PNEC of 190 ng/L was recently derived for triclocarban (Tamura et al. 2012). A LOEC of 130 ng/L (NOEC of 60 ng/L) was previously reported for *Mysidopsis bahia* reproduction rate (U.S. Environmental Protection Agency 2008). There is limited information about the occurrence of triclocarban in the environment in general,

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compared to triclosan. Halden and Paull (2005) predicted mean and median concentrations of 213 and 109 ng/L, respectively, in US streams, which warrants further chemical monitoring efforts.

DEET was analyzed but results were not presented due to concerns that some LC-MS/MS methods, including ours, may overestimate DEET concentrations due to an unidentified natural substance that is being incorrectly measured as DEET (Snyder, pers. comm.). A more robust chemical analysis methodology for DEET may be required to accurately quantify this compound in the environment.

3.1.6. Industrial compounds

The flame retardant TCEP was the only industrial compound examined. TCEP was detected in 44% of samples, with a maximum concentration of 184 ng/L (detected in a SA sample downstream of a WWTP; Table 3). Similarly, Kolpin et al. (2002) detected TCEP in 60% of samples, but reported significantly higher maximum and median concentrations (54,000 ng/L, 100 ng/L). Focazio et al. (2008) detected TCEP in 20% of samples, but concentrations were less than the quantification limit (500 ng/L). Mean and maximum concentrations of 203 ng/L and 2,019 ng/L, respectively, were found in five German rivers (Quednow and Puttmann 2009). While it was frequently detected, TCEP poses a negligible risk considering its PNEC of 65,000 ng/L (Quednow and Puttmann 2009).

3.1.7. Pesticides

Pesticides were not commonly detected in our water samples. As of 2002, simazine (LOQ = 5 ng/L) and atrazine (LOQ = 5 ng/L) were the most widely used herbicides in Australia (Radcliffe, 2002), however they were only detected in 14% and 11% of samples, respectively. The fungicide 2-phenylphenol (LOQ = 10 ng/L) was detected in 13% of

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samples, although it was not among the most frequently used fungicides in Australia (Radcliffe 2002). Linuron (LOQ = 5 ng/L), which has the same mode of action as atrazine and simazine, has also been used frequently in Australia, but was only detected in three percent of samples; predominantly in agricultural samples (66% of detections). Chlorpyrifos (LOQ = 5 ng/L) and diazinon (LOQ = 5 ng/L) have been the most widely used insecticides in Australia (Radcliffe, 2002); but despite its wide use, chlorpyrifos was detected only twice at very low concentrations (5 ng/L) and diazinon was never detected. Trifluralin was not detected either (LOQ = 150 ng/L), despite its wide use as a pre-emergent control for weeds (Radcliffe, 2002). It is, however, important to note that chlorpyrifos, diazinon and trifluralin were only analyzed in the Spring sampling event.

Simazine had a maximum concentration of 3,930 ng/L (Table 3), which exceeded the PNEC of 3,200 ng/L derived using the 95th percentile and may pose a risk (ANZECC/ARMCANZ 2000). However it should be noted that it was only exceeded in one sampling event. The maximum concentration was also higher than those found in different studies in Australia, the US and Europe. An Australian study of 39 WWTP effluents reported a maximum concentration for simazine of 1,727 ng/L (Allinson et al. 2012). A European survey of river waters reported a detection frequency of 26%, a maximum concentration of 169 ng/L and an average concentrations of 10 ng/L (Loos et al. 2009). An EU ground water survey reported a higher detection frequency of 43% but a lower maximum concentration of 127 ng/L and an average of 7 ng/L (Loos et al. 2010). In a US shallow groundwater study of 1,034 sites, simazine had a detection frequency of 18% and a maximum concentration of 1,300 ng/L (Kolpin et al. 1998), while a surface water study including 151 water samples from 71 streams (and five reservoirs) detected simazine in 7 – 47% of samples (depending on sample type) and a maximum concentration of 14,150 ng/L, while median concentrations were all below the reporting limit (<50 ng/L; Battaglin et al. 2003).

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458 The maximum concentration for 2-phenylphenol (92 ng/L) occurred in a sample collected
459 downstream of a WWTP in VIC. This concentration was lower than the sole concentration
460 measured from 39 different WWTP effluent samples in the same state (240 ng/L) (Allinson et
461 al. 2012). A PNEC of 900 ng/L was determined using a reproduction test with *Daphnia*
462 *magna* (Bayer 2001), which results in a Hazard Quotient (HQ) of 0.1 for 2-phenylphenol.
463 This indicates that there may be cause for concern at the maximum concentration.
464 Atrazine was detected in 11% of samples, with a maximum concentration of 209 ng/L (Table
465 3). Kolpin et al. (1998) reported a much higher detection frequency (38%) and maximum
466 concentration (3,600 ng/L). In Europe, a detection frequency of 68%, a maximum
467 concentration of 46 ng/L and an average concentration of 3 ng/L were reported in surface
468 waters (Loos et al. 2009). Atrazine was detected in 56% of groundwater samples in Europe
469 with a maximum concentration of 253 ng/L and an average of 8 ng/L (Loos et al. 2010).
470 Atrazine was detected twice in WWTP effluents from across VIC with a maximum
471 concentration of 63 ng/L (Allinson et al. 2012). Interestingly, Australian WWTP effluent
472 contained less atrazine than river waters investigated in this study, again clearly indicating
473 that pesticides are likely to be attributable to other activities (such as agriculture, road
474 maintenance, etc). Atrazine has a PNEC of 13,000 ng/L (ANZECC/ARMCANZ 2000) and as
475 such, the maximum concentration of 209 ng/L is unlikely to be cause for concern, although
476 sampling design did not take into account run-off events, when environmental concentrations
477 could be elevated. Furthermore, there is still a vigorous scientific debate about its potential
478 endocrine effects (APVMA 2008).

479 It should be noted that we only measured a small number of pesticides, and that there is a
480 large and growing body of literature on many different types of pesticides detected in
481 Australian rivers (*e.g.*, Allinson et al. 2012; Church et al. 2004; Davis et al. 2008; Lewis et al.
482 2009; Sanchez-Bayo and Hyne 2014; Schäfer et al. 2011).

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3.2. Conclusions

A median of three TrOCs out of 42 was detected per sample, with a maximum of 18. The six most frequently detected compounds in this study were: salicylic acid (82%), caffeine (65%), paracetamol (45%), TCEP (44%), carbamazepine (27%) and triclosan (25%). Most pharmaceutical detected were at concentrations posing negligible risk. However, carbamazepine and sulfamethoxazole exceeded their PNECs five and four times each, respectively. Maximum concentrations of other pharmaceuticals (fluoxetine, gemfibrozil, naproxen, paracetamol) and PCPs (caffeine, triclocarban and triclosan) left only small margins of safety when compared to their respective PNECs. The pesticide simazine exceeded its PNEC in one sample, indicating potential risk. Chlorpyrifos, linuron and 2-phenylphenol concentrations were below their respective PNECs, but had thin margins of safety. TCEP was commonly detected but unlikely to be cause for concern.

3.3. Limitations and future research

The PNEC values used to calculate Hazard Quotients (HQs) and margins of safety were based on international studies, and it is unclear at this stage whether those levels would protect the unique Australian wildlife. Further work is needed to establish PNECs specific to the Australian environment.

The analytical issues with DEET and salicylic acid need to be overcome in the future to determine the actual impact that anthropogenic use of these chemicals have on the environment. This study relied on grab sampling, and further studies with composite or passive sampling techniques may provide a better measure of concentrations over longer time windows.

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This study measured "only" 42 TrOCs and many more are likely present in the Australian environment, including environmental transformation products. While most compounds were present below PNEC values, their potential for interaction and mixture toxicity needs to be investigated using effects based assessment (*e.g.*, using *in vitro* and *in vivo* techniques). Finally, *in situ* studies at the most polluted sites identified would help determine if the PNEC exceedances reported lead to significant environmental disturbances.

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733 **Figure titles -**

734 Figure 1 - Location of sampling sites across mainland Australia. State and territory capitals
735 are depicted by white stars, while black circles represent sampling locations. The population
736 density graph was obtained from the Australian Bureau of Statistics (2012).

737

738 Figure 2. (top) Frequency of detection for the five most detected compounds for each land-
739 use. Salicylic acid and caffeine were the most and second most commonly detected
740 compounds in each land-use. (bottom) Frequency of detection for the five most detected
741 compounds in each state. Salicylic acid and caffeine were again the first and second most
742 detected compounds, respectively, in all six states and territories. Numbers in brackets
743 represent the total number of samples analyzed for the respective compound. "TCEP" =
744 tris(2-Chloroethyl) phosphate.

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745 **Tables –**

746

747 Table 1. The number of samples collected during the four separate sampling events
748 and the dominant land-use at each site. WWTP = wastewater treatment plant.

749

Dominant adjoining land-use	Autumn May-11	Winter Aug-11	Spring Nov-11	Summer Feb-12
Agricultural	20	20	20	20
Industrial	7	7	7	7
Residential	19	19	18	18
WWTP	13	13	12	12
Undeveloped	14	14	12	13
Total	**73**	**73**	**69**	**70**

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750 Table 2. Chemical limit of quantification (LOQ) and number of detections above the LOQ throughout four sampling events during a one-year
751 period for targeted trace organic pollutants (TrOCs). “CASRN” = Chemical Abstracts Service Registry Number; “NA” = not analyzed; "NR" =
752 not reported (DEET only).

753

				Detection Frequency (%)			
				Autumn	Winter	Spring	Summer
			LOQ	May-11	Aug-11	Nov-11	Feb-12
Contaminant	**CASRN**	**Use**	**(ng/L)**	**n=73**	**n=73**	**n=69**	**n=70**
Industrial compound							
tris(2-Chloroethyl) phosphate (TCEP)	115-96-8	flame retardant	10	33	42	45	56
Pharmaceuticals							
Amitriptyline	50-48-6	antidepressant	10	0	3	3	0
Atenolol	29122-68-7	beta blocker	5	7	7	4	9
Atorvastatin	134523-00-5	antilipidemic	5	0	NA	NA	NA
o-Hydroxy atorvastatin	265989-46-6	atorvastatin metabolite	5	7	NA	NA	NA
p-Hydroxy atorvastatin	214217-86-6	atorvastatin metabolite	5	5	NA	NA	NA
Carbamazepine	298-46-4	anticonvulsant	5	25	33	25	27
Clozapine	5786-21-0	antipsychotic	5	3	7	1	3
Diazepam	439-14-5	benzodiazepine tranquilizer	5	0	1	0	1
Enalapril	75847-73-3	angiotensin-converting enzyme inhibitor	10	0	NA	NA	0
Fluoxetine	54910-89-3	selective serotonin uptake inhibitor	5	1	1	3	1
Gemfibrozil	25812-30-0	antilipidemic	5	10	16	10	6
Hydroxyzine	68-88-2	antihistamine	10	0	NA	0	0
Ibuprofen	15687-27-1	anti-inflammatory	5	7	5	3	3
Ketoprofen	22071-15-4	anti-inflammatory	10	0	0	0	0
Meprobamate	57-53-4	anti-anxiety agent	10	0	NA	0	0

Methotrexate	21672	antifolate	50	NA	NA	0	NA
Naproxen	22204-53-1	anti-inflammatory	5	4	4	4	1
Omeprazole	73590-58-6	antigastroesophageal reflux	5	0	1	0	0
Paracetamol	103-90-2	antipyretic	5	38	47	NA	50
Phenytoin	57-41-0	antiepileptic	5	16	21	19	0
Primidone	125-33-7	anticonvulsant	5	22	8	16	10
Risperidone	106266-06-2	antipsychotic	5	0	0	0	0
Salicylic acid	69-72-7	antiacne, acetylsalicylic acid metabolite	20	78	64	100	86
Simvastatin	79902-63-9	antilipidemic	5	0	0	0	0
Simvastatin-hydroxyacid	121009-77-6	simvastatin metabolite	5	0	0	0	0
Sulfamethoxazole	723-46-6	antibiotic	5	11	10	10	4
Triamterene	396-01-0	for hypertension and edema	5	0	1	3	0
Trimethoprim	738-70-5	antibiotic	5	5	7	4	3
Verapamil	52-53-9	antiarrhythmic	5	0	1	1	0
Personal care products							
Caffeine	1958-08-02	stimulant	10	71	49	NA	76
N,*N*-Diethyl-*meta*-toluamide (DEET)*	134-62-3	insect repellent	5	NR*	NR*	NR*	NR*
Propylparaben	94-13-3	preservative	10	0	4	33	11
Triclocarban	101-20-2	antibacterial	10	0	0	6	0
Triclosan	3380-34-5	antibacterial	10	33	19	22	26
Pesticides							
Atrazine	1912-24-9	herbicide	5	5	16	9	13
Chlorpyrifos	2921-88-2	insecticide	5	NA	NA	3	NA
Diazinon	333-41-5	insecticide	5	NA	NA	0	NA
Linuron	330-55-2	herbicide	5	1	4	4	3
2-Phenylphenol	90-43-7	biocide	10	3	3	10	39
Simazine	122-34-9	herbicide	5	NA	NA	10	17

Trifluralin	1582-09-8	herbicide	150	NA	NA	0	NA

*Not reported, see section 3.1.5 for more information.

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755 Table 3. Summary of the monitoring data of trace organic compounds from 285 samples, spanning 73 locations across mainland Australia, with
756 four sampling events over a one-year period. "NA" = Not available. Compounds with a hazard quotient >0.1 are highlighted in bold.
757

Compound	# samples analyzed (n)	Detection frequency (%)	Mean ± SE (ng/L)	50th percentile (ng/L)	95th percentile (ng/L)	Maximum value (ng/L)	Predicted No Effect Concentrations (PNEC)* (ng/L)	Hazard Quotient (Max/PNEC)
Industrial compound								
tris(2-Chloroethyl) phosphate (TCEP)	285	44%	19 ± 2	<10	89	184	65,000 [a]	0.0028
Pharmaceuticals								
Amtriptyline	285	1%	<10	<10	<10	62	2500 [b]	0.025
Atenolol	285	7%	<5	<5	7	133	10,000 [c]	0.013
Atorvastatin	73	0	<5	<5	<5	<5	24,000 [b]	<0.00021
o-Hydroxy atorvastatin	73	7%	<5	<5	7	20	NA	NA
p-Hydroxy atorvastatin	73	5%	<5	<5	7	34	NA	NA
Carbamazepine	**285**	**27%**	**30 ± 6**	**<5**	**171**	**682**	**500 [b]**	**1.4**
Clozapine	285	4%	<5	<5	<5	90	16,000 [d]	0.0056
Diazepam	285	1%	<5	<5	<5	8	4,300 [e]	0.0019
Enalapril	212	0	<10	<10	<10	<10	180,000 [b]	<0.00006
Fluoxetine	**285**	**2%**	**<5**	**<5**	**<5**	**22**	**47 [b]**	**0.47**
Gemfibrozil	**285**	**11%**	**7 ± 1**	**<5**	**15**	**213**	**1,000 [f]**	**0.21**
Hydroxyzine	212	0	<10	<10	<10	<10	[3,900 [g]]	<0.0025
Ibuprofen	285	5%	<5	<5	<5	44	1,650 [b]	0.027
Ketoprofen	285	0	<10	<10	<10	<10	2,000 [h]	<0.005
Meprobamate	212	0	<10	<10	<10	<10	NA	NA

Methotrexate	69	0	<50	<50	<50	<50	45,000 [i]	<0.0011
Naproxen	**285**	**4%**	**<5**	**<5**	**<5**	**347**	**640 [b]**	**0.54**
Omeprazole	285	< 1%	<5	<5	<5	5	[210 [j]]	0.024
Paracetamol	**216**	**45%**	**85 ± 38**	**<5**	**271**	**7,150**	**9,200 [k]**	**0.78**
Phenytoin	285	14%	8 ± 1	<5	32	145	>100,000 [l]	<0.0015
Primidone	285	14%	6 ± 1	<5	18	259	>100,000 [l]	<0.0025
Risperidone	212	0	<5	<5	<5	<5	[690 [m]]	<0.0073
Salicylic acid	285	82%	82 ± 9	42	278	1,530	60,000 [f]	0.025
Simvastatin	285	0	<5	<5	<5	<5	9,600 [b]	<0.0005
Simvastatin-hydroxyacid	285	0	<5	<5	<5	<5	NA	NA
Sulfamethoxazole	**284**	**9%**	**<5**	**<5**	**10**	**67**	**26.8 [b]**	**2.5**
Triamterene	285	1%	<5	<5	<5	14	[1,900 [n]]	0.0074
Trimethoprim	285	5%	5 ± 2	<5	<5	657	180,000 [o]	0.0037
Verapamil	284	1%	<5	<5	<5	36	54,000 [b]	0.00067
Personal care products								
Caffeine	**216**	**65%**	**130 ± 28**	**19**	**453**	**3,770**	**5,200 [l]**	**0.73**
DEET**	NA	NA	NA	NA	NA	NA	NA	NA
Propylparaben	285	12%	<10	<10	20	218	20,000 [p]	0.011
Triclocarban	**285**	**1%**	**<10**	**<10**	**<10**	**58**	**190 [q]**	**0.31**
Triclosan	**285**	**25%**	**<10**	**<10**	**24**	**87**	**500 [r]**	**0.17**
Pesticides								
Atrazine	285	11%	5 ± 1	<5	12	209	13,000 [s]	0.017
Chlorpyrifos	**69**	**3%**	**<5**	**<5**	**<5**	**5**	**10 [s]**	**0.5**
Diazinon	69	0	<5	<5	<5	<5	10 [s]	<0.5
Linuron	**285**	**3%**	**<5**	**<5**	**<5**	**72**	**500 [t]**	**0.14**
2-Phenylphenol	**285**	**13%**	**<10**	**<10**	**19**	**92**	**900 [u]**	**0.10**
Simazine	**139**	**14%**	**52 ± 29**	**<5**	**122**	**3,930**	**3,200 [s]**	**1.2**

Trifluralin	69	0	<150	<150	<150	<150	2,600 [v]	<0.058

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759 [a]Quednow and Puttmann 2009 [b]Agerstrand and Ruden 2010 [c]Derived based on no observable effect concentration (NOEC) for condition index in fathead
760 minnow of 1 mg/L, as reported in Winter et al. (2008) with an uncertainty factor (UF) of 100 [d]Escher et al. 2011 [e]Carlsson et al. 2006 [f]Wang et al. 2010
761 [g]Derived based on EC_{50} for green algae (96h) of 3.9 mg/L, as calculated by ECOSAR, with a UF of 1000 [h]Derived based on EC_{50} for growh inhibition of *P.*
762 *subcapitata* of 2 mg/L, as reported in Harada et al. 2008, with a UF of 1000 [i]Derived based on EC_{50} for growth inhibition of *T. pyriformis* of 45 mg/L, as
763 reported in Henschel et al. 1997, with a UF of 1000 [j]Derived based on EC_{50} for green algae (96h) of 0.21 mg/L, as calculated by ECOSAR, with a UF of 1000
764 [k]Schowanek and Webb 2002 [l]Komori et al. 2013 [m]Derived based on EC_{50} for green algae (96h) of 0.69 mg/L, as calculated by ECOSAR, with a UF of 1000
765 [n]Derived based on LC_{50} for daphnid (48h) of 1.9 mg/L, as calculated by ECOSAR, with a UF of 1000 [o]Halling-Sorensen et al. 2000 [p]Yamamoto et al. 2011
766 [q]Derived from a NOEC based on an 8d chronic toxicity test with *C. dubia* reported in Tamura et al. (2012), with a UF of 10 [r]Perez et al. 2013
767 [s]ANZECC/ARMCANZ 2000 95th percentile [t]Crane et al. 2007 [u]Derived from a NOEC based on a *D. magna* reproduction test in Bayer 2001, with a UF of 10
768 [v]ANZECC/ARMCANZ 2000, 99th percentile

769 * low reliability PNEC derived from QSAR data are indicated in brackets, **Not reported, see section 3.1.5 for more information.

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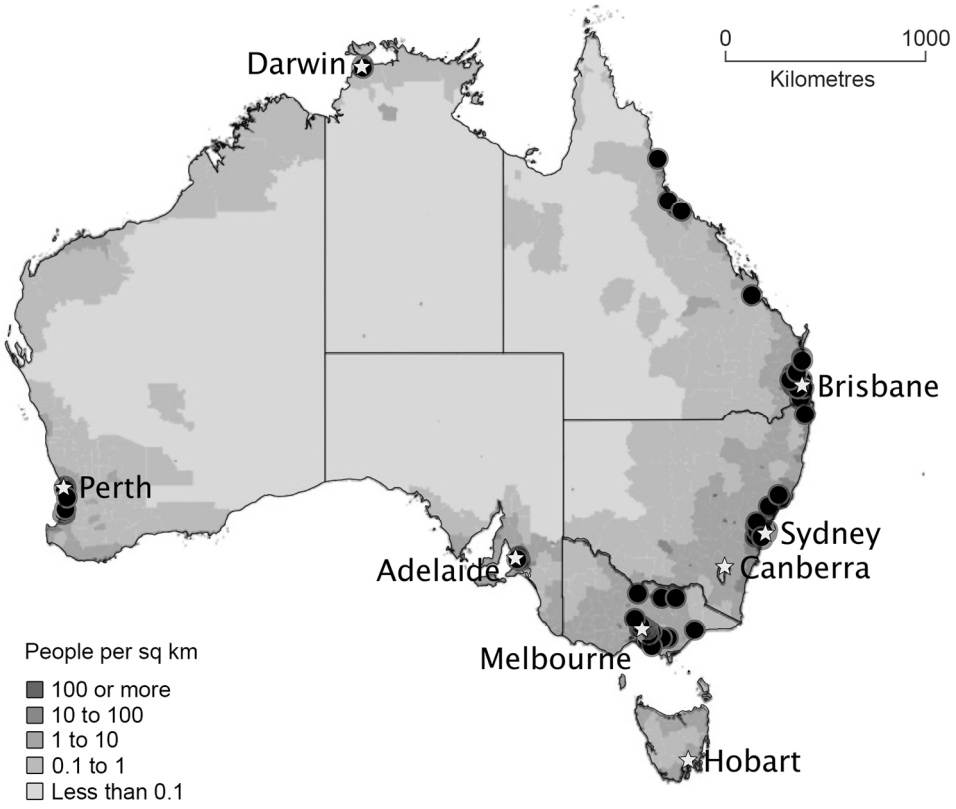

Figure 1 - Location of sampling sites across mainland Australia. State and territory capitals are depicted by white stars, while black circles represent sampling locations. The population density graph was obtained from the Australian Bureau of Statistics (2012).
285x240mm (150 x 150 DPI)

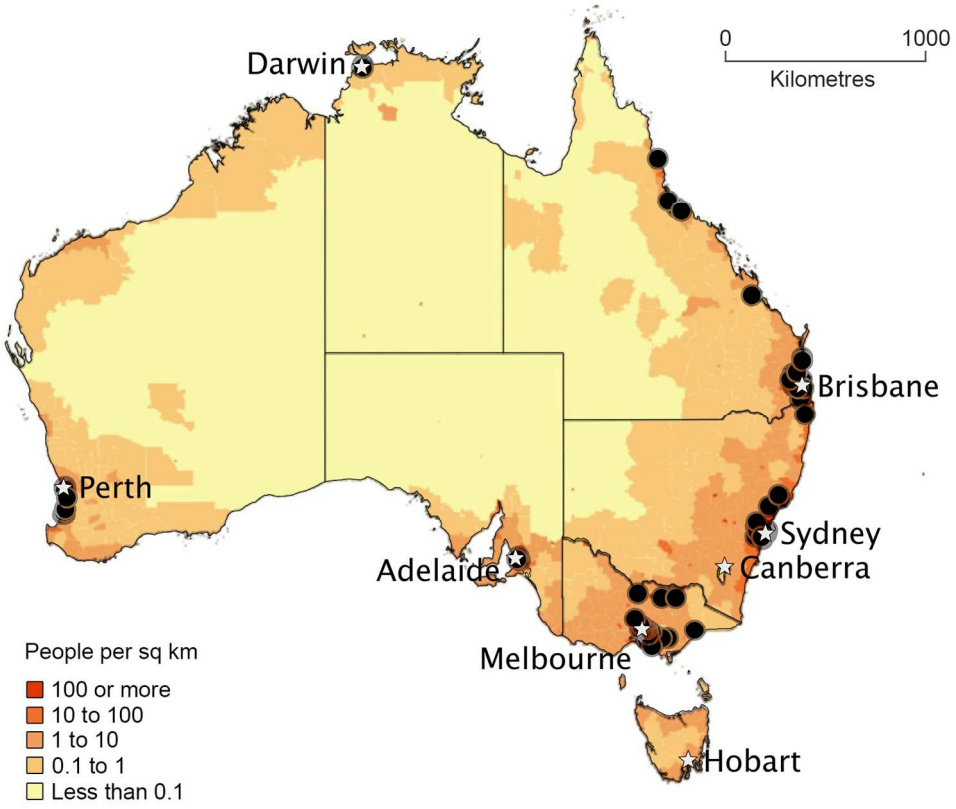

Figure 1 - Location of sampling sites across mainland Australia. State and territory capitals are depicted by white stars, while black circles represent sampling locations. The population density graph was obtained from the Australian Bureau of Statistics (2012).
285x240mm (150 x 150 DPI)

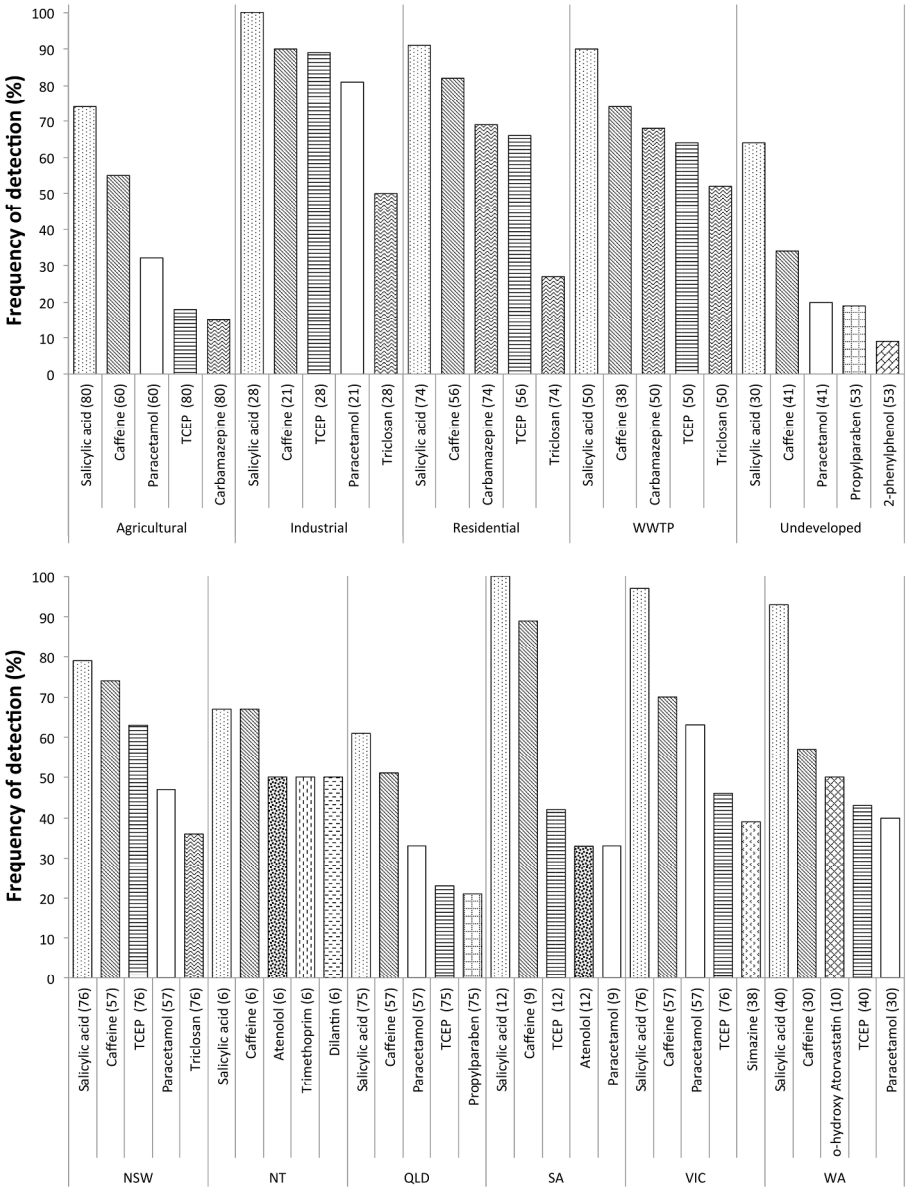

Figure 2. (top) Frequency of detection for the five most detected compounds for each land-use. Salicylic acid and caffeine were the most and second most commonly detected compounds in each land-use. (bottom) Frequency of detection for the five most detected compounds in each state. Salicylic acid and caffeine were again the first and second most detected compounds, respectively, in all six states and territories. Numbers in brackets represent the total number of samples analysed for the respective compound. "TCEP" = tris(2-Chloroethyl) phosphate.
255x327mm (300 x 300 DPI)

SUPPLEMENTARY INFORMATION FOR

A national survey of trace organic contaminants in Australian rivers

Philip D. Scott[a], Michael Bartkow[b], Stephen J. Blockwell[c], Heather M. Coleman[d], Stuart J. Khan[d], Richard Lim[e], James A. McDonald[d], Helen Nice[f], Dayanthi Nugegoda[g], Vincent Pettigrove[h], Louis A. Tremblay[i,j], Michael St. J. Warne[k], and Frederic D.L. Leusch[a,*]

[a] School of Environment, Griffith University, Southport, Queensland, 4222, Australia

[b] Seqwater, PO Box 16146, Brisbane City East, Queensland, 4002, Australia

[c] Sydney Water Corporation, PO Box 399, Parramatta, New South Wales, 2124, Australia

[d] School of Civil & Environmental Engineering, University of New South Wales, New South Wales, 2052, Australia

[e] School of the Environment, University of Technology Sydney, PO Box 123, Broadway, New South Wales, 2007, Australia

[f] Water Science Branch, Department of Water, Government of Western Australia, PO Box K822, Perth, Western Australia, 6842, Australia

[g] School of Applied Sciences, Royal Melbourne Institute of Technology, PO Box 71, Bundoora, Victoria, 3083, Australia

[h] Melbourne Water, PO Box 4342, Melbourne, Victoria, 3001, Australia

[i] Cawthron Institute, 98 Halifax Street East, Nelson, 7042, New Zealand

[j] School of Biological Sciences, University of Auckland, PO Box 92019, Auckland, 1142, New Zealand

[k] Water Quality and Investigations, Department of Science, Information, Technology, Innovation and the Arts, Queensland Government, GPO Box 5078, Brisbane, Queensland, 4001, Australia

* Corresponding Author.

e: f.leusch@griffith.edu.au

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p: +61 7 5552 7832

Mailing address:

Dr Frederic Leusch

Smart Water Research Centre (G51)

Griffith University, Gold Coast Campus

Southport, Queensland, 4222

Australia

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Table S1. Catchment composition based on primary land-use. Catchment assessments were performed for each sampling site to assess the impact of agricultural, industrial, residential, wastewater treatment plant (WWTP) effluent, and undeveloped inputs at each sampling location. The dominant land-use was used for grouping.

	Catchment composition (percent total catchment)				
Site	**Agricultural**	**Industrial**	**Residential**	**WWTP**	**Undeveloped**
Agricultural sites (n=20)					
1	40	0	20	30	10
2	70	10	10	10	0
3	50	0	10	20	20
4	60	0	0	0	40
5	95	0	0	0	5
6	90	0	10	0	0
7	90	0	10	0	0
8	80	20	0	0	0
9	80	10	10	0	0
10	80	0	10	0	10
11	100	0	0	0	0
12	100	0	0	0	0
13	90	0	0	0	10
14	80	0	20	0	0
15	70	0	30	0	0
16	100	0	0	0	0
17	75	0	5	0	20
18	70	0	30	0	0
19	100	0	0	0	0
20	60	0	0	0	40
Industrial sites (n=7)					
21	0	60	40	0	0
22	0	80	20	0	0
23	0	80	20	0	0
24	0	80	20	0	0
25	0	100	0	0	0
26	0	100	0	0	0
27	0	90	10	0	0
Residential sites (n=19)					
28	0	20	80	0	0
29	0	20	60	20	0
30	0	0	90	0	10
31	0	0	100	0	0
32	0	0	50	0	50
33	0	5	65	0	30
34	0	0	60	0	40
35	0	20	80	0	0
36	0	10	90	0	0

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37	0	30	70	0	0
38	0	20	80	0	0
39	0	20	80	0	0
40	0	0	100	0	0
41	0	0	100	0	0
42	20	0	60	0	20
43	0	20	80	0	0
44	0	0	80	0	20
45	0	20	80	0	0
46	0	0	80	0	20
WWTP sites (n=13)					
47	0	0	0	60	40
48	15	5	30	50	0
49	5	15	40	40	0
50	0	10	40	50	0
51	0	20	20	60	0
52	20	0	0	60	20
53	0	0	0	100	0
54	20	0	20	50	10
55	20	0	0	60	20
56	30	0	0	70	0
57	20	0	0	80	0
58	0	0	0	80	20
59	30	0	0	60	10
Undeveloped sites (n=14)					
60	0	0	10	0	90
61	10	0	10	0	80
62	20	0	0	0	80
63	0	0	10	0	90
64	20	0	10	0	70
65	0	0	0	0	100
66	0	0	0	0	100
67	0	0	10	0	90
68	30	0	0	30	40
69	40	0	0	0	60
70	0	0	0	0	100
71	0	0	0	0	100
72	0	10	0	0	90
73	0	0	10	0	90

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Table S2. Basic water parameters and meteorological data. Ranges reported here are based on four sampling events. pH, water temperature, dissolved oxygen (DO) and electro-conductivity (EC) determined via multi-meter. Nitrate, nitrite, total chlorine, free chlorine, total hardness, total alkalinity, pH (Hach strip) all determined using Hach strips (Section 2.3). Average atmospheric temperature and total precipitation values calculated for the week prior to sampling day (data downloaded for the nearest weather station from the Australian Bureau of Meteorology). "NA" = not available.

Site Number	pH	Water temperature (ºC)	Dissolved oxygen (mg/L)	Electro-conductivity (µS/cm^2)	Nitrate (ppm)	Nitrite (ppm)	Total chlorine (ppm)	Free chlorine (ppm)	Total hardness (ppm; $CaCO_3$)	Total alkalinity (ppm; $CaCO_3$)	pH (Hach strip)	Atmospheric temperature (ºC)	Precipitation (mm)
New South Wales													
1	7.1 - 7.9	14 - 25	8.2 - 10.1	182 - 243	0.15 - 0.5	0 - 1	0 - 0.01	0	50 - 120	40 - 80	6.8 - 7.2	9.8 - 21.7	1.4 - 66.4
2	7 - 7.8	15 - 26	7.7 -8 10.5	185 - 277	0 - 0.5	0 - 0.5	0 - 0.06	0	50 - 50	40 - 80	6.8 - 7.2	10.3 - 22.1	0.4 - 46.2
3	7.3 - 7.7	13.4 - 26.2	6.1 - 8.9	643 - 1421	0.15 - 1	0 - 1.5	0	0	7 - 120	80 - 120	7.2 - 7.6	10.3 - 22.1	0.4 - 46.2
4	7.2 - 8	13.9 - 23.2	6.3 - 8.5	185 - 1078	0 - 0.5	0.15 - 1.5	0	0	7 - 250	50 - 180	7.2 - 7.8	11.7 - 23.2	5.8 - 44.1
5	5.2 - 7.8	17.7 - 26.3	6.2 - 9.5	0 - 1262	0.15 - 2	0 - 1	0	0	50 - 120	40 - 120	6.8 - 7.2	14.5 - 21.5	1.2 - 72.4
6	7.1 - 8	22.4 - 24.1	4.3 - 8.3	200 - 325	0.15 - 0.5	0 - 1	0	0	50 - 50	40 - 80	6.8 - 7.8	9.2 - 23.6	2.6 - 82.2
7	6.9 - 7.8	15.4 - 22	4.5 - 9.3	63 - 4686	0 - 1	0 - 1	0	0	25 - 425	60 - 120	6.8 - 7.8	11.2 - 22.6	7.8 - 40.8
8	7.3 - 7.5	10.2 - 20.7	5.4 - 90	230 - 397	0 - 2	0 - 0.15	0	0	120 - 120	60 - 80	6.8 - 7.2	12 - 23.2	2 - 71
9	7.2 - 7.6	12.2 - 24.4	6.3 - 10.4	89 - 224	0.15 - 2	0 - 0.15	0	0	50 - 50	40 - 120	6.8 - 7.2	14.3 - 22.9	10.6 - 120.2
10	6.2 - 7.6	17 - 25.5	3.4 - 6.6	9 - 41	0.15 - 2	0 - 1	0	0	25 - 425	180 - 240	7.2 - 7.8	12.9 - 22.2	1.2 - 58.8
11	7.3 - 8.7	15 - 24	1.9 - 19.2	9 - 1055	0 - 2	0 - 1	0	0	25 - 425	120 - 240	7.2 - 8.4	11.7 - 20.8	8 - 63
12	6.9 - 7.9	17 - 25.2	1.9 - 8.3	16 - 47	0 - 2	0 - 0.15	0	0	25 - 425	120 - 240	6.8 - 7.8	12.9 - 22.2	1.2 - 58.8
13	7.1 - 7.7	12.5 - 21.2	2.3 - 8.7	102 - 977	0 - 1.5	0.15 - 0.65	0	0	50 - 250	120 - 240	6.8 - 7.6	20.6 - 21.1	67.4 - 74.4
14	7.2 - 7.5	11 - 22.7	1.6 - 6.6	685 - 1414	0 - 0.5	0.05 - 1	0	0	10 - 120	120 - 180	6.8 - 7.8	11.1 - 23.2	2.4 - 39.6
15	6.8 - 7.6	12.4 - 22	4.2 - 8.8	307 - 1038	0.15 - 3.5	0 - 0.5	0	0	120 - 250	40 - 240	7 - 7.8	11.1 - 21.8	6.4 - 60.4
16	7.1 - 8	10.8 - 22.5	7.1 - 10.8	60 - 148	0.15 - 1.5	0 - 1	0	0	25 - 50	20 - 100	6.8 - 7.2	12 - 20.3	41.4 - 109.4
17	6.9 - 7.6	11.1 - 26.8	8 - 10.4	75 - 121	0 - 1.5	0 - 0.5	0	0	25 - 50	20 - 40	6.8 - 7.2	10.9 - 23.7	0.6 - 51.6
18	5 - 6	10.1 - 18	9.1 - 10.7	138 - 172	0.15 - 1	0 - 0.5	0	0	25 - 50	20 - 40	6.2 - 7	11.1 - 20.6	0 - 83.6
19	6.4 - 7.7	11.3 - 20.9	9.1 - 10.9	109 - 171	0 - 0.15	0 - 1	0	0	25 - 85	40 - 80	6.8 - 6.8	11.1 - 20.6	0 - 83.6
Northern Territory													
20	7.2 - 7.2	25.6 - 25.6	NA	NA	1.5 - 1.5	0.23 - 2	0	0	50 - 120	120 - 180	7.8 - 8.4	0 - 31.2	0

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21	7.1 - 7.7	27 - 27	5.3 - 6.9	NA	0.5 - 1.5	0.15 - 1	0	0	50 - 50	120 - 120	7.2 - 8.4	0 - 26.1	0 - 0.6
22	7.9 - 8.1	25.7 - 25.7	0.5 - 6.4	NA	0	0 - 1.5	0	0	25 - 425	180 - 220	7.8 - 7.9	0 - 25.7	0 - 0.6
Queensland													
23	7.8 - 8.4	13.3 - 24.2	2.8 - 8.2	464 - 729	0 - 0.15	0 - 0.5	0	0	120 - 250	160 - 240	7.2 - 8.4	11.7 - 22.9	0 - 69.2
24	7.7 - 8.3	16 - 26.2	7.7 - 11.3	513 - 780	0 - 1	0 - 1	0	0	120 - 338	120 - 240	7.8 - 7.8	11.1 - 25.1	0 - 32.8
25	8.1 - 8.2	15.4 - 24.8	7.2 - 9.5	303 - 684	0 - 0.2	0 - 0.05	0	0	120 - 200	120 - 180	7.8 - 7.8	13.8 - 24.9	0.2 - 12.8
26	6.4 - 7.5	20.1 - 31.2	2.2 - 7.6	227 - 1049	0 - 1	0 - 0.15	0	0	120 - 250	80 - 240	6.8 - 8.4	19.1 - 28.4	0 - 155.2
27	6.1 - 6.8	20.2 - 27.5	7.7 - 8.5	38 - 41	0 - 1	0 - 1	0	0	0 - 25	0 - 80	6.2 - 6.8	19.2 - 28.4	0 - 230.5
28	7.5 - 8.6	20.4 - 29.4	8.1 - 9	237 - 729	0 - 1	0 - 0.5	0	0	50 - 250	180 - 240	7.8 - 8.4	16 - 27.6	0.2 - 86.2
29	7.9 - 8.3	14.8 - 26.6	6.1 - 13.5	452 - 1732	0 - 0.25	0 - 0.15	0	0	120 - 425	180 - 240	7.8 - 8.4	13.8 - 24.9	0.2 - 12.8
30	7.9 - 8.2	15.6 - 26	7.4 - 9.7	371 - 701	0 - 0.5	0 - 0.15	0	0	120 - 425	80 - 240	7.2 - 7.8	16.4 - 25.3	0 - 38.4
31	6.2 - 7.6	16.1 - 28.7	2.7 - 7.1	310 - 440	0 - 2	0 - 0.15	0	0	120 - 120	40 - 120	6.2 - 7.8	14.5 - 24.7	0 - 28.2
32	7.9 - 8.9	17.5 - 29.2	1.2 - 9	48 - 672	0 - 0	0 - 0.5	0	0	120 - 250	120 - 240	7.8 - 8.4	15.7 - 25.2	0 - 38.4
33	7.3 - 7.5	15.8 - 25.2	7.8 - 9.5	160 - 578	0.1 - 1	0 - 1	0	0	100 - 120	40 - 180	7 - 7.9	13.6 - 24.9	0 - 29.6
34	7.3 - 8	26.5 - 27.6	4.1 - 4.4	370 - 864	0.1 - 2	0 - 0.5	0	0	120 - 250	8 - 240	7.5 - 19.1	12.2 - 24.2	0 - 11.8
35	7.7 - 8.2	13 - 25.2	6 - 10.2	818 - 2309	0 - 0.15	0 - 0.05	0	0	250 - 425	240 - 240	7.8 - 8.4	14 - 25.2	0 - 48
36	6.3 - 7.7	22 - 30	2.4 - 7.1	69 - 278	0 - 0.15	0 - 0.15	0	0	25 - 75	40 - 120	6 - 6.8	20.9 - 27.8	0.2 - 74
37	6.8 - 8.2	21.9 - 26.3	5.6 - 10.2	45 - 100	0 - 0.15	0 - 0.5	0	0	25 - 50	40 - 240	7.2 - 7.2	19.1 - 28.3	0 - 126.6
38	7.7 - 8.9	15.2 - 25.8	9.4 - 10.3	57 - 70	0 - 0	0	0	0	25 - 120	40 - 40	6.8 - 7.8	14.8 - 24.7	4.8 - 14
39	4.9 - 7.8	28.7 - 29.1	5.1 - 8.2	70 - 1023	0.15 - 1	0 - 0.15	0	0	0 - 425	0 - 80	6.8 - 19.2	16.1 - 25.6	0 - 54.2
40	7.8 - 8.2	14.6 - 22	1.2 - 7.7	210 - 432	0 - 0.1	0 - 0.5	0	0	50 - 120	40 - 120	6.8 - 7.2	14.1 - 22.8	0.2 - 46.8
41	7.1 - 8.2	10 - 26.9	7.1 - 7.9	370 - 590	0 - 1	0 - 0.15	0	0	7 - 425	8 - 240	6.8 - 18	16.1 - 25.6	0 - 54.2
South Australia													
42	6.9 - 11.3	11.8 - 20.8	6.9 - 9.1	1154 - 2167	0 - 2	0 - 1	0 - 0.5	0	25 - 120	240 - 240	7.2 - 8.4	9.8 - 21.6	0 - 19.2
43	6.8 - 8.3	11.9 - 20.2	6.7 - 10.6	622 - 821	0 - 1	0	0	0	7 - 250	180 - 240	8.4 - 8.4	9.8 - 18	0.2 - 19.2
44	7.3 - 8	11.5 - 19.7	7.2 - 24.1	271 - 385	0 - 1	0 - 0.15	0	0	3 - 120	40 - 80	6.8 - 7.2	8.2 - 18	0.2 - 19.2
Victoria													
45	6.9 - 7.2	13.4 - 26.9	5.2 - 7.3	90 - 142	0 - 1	0 - 0.15	0	0	50 - 50	40 - 80	6.8 - 8.8	10.1 - 28.9	0 - 23.9
46	6.1 - 6.7	12 - 30.1	5 - 6.8	102 - 437	0 - 1	0 - 0.15	0	0	50 - 120	40 - 40	6.8 - 7.2	9.9 - 18.7	6 - 42
47	6.7 - 7.1	13.6 - 27.3	5.7 - 7.9	42 - 54	0 - 1	0 - 0.15	0	0	25 - 25	0 - 80	6.8 - 6.8	9.8 - 19.9	0.2 - 45.2

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48	6.6 - 7.1	8.3 - 21.4	6.4 - 9.6	112 - 246	0 - 1	0 - 0.15	0	0	50 - 50	40 - 40	6.8 - 6.8	8.8 - 19.9	2.6 - 29.8
49	6.2 - 6.9	9 - 23.9	5.9 - 9.5	217 - 260	0.15 - 1	0 - 1	0	0	3 - 50	40 - 80	6.2 - 6.8	8.2 - 19.9	2.6 - 29.8
50	6.4 - 7.5	12.1 - 25.4	3.8 - 6.9	400 - 1774	0 - 1	0 - 1	0	0	7 - 425	40 - 120	6.8 - 7.8	9.7 - 19.8	5 - 58.4
51	6.1 - 8.3	11 - 20.5	6 - 7.2	101 - 148	0 - 1	0	0	0	2 - 50	40 - 40	6.8 - 6.8	6.9 - 17.5	13.6 - 62.4
52	6.8 - 7.5	15 - 26.6	6.5 - 7.4	15 - 686	0 - 1	0 - 1	0	0	50 - 120	40 - 120	6.8 - 7.2	10.1 - 21	0.4 - 37.4
53	6.4 - 7.8	9.8 - 26.3	5 - 7.9	159 - 2550	0 - 1	0 - 1	0	0	0 - 425	40 - 240	6.8 - 7.8	11.4 - 20.8	6 - 37.8
54	7 - 7.4	12.3 - 22.2	5 - 6.9	9 - 780	0 - 1	0 - 0.15	0	0	50 - 120	40 - 120	6.8 - 68	11.9 - 20.8	6.6 - 20.4
55	5.9 - 7.1	13.3 - 22.5	3.1 - 4.9	509 - 1231	0.15 - 1	0 - 0.15	0	0	120 - 120	40 - 120	6.2 - 7.2	11.1 - 19.2	12.2 - 48.3
56	6.1 - 7.1	14.1 - 20.4	4.7 - 5.7	176 - 242	0 - 1	0 - 1	0	0	50 - 120	40 - 80	6.8 - 6.8	11 - 19.5	11.4 - 45.8
57	6 - 7.1	13.2 - 19.2	3.1 - 6.9	266 - 2089	0.15 - 1	0 - 0.15	0	0	120 - 425	40 - 240	6.8 - 68	11.2 - 20.1	1.2 - 51.8
58	6.8 - 7.9	10.1 - 18.8	4.4 - 6	125 - 600	0.15 - 1	0 - 0.3	0	0	50 - 120	80 - 120	6.8 - 7.8	11.6 - 20.8	6.6 - 31.4
59	6.9 - 8	11 - 19.9	5.9 - 7.8	167 - 1123	0.15 - 1	0 - 0.15	0	0	50 - 250	80 - 240	6.8 - 8.4	10.5 - 19.6	3.2 - 39.4
60	6.9 - 8	11.3 - 23.9	7.2 - 8.8	1384 - 2129	0 - 1	0 - 0.15	0	0	120 - 250	240 - 240	7.8 - 8.5	10.6 - 19.8	3.2 - 39.4
61	7 - 8.5	11.6 - 24.5	7 - 9.7	211 - 572	0 - 1	0 - 0.15	0	0	50 - 120	80 - 240	7.2 - 8.4	10.7 - 20.1	1.2 - 17.8
62	5.6 - 7.3	10.5 - 22.3	4.4 - 10.2	375 - 3120	0 - 1	0 - 0.15	0	0	25 - 425	240 - 240	6.8 - 8.4	10.6 - 19.7	1.4 - 6.4
63	6.1 - 7.1	6 - 16.7	4.4 - 9.7	76 - 151	0 - 1	0 - 0.15	0	0	0 - 25	40 - 40	6.2 - 6.8	7.1 - 17.5	3 - 14.4
Western Australia													
64	7.2 - 8	15.4 - 23	5.2 - 11.1	485 - 694	0.15 - 1	0 - 1	0 - 1	0	120 - 120	40 - 180	7 - 7.8	12.8 - 21.7	5.2 - 75.8
65	7.4 - 7.7	16.7 - 22.4	3.3 - 10.1	394 - 905	0.15 - 2	0 - 1	0	0	50 - 120	80 - 240	6.2 - 7.2	11.9 - 22.1	0 - 64.1
66	7.2 - 9.2	15.2 - 26.6	5.6 - 13	107 - 1282	0 - 1.5	0 - 1	0	0	120 - 250	80 - 120	7.2 - 7.2	12.8 - 21.7	5.2 - 75.8
67	7.3 - 9.2	16 - 29.4	8.1 - 16.4	148 - 767	0.3 - 1	1 - 2	0	0	120 - 120	80 - 180	7.2 - 7.2	12.4 - 21.7	5.2 - 154.4
68	7.1 - 8.2	12.5 - 21.4	7.9 - 10.1	225 - 314	0 - 2	0 - 1	0	0	50 - 120	40 - 40	6.8 - 7.2	11.8 - 22.1	0 - 156.9
69	7.1 - 7.5	19.9 - 26.7	4.5 - 10.8	146 - 865	0 - 2	0 - 1	0	0	50 - 250	80 - 240	6.2 - 7.8	14.6 - 25.5	0 - 33.2
70	6.9 - 7.9	18.6 - 26.5	2.1 - 8.5	547 - 696	0 - 1	0 - 1	0	0	120 - 120	40 - 80	6.2 - 7.2	14.9 - 25.3	0 - 29.4
71	6.9 - 7.6	19.8 - 27.5	6.1 - 7.6	434 - 918	0.15 - 2	0 - 1	0	0	25 - 425	80 - 180	7.2 - 7.8	14.9 - 25.3	0 - 35.6
72	7.3 - 7.9	19.3 - 25.4	7 - 7.3	146 - 665	0 - 1	0.15 - 1	0	0	50 - 120	40 - 120	6.8 - 7.2	14.6 - 24.1	0 - 33.2
73	7 - 8	12.2 - 21.7	6 - 10.6	248 - 309	0.15 - 5	0 - 1	0	0	3 - 50	40 - 40	6.8 - 7.2	12.1 - 21.7	6.7 - 70
Laboratory Blank													
74	8.4 - 8.8	21.7 - 22.1	5.2 - 7.6	0 - 2	0	0	0	0	25 - 25	40 - 40	6.2 - 7.8	NA	NA

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Table S3. Transition for compounds using ESI positive mode.

Compound	Precursor Ion (m/z)	Product Ion (m/z)
Atenolol 1	267.2	145.1
Atenolol 2	267.2	190.2
Atenolol-D7	274.1	145.1
Paracetamol	152.1	110.1
Paracetamol-$^{15}N^{13}C$	155	111
Sulfamethoxazole 1	254	156.1
Sulfamethoxazole 2	254	92
Sulfamethoxazole-D4	258.1	160.1
Caffeine 1	195	138.1
Caffeine 2	195	110.1
Caffeine-D9	204.1	144.2
Trimethoprim 1	291.1	230.2
Trimethoprim 2	291.1	261.1
Trimethoprim-D9	300.3	234.2
tris(2-Chloroethyl) phosphate (TCEP) 1	284.9	223
tris(2-Chloroethyl) phosphate (TCEP) 2	284.9	62.9
Phenytoin 1	253.1	182.1
Phenytoin 2	253.1	104.1
Phenytoin -D10	263.1	192.2
Carbamazepine 1	237	194.2
Carbamazepine 2	237	192.1
Carbamazepine-D10	247.1	204.3
Fluoxetine 1	310	44.1
Fluoxetine 2	310	148.2
Fluoxetine-D5	315.1	44.2
Enalapril 1	377.1	234.1
Enalapril 2	377.1	91.1
Enalapril-D5	382.2	239.2
Risperidone 1	411.1	191.2
Risperidone 2	411.3	110
Risperidone-D4	415.1	195.2
Atrazine 1	216	174.2
Atrazine 2	216	96.1
Atrazine-D5	221.3	179.1
Linuron 1	249	182.2
Linuron 2	249	160.1
Linuron-D6	255	160.1
Atorvastatin 1	559.1	440.1
Atorvastatin 2	559.1	250.3
Atorvastatin-D5	564.2	445.4
o-Hydroxy atorvastatin 1	575.2	440.2
o-Hydroxy atorvastatin 2	575.2	466.1
o-Hydroxy atorvastatin D5	580.2	445.1

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Compound	Precursor Ion (m/z)	Product Ion (m/z)
p-Hydroxy atorvastatin 1	575.2	440.2
p-Hydroxy atorvastatin 2	575.2	466.1
p-Hydroxy atorvastatin D5	580.2	445.1
Omeprazole 1	346.2	198.2
Omeprazole 2	346.2	136.1
Omeprazole D3	349.2	198
Clozapine 1	327.1	270.2
Clozapine 2	327.1	192.1
Clozapine_D4	331.2	272
Amtriptyline 1	278.2	233
Amtriptyline 2	278.2	117.1
Amtriptyline-D6	284.4	233.1
DEET 1	192.2	119
DEET 2	192.2	108.9
DEET-D7	199.2	126.1
Primidone 1	219.2	162.2
Primidone 2	219.2	119
Primidone-D5	224.2	167
Verapamil 1	455.4	165.1
Verapamil 2	455.4	150
Verapamil-D6	461.4	165.2
Triamterene 1	254.2	237
Triamterene 2	254.2	104
Triamterene-D5	259.2	242.2
Propylparaben 1	181.2	139.1
Propylparaben 2	181.2	121
Meprobamate 1	218.9	158.2
Meprobamate 2	218.9	115.1
Meprobamate-D3	221.9	161.2
Hydroxyzine 1	375.3	201.1
Hydroxyzine 2	375.3	165.1
Hydroxyzine-D8	383.3	201.1
Methotraxate 1	455.2	308.2
Methotraxate 2	455.2	175
Chlorpyrifos 1	349.9	197.9
Chlorpyrifos 2	349.9	115
Diazinon 1	305.1	169.1
Diazinon 2	305.1	115
Simazine 1	202.1	132.1
Simazine 2	202.1	124.1
Simazine-D10	212.2	137.1
Trifluralin 1	336.2	236.1
Trifluralin 2	336.2	251.8
Trifluralin-D14	350.2	238
Diazepam 1	285.1	193.1

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Compound	Precursor Ion (m/z)	Product Ion (m/z)
Diazepam 2	285.1	154.2
Diazepam-D5	290.1	198.1

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Table S4. Transitions for compounds using ESI negative mode.

Compound	Precursor Ion (m/z)	Product Ion (m/z)
Ketoprofen	252.8	208.8
Ketoprofen-D3	255.6	211.7
Naproxen 1	228.9	184.6
Naproxen 2	228.9	169.8
Naproxen-D3	231.9	187.8
Ibuprofen 1	204.9	160.8
Ibuprofen 2	204.9	158.8
Ibuprofen-D3	208	163.9
Gemfibrozil 1	248.9	120.8
Gemfibrozil 2	248.9	126.8
Gemfibrozil-D6	254.9	120.9
Triclosan	286.6	35
Triclosan-D3	289.7	34.9
Simvastatin-hydroxyacid 1	435.1	318.9
Simvastatin-hydroxyacid 2	435.1	114.9
Simvastatin-hydroxyacid-D6	441.1	319
Simvastatin 1	399	114.9
Simvastatin 2	399	282.8
Simvastatin-D6	405.4	121.1
Salicilic acid 1	136.9	92.8
Salicilic acid 2	136.9	65
Salicilic acid-D6	140.9	96.9
Triclocarban 1	312.9	159.8
Triclocarban 2	312.9	125.7
Triclocarban-D4	317	159.8
Propylparaben 1	179	135.7
Propylparaben 2	179	136.9
2-Phenylphenol 1	168.9	114.8
2-Phenylphenol 2	168.9	140.8

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