SUPPLEMENTAL MATERIAL FOR

Influence of hydrologic and anthropogenic drivers on emerging organic contaminants in drinking water sources in the Susquehanna River Basin

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Table S1. Physicochemical characteristics and EC50 or LC50 (mg/L) criteria used for risk assessment.

Compound	Physicochemical characteristics				EC50 or LC50 (mg/L)		
	[a]Chemical Formula	[a]Molar Mass (g/mol)	[a]pK_a	[a]Log Kow	Fish	Algae	*Daphnia*
Human Antibiotics							
Ampicillin	$C_{16}H_{19}N_3O_4S$	349.40	2.5; 7.3	1.35	--	[b]>1000	--
Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	253.28	1.6; 5.7	0.89	[c]890	[c]51	[d]189.2
Ofloxacin	$C_{18}H_{20}FN_3O_4$	361.37	5.97; 9.28	-0.39	[e]16	[e]4.74	[f]31.75
Trimethoprim	$C_{14}H_{18}N_4O_3$	290.32	7.12	0.91	[g]92.66	[g]83.8	[g]8.21
Antidiuretic							
Metformin	$C_4H_{12}ClN_5$	165.63	12.4	-0.5	[h]*383.3	[h]320	[h]81.4
Antihistamine							
Cimetidine	$C_{10}H_{16}N_6S$	252.34	6.8	0.40	--	--	--
Analgesics							
Acetaminophen	$C_8H_9NO_2$	151.17	9.38	0.46	[i]378	[i]132	[i]9.2
Naproxen	$C_{14}H_{14}O_3$	230.26	4.15	3.18	[c]34	[c]22	[c]15
Stimulant							
Caffeine	$C_8H_{10}N_4O_2$	194.19	10.4	-0.07	[j]90	--	[k]16
Metabolites							
Theobromine	$C_7H_8N_4O_2$	180.17	9.9	-0.78	--	--	--
Antimicrobial							
Triclosan	$C_{12}H_7Cl_3O_2$	289.54	7.9	4.73	--	--	--
Veterinary Antibiotics							
Chlortetracycline	$C_{22}H_{24}Cl_2N_2O_8$	515.34	--	--	[l]*78.9	[l]3.1	--
Erythromycin	$C_{37}H_{67}NO_{13}$	733.94	8.88	3.06	[l]*>100	[l]0.02	[l]22.45
Tetracycline	$C_{22}H_{25}ClN_2O_8$	480.90	3.30	-1.37	--	[l]2.2	[l]44.8
Oxytetracycline	$C_{22}H_{25}ClN_2O_9$	496.90	9.5	-0.90	[l]*110-215.4	[l]4.5	[l]22.64
Sulfadiazine	$C_{10}H_{10}N_4O_2S$	250.28	6.36	--	--	[l]0.135	[l]221
Sulfadimethoxine	$C_{12}H_{14}N_4O_4S$	310.33	--	--	[l]*>100	[l]2.3	[i]248
Sulfamethazine	$C_{12}H_{14}N_4O_2S$	278.33	2.07; 7.49	0.14	[l]*>100	--	[l]202
Tylosin	$C_{46}H_{77}NO_{17}$	916.11	7.73	1.63	--	[l]0.034	[l]680
Neonicotinoid Insecticide							
Thiamethoxam	$C_8H_{10}ClN_5O_3S$	291.71	--	-0.13	[m]3.7	[m]81.8	[m]>100

K_a: Acid dissociation constant; K_{ow}: Octanol water partition coefficient; EC50: Effective concentration; LC50: Lethal concentration -- No values; Sources: [a]https://pubchem.ncbi.nlm.nih.gov; [b]Eguchi et al., 2004; [c]Sanderson et al., 2003; [d]Santos et al., 2010; [e]Ferrari et al., 2004; [f]Isidori et al., 2005; [g]De Liguoro et al., 2012; [h]Lee, 2008; [i]Grung et al., 2008; [j]Moore et al., 2008; [k]Lilius et al., 1995; [l]Santos et al., 2010; [m]Finnegan et al., 2017.

Table S2. Summary statistics for seasonal variations during Phase I (row 1: mean ± standard deviation, row 2: detection frequency).

Compound	Spring		Summer		Fall		Winter	
	Riverine	*Reservoir*	*Riverine*	*Reservoir*	*Riverine*	*Reservoir*	*Riverine*	*Reservoir*
Acetaminophen	0.08 ± 0.04	<LOD	0.24 ± 0.22	0.05 ± 0	0.10 ± 0.09	0.16 ± 0.12	0.22 ± 0.15	0.37 ± 0.35
	22%	0%	78%	50%	33%	25%	67%	67%
Ampicillin	0.72 ± 0.66	<LOD	0.37 ± 0.17	<LOD	0.05 ± 0	0.05 ± 0	0.05 ± 0	0.05 ± 0
	22%	0%	33%	0%	33%	8%	11%	11%
Caffeine	4.72 ± 4.30	0.06 ± 0.01	0.11 ± 0.05	2.43 ± 2.78	0.33 ± 0.02	0.08 ± 0	3.28 ± 1.01	2.88 ± 0.58
	56%	22%	56%	50%	22%	8%	33%	33%
Naproxen	5.76 ± 3.34	1.33 ± 0.89	0.61 ± 0.20	0.05 ± 0	230.33 ± 0	91.62 ± 1489	5.09 ± 0	<LOD
	33%	33%	33%	25%	11%	25%	11%	0%
Ofloxacin	7.60 ± 5.54	1.14 ± 0	1.75 ± 0	<LOD	17.87 ± 0.62	13.64 ± 8.07	3.07 ± 0	8.96 ± 0
	44%	11%	11%	0%	22%	42%	11%	11%
Sulfamethoxazole	0.07 ± 0.03	0.12 ± 0.10	0.16 ± 0.11	0.26 ± 0.55	0.06 ± 0.02	0.05 ± 0	1.16 ± 2.26	4.85 ± 3.21
	67%	22%	100%	58%	78%	8%	67%	44%
Trimethoprim	22.69 ± 22.3	0.42 ± 0.34	1.13 ± 1.21	0.28 ± 0.30	<LOD	0.56 ± 0.67	0.28 ± 0.01	0.48 ± 0.02
	33%	22%	44%	58%	0%	17%	33%	33%

LOD = Limit of detection (0.01 µg/L) for all compounds except ofloxacin (0.3µg/L).

Table S3. Summary statistics for seasonal variations at site E during Phase II (concentration values: mean ± standard deviation).

Compound	Concentration (µg/L)		% Detection Frequencies	
	Winter	Spring	Winter	Spring
Acetaminophen	0.14±0.09	0.14±0.06	100%	97%
Caffeine	0.08±0.05	0.06±0.02	97%	93%
Metformin	0.09±0.06	0.17±0.14	88%	86%
Naproxen	<LOD	0.05	2%	45%
Ofloxacin	3.31	0.01	2%	2%
Oxytetracycline	0.41	<LOD	2%	0%
Sulfadimethoxine	0.18	<LOD	2%	0%
Sulfamethazine	0.04	<LOD	2%	0%
Sulfamethoxazole	<LOD	0.11±0.1	0%	43%
Tetracycline	0.39	<LOD	2%	0%
Theobromine	0.07±0.06	0.06±0.02	100%	96%
Thiamethoxam	<LOD	0.06±0.09	0%	49%

LOD = Limit of detection (0.01 µg/L) for all compounds except ofloxacin (0.3 µg/L).

Table S4. Calculated predicted no effect concentrations (PNEC) and seasonal risk quotients (RQ) for fish, algae, and *Daphnia* during Phase I.

Riverine Sources

	Compound	**PNEC** (µg/L)	**Seasonal Risk Quotient (RQ)** Fall	Spring	Summer	Winter
Fish	Acetaminophen	378	3.0E-04	2.0E-04	6.0E-04	6.0E-04
	Ampicillin	--	--	--	--	--
	Caffeine	90	3.6E-03	5.3E-02	1.2E-03	3.7E-02
	Naproxen	34	6.8	1.7E-01	1.8E-02	1.5E-01
	Ofloxacin	16	1.12	4.7E-01	1.1E-01	1.9E-01
	Sulfamethoxazole	890	1.0E-04	1.0E-04	2.0E-04	1.3E-03
	Trimethoprim	92.66	0	2.4E-01	1.2E-02	3.0E-03
Daphnia	Acetaminophen	9.2	1.14E-02	8.2E-03	2.63E-02	2.38E-02
	Ampicillin	--	--	--	--	--
	Caffeine	16	2.04E-02	2.95E-01	7.00E-03	2.05E-01
	Naproxen	15	1.54E+01	3.84E-01	4.09E-02	3.39E-01
	Ofloxacin	31.75	5.63E-01	2.39E-01	5.52E-02	9.66E-02
	Sulfamethoxazole	189.2	3.0E-04	4.0E-04	8.0E-04	6.10E-03
	Trimethoprim	8.21	0	2.76	1.37E-01	3.38E-02
Algae	Acetaminophen	132	8.0E-04	6.0E-04	1.8E-03	1.7E-03
	Ampicillin	1000	1.0E-04	7.0E-04	4.0E-04	1.0E-04
	Caffeine	--	--	--	--	--
	Naproxen	22	1.05E+01	2.62E-01	2.79E-02	2.31E-01
	Ofloxacin	4.74	3.77	1.6	3.7E-01	6.47E-01
	Sulfamethoxazole	51	1.2E-03	1.3E-03	3.1E-03	2.28E-02
	Trimethoprim	83.8	0	2.71E-01	1.34E-02	3.3E-03

Reservoir Sources

	Compound	**PNEC** (µg/L)	**Seasonal Risk Quotient (RQ)** Fall	Spring	Summer	Winter
Fish	Acetaminophen	378	4.0E-04	0	1.0E-04	1.0E-03
	Ampicillin	--	--	--	--	--
	Caffeine	90	9.0E-04	7.0E-04	2.7E-02	3.2E-02
	Naproxen	34	2.69	3.9E-02	1.5E-03	0
	Ofloxacin	16	8.52E-01	7.13E-02	0	5.6E-01
	Sulfamethoxazole	890	1.0E-04	1.0E-04	3.0E-04	5.5E-03
	Trimethoprim	92.66	6.1E-03	4.5E-03	3.0E-03	5.2E-03
Daphnia	Acetaminophen	9.2	1.69E-02	0	5.4E-03	3.99E-02
	Ampicillin	--	--	--	--	--
	Caffeine	16	5.2E-03	3.8E-03	1.52E-01	1.8E-01
	Naproxen	15	6.11	8.84E-02	3.3E-03	0
	Ofloxacin	31.75	4.3E-01	3.59E-02	0	2.82E-01
	Sulfamethoxazole	189.2	3.0E-04	6.0E-04	1.4E-03	2.57E-02
	Trimethoprim	8.21	6.86E-02	5.1E-02	3.36E-02	5.83E-02
Algae	Acetaminophen	132	1.2E-03	0	4.0E-04	2.8E-03
	Ampicillin	1000	1.0E-04	0	0	1.0E-04
	Caffeine	--	--	--	--	--
	Naproxen	22	4.16	6.03E-02	2.3E-03	0
	Ofloxacin	4.74	2.88	2.41E-01	0	1.89
	Sulfamethoxazole	51	1.0E-03	2.3E-03	5.0E-03	9.52E-02
	Trimethoprim	83.8	6.7E-03	5.0E-03	3.3E-03	5.7E-03

RQ = 0 when surface water concentrations were <LOD; -- = No values.

Table S5. Calculated predicted no effect concentrations (PNEC) and risk quotients (RQ) for fish, algae, and *Daphnia* during Phase II.

	Compound	PNEC (µg/L)	Risk Quotient (RQ) January	February	March	May	June
Fish	Acetaminophen	378	3.0E-04	4.0E-04	4.0E-04	3.0E-04	4.0E-04
	Ampicillin	--	--	--	--	--	--
	Caffeine	90	1.4E-03	7.0E-04	6.0E-04	4.0E-04	7.0E-04
	Metformin	383.3	3.0E-04	4.0E-04	1.0E-04	2.0E-04	7.0E-04
	Naproxen	34	2.0E-04	0	0	1.0E-04	1.2E-03
	Ofloxacin	16	2.3E-02	0	0	0	4.0E-04
	Sulfamethoxazole	890	0	0	0	0	1.0E-04
	Trimethoprim	92.66	0	0	0	0	0
	Triclosan	--	--	--	--	--	--
	Chlortetracycline	78.9	0	0	0	0	0
	Erythromycin	100	0	0	0	0	0
	Oxytetracycline	162.7	3.0E-04	0	0	0	0
	Tetracycline	--	--	--	--	--	--
	Theobromine	--					
	Thiamethoxam	3.7	0	0	0	1.23E-02	2.05E-02
	Cimetidine	--	--	--	--	--	--
	Tylosin	--	--	--	--	--	--
	Sulfadiazine	--	--	--	--	--	--
	Sulfadimethoxine	100	2.0E-04	0	0	0	0
	Sulfamethazine	100	4.0E-05	0	0	0	0
Algae	Acetaminophen	132					
	Ampicillin	1000	8.0E-04	1.0E-03	1.0E-03	1.0E-03	1.1E-03
	Caffeine	--	0	0	0	0	0
	Metformin	320	--	--	--	--	--
	Naproxen	22	4.0E-04	5.0E-05	1.0E-04	3.0E-04	8.0E-04
	Ofloxacin	4.74	3.0E-04	0	0	1.0E-04	1.8E-03
	Sulfamethoxazole	51	7.75E-02	0	0	0	1.2E-03
	Trimethoprim	83.8	0	0	0	1.0E-04	2.5E-03
	Triclosan	--	0	0	0	0	0
	Chlortetracycline	3.1	--	--	--	--	--
	Erythromycin	0.02	0	0	0	0	0
	Oxytetracycline	4.5	0	0	0	0	0
	Tetracycline	2.2	1.01E-02	0	0	0	0
	Theobromine	--	1.99E-02	0	0	0	0
	Thiamethoxam	81.8	--	--	--	--	--
	Cimetidine	--	0	0	0	6.0E-04	9.0E-04
	Tylosin	0.034	--	--	--	--	--
	Sulfadiazine	0.034	0	0	0	0	0
	Sulfadimethoxine	0.135	0	0	0	0	0
	Sulfamethazine	2.3	1.0E-01	0	0	0	0

Daphnia	Acetaminophen	9.2	1.0E-02	2.0E-02	2.0E-02	1.4E-02	1.53E-02
	Ampicillin	--	--	--	--	--	--
	Caffeine	16	8.1E-03	3.8E-03	3.2E-03	3.0E-03	4.0E-03
	Metformin	81.4	1.5E-03	2.0E-04	5.0E-04	1.0E-03	3.0E-03
	Naproxen	15	0	0	0	2.0E-04	3.0E-03
	Ofloxacin	31.75	0	0	0	0	2.0E-04
	Sulfamethoxazole	189.2	0	0	0	1.0E-05	7.0E-04
	Trimethoprim	8.21	0	0	0	0	0
	Triclosan	--	--	--	--	--	--
	Chlortetracycline	--	--	--	--	--	--
	Erythromycin	22.45	0	0	0	0	0
	Oxytetracycline	22.64	2.0E-03	0	0	0	0
	Tetracycline	44.8	1.0E-03	0	0	0	0
	Theobromine	--	--	--	--	--	--
	Thiamethoxam	100	0	0	0	5.0E-04	8.0E-04
	Cimetidine	--	--	--	--	--	--
	Tylosin	680	0	0	1.0E-03	0	0
	Sulfadiazine	221	0	0	0	0	0
	Sulfadimethoxine	248	1.0E-04	0	0	0	0
	Sulfamethazine	202	2.0E-05	0	0	0	0

RQ = 0 when surface water concentrations were <LOD; -- = No values.

Table S6. Predicted concentrations in fish, predicted human dose and human health risk quotients.

Compound	**Calculated Bioconcentration Factor**	**Predicted Concentration in Fish** (µg kg$^{-1}_{wt}$)	**Predicted Human Dose** (µg kg$^{-1}_{wt}$ d^{-1})	**Acceptable Daily Intake (ADI)** (µg Kg^{-1} d^{-1})	**Human Health Risk Quotient (RQ)**
Acetaminophen	0.5	0.07	2.48E-05	340[a]	7.3E-08
Ampicillin	2.8	0.5	2.0E-04	0.5[b]	3.0E-04
Caffeine	0.17	0.3	1.0E-04	30[c]	3.36E-06
Naproxen	0.07	4214	1.4	5.7[d]	2.0E-01
Ofloxacin	100.7	0.6	2.0E-04	7.1[d]	3.0E-05
Sulfamethoxazole	0.09	1.0	3.0E-04	130[a]	2.46E-06
Trimethoprim	1.1	3.8	1.3E-03	4.2[a]	3.0E-04

Sources: [a]Schwab et al., 2005; [b] Vragović et al., 2012; [c]McEachran et al., 2017; [d]Prosser & Sibley, 2015.

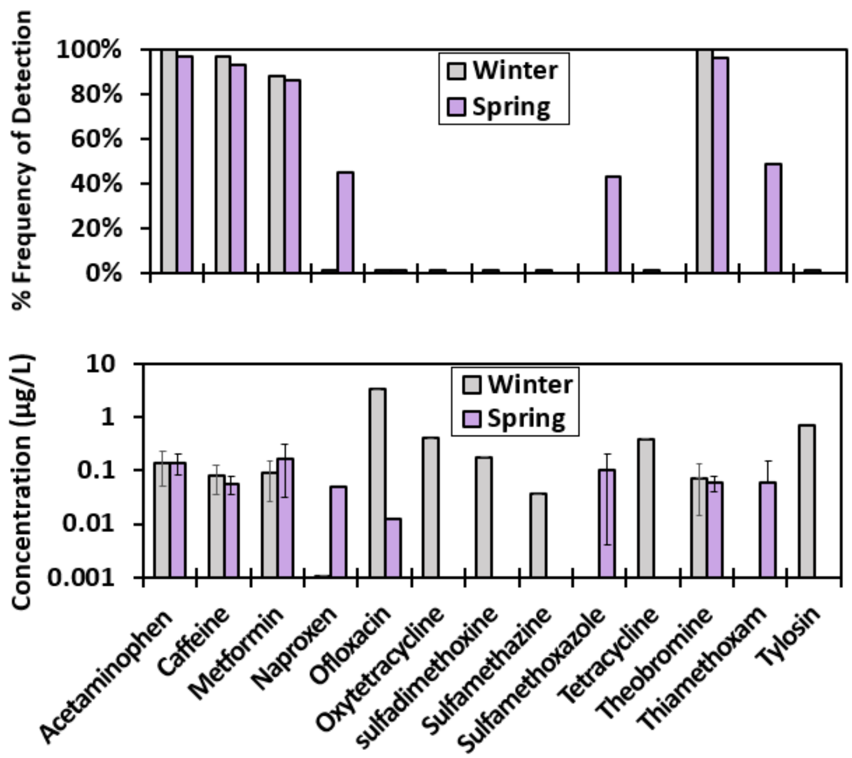

Figure S1. Seasonal variations in detection frequencies greater than the limit of detection (>LOD) and mean concentrations in samples collected in Phase II. Standard deviations are shown as error bars for compounds with values >LOD in more than one sample.

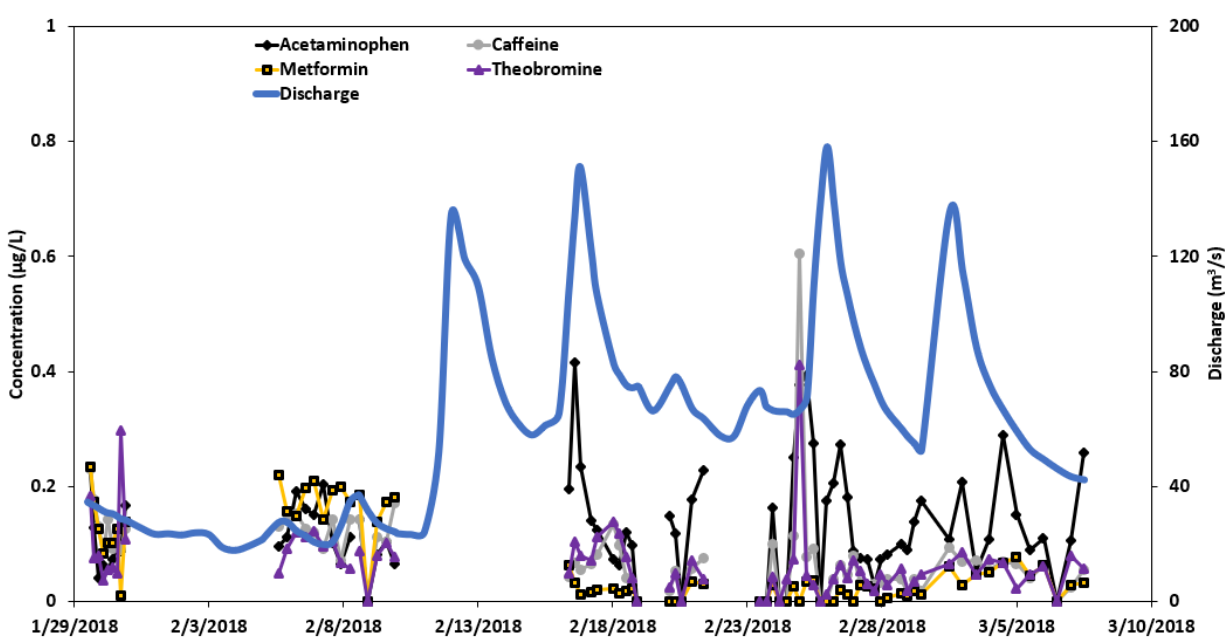

Figure S2. Fluxes of dissolved emerging organic contaminants (EOCs) with discharge in January through March, Phase II.

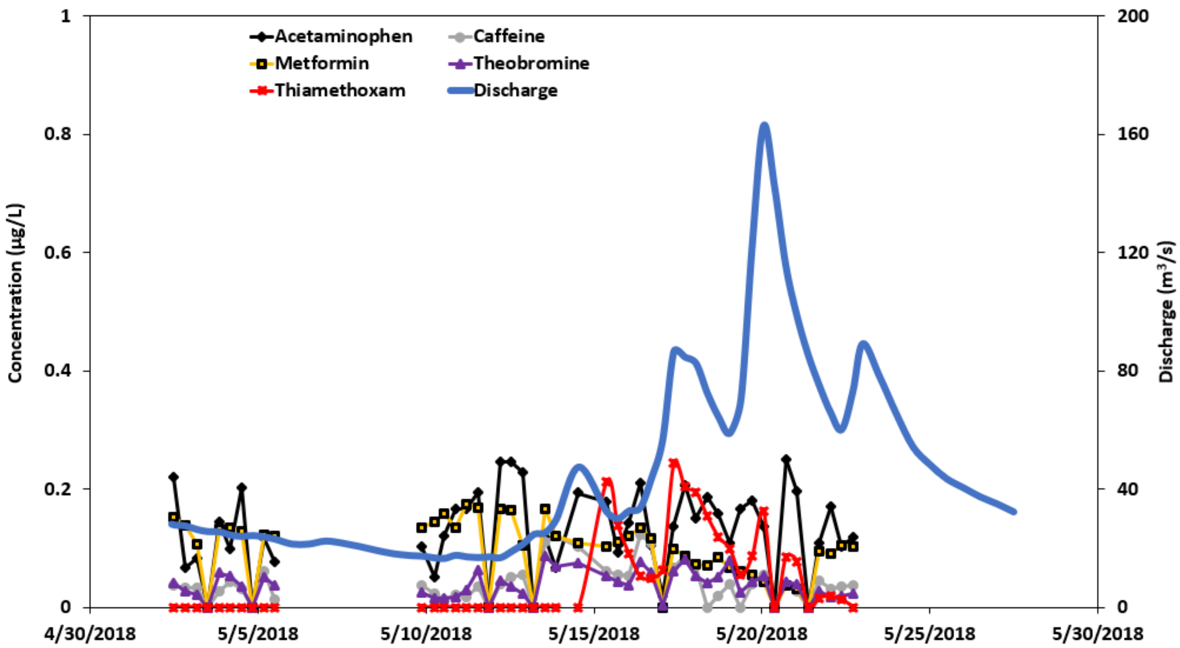

Figure S3. Fluxes of dissolved emerging organic contaminants (EOCs) with discharge in April and May, Phase II.

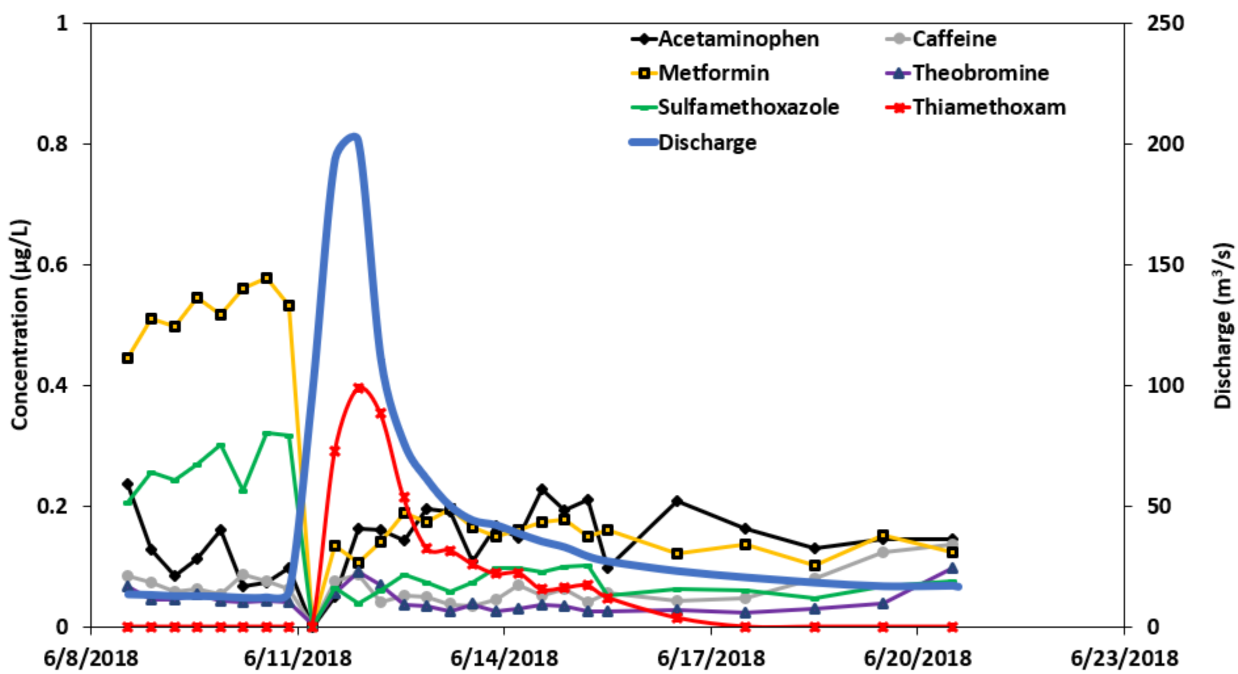

Figure S4. Fluxes of dissolved emerging organic contaminants (EOCs) with discharge in June, Phase II.

Relationships with Water Quality Indicators

In general, sulfamethoxazole (r=-0.22), caffeine (r=-0.40), and theobromine (r=-0.39) were significantly inversely correlated with temperature ($p<0.01$). Increased temperatures generally correspond with increased solar UV radiation, which increases biodegradation and photodegradation rates. In a water-sediment system, sulfamethoxazole's biodegradation rates have been observed to increase by over 40% at elevated temperatures independent of initial concentrations (Xu et al., 2011). Metformin (r=0.38), thiamethoxam (r=0.32), and naproxen (r=0.49) depicted significant ($p<0.01$) positive correlation with temperature. For thiamethoxam and naproxen, correlations may be representative of temporal variability especially since concentrations were higher in samples collected during warmer temperatures. Metformin concentrations decreased with increasing dissolved oxygen concentrations ($p<0.01$; r=-0.30). Although metformin is not readily biodegradable in aquatic environments (Scheurer et al., 2012), biodegradation rates in soil have increased (80-92%) under aerobic conditions (Mrozik and Stefańska, 2014) indicating a likelihood to degrade in water-sediment interphase under high dissolved oxygen levels. Naproxen showed similar patterns with dissolved oxygen ($p<0.01$; r=-0.28). However, as naproxen is a moderately hydrophobic compound, sorption to sediment can reduce aqueous concentrations (Kunkel and Radke, 2008).

Bernot et al. (2013) reported total dissolved carbon in surface water as a significant aqueous regulator of concentrations of pharmaceuticals and personal care products (PPCPs). In this study, trimethoprim (r=-0.16), ampicillin (r=-0.14), and naproxen (r=-0.12), had weak inverse relationships with total organic carbon. Increasing total organic carbon may provide a sink for concentration as emerging organic contaminants can combine with organic matter to reduce aqueous concentrations, especially for hydrophobic compounds. Sorption in natural environments is further influenced by compound characteristics such as structure and pKa and by aqueous phase characteristics such as pH and temperature. Hydrophilic compounds, ofloxacin (r=-0.26) and caffeine (r=-0.15), also had weak negative correlations with total organic carbon. The heterocyclic-N group in caffeine increases caffeine's ability to form hydrogen bonds to increase sorption potential (Nam et al., 2014). Similarly, the sorption capacity for quinolones, such as ofloxacin, are pH dependent, with their highest sorption potential near a neutral pH (Fu et al., 2017). This pH dependence is demonstrated in part with increasing ofloxacin concentrations as water pH increases (r=0.14).

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