Erratum: Schaefer et al. (2013)

SAN FRANCISCO ESTUARY AND WATERSHED SCIENCE, VOLUME 11, ISSUE 2, ARTICLE 3, JUNE 2013

Fate and Transport of Three Pharmaceuticals in the Sacramento–San Joaquin Delta

Minta M. Schaefer¹*, Laura A. Doyle², William E. Fleenor², and Michael L. Johnson¹

An error in the environmental concentrations included in Table 1, Available POCIS sampling rates and concentrations, was identified after publication of this paper in Volume 11, Issue 2 of the online journal San Francisco Estuary and Watershed Science. The chief scientist at the Sacramento Regional County Sanitation District (Regional San) contacted the authors because the environmental concentrations reported in Table 1 were much higher than the results of Regional San monitoring in the same portion of the Sacramento River. When preparing a written description for Regional San to show how the mass that was extracted from the Polar Organic Chemical Integrative Sampler (POCIS) membranes was translated to environmental concentrations, an error was discovered in the spreadsheet that was used to complete the calculations. The environmental concentrations were a critical part of the fate and transport modeling because they were used to calculate pharmaceutical loading for each wastewater treatment plant included in the model. As a result of the spreadsheet error, the input pharmaceutical concentrations in the original model runs were 228 times higher than they should have been (a POCIS membrane is 228 milligrams). After the error was discovered, the spreadsheet was corrected, the pharmaceutical loading recalculated, and the model was rerun.

The erroneous and corrected versions of Table 1 are shown on the following page.

The only difference between the original and new model runs is the pharmaceutical loading boundary condition; all other aspects of the approach are the same. The new model results range from two to three orders of magnitude lower than the original model results. Both the original and updated model results show that widespread spatial distribution of

* Corresponding author: 2600 Capitol Avenue, Suite 200, Sacramento, CA 95816; email: mintaschaefer@gmail.com
1 Center for Watershed Sciences, University of California, Davis
2 Department of Civil and Environmental Engineering, University of California, Davis
pharmaceuticals in the Delta is possible, however the updated model results significantly underestimates the concentrations found in some portions of the Delta. The monitoring data collected by the National Water Research Institute and United States Geological Survey were more consistent with the original model results than with the updated calculated concentrations. Additional data on the presence of these and other PPCPs in the Delta might help clarify this discrepancy and could be used to calibrate and validate future models.

The following pages reflect the original publication of the paper and include revisions to all text, tables, and figures based on the corrected environmental concentrations spreadsheet and updated model results. Revised content is indicated by red, strikethrough text (sample) on the original pages and is followed by yellow highlighted text (sample) on the corrected pages.

### ORIGINAL Table 1 Available POCIS sampling rates and concentrations

| Analyte         | Site 1 | Site 2 | Site 3 | Site 4 | Sampling rate (RS) | Site 2 | Site 3 | Site 4 |
|-----------------|--------|--------|--------|--------|-------------------|--------|--------|--------|
| Carbamazepine   | ND     | ND     | 45.6   | 43.2   | 0.360             | ND     | 285.9  | 268.9  |
| Fluoxetine      | ND     | 17.6   | 20.8   | 20.8   | 0.196             | 206.8  | 244.4  | 244.4  |
| Trimethoprim    | ND     | 2.0    | 28.3   | 26.3   | 0.348             | 12.8   | 181.0  | 168.2  |
| Gemfibrozil     | ND     | 19.3   | ND     | 214.0  | 0.192             | 231.5  | ND     | 2566.9 |

*ND indicates the analyte was not detected at this site.*

### CORRECTED Table 1 Available POCIS sampling rates and concentrations

| Analyte         | Site 1 | Site 2 | Site 3 | Site 4 | Sampling rate (RS) | Site 2 | Site 3 | Site 4 |
|-----------------|--------|--------|--------|--------|-------------------|--------|--------|--------|
| Carbamazepine   | ND     | ND     | 45.6   | 43.2   | 0.348             | ND     | 1.3    | 1.3    |
| Fluoxetine      | ND     | 17.6   | 20.8   | 20.8   | 0.196             | 0.9    | 1.1    | 1.1    |
| Trimethoprim    | ND     | 2.0    | 28.3   | 26.3   | 0.360             | 0.1    | 0.8    | 0.7    |
| Gemfibrozil     | ND     | 19.3   | ND     | 214.0  | 0.192             | 1.0    | ND     | 11.3   |

*ND indicates the analyte was not detected at this site.*
Fate and Transport of Three Pharmaceuticals in the Sacramento–San Joaquin Delta

Minta M. Schaefer†, Laura A. Doyle‡, William E. Fleenor‡, and Michael L. Johnson†

ABSTRACT
Pharmaceuticals and personal care products (PPCPs) are found in surface waters worldwide. Wastewater treatment plant effluent is a major source of these contaminants. The Sacramento–San Joaquin Delta (Delta) is a unique aquatic ecosystem, a source of drinking water for over 25 million Californians, and a primary source of water for Central Valley agriculture. The sharp decline of four pelagic fish species in the Delta in the last decade is just one of several indicators that the ecosystem is severely impaired. Several wastewater treatment plants (WWTPs) discharge into the Delta, directly or through tributaries. The presence of PPCPs in the Delta has received very little attention relative to the immense effort underway to rehabilitate the ecosystem. This study determined concentrations of PPCPs in the Sacramento River in the vicinity of the Sacramento Regional Wastewater Treatment Plant using passive sampler monitoring. These data were used to estimate loads of three of the detected pharmaceuticals (carbamazepine, fluoxetine, and trimethoprim) from nine other WWTPs that discharge to the Delta. The 2-D, finite element, Resource Management Associates (RMA) Delta Model was then applied to determine the distribution that might result from these discharges. The model was run for the 2006, 2007, and 2009 water years. Results indicate that it is feasible that WWTP discharges could result in chronic presence of these pharmaceuticals at low ng L⁻¹ levels at all 45 model output locations and, therefore, aquatic organisms within the Delta may be continually exposed to these contaminants.

KEYWORDS
RMA, pharmaceuticals, PPCP, fluoxetine, trimethoprim, carbamazepine, passive sampling, POCIS, modeling, water quality

INTRODUCTION
Pharmaceuticals and personal care products (PPCPs) are recognized water pollutants and can be found at trace levels in surface water and groundwater around the world (Barnes et al. 2008; Kolpin et al. 2002; Petrović 2007). Adverse effects from endocrine disruption and other biochemical pathways on a variety of aquatic organisms have been demonstrated, and examples include feminization of fish, deformities in amphipod crustaceans, reduced biomass and diversity in algal populations, and altered behavior in fish and tadpoles (Brain et al. 2008; Fraker and Smith 2004; Henry and Black 2008; Kidd et al. 2007; Routledge...
et al. 1998; Vandenberghe et al. 2003; Wilson et al. 2003). PPCPs are present in drinking water although the effects on human health are unknown (Benotti et al. 2008). Despite thousands of studies, including those on complex mixtures of PPCP compounds, determining whether PPCPs in surface water represent a significant environmental problem is unclear.

Wastewater treatment plant (WWTP) effluent is the most significant environmental source of PPCPs (Daughton and Ternes 1999; Petrović and Barceló 2007). After consumption or use, PPCP compounds and metabolites are excreted through urine and feces or washed from the body and released into wastewater streams and septic systems (Daughton and Ternes 1999). In addition to excretion, PPCPs are directly disposed of into home plumbing systems. The relative contributions of excretion and disposal are unknown although it is expected that the contribution from disposal is relatively minor (Heberer 2002). Existing wastewater treatment systems were not designed to remove the compounds found in PPCPs and a cost-effective treatment option is not currently available (Bolonga et al. 2008; Ternes 1999). However, wastewater treatment processes reduce the concentrations of many PPCPs to varying degrees (Petrović and Barceló 2007). Therefore, PPCPs remaining after wastewater treatment are the contaminants in question. Currently, PPCPs are not regulated as water contaminants by the federal or California state governments.

Several WWTPs discharge into the Sacramento–San Joaquin Delta (Delta), which is a unique aquatic ecosystem, a source of drinking water for over 25 million Californians, and a primary source of water for Central Valley agriculture. The health of the Delta ecosystem has been in steady decline for many years as a result of multiple stressors, including large-scale drinking water exports via the State Water Project (SWP) and Central Valley Project (CVP), contaminants in agricultural and urban runoff, power plant diversions, invasive species, municipal wastewater and industrial discharges, and highly regulated tributary river systems (CALFED 2008). Given the large population that is served by numerous WWTPs that discharge to the Delta, it is possible that PPCPs are another important stressor that contributes to this ecosystem decline.

Data on the presence of PPCPs in the Delta are very limited. None of the ongoing monitoring programs in the Delta include PPCPs. Occurrence data consist of results from a few short-term studies. A variety of PPCPs—including antibiotics, steroid hormones, caffeine, antidepressants, lipid regulators, antihypertensives, anticoagulants, and other compounds—were detected in Delta waters during these studies (Guo et al. 2010; Kolpin et al. 2002; Oros et al. 2003). A 2006 study evaluated water from 16 sites within the Delta and Napa River for the presence of steroid hormones and evidence of endocrine disruption by completing chemical analyses and bioassays on rainbow trout (Oncorhynchus mykiss). Natural and synthetic steroid hormones were either not present in the samples or were in concentrations that were below quantification limits. In contrast, high estrogenic activity was found in the bioassay results at 6 of the 16 sites. The inconsistency between the chemical and bioassay results was attributed to the possibility that other compounds could be responsible for the observed estrogenicity in rainbow trout (Lavado et al. 2008). Another study demonstrated a higher frequency of feminization of fall-run chinook salmon (Oncorhynchus tshawytscha) from the Sacramento and San Joaquin river basins when compared to hatchery populations (Williamson and May 2002). Though the issue of PPCPs in the Delta has received very little attention to date, especially when considering the immense efforts that are underway to understand and manage the Delta as a viable ecosystem and water source, the few studies that have been conducted suggest PPCPs cannot be eliminated as an important stressor of the Delta ecosystem and that they are possibly relevant to human health. However, the distribution and fate of these compounds remains unclear.

The purpose of this study was to address whether PPCP releases from WWTPs in the Delta watershed could result in regional contamination, and to estimate the approximate (order of magnitude) concentrations at which such contamination might be found. This was accomplished by: (1) collecting data on the concentrations of PPCPs in the Delta near a large
WWTP; (2) using a two-dimensional (2-D) hydrodynamic and water quality model to estimate PPCP concentrations throughout the Delta resulting from other WWTP inputs, assuming similar PPCP loading among WWTPs; and (3) comparing the estimated concentrations to data from the literature. The monitoring effort included four sites along the Sacramento River near the effluent of the Sacramento Regional Wastewater Treatment Plant (SRWTP). Passive sampling devices, including Polar Organic Chemical Integrative Sampler (POCIS) and Semipermeable Membrane Device (SPMD), were used at all four sites and remained in situ for 33 days in May and June 2009. A passive sampler membrane extract was screened for 30 analytes, including several antibiotics, an antibiotic metabolite, a lipid regulator, an anti-inflammatory, an anti-depressant, a natural estrogen hormone, an anti-epileptic, caffeine, an antibacterial, two surfactants, and four polycyclic musks. Three of the detected compounds, carbamazepine, fluoxetine, and trimethoprim were considered in the fate and transport analysis. Loads of each of the three compounds were estimated for each WWTP based on the assumption that the loads were proportional to discharge. For the 2006, 2007, and 2009 water years, the distribution of the three compounds was modeled using the Resource Management Associates (RMA) Delta Model, based on the calculated loads and estimated decay rates. The WWTPs considered in the fate and transport analysis include Delta Diablo, Discovery Bay, Fairfield, Mountain House, Rio Vista Beach, Rio Vista Northwest, Sacramento Regional, Stockton, Tracy, and White Slough (City of Lodi).

METHODS

Sacramento River Sampling

Using passive sampling devices we monitored four sites for 30 PPCPs within the Sacramento River near the effluent of the Sacramento Regional Wastewater Treatment Plant (SRWTP). The location of each monitoring site and the regional setting of the monitoring study area are provided in Figure 1. One monitoring site was located upstream and three sites were downstream of the SRWTP effluent. Effluent is discharged into the Sacramento River via a 122-m (400-ft) diffuser that spans the river bed perpendicular to flow just south of the Freeport Bridge. Site selection was based on distance from the SRWTP discharge, the two locations regularly monitored by SRWTP to comply with National Pollutant Discharge Elimination System (NPDES) permit requirements, and the presence of objects to which the passive sampling devices could be attached. Site 1 (38°27’22.22”N/121°30’5.25”W) was used as a control; it is located at the southernmost portion of Freeport Marina located upstream of the Freeport Bridge along the east bank of the river and approximately 100 m upstream from the treatment plant effluent. Site 2 (38°27’14.73”N/121°30’9.53”W) was approximately 9 m from the west bank and 525 m downstream from the effluent diffuser. Site 3 was at Cliff’s Marina, approximately 1,180 m downstream of the plant discharge (38°26’40.41”N/121°30’3.98”W). A private dock 1,900 m downstream of the effluent at the east bank was the location of Site 4 (38°26’18.62”N/121°30’16.11”W). The sites monitored for NPDES permit compliance are at the Freeport Bridge and Cliff’s Marina.

Passive sampling devices used in this study included three POCIS and SMPDs at each monitoring location. The POCIS membranes are designed to sequester hydrophilic polar organic compounds while the SPMD membranes trap hydrophobic compounds (Alvarez et al. 2004; MacLeod et al. 2007). Most PPCPs are polar organic compounds (Petrović and Barceló 2007). Both types of sampling devices were used to be thorough and because surfactants and musks, which exhibit hydrophobicity, were included as analytes. See Appendix A for detail on passive sampler deployment.

Passive sampler membrane extract was screened for 30 analytes including the antibiotics carbadox, chlorotetracycline, doxycycline, lincomycin, oxytetracycline, roxithromycin, sulfadimethoxine, sulfachloropyridazine, sulfamerazine, sulfamethazine, sulfathiazole, sulfamethizole, sulfamethoxazole, tetracycline, trimethoprim, and tylosin; erythromycin hydrate (antibiotic metabolite); caffeine (stimulant); gemfibrozil (lipid regulator); ibuprofen (non-steroidal anti-inflammatory); triclosan (antibacterial); 17β-estradiol
Figure 1 The Sacramento-San Joaquin Delta, wastewater discharge locations, and Sacramento River monitoring sites
(natural estrogen hormone); carbamazepine (anti-ionization (API-ES) source in positive and negative ion modes. Method detection limits ranged from 2 to 50 ng L$^{-1}$. We analyzed surfactants by using high-performance liquid chromatography with a fluorescence detector and confirmed it with a liquid chromatography mass detector operated in negative and positive mode for nonylphenol and nonylphenol ethoxylate, respectively. The reporting limit is 20 ng L$^{-1}$. Analysis for musks followed the EPA Method 8270 M. We analyzed the POCIS extract for musks by gas chromatography with a Mass Spectrometer Ion Trap Detector (operated in MS/MS mode). We analyzed the SPMD extract musks in the same manner as we did for pharmaceutical analytes.

Analytical results from passive sampling devices were reported in terms of mass per membrane filter. Empirically-determined, compound-specific linear uptake sampling rates, where available, were used to calculate an average concentration applicable to the river water over the monitoring period. Sampling rates have been determined for carbamazepine, fluoxetine, gemfibrozil, and trimethoprim and were used to calculate average concentrations for each compound at each monitoring site (MacLeod et al. 2007) (Table 1). Where sampling rates were not available, results are presented in ng per membrane (complete analytical results provided in Appendix A). None of the analytes were detected in the SPMD extract and, therefore, information on sampling rates focuses on the POCIS membranes. Analyte uptake by the POCIS devices is governed by analyte diffusion through the aqueous boundary layer that surrounds the membrane, and is independent of concentration in the sampled water body (Alvarez et al. 2004). Equation 1 developed by Huckins et al. (2000) relates the sampling rate ($R_s$); concentrations in water ($C_W$) and sorbent ($C_S$) (MacLeod et al. 2007); mass of the membrane (Williamson and May 2002); and time in situ in days ($t$) and is appropriate for POCIS and SPMDs (Alvarez et al. 2004; Huckins et al. 2000). The mass of a POCIS membrane is 228 mg and the sampling time is 33 days.

$$C_W = C_s M_s / R_s t$$

Transport Modeling

Carbamazepine, fluoxetine, and trimethoprim were selected from the list of detected analytes for use in the transport model. We selected these compounds because they have published POCIS sampling rates and are frequently detected in PPCP monitoring studies (Kolpin et al. 2002; Petrović and Barceló 2007). Decay rates 0.011 day$^{-1}$, 0.033 day$^{-1}$, 0.017 day$^{-1}$ were applied to the transport of carbamazepine, fluoxetine, and trimethoprim, respectively. Corresponding half-lives are 63, 21, and 42 days, respectively. We developed decay rates for each modeled pharmaceutical based on existing fate and monitoring studies. The basis for the selection of specific decay rates is provided in Appendix A. Dilution, advection, direct and indirect photolysis, adsorption to sediment, biodegradation, and bioaccumulation act on PPCPs in surface water (Petrović and Barceló 2007). Therefore, a decay rate that represents the cumulative effect of these processes is a critical model parameter. It is important to note that each of the processes listed above are relevant at different time-scales and vary in importance by the PPCP compound in question, as well as the character of the receiving water body. Dilution and advection are important in the transport of any compound found in WWTP effluent, and generally result in a reduction in concentration with distance from the point of discharge. Exceptions have been found in small systems where low or slow moving flow resulted in virtually no dilution downstream of the point of discharge (Petrović and Barceló 2007). Given that the receiving water bodies considered in this study vary in character, we recognize that the application of one decay rate for each modeled compound is a potential oversimplification of these local systems within the Delta.

We used the RMA Delta Model to analyze the movement of carbamazepine, fluoxetine, and trimethoprim through the Delta. The RMA Delta Model is a 2-D, depth averaged, finite element, hydrodynamic (RMA2) and water quality (RMA11) numerical model specific to the Delta. In the finite element grid, the Delta is represented through 2D quadrilaterals and triangles and one-dimensional (1-D) river and channel reaches that include the Delta as legally defined in the California Water Code Section 12220 as well as
Suisun Bay, sloughs and creeks that surround Suisun Marsh, Honker Bay, Grizzly Bay, and the Carquinez Strait (CA Water Code Section 12220). Elements range in size from 10 to 100 m on any side.

The RMA2 portion of the model is applicable to far-field problems for vertically homogenous fluids with a free surface. The program computes water surface elevations, or stage, and horizontal velocity by the Bubnov–Galerkin finite element approximation for spatial derivatives and a modified Crank–Nicholson for time derivatives using the momentum equation in the x and y direction and the continuity equation, shown as Equations 2 through 4 below, respectively.

RMA2 was developed in 1973 and has been continually improved and calibrated by RMA, the Coastal and Hydraulics Laboratory at the U.S. Army Corps of Engineers’ Engineer Research and Development Center, and others. The RMA Delta model is highly calibrated and frequently used to study flooding, seal level rise, reservoir and gate operations, water supply export strategies, water quality, and other topics in the Delta (King 1998; King and Norton 1978; King and Rachiele 1990).

Variables in Equations 2 through 5 are: $x, y =$ horizontal Cartesian coordinates; $t =$ time; $u, v =$ horizontal velocity components; $h =$ depth; $a =$ bottom elevation; $\varepsilon_x, \varepsilon_y, \epsilon_y, \epsilon_x =$ turbulent eddy coefficients; $g =$ acceleration due to gravity; $C =$ Chezy bottom friction coefficient in Equations 2 through 4 and constituent concentration in Equation 5; $V =$ total water velocity; $q_s =$ tributary flow; $\Omega_v, \Omega_u =$ coriolis forcing; $W_x, W_y =$ wind stress; $q_1 =$ inflow per unit area; $Dx, Dry, Dy =$ diffusion coefficients; $R =$ growth rate; $\theta_s =$ source rate $= -kC$, and $k$ is the decay rate.

Each pharmaceutical was defined as an arbitrary constituent subject to first order kinetics in RMA11.

\[
\rho \ h \ \frac{\partial u}{\partial t} + u \ \frac{\partial u}{\partial x} + v \ \frac{\partial u}{\partial y} + gh \ \frac{\partial a}{\partial x} + \frac{g}{C} \ u |V| + u q_s - \ v h + g h^2 \ \frac{\partial \rho}{\partial x} - \ \frac{\partial}{\partial x} \ \varepsilon_x \ \frac{\partial u}{\partial x} - \ \frac{\partial}{\partial y} \ \varepsilon_y \ \frac{\partial u}{\partial y} - W_x = 0
\] (2)

\[
\rho \ h \ \frac{\partial v}{\partial t} + u \ \frac{\partial v}{\partial x} + v \ \frac{\partial v}{\partial y} + gh \ \frac{\partial a}{\partial y} + \frac{g}{C} \ v |V| + v q_s - \ u h + g h^2 \ \frac{\partial \rho}{\partial y} - \ \frac{\partial}{\partial x} \ \varepsilon_x \ \frac{\partial v}{\partial x} - \ \frac{\partial}{\partial y} \ \varepsilon_y \ \frac{\partial v}{\partial y} - W_y = 0
\] (3)

\[
\frac{\partial h}{\partial t} + h \ \frac{\partial u}{\partial x} + v \ \frac{\partial v}{\partial y} + u \ \frac{\partial h}{\partial x} + v \ \frac{\partial h}{\partial y} - q_s = 0
\] (4)

The RMA11 water quality model uses the RMA2 velocity and stage output and the following equation to calculate steady-state transport.

\[
h \ \frac{\partial C}{\partial t} + u \ \frac{\partial C}{\partial x} + v \ \frac{\partial C}{\partial y} - \ \frac{\partial}{\partial x} \ D_x \ \frac{\partial C}{\partial x} + D_y \ \frac{\partial C}{\partial y} - \ \frac{\partial}{\partial y} \ D_x \ \frac{\partial C}{\partial y} + D_y \ \frac{\partial C}{\partial y} + (q_1 - R_h) C - h \ \theta_s = 0
\] (5)
Inputs from all WWTPs that discharge to areas included in the RMA Delta Model finite element grid were considered in the analysis. The WWTPs included Delta Diablo, Discovery Bay, Fairfield, Mountain House, Rio Vista Beach, Rio Vista Northwest, Sacramento Regional, Stockton, Tracy, and White Slough (City of Lodi) (Figure 1). The SRWTP treats wastewater generated by a residential population of 1.3 million, in addition to that generated by commercial and industrial customers within a 368-mi² area. According to the 2020 Master Plan for the facility, in the year 2000, average flows were approximately 154 million gallons per day (mgd) (SRCSD 2008). It is assumed that the communities served by the ten WWTPs included in this study do not differ significantly in their access to medical treatment, prescription drugs, or personal care products and, thus, were considered spatially and temporally uniform in terms of general PPCP consumption and use of the three compounds considered in the model. Even if it is assumed that the populations served by the WWTPs do not vary in terms of access to PPCPs, it is expected that actual concentrations in the effluent of the WWTPs included in this study would vary because level of treatment and treatment methods differ among WWTPs. Several chemical and physical characteristics of each class of compounds determine the degree to which a specific treatment technology is effective. The actual concentrations of PPCPs in the WWTP effluent could vary by up to two orders of magnitude (Petrović and Barceló 2007).

We considered effluent inputs from each WWTP to be proportional to those from the SRWTP, and calculated the inputs for each pharmaceutical using the concentrations determined from the POCIS sampling of the Sacramento River and the effluent flow time series from each WWTP. We generated time series for each pharmaceutical at each WWTP by calculating the contaminant load-per-unit flow for the SRWTP during the monitoring period and multiplying the calculated load per unit flow by the effluent flow time-series for each WWTP, including SRWTP flows for periods outside of the month monitored. Effluent flow time-series were obtained from the USEPA Online Tracking Information System (OTIS) (http://www.epa-otis.gov/cgi-bin/eflouentsquery.cgi?tool=otis) and the Central Valley Regional Water Quality Control Board (USEPA OTIS).

Initializing the model included the application of several boundary condition data sets. The downstream model boundary is in the Carquinez Strait near Martinez and the Benicia–Martinez Bridge. Upstream boundaries to the model include the Sacramento and San Joaquin rivers along with the Calaveras, Cosumnes, and Mokelumne rivers, the Yolo Bypass, and Rock Slough. Exports from the SWP, CVP, North Bay Aqueduct, and the Contra Costa Water District intake at Old River are included in the model. Delta island diversions and return flows—or Delta island consumptive use (DICU)—and operation of the Delta Cross Channel, Suisun Marsh Salinity Control Gate, and all four temporary barriers in the south Delta, including those at Grant Line Canal, Middle River, head of Old River, and Old River at Tracy are included in the RMA model. The California Department of Water Resources provided boundary condition data sets for flow and salinity. We assumed initial PPCP concentrations to be zero with a 2-month spin-up with inputs beginning in August, or 2 months before the start of the water year. We modeled the 2006, 2007, and 2009 water years so that a recent wet and dry year (2006 and 2007, respectively) were modeled along with the water year from which the PPCP concentrations were monitored (2009). Forty-five locations throughout the grid were selected as stations for model output; these included locations commonly monitored as part of various water quality programs in the Delta and sites where data were available to validate the model (Figure 1, Appendix A). Developers of the RMA Delta Model have determined that the most appropriate time step for the system is 7.5 min, and we used this time step in each model run.

RESULTS AND DISCUSSION

Sacramento River Sampling

Caffeine, trimethoprim, sulfamethoxazole, gemfibrozil, fluoxetine, ibuprofen, carbamazepine, xylene, nonylphenol, and nonylphenol ethoxylates were detected at one or more monitoring site (complete
analytical results provided in Appendix A). None of the analytes were detected at Site 1 upstream of the SRWTP effluent diffuser. At Site 2, caffeine, trimethoprim, sulfamethoxazole, gemfibrozil, fluoxetine, and xylene were detected. Trimethoprim, sulfamethoxazole, ibuprofen, carbamazepine, fluoxetine, nonylphenol, and nonylphenol ethoxylate were detected at Site 3. Compounds detected at Site 4 included trimethoprim, sulfamethoxazole, gemfibrozil, carbamazepine, fluoxetine, nonylphenol, nonylphenol ethoxylate, and xylene. The mass detected in the POCIS membrane extract ranged from 2.0 ng of trimethoprim at Site 2 to 1,140 ng of xylene, also at Site 2. Of the compounds that were detected, four have published POCIS sampling rates which were used in Equation 1 to calculate the corresponding concentration in ng L⁻¹ in the water column (MacLeod et al. 2007) (Table 1). Concentrations in the Sacramento River ranged from 12.8 ng L⁻¹ of trimethoprim at Site 2 and 2,566.9 ng L⁻¹ of gemfibrozil at Site 4. Observed concentrations in ng L⁻¹ or ppt levels are consistent with other monitoring studies of various water bodies (Kolpin et al. 2002; Petrović and Barceló 2007).

Transport Modeling

Results include the average monthly concentrations at each location for the months of October, January, April, and July of each simulated water year (see Tables 2 through 4 in Appendix A). Model results included the presence of all three pharmaceuticals throughout the year at concentrations below ±2 ng L⁻¹ at all output points. The maximum calculated concentration for carbamazepine was 11.77 ng L⁻¹ in January 2009 at the Stockton Ship Channel at Burns Cutoff. All calculated carbamazepine concentrations were greater than zero except during April 2006 at the Grant Line Canal at Tracy Road, Middle River at Mowry, Middle River at Tracy Boulevard, the San Joaquin River at Mossdale, and French Camp Slough. Calculated concentrations of fluoxetine and trimethoprim were zero in April 2006 at the same five locations. Results showed fluoxetine at a maximum of 6.74 ng L⁻¹ at Sacramento River North of Merritt Island in October 2008. Model results included maximum concentrations of trimethoprim of 6.11 ng L⁻¹ in January 2009 at the Stockton Ship Channel at Burns Cutoff. The WWTP discharge data available for model input was limited to a monthly time step and, therefore, any diurnal variation was not captured in the model. The calculated concentrations of all three pharmaceuticals were consistently above zero throughout the Delta, and did not fluctuate widely.

As stated above, data on PPCPs in the Delta are very limited. Data collected in 2009 as part of an evaluation of the presence of PPCPs in drinking water sources conducted by the National Water Research Institute (NWRI), Orange County Water District (OCWD), and the Metropolitan Water District of Southern California (MWD) were used to validate model results (Guo et al. 2010). Monitoring results from the NWRI study at the Sacramento River at Hood, San Joaquin River at Holt, Harvey O. Banks Pumping Plant, and the San Joaquin River at

| Analyte       | Site 1 | Site 2 | Site 3 | Site 4 | Sampling rate (RS) | Site 2 | Site 3 | Site 4 |
|---------------|--------|--------|--------|--------|--------------------|--------|--------|--------|
| Carbamazepine | NDₐ    | ND     | 45.6   | 43.2   | 0.360              | ND     | 301.8  | 285.9  |
| Fluoxetine    | ND     | 17.6   | 20.8   | 20.8   | 0.196              | 206.8  | 244.4  | 244.4  |
| Trimethoprim  | ND     | 2.0    | 28.3   | 26.3   | 0.348              | 22.8   | 181.9  | 168.2  |
| Gemfibrozil   | ND     | 19.3   | ND     | 214.0  | 0.192              | 231.5  | ND     | 2566.9 |

ₐ ND indicates the analyte was not detected at this site.
CORRECTED PAGE 8

ERRATUM: SAN FRANCISCO ESTUARY & WATERSHED SCIENCE

analytical results provided in Appendix A). None of the analytes were detected at Site 1 upstream of the SRWTP effluent diffuser. At Site 2, caffeine, trimethoprim, sulfamethoxazole, gemfibrozil, fluoxetine, and xylene were detected. Trimethoprim, sulfamethoxazole, ibuprofen, carbamazepine, fluoxetine, nonylphenol, and nonylphenol ethoxylate were detected at Site 3. Compounds detected at Site 4 included trimethoprim, sulfamethoxazole, gemfibrozil, carbamazepine, fluoxetine, nonylphenol, nonylphenol ethoxylate, and xylene. The mass detected in the POCIS membrane extract ranged from 2.0 ng of trimethoprim at Site 2 to 1,140 ng of xylene, also at Site 2. Of the compounds that were detected, four have published POCIS sampling rates which were used in Equation 1 to calculate the corresponding concentration in \( \text{ng L}^{-1} \) in the water column (MacLeod et al. 2007) (Table 1). Concentrations in the Sacramento River ranged from 0.1 ng \( \text{L}^{-1} \) of trimethoprim at Site 2 and 11.3 ng \( \text{L}^{-1} \) of gemfibrozil at Site 4. Observed concentrations in ng \( \text{L}^{-1} \) or ppt levels are consistent with other monitoring studies of various water bodies (Kolpin et al. 2002; Petrović and Barceló 2007).

Transport Modeling

Results include the average monthly concentrations at each location for the months of October, January, April, and July of each simulated water year (see Tables 2 through 4 in Appendix A). Model results included the presence of all three pharmaceuticals throughout the year at concentrations below 0.06 ng \( \text{L}^{-1} \) at nearly all output points. The maximum calculated concentration for all three pharmaceuticals occurred at the Stockton Ship Channel at Burns Cutoff output location and the January 2009 time period. Maximum calculated concentrations of carbamazepine, fluoxetine, and trimethoprim were 0.06, 0.04, and 0.05 ng \( \text{L}^{-1} \), respectively. The WWTP discharge data available for model input was limited to a monthly time step and, therefore, any diurnal variation was not captured in the model. The calculated concentrations of all three pharmaceuticals were consistently above zero throughout the Delta, and did not fluctuate widely.

As stated above, data on PPCPs in the Delta are very limited. Data collected in 2009 as part of an evaluation of the presence of PPCPs in drinking water sources conducted by the National Water Research Institute (NWRI), Orange County Water District (OCWD), and the Metropolitan Water District of Southern California (MWD) were used to validate model results (Guo et al. 2010). Monitoring results from the NWRI study at the Sacramento River at Hood, San Joaquin River at Holt, Harvey O. Banks Pumping Plant, and the San Joaquin River at

---

Table 1 Available POCIS sampling rates and concentrations

| Analyte       | Site 1 | Site 2 | Site 3 | Site 4 | Sampling rate (RS) | Site 2 | Site 3 | Site 4 |
|---------------|--------|--------|--------|--------|-------------------|--------|--------|--------|
| Carbamazepine | ND\(^a\) | ND     | 45.6   | 43.2   | 0.348             | ND     | 1.3    | 1.3    |
| Fluoxetine    | ND     | 17.6   | 20.8   | 20.8   | 0.196             | 0.9    | 1.1    | 1.1    |
| Trimethoprim  | ND     | 2.0    | 28.3   | 26.3   | 0.360             | 0.1    | 0.8    | 0.7    |
| Gemfibrozil   | ND     | 19.3   | ND     | 214.0  | 0.192             | 1.0    | ND     | 11.3   |

\(^a\) ND indicates the analyte was not detected at this site.
The monitoring results included concentrations of carbamazepine in April, July, and October 2008 and January 2009. The level of agreement between these data and the model results varies. Of the sixteen comparisons shown in Figure 2, three vary by less than 25%, 8 vary by less than 50% and six vary by more than 75%, including all four comparisons at the San Joaquin River at Mossdale. This variability in the level of agreement underscores the need for an understanding of the how concentrations of PPCP compounds in WWTP discharges to the Delta may differ.

The model results can also be compared to a national reconnaissance study conducted by the United States Geological Survey (USGS) in 1999 to 2000. Among the 139 sites included in the USGS study, one site (Sacramento River at Freeport) was within the Delta, and four sites (Mud Slough near Gustine, Orestimba Creek near Crows Landing, San Joaquin River near Vernalis, and French Camp Slough near Stockton) were tributary to the Delta (Kolpin et al. 2002). Fluoxetine concentrations were estimated in the USGS study because of an average recovery of less than 60% in the laboratory. The estimated maximum concentration at all four sites was 12 ng L\(^{-1}\). Carbamazepine and trimethoprim were not included in the list of analytes in the USGS study. While the model results indicate that carbamazepine, fluoxetine, and trimethoprim are persistent throughout the year in the Delta at low ng L\(^{-1}\) concentrations, addi-
Mossdale were compared to model results (Table 2). The NWRI monitoring results included concentrations of carbamazepine in April, July, and October 2008 and January 2009. This large difference between the modeled and monitored results underscores the need for an understanding of how the concentrations of PPCP compounds in WWTP discharges to the Delta may differ.

The model results can also be compared to a national reconnaissance study conducted by the United States Geological Survey (USGS) in 1999 to 2000. Among the 139 sites included in the USGS study, one site (Sacramento River at Freeport) was within the Delta, and four sites (Mud Slough near Gustine, Orestimba Creek near Crows Landing, San Joaquin River near Vernalis, and French Camp Slough near Stockton) were tributary to the Delta (Kolpin et al. 2002). Fluoxetine concentrations were estimated in the USGS study because of an average recovery of less than 60% in the laboratory. The estimated maximum concentration at all four sites was 12 ng L⁻¹. Carbamazepine and trimethoprim were not included in the list of analytes in the USGS study. As with the NWRI data, the model results are significantly lower than the USGS data. Additional data on the presence of these and other PPCPs in the Delta might help clarify this discrepancy and could be used to calibrate and validate future models.
tional data on the presence of these and other PPCPs in the Delta is required to more thoroughly calibrate and validate the model.

Ecological Implications

The ecological implications of the presence of carbamazepine, fluoxetine, trimethoprim, and presumably other pharmaceuticals within the Delta are unknown. Of the three pharmaceuticals analyzed in this study, the toxicity of fluoxetine to aquatic organisms has been the most studied. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI). This class of drugs induces an extracellular supply of serotonin, a mood-regulating neurotransmitter and neurohormone (Kreke and Dietrich 2008). Serotonin is highly conserved and found in vertebrates and invertebrates (Beulig and Fowler 2008; Kreke and Dietrich 2008). Limited research indicates that SSRIs may result in decreased activity in freshwater crustaceans and fish. After exposure to 10 and 100 ng L\(^{-1}\) of fluoxetine, the freshwater crustacean *Gammarus pulex* exhibited significantly reduced activity while behavior at higher concentrations of 1 µg L\(^{-1}\) to 1 mg L\(^{-1}\) was equivalent to the control population (De Lange et al. 2006). Goldfish exposed to 81 µg L\(^{-1}\) of fluoxetine were less active when compared to the control group in a study that evaluated active avoidance learning in the fish (Beulig and Fowler 2008). Decreased activity resulting from SSRI exposure could have population-level ecological effects though no studies have investigated the possibility. Studies also indicate that SSRIs and their metabolites may bioaccumulate in fish. Fluoxetine, norfluoxetine, sertraline, and desmethylsertraline were found in brain, liver, and lateral muscle tissues of bluegill (*Lepomis macrochirus*), channel catfish (*Ictalurus punctatus*), and black crappie (*Pomoxis nigromaculatus*) from an effluent-dominated stream in Texas (Brooks et al. 2005). Brain tissue had the highest concentrations followed by liver and then muscle. The fluoxetine metabolites norfluoxetine and desmethylsertraline were found in higher concentrations than their parent compounds in all tissues of each species, which is consistent with the behavior of SSRIs in human and rat tissues (Brooks et al. 2005). The ecological implications of SSRIs in fish tissues are unknown.

The effect of carbamazepine and trimethoprim on aquatic organisms is largely unknown. The midge *Chironomus riparius* was exposed to carbamazepine in sediment at 0.16 to 100 mg kg\(^{-1}\) dry weight. At 70 to 100 µg kg\(^{-1}\) there was a blockage of pupation and emergence (Oetken et al. 2005). In the same study, the oligochaete *Lumbriculus* variegates was exposed to 0.625 to 10 mg kg\(^{-1}\) dry weight in sediment and the freshwater snail *Potamopyrgus antipodarum* was placed in aqueous concentrations of 0.4 to 250 mg L\(^{-1}\) with no statistically significant adverse effects. Another study found that the composition and function of organisms within riverine biofilm communities were significantly modified after exposure to 10 µg L\(^{-1}\) of carbamazepine with significant reductions in bacterial and cyanobacterial biomass, increases in aerobic heterotrophic bacterial and fungal plate counts, and no impact to algal biomass (Lawrence et al. 2005). A study evaluating the cytotoxic and oxidative effects of various PPCPs on rainbow trout (*Oncorhynchus mykiss*) found that carbamazepine may adversely impact liver function (Gagne et al. 2006). There are no studies of the chronic toxicity of trimethoprim at environmentally relevant concentrations. However, trimethoprim, an antibiotic, inhibits the folate biosynthetic pathway in aquatic plants as it does in bacteria. Folates are required by plants for lignin formation and photosynthesis (Brain et al. 2008). Trimethoprim caused inhibited growth and ejection of the symbiotic algae within the digestive cells of green hydra in one study (McAuley 1981). Though it is very difficult to draw meaningful conclusions about the Delta from the effects described above, these studies provide evidence that many parts of the food web, including plants, biofilm, macroinvertebrates, zooplankton, and fish could be adversely affected by one or more of the compounds included in this study, which are three of potentially hundreds or thousands of PPCP compounds present in Delta waters. Though the studies described above give some indication of potential effects on aquatic species and ecosystems, these and other research efforts do not provide a clear picture of the effects these compounds may have at the concentrations estimated and observed in the Delta.
Ecological Implications

The ecological implications of the presence of carbamazepine, fluoxetine, trimethoprim, and presumably other pharmaceuticals within the Delta are unknown. Of the three pharmaceuticals analyzed in this study, the toxicity of fluoxetine to aquatic organisms has been the most studied. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI). This class of drugs induces an extracellular supply of serotonin, a mood-regulating neurotransmitter and neurohor- mone (Kreke and Dietrich 2008). Serotonin is highly conserved and found in vertebrates and invertebrates (Beulig and Fowler 2008; Kreke and Dietrich 2008). Limited research indicates that SSRIs may result in decreased activity in freshwater crustaceans and fish. After exposure to 10 and 100 ng L\(^{-1}\) of fluoxetine, the freshwater crustacean Gammarus pulex exhibited significantly reduced activity while behavior at higher concentrations of 1 \(\mu\)g L\(^{-1}\) to 1 mg L\(^{-1}\) was equivalent to the control population (De Lange et al. 2006). Goldfish exposed to 81 \(\mu\)g L\(^{-1}\) of fluoxetine were less active when compared to the control group in a study that evaluated active avoidance learning in the fish (Beulig and Fowler 2008). Decreased activity resulting from SSRI exposure could have population-level ecological effects though no studies have investigated the possibility. Studies also indicate that SSRIs and their metabolites may bioaccumulate in fish. Fluoxetine, norfluoxetine, sertraline, and desmethylsertraline were found in brain, liver, and lateral muscle tissues of bluegill (Lepomis macrochirus), channel catfish (Ictalurus punctatus), and black crappie (Pomoxis nigromaculatus) from an effluent-dominated stream in Texas (Brooks et al. 2005). Brain tissue had the highest concentrations followed by liver and then muscle. The fluoxetine metabolites norfluoxetine and desmethylsertraline were found in higher concentrations than their parent compounds in all tissues of each species, which is consistent with the behavior of SSRIs in human and rat tissues (Brooks et al. 2005). The ecological implications of SSRIs in fish tissues are unknown.

The effect of carbamazepine and trimethoprim on aquatic organisms is largely unknown. The midge Chironomus riparius was exposed to carbamazepine in sediment at 0.16 to 100 mg kg\(^{-1}\) dry weight. At 70 to 100 mg kg\(^{-1}\) there was a blockage of pupation and emergence (Oetken et al. 2005). In the same study, the oligochaete Lumbriculus variegates was exposed to 0.625 to 10 mg kg\(^{-1}\) dry weight in sediment and the freshwater snail Potamopyrgus antipodarum was placed in aqueous concentrations of 0.4 to 250 mg L\(^{-1}\) with no statistically significant adverse effects. Another study found that the composition and function of organisms within riverine biofilm communities were significantly modified after exposure to 10 \(\mu\)g L\(^{-1}\) of carbamazepine with significant reductions in bacterial and cyanobacterial biomass, increases in aerobic heterotrophic bacterial and fungal plate counts, and no impact to algal biomass (Lawrence et al. 2005). A study evaluating the cytotoxic and oxidative effects of various PPCPs on rainbow trout (Oncorhynchus mykiss) found that carbamazepine may adversely impact liver function (Gagne et al. 2006). There are no studies of the chronic toxicity of trimethoprim at environmentally relevant concentrations. However, trimethoprim, an antibiotic, inhibits the folate biosynthetic pathway in aquatic plants as it does in bacteria. Folates are required by plants for lignin formation and photosynthesis (Brain et al. 2008). Trimethoprim caused inhibited growth and ejection of the symbiotic algae within the digestive cells of green hydra in one study (McAuley 1981). Though it is very difficult to draw meaningful conclusions about the Delta from the effects described above, these studies provide evidence that many parts of the food web, including plants, biofilm, macroinvertebrates, zooplankton, and fish could be adversely affected by one or more of the compounds included in this study, which are three of potentially hundreds or thousands of PPCP compounds present in Delta waters. Though the studies described above give some indication of potential effects on aquatic species and ecosystems, these and other research efforts do not provide a clear picture of the effects these compounds may have at the concentrations estimated and observed in the Delta.
CONCLUSION

The model results indicate that it is possible that carbamazepine, fluoxetine, and trimethoprim are persistent all year in the Delta at low ng L$^{-1}$ concentrations. Previous studies are very few and associated data are limited; however, the results of those efforts also indicate that PPCPs may be present in the Delta. At this stage of understanding about their potential effects, PPCPs cannot be eliminated as a stressor on the struggling Delta ecosystem. Current understanding about the risks of exposure could be improved with additional data about the occurrence of PPCPs in the Delta, variability of concentrations in effluent from WWTPs that discharge to the Delta, and potential variation in applicable decay rates. Additional fate and transport and focused ecotoxicity studies are also necessary. Passive sampling devices and the RMA Delta Model are useful tools that could support that work. Such studies would be of great value in advancing our understanding of the influence of PPCPs on the health of the Delta ecosystem.

ACKNOWLEDGEMENTS

Support for this research was provided by the State Water Resources Control Board and the Center for Watershed Sciences and Hydrologic Sciences Graduate Group at the University of California, Davis. Special thanks to Henry Calanchini and Carson Jeffries for their greatly appreciated assistance in the field, and Dave Crane and Abdu Mekebri (California Department of Fish and Wildlife, Fish and Wildlife Water Pollution Control Laboratory), Cathy Johnson (U.S. Fish and Wildlife Service), and Terri Spencer (Environmental Sampling Technologies).

REFERENCES

Alvarez D, Petty J, Huckins J, Jones Lepp T, Getting D, Goddard J, Manahan S. 2004. Development of a passive, in situ, integrative sampler for hydrophilic organic contaminants in aquatic environments. Environ Toxicol Chem 23(7):1640–1648.

Barnes K, Kolpin D, Furlong E, Zaugg S, Meyer M, Barber L. 2008. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States—(i) groundwater. Sci Tot Environ 402(2–3):192–200.

Benotti M, Trenholm R, Vanderford B, Holady J, Stanford B, Snyder S. 2008. Pharmaceuticals and endocrine disrupting compounds in U.S. drinking water. Environ Sci Tech 43(3):597–603.

Beulig A, Fowler J. 2008. Fish on prozac: Effect of serotonin re-uptake inhibitors on cognition in goldfish. Behav Neurosci 122(4):423-432. Available from: http://psycnet.apa.org/?fa=main.doiLanding&doi=10.1037/0735-7044.122.2.426

Bolonga N, Ismaila AF, Salimb MR, Matsuurad T. 2008. A review of the effects of emerging contaminants in wastewater and options for their removal. Desalination 239:229–246.

Brain R, Hanson M, Solomon K, Brooks B. 2008. Aquatic plants exposed to pharmaceuticals: effects and risks. Rev Environ Contam Toxicol. 192:67–115.

Brooks BW, Chambliss CK, Stanley JK, Ramirez A, Banks KE, Johnson RD, Lewis RJ. 2005. Determination of select antidepressants in fish from an effluent-dominated stream. Environ Toxicol Chem 24(2):464–469.

[CALFED] California Bay-Delta Authority. 2008. The state of Bay-Delta science. Sacramento (CA): CALFED Science Program. 174 p. Available from: http://www.science.calwater.ca.gov/pdf/publications/sbds/sbds_final_update_122408.pdf

Daughton CG, Ternes TA. 1999. Pharmaceuticals and personal care products in the environment: agents of subtle change? Environ Health Persp 107:907–938.

De Lange HJ, Noordoven W, Murk AJ, Lurling M, Peeters E. 2006. Behavioural responses of Gammarus pulex (Crustacea, Amphipoda) to low concentrations of pharmaceuticals. Aquat Toxicol 78(3):209–216.

Fraker S, Smith G. 2004. Direct and interactive effects of ecologically relevant concentrations of organic wastewater contaminants on Rana pipiens tadpoles. Environ Toxicol 19(3):250–256.
CONCLUSION

The model results indicate that it is possible that carbamazepine, fluoxetine, and trimethoprim are persistent all year in the Delta at sub ng L \(^{-1}\) concentrations. Previous studies are very few and associated data are limited; however, the results of those efforts also indicate that PPCPs may be present in the Delta at low ng L \(^{-1}\) concentrations. Current understanding about the risks of exposure could be improved with additional data about the occurrence of PPCPs in the Delta, variability of concentrations in effluent from WWTPs that discharge to the Delta, and potential variation in applicable decay rates. Additional fate and transport and focused ecotoxicity studies are also necessary. Passive sampling devices and the RMA Delta Model are useful tools that could support that work. Such studies would be of great value in advancing our understanding of the influence of PPCPs on the health of the Delta ecosystem.

ACKNOWLEDGEMENTS

Support for this research was provided by the State Water Resources Control Board and the Center for Watershed Sciences and Hydrologic Sciences Graduate Group at the University of California, Davis. Special thanks to Henry Calanchini and Carson Jeffres for their greatly appreciated assistance in the field, and Dave Crane and Abdu Mekebri (California Department of Fish and Wildlife, Fish and Wildlife Water Pollution Control Laboratory), Cathy Johnson (U.S. Fish and Wildlife Service), and Terri Spencer (Environmental Sampling Technologies).

REFERENCES

Alvarez D, Petty J, Huckins J, Jones Lepp T, Getting D, Goddard J, Manahan S. 2004. Development of a passive, in situ, integrative sampler for hydrophilic organic contaminants in aquatic environments. Environ Toxicol Chem 23(7):1640–1648.

Barnes K, Kolpin D, Furlong E, Zaugg S, Meyer M, Barber L. 2008. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the united states—(i) groundwater. Sci Tot Environ 402(2–3):192–200.

Benotti M, Trenholm R, Vanderford B, Holady J, Stanford B, Snyder S. 2008. Pharmaceuticals and endocrine disrupting compounds in U.S. drinking water. Environ Sci Tech 43(3):597–603.

Beulig A, Fowler J. 2008. Fish on prozac: Effect of serotonin re-uptake inhibitors on cognition in goldfish. Behav Neurosci 122(4):423-432. Available from: http://psycnet.apa.org/?fa=main.doiLanding&doi=10.1037/0735-7044.122.2.426

Bologna N, Ismaila AF, Salimb MR, Matsuurad T. 2008. A review of the effects of emerging contaminants in wastewater and options for their removal. Desalination 239:229–246.

Brain R, Hanson M, Solomon K, Brooks B. 2008. Aquatic plants exposed to pharmaceuticals: effects and risks. Rev Environ Contam Toxicol. 192:67–115.

Brooks BW, Chambliss CK, Stanley JK, Ramirez A, Banks KE, Johnson RD, Lewis RJ. 2005. Determination of select antidepressants in fish from an effluent-dominated stream. Environ Toxicol Chem 24(2):464–469.

[CALFED] California Bay-Delta Authority. 2008. The state of Bay–Delta science. Sacramento (CA): CALFED Science Program. 174 p. Available from: http://www.science.calwater.ca.gov/pdf/publications/sbds/sbds_final_update_122408.pdf

Daughton CG, Ternes TA. 1999. Pharmaceuticals and personal care products in the environment: agents of subtle change? Environ Health Persp 107:907–938.

De Lange HJ, Noordoven W, Murk AJ, Lurling M, Peeters E. 2006. Behavioural responses of Gammarus pulex (Crustacea, Amphipoda) to low concentrations of pharmaceuticals. Aquat Toxicol 78(3):209–216.

Fraker S, Smith G. 2004. Direct and interactive effects of ecologically relevant concentrations of organic wastewater contaminants on Rana pipiens tadpoles. Environ Toxicol 19(3):250–256.
Gagne F, Blaise C, Andre C. 2006. Occurrence of pharmaceutical products in a municipal effluent and toxicity to rainbow trout (Oncorhynchus mykiss) hepatocytes. Ecotoxicol Environ Safety 64(3):329–336.

Guo CY, Krasner SW, Fitzsimmons S, Woodside G, Yamachika N. 2010. Source, fate, and transport of endocrine disruptors, pharmaceuticals, and personal care products in drinking water sources in California. Fountain Valley (CA): National Water Research Institute. 103 p. + appendices. Available from: http://www.nwri-usa.org/pdfs/NWRIFinalReportEDCsPPCPsMay2010.pdf

Heberer T. 2002. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. Toxicol Lett 131(1–2):5–17.

Henry T, Black M. 2008. Acute and chronic toxicity of fluoxetine (selective serotonin reuptake inhibitor) in western mosquitofish. Arch Environ Contam Toxicol 54(2):325–330.

Huckins JN, Petty JD, Prest HF, Clark RC, Alvarez DA, Orazio CE, Lebo JA, Cranor WL, Johnson BT. 2000. A guide for the use of semipermeable membrane devices (SPMDs) as samplers of waterborne hydrophobic organic contaminants Washington (DC): American Petroleum Institute. API Publication No. 4690.

Kidd K, Blanchfield P, Mills K, Palace V, Evans R, Lazorchak J, Flick R. 2007. Collapse of a fish population after exposure to a synthetic estrogen. Proc Nat Acad Sci 104(21):8897.

King IP. 1998. RMA-11: A three dimensional finite element model for water quality in estuaries and streams. Davis (CA): Department of Civil and Environmental Engineering, University of California, Davis.

King IP, Rachiele RR. 1990. Multi-dimensional modeling of hydrodynamics and salinity in San Francisco Bay. ASCE Conference on Estuarine and Coastal Modeling p. 511–521. Available from: http://cedb.asce.org/cgi/WWWdisplay.cgi?66224

Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: A national reconnaissance. Environ Sci Technol 36(6):1202–1211.

Kreke N, Dietrich DR. 2008. Physiological endpoints for potential SSRI interactions in fish. Critical Rev Toxicol 38(3):215–247.

Lavado R, Loyo–Rosales, Jorge E., Kolodziej, Edward P, Sedlak, David L, Schlenk D. 2008. Evaluation of steroid estrogen and estrogenic activity in surface waters from central California. Mar Environ Res 66:121–125.

Lawrence JR, Swerhone GDW, Wassenaar LI, Neu TR. 2005. Effects of selected pharmaceuticals on riverine biofilm communities. Can J Microbiol 51(8):655–669.

MacLeod S, McClure E, Wong C. 2007. Laboratory calibration and field deployment of the polar organic chemical integrative sampler for pharmaceuticals and personal care products in wastewater and surface water. Environ Toxicol Chem 26(12):2517–2529.

McAuley PJ. 1981. Ejection of algae in the green hydra symbiosis. J Exp Zool 217(1):23–31.

Oetken M, Nentwig G, Loffler D, Ternes T, Oehlmann J. 2005. Effects of pharmaceuticals on aquatic invertebrates. Part I. The antiepileptic drug carbamazepine. Arch Environ Contam Toxicol 49(3):353–361.

Oros D, Jarman W, Lowe T, David N, Lowe S, Davis J. 2003. Surveillance for previously unmonitored organic contaminants in the San Francisco Estuary. Mar Pollut Bull 46(9):1102–1110.

Petrović M, Barceló D, editors. 2007. Analysis, fate and removal of pharmaceuticals in the water cycle. In: Wilson & Wilson’s Comprehensive Analytical Chemistry. Amsterdam: Elsevier. 564 p.
Routledge E, Sheahan D, Desbrow C, Brighty G, Waldock M, Sumpter J. 1998. Identification of estrogenic chemicals in STW effluent. 2. In vivo responses in trout and roach. Environ Sci Technol 32(11):1559–1565.

[Regional San] Sacramento Regional County Sanitation District. 2008. Final executive summary. In: Sacramento Regional Wastewater Treatment Plant 2020 master plan. Sacramento (CA): Sacramento Regional County Sanitation District. 42 p. Available from: http://www.regionalsan.com/sites/main/files/file-attachments/exec-sum_0.pdf

Ternes T. 1999. Preface. Drugs and hormones as pollutants of the aquatic environment: determination and ecotoxicological impacts. Sci Tot Environ 225(1–2):1–2.

U.S. Environmental Protection Agency Online Tracking Information System [Internet]. [updated 2012 Feb 12]. USEPA; [cited 2011 Dec 1]. Available from: http://www.epa-otis.gov/cgi-bin/effluentsquery.cgi?tool=otis Available from: http://echo.epa.gov/

Vandenbergh G, Adriaens D, Verslycke T, Janssen C. 2003. Effects of 17 [alpha]–ethinylestradiol on sexual development of the amphipod *Hyalella azteca*. Ecotoxicol Environ Safety 54(2):216–222.

Williamson K, May B. 2002. Incidence of phenotypic female Chinook salmon positive for the male Y-chromosome-specific marker OtY1 in the Central Valley, California. J Aquat Anim Health 14(3):176–183.

Wilson B, Smith V, Denoyelles Jr F, Larive C. 2003. Effects of three pharmaceutical and personal care products on natural freshwater algal assemblages. Environ Sci Technol 37(9):1713–1719.