Environ. Sci. Technol. **2009,** *43,* 597–603

Pharmaceuticals and Endocrine Disrupting Compounds in U.S. Drinking Water

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Received July 3, 2008. Revised manuscript received October 3, 2008. Accepted October 13, 2008.

The drinking water for more than 28 million people was screened for a diverse group of pharmaceuticals, potential endocrine disrupting compounds (EDCs), and other unregulated organic contaminants. Source water, finished drinking water, and distribution system (tap) water from 19 U.S. water utilities was analyzed for 51 compounds between 2006 and 2007. The 11 most frequently detected compounds were atenolol, atrazine, carbamazepine, estrone, gemfibrozil, meprobamate, naproxen, phenytoin, sulfamethoxazole, TCEP, and trimethoprim. Median concentrations of these compounds were less than 10 ng/L, except for sulfamethoxazole in source water (12 ng/L), TCEP in source water (120 ng/L), and atrazine in source, finished, and distribution system water (32, 49, and 49 ng/L). Atrazine was detected in source waters far removed from agricultural application where wastewater was the only known source of organic contaminants. The occurrence of compounds in finished drinking water was controlled by the type of chemical oxidation (ozone or chlorine) used at each plant. At one drinking water treatment plant, summed monthly concentrations of the detected analytes in source and finished water are reported. Atenolol, atrazine, DEET, estrone, meprobamate, and trimethoprim can serve as indicator compounds representing potential contamination from other pharmaceuticals and EDCs and can gauge the efficacy of treatment processes.

Introduction

Pharmaceuticals and endocrine disrupting compounds (EDCs) are subclasses of organic contaminants that have been detected in wastewater and surface waters throughout the world (*1*–*4*). Their occurrence is most often a result of municipal wastewater discharge, as these compounds are not completely removed during treatment (*4*). Other sources of pharmaceuticals and EDCs in water include runoff from agricultural fields, concentrated animal feeding operations, landfill leachates, and urban runoff (*5*–*7*). Scientists and regulators are concerned about what level of risk may be associated with the presence of pharmaceuticals and EDCs in drinking water, as many drinking water treatment plants (DWTPs) use source water impacted by wastewater. While some researchers have postulated that the long-term risk to humans from any single pharmaceutical at sub-μg/L levels is negligible (*8*), it is not clear what toxicological implications chronic exposure to suites of trace contaminants may pose (*9, 10*). The degree to which this issue has drawn interest across disciplines is illustrated by the voices of concern stemming from medical professionals, environmental scientists, drinking water municipalities, government agencies, and the general media (*9, 11*–*13*). However, if risk assessors and epidemiologists are to link any potential health outcomes with pharmaceutical and EDC exposure, a better understanding of their occurrence in drinking water is critical.

There is relatively sparse information regarding pharmaceutical and EDC occurrence in drinking water. Researchers in Germany measured ng/L concentrations of clofibric acid in Berlin tap water (*14*), a case which remains a strong illustration of the sometimes close wastewater to drinking water coupling of unintended water reuse. The elimination of pharmaceuticals at German DWTPs was attributed to ozone oxidation or adsorption to granular activated carbon (*15*): finished drinking water concentrations of five compounds were <10 ng/L. The occurrence of 106 organic wastewater contaminants, including some pharmaceuticals and potential EDCs, at different stages of a U.S. DWTP was documented by Stackelberg et al. (*16*): 18 compounds were measured in finished drinking water at concentrations up to 258 ng/L. Bruchet et al. (*17*) investigated the occurrence of 21 antibiotics and X-ray contrast agents in the Seine River, through groundwater recharge, and in finished drinking water. In this case, only four X-ray contrast agents persisted into finished drinking water at concentrations up to 60 ng/L. Selected antibiotics were measured in the finished water of three DWTPs in the U.S. at concentrations up to 5 ng/L (*18*). As a precursor to the data presented in this study, concentrations of a more limited set of pharmaceuticals and EDCs were measured in source and finished drinking water from 20 utilities in the U.S. (*19*) (see Supporting Information Table S1).

This paper describes results from a comprehensive survey of 20 pharmaceuticals, 25 known or potential EDCs, and 6 other wastewater contaminants in source water, finished drinking water, and distribution system (tap) water from 19 U.S. DWTPs sampled during 2006–2007. The results provide an assessment of the actual concentrations to which people are exposed from drinking water. Occurrence data were used to propose a set of indicator compounds that can predict the presence of other pharmaceuticals and EDCs as well as monitor the efficacy of treatment processes.

Experimental Section

Selection of Compounds. A fundamental challenge faced by scientists and regulators is deciding upon which compounds to investigate. More than 3000 pharmaceuticals are currently approved for prescription in the U.S., and hundreds of others are approved for over-the-counter use, used in personal care products, or used as adjuncts in the formulation of these materials (*20*). The 51 compounds targeted in this work (Table 1) were chosen using a comprehensive multistep selection process. The selection process and the fit of each selected chemical to qualifying criteria are described in detail elsewhere (*21*). In brief, 20 pharmaceuticals and pharmaceutical metabolites were selected based on the following criteria: (a) prescription drug status, (b) volume of use, (c) toxicity, (d) occurrence and public interest, (e) pharmaceutical class, and (f) availability of analytical standards. Note that four prescription pharmaceutical metabolites (*o*-hydroxy

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10.1021/es801845a CCC: $40.75
Published on Web 12/17/2008

TABLE 1. Fifty-one Pharmaceuticals and EDCs Targeted in This Work

chemical	CAS number	description
pharmaceuticals		
atenolol	29122−68−7	beta-blocker
atorvastatin	134523−03−8	antilipidemic
carbamazepine	298−46−4	anticonvulsant
diazepam	62−73−7	antianxiety
diclofenac	15307−79−6	nonsteroidal anti-inflammatory
enalapril	76095−16−4	angiotensin-converting enzyme inhibitor
fluoxetine	59333−67−4	antidepressant
gemfibrozil	25812−30−0	antilipidemic
o-hydroxy atorvastatin	214217−86−6	metabolite of atorvastatin
p-hydroxy atorvastatin	214217−88−6	metabolite of atorvastatin
meprobamate	57−53−4	antianxiety
naproxen	22204−53−1	nonsteroidal anti-inflammatory
norfluoxetine	83891−03−6	metabolite of fluoxetine
phenytoin	57−41−0	anticonvulsant
risperidone	106266−06−2	antipsychotic
simvastatin	79902−63−9	antilipidemic
simvastatin hydroxy acid	12009−77−6	metabolite of simvastatin
sulfamethoxazole	723−46−6	antibiotic
triclosan	3380−34−5	antibacterial/antimicrobial
trimethoprim	738−70−5	antibiotic
known or potential EDCs		
atrazine	1912−24−9	herbicide
benzophenone	119−61−9	uv stabilizer
butylated hydroxy anisole (BHA)	25013−16−5	food preservative
17β-estradiol	50−28−2	steroid hormone
estrone	53−16−7	steroid hormone
17α-ethynylestradiol	57−63−6	synthetic steroid hormone
bisphenol A	80−05−7	component of plastics
butylbenzyl phthalate	85−68−7	plasticizer
diazinon	333−41−5	insecticide
diethylhexyl phthalate	117−81−7	plasticizer
galaxolide (HHCB)	1222−05−5	fragrance
β-hexachlorocyclohexane (β-HCH)[a]	319−85−7	insecticide constituent
α-hexachlorocyclohexane (α-HCH)[a]	319−84−6	insecticide constituent
γ-hexachlorocyclohexane (γ-HCH, or Lindane)[a]	58−89−9	insecticide
δ-hexachlorocyclohexane (δ-HCH)[a]	319−86−8	insecticide constituent
linuron	330−55−2	herbicide
methoxychlor	72−43−5	insecticide
musk ketone	81−14−1	fragrance
nonylphenol	104−40−7	nonionic surfactant degradation product
octachlorostyrene	29082−74−4	pesticide
octylphenol	27193−28−8	surfactant degradate
progesterone	57−83−0	steroid hormone
testosterone	58−22−0	steroid hormone
tonalide (AHTN)	108−88−3	fragrance
vinclozolin	50471−44−8	fungicide
other chemicals		
butylated hydroxy toluene (BHT)	128−37−0	food preservative
metolachlor	51218−45−2	herbicide
n,n-diethyl-*meta*-toluamide (DEET)	134−62−3	insect repellant
traseolide (AITI)	68140−48−7	fragrance
tris(2-chloroethyl) phosphate (TCEP)	115−96−8	flame retardant
tris(1,3-dichloro-2-propyl) phosphate (TCPP)	13674−84−5	flame retardant

[a] Technical-grade HCH is pesticide mixture including α-, β-, δ-, and γ-HCH isomers. γ-HCH is the main insecticidal constituent.

atorvastatin, *p*-hydroxy atorvastatin, norfluoxetine, and simvastatin hydroxy acid) and triclosan (an antimicrobial agent used in personal care products) are not technically pharmaceuticals but are included in this group. Twenty-five known or potential EDCs, including natural and synthetic steroid hormones and other chemicals, were selected based on criteria including (a) status as an EDC, (b) occurrence and exposure, (c) effects, (d) mode of action, and (e) public interest in specific contaminants. Although not specifically considered EDCs, six additional compounds were selected because they have been frequently detected in wastewater effluents or source waters and were easily measured along with other target chemicals. For the purposes of discussion, all 51 compounds will be hereafter referred to as pharmaceuticals and EDCs. Additional discussion of the selection criteria is included in the "Selection of Compounds" section of the Supporting Information.

Drinking Water Treatment Plants. Samples were collected from 19 DWTPs across the U.S., representing the drinking water for more than 28 million Americans. Table 2 lists the general treatment schemes for each DWTP as well as the number of samples collected at each site. Specifics of the sample collection are presented in the Supporting Information under "Sample Collection." A total of 222

TABLE 2. Summary of Treatment Schematics of Nineteen DWTPs As Well As Number of Source Water, Finished Water, and Distribution System Samples Collected at Each. Samples Collected from Similar Sites Were Averaged so as to Avoid Bias. See Supporting Information for Tables of Raw Data (Tables S2, S3, and S4)

DWTP	treatment processes[a]	source	finished	distribution
DWTP-1	C/F → sed. → f-Cl_2 → filt. → NH_2Cl	4	4	4[b]
DWTP-2	ClO_2 (preox.) → C/F → sed. → filt. → UV → f-Cl_2	2	1	1
DWTP-3	ClO_2 (preox.) → C/F → sed. → filt. → UV → f-Cl_2	1	2	1
DWTP-4	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 → filt. → f-Cl_2	2	2	2[b]
DWTP-5	f-Cl_2 (preox.) → O_3 → C/F → filt. → f-Cl_2	1	0	0
DWTP-6	f-Cl_2 (preox.) → O_3 → C/F → filt. → f-Cl_2	2	1	3
DWTP-7	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 → filt. → NH_2Cl	4	4	0
DWTP-8	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 → filt. → NH_2Cl	4	4	0
DWTP-9	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 → filt. → NH_2Cl	4	4	0
DWTP-10	f-Cl_2 (preox.) → C/F → sed. → filt. → NH_2Cl	3	3	3
DWTP-11	f-Cl_2 (preox.) → C/F → sed. → filt. → NH_2Cl	2	3	3
DWTP-12	f-Cl_2 → NH_2Cl	3	3	2
DWTP-13	f-Cl_2 (preox.) → O_3 → C/F → sed. → NH_2Cl	2	1	1
DWTP-14	filt. → O_3 → NH_2Cl	2	1	1
DWTP-15	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 →filt. → NH_2Cl	2	1	1
DWTP-16	C/F → sed. → O_3 → dm-filt. → NH_2Cl	2	1	1
DWTP-17	f-Cl_2 (preox.) → C/F → sed. → f-Cl_2 → filt. → NH_2Cl	2	1	1
DWTP-18	O_3 (preox. and int. ox.) → C/F → sed. → GAC/sand bio-filt. → NH_2Cl	1	1	0
DWTP-19	O_3 (preox. and int. ox.) → C/F → sed. → GAC/sand bio-filt. → NH_2Cl	1	1	0

[a] C/F: coagulation/flocculation; sed.: sedimentation; f-Cl_2: chlorine (hypochlorite); filt.: filtration; NH_2Cl: chloramine; ClO_2: chlorine dioxide: pre-ox.: pre-oxidation; O_3: ozonation; dm-filt.: dual-media filtration; int. ox.: intermediate oxidation; GAC/sand bio-filt.: granular activated carbon/sand biofiltration. [b] distribution system samples at DWTP-1 and DWTP-4 were collected from two discrete sampling locations.

samples were analyzed, including blanks and QA/QC samples. Distribution sites (i.e., tap water) were sampled at 10 of the 19 facilities, with a preference toward collection points with longer retention times within a system. In cases where samples were collected on more than one occasion from the same location, results were averaged for interpretation.

All DWTPs employ various combinations of coagulation, flocculation, sedimentation, primary disinfection, filtration, and secondary disinfection (Table 2). Seven of the facilities use ozone as a primary disinfectant, while the remaining facilities use chlorine or chlorine dioxide. The source water of all DWTPs is surface water, except for DWTP-12, which uses groundwater. DWTP-1 withdraws water from a lake receiving water from two tributary lakes and treated effluent from a wastewater treatment plant. DWTPs-2, -3, -5, and -6 withdraw water from reservoirs, each of which contains wastewater effluent from upstream tributaries. DWTPs-4, -7, 8-, -9, -13, and -15 withdraw water directly from large rivers with upstream wastewater sources. DWTPs-16, -17, -18, and -19 withdraw water from reservoirs with no direct input of wastewater but where recreational use is permitted (e.g., swimming, fishing, and boating), whereas DWTPs-10, -11 and, -14 withdraw water from reservoirs with no direct input of wastewater and where no recreational use is permitted.

Methods. Source, finished, and distribution system samples were collected making every effort to follow the same plug of water through each plant. For each sample, two liters of water were collected in silanized, amber glass bottles, preserved with sodium azide, and disinfection residual was quenched with ascorbic acid. All compounds were extracted by solid phase extraction (SPE) and analyzed using either liquid chromatography or gas chromatography with tandem mass spectrometry (LC-MS/MS and GC-MS/MS, respectively). All methods have been previously published (*22*−*24*), though a few modifications were made for this study. Additional details pertaining to sampling, SPE, and instrument parameters are available in the Supporting Information under "Sample Collection" and "Analytical Methods."

Results and Discussion

A summary of the occurrence of pharmaceuticals and EDCs in source, finished, and distribution system water is shown in Table 3. Thirty-four of the 51 targeted compounds were detected in at least one sample, while the remaining 17 compounds were not detected in any samples. Eleven compounds (atenolol, atrazine, carbamazepine, estrone, gemfibrozil, meprobamate, naproxen, phenytoin, sulfamethoxazole, tris(2-chloroethyl) phosphate (TCEP), and trimethoprim) were detected in more than half of the source waters, while only atrazine, meprobamate, and phenytoin were detected in more than half of finished waters or distribution systems. All raw data are available in Supporting Information Tables S2, S3, and S4.

Occurrence of Pharmaceuticals and EDCs in Source Water Samples. Targeted compounds were detected most frequently in source waters as compared to treated drinking waters (Table 3 and Supporting Information Table S2). At least one compound was detected in all 19 source waters. The 11 compounds which were detected in greater than half of source waters were atenolol, atrazine, carbamazepine, estrone, gemfibrozil, meprobamate, naproxen, phenytoin, sulfamethoxazole, TCEP, and trimethoprim. The three DWTPs (-10, -11, and -14) utilizing water from reservoirs with no direct input of wastewater and where no recreational use is permitted had the lowest numbers of individual compounds detected in source waters (3, 3, and 2 compounds detected). The four DWTPs (-16, -17, -18, and -19) utilizing water from reservoirs with no direct input of wastewater, but where recreational use is allowed, had similar numbers of individual compounds detected in their source waters as compared to those DWTPs withdrawing water from wastewater impacted sources.

Atrazine is a widely used herbicide and was detected in the source water of almost every DWTP, including those far-removed from areas with no agricultural atrazine application. The frequent detection of atrazine suggests that it is a widespread environmental contaminant. For example, it was one of the most commonly detected compounds in the 22-month monitoring program at DWTP-6 (see Supporting Information Tables S5 and S6), a plant located in an arid region of the U.S. where there is no known atrazine use (*25*). However, atrazine has previously been detected in wastewater effluent influencing the reservoir of this DWTP (*24*). Detectable levels of atrazine have been measured in some foods (*26*) which may explain the loading to this wastewater

TABLE 3. MRLs, Maximum Concentrations(max), Median Concentrations(med), the Number of Detections (no.) of Pharmaceuticals and EDCs in Source Water, Finished Water, And Distribution Systems As Well As Literature Chlorine and Ozone Removal Efficiencies. All Concentrations Are Presented in ng/L[a]

		source ($n = 19$)			finished ($n = 18$)			distribution ($n = 15$)			removal (%)	
	MRL	max.	med.	no.	max.	med.	no.	max.	med.	no.	f-cl_2	ozone
pharmaceuticals												
atenolol	0.25	36	2.3	12	18	1.2	8	0.84	0.47	8	n	n
atorvastatin	0.25	1.4	0.80	3	<MRL	<MRL		<MRL	<MRL		n	n
carbamazepine	0.50	51	4.1	15	18	6.0	8	10	6.8	6	<20[b], ~95[c], >95[d], 9[e]	>95[f], 99[g], >95[h], >95[I]
diazepam	0.25	0.47	0.43	2	0.33	0.33	1	<MRL	<MRL		20−50[b], ~75[c], ~75[d]	50−80[f], 81[g],
diclofenac	0.25	1.2	1.1	4	<MRL	<MRL		<MRL	<MRL		>80[b], ~95[c], ~95[d]	>95[f], 95[g], >95[h], >95[I]
fluoxetine	0.50	3.0	0.80	3	0.82	0.71	2	0.64	0.64	1	<20[b], ~50[c], ~15[d]	>95[f], 91[g],
gemfibrozil	0.25	24	2.2	11	2.1	0.48	7	1.2	0.43	4	50−80[b], >95[c], >95[d], 0[e]	>95[f], 98[g],
o-hydroxy atorvastatin	0.50	1.2	0.70	3	<MRL	<MRL		<MRL	<MRL		n	n
p-hydroxy atorvastatin	0.50	2.0	1.0	3	<MRL	<MRL		<MRL	<MRL		n	n
meprobamate	0.25	73	8.2	16	42	5.7	14	40	5.2	11	<20[b], ~25[c], ~10[d]	20−50[f], 60[g],
naproxen	0.50	32	0.90	11	<MRL	<MRL		<MRL	<MRL		>80[b], ~95[c], ~95[d]	>95[f], 91[g],
norfluoxetine	0.50	<MRL	<MRL	-	<MRL	<MRL		0.77	0.77	1	n	n
phenytoin	1.0	29	5.1	14	19	6.2	10	16	3.6	10	<20[b], ~60[c], ~20[d]	50−80[f], 86[g],
risperidone	2.5	<MRL	<MRL		<MRL	<MRL		2.9	2.9	1	n	n
sulfamethoxazole	0.25	110	12	17	3.0	0.39	4	0.32	0.32	1	>80[b], ~90[c], >95[d], 48[e]	>95[f], 88[g], >95[I]
triclosan	1.0	6.4	3.0	6	1.2	1.2	1	<MRL	<MRL		>80[b], >95[c], >95[d], ~96[e]	>95[f], 92[g],
trimethoprim	0.25	11	0.80	11	<MRL	<MRL		<MRL	<MRL		>80[b], >95[c], >95[d], 42[e], 100[e]	>95[f], 98[g], >95[j]
known or potential EDCs												
atrazine	0.25	870	32	15	870	49	15	930	50	12	<20[b], ~35[c], ~5[d], 44[e]	20−50[f], 47[g],
17β-estradiol	0.50	17	17	1	<MRL	<MRL		<MRL	<MRL		>80[b], >95[c], >95[d]	>95n[f], 98[g],
estrone	0.20	0.90	0.30	15	<MRL	<MRL		<MRL	<MRL		>80[b], >95[c], >95[d]	>95[f], 99[g],
17α-ethynylestradiol	1.0	1.4	1.4	1	<MRL	<MRL		<MRL	<MRL		>80[b], >95[c], >95[d]	>95[f], 99[g], >95[I]
bisphenol A	5.0	14	6.1	3	25	25	1	<MRL	<MRL		~97[e]	n
butylbenzyl phthalate	50	54	53	2	<MRL	<MRL		<MRL	<MRL		n	n
diethylhexyl phthalate	120	170	150	2	<MRL	<MRL		<MRL	<MRL		11[e]	n
galaxolide	25	48	3	4	33	31	2	<MRL	<MRL		~55[c], ~45[c], 4[e]	n
linuron	0.50	9.3	4.1	5	6.2	6.1	2	<MRL	<MRL		n	n
nonylphenol	80	130	100	8	100	93	2	110	97	2	~89[e]	*n*
progesterone	0.50	3.1	2.2	4	0.57	0.57	1	<MRL	<MRL		<20[b], ~65[c], ~60[d]	>80[f], 91[g],
testosterone	0.50	1.2	1.1	2	<MRL	<MRL		<MRL	<MRL		<20[b], ~65[c], ~55[d]	>80[f], 94[g],
other chemicals												
BHT	25	49	49	1	26	26	1	<MRL	<MRL		n	n
metolachlor	10	81	17	7	27	16	6	22	18	3	<20[b], ~35[c], ~30[d], 1[e]	>80[f], 83[g],
DEET	25	110	85	6	93	63	6	63	49	4	<20[b], ~35[c], ~5[d], 0[e]	50−80[f], 80[g],
TCEP	50	530	120	10	470	120	7	200	150	6	<20[b], ~10[c], 0[d], 0[e]	<20[f], <5[g],
TCPP	50	720	180	8	510	210	5	240	220	6	n	n

[a] Not detected in any samples were benzophenone, BHA, diazinon, enalapril, α-HCH, β-HCH, δ-HCH, γ-HCH, methoxychlor, musk ketone, octachlorostyrene, octylphenol, simvastatin, simvastatin hydroxy acid, tonalide, traseolide, and vinclozolin; n, no information available. [b] 3 mg/L chlorine for 24 h in surface water (*19*). [c] 3.8 mg/L chlorine for 24 h in surface water @ pH 5.5 (*28*). [d] 3.5 mg/L chlorine for 24 h in surface water @ pH 5.5 (*28*). [e] 1.2 mg/L chlorine for 24 h in drinking water (*30*). [f] 1.3 and 2.7 mg/L ozone for 24 min in surface water (*19*). [g] Average of four treatments of 3−8.2 mg/L ozone in surface water (*28*). [h] Various ozone concentrations (0.5−3 mg/L) in flocculated drinking water (*15*). [I] Various ozone concentrations (0.5−2 mg/L) in bank filtrate or surface water (*29*). [j] 0.3 mg/L ozone for 1.3 min in surface water (*31*).

treatment plant and DWTP. In this study, the largest atrazine source water concentrations were measured in source waters proximate to agricultural areas where it is heavily applied.

In some samples, pharmaceutical parent-metabolite compounds were detected together, whereas in others they were not. The hydroxylated metabolites of atorvastatin occurred when the parent compound, atorvastatin, was also detected. Norfluoxetine was not detected in any source waters, including the three in which its parent compound fluoxetine was detected. Neither simvastatin nor its metabolite, simvastatin hydroxy acid, was detected in any source waters.

The most prescribed pharmaceutical in 2006 and 2007 in the U.S. (*27*), atorvastatin, was detected in only three source waters and was not detected in any finished or distribution waters. Conversely, the most frequently detected prescription pharmaceuticals (carbamazepine, gemfibrozil, meprobamate, sulfamethoxazole, and trimethoprim) were not included in the top 200 prescribed pharmaceuticals for 2006 or 2007. Only atenolol (ranked no. 99 in 2007) and phenytoin (ranked no. 128 in 2006 and no. 151 in 2007) were frequently detected in source water. Thus, prescription information alone is a poor proxy for source water occurrence because it does not take into account the dosage, pharmacokinetics, removal during wastewater treatment, or environmental fate.

Occurrence of Pharmaceuticals and EDCs in Finished Water Samples. Compounds were detected less frequently in finished waters as compared to source waters (Table 3 and Supporting Information Table S3). Sixteen of the 18 finished waters had detectable concentrations of at least one target compound. The two finished waters with no detectable concentrations of any targeted compound were from DWTP-11 and DWTP-14. These were two of the three DWTPs withdrawing water from reservoirs with no direct input of wastewater and where no recreational use is permitted. Median concentrations of detected pharmaceuticals and EDCs in finished drinking water were less than 10 ng/L, except for atrazine (49 ng/L), bisphenol A (25 ng/L), galaxolide (31 ng/L), nonylphenol (93 ng/L), BHT (26 ng/L), metolachlor (16 ng/L), DEET (63 ng/L), tris(1,3-dichloro-2-propyl) phosphate (TCPP) (120 ng/L), and TCPP (210 ng/L). Some of these median concentrations, however, were biased by low frequencies of detection.

The persistence of pharmaceuticals and EDCs into finished drinking waters targeted in this work is governed by pharmaceutical and EDC occurrence in source water and subsequent removal during chlorine or ozone oxidation. Though there are other processes at each DWTP (Table 2), those most responsible for the removal of pharmaceuticals and EDCs are oxidation by chlorine or ozone (*19*). Additionally, though chloramines are employed at some DWTPs, chlorine (f-Cl_2 in Table 2) is a stronger oxidant and has been shown to be more effective at oxidizing pharmaceuticals and EDCs (*19*). Thus, the presence of pharmaceuticals in finished drinking water can be explained by whether a DWTP employs chlorine or ozone. Though many ozone plants also utilize chlorine, ozone is a stronger oxidant and for the purposes of this discussion, these DWTPs are considered ozone plants.

Table 3 lists literature removal efficiencies for each compound by chlorine and ozone during simulated drinking water treatment. Of the 11 most frequently detected compounds in source water, naproxen, trimethoprim, and estrone were not detected in any finished waters. Each of these compounds has been shown to be efficiently oxidized by either chlorine or ozone. Conversely, atrazine, meprobamate, and phenytoin, detected in more than half of finished waters, are resistant to chlorine or ozone oxidation (measured atrazine concentrations in finished water were always well below the U.S. Environmental Protection Agency mandated maximum contaminant level of 3000 ng/L). TCEP was also detected in several finished water samples, consistent with the fact it is poorly oxidized by either chlorine or ozone. Carbamazepine was measured in finished waters at DWTPs employing chlorine but not at those employing ozone. The removal of carbamazepine by chlorine varies depending on pH: at lower pH values carbamazepine is removed more efficiently than at higher pH values (*28*). Carbamazepine is efficiently removed by ozone. Sulfamethoxazole was detected in only three finished waters at DWTPs employing chlorine, at concentrations approaching the method reporting limit (MRL), consistent with efficient oxidation by chlorine. Sulfamethoxazole was, however, detected in the finished water of one DWTP employing ozone, well above the MRL and at a level similar to its concentration in the corresponding source water. The reason for this is not known. Gemfibrozil was not detected in finished waters at DWTPs employing ozone, consistent with efficient removal by ozonation. Gemfibrozil was measured in seven finished waters at DWTPs employing chlorine, though finished water concentrations were much lower than source water concentrations. There are conflicting data pertaining to how efficiently gemfibrozil is removed by chlorine. Though there is no information in the literature pertaining to the removal of atenolol by chlorine or ozone, its behavior can be inferred from this study. Atenolol was not detected in the finished water of any DWTP employing ozone. It was, however, detected in the finished water of seven plants employing chlorine and no O_3. Additionally, measured finished water concentrations of atenolol were 18−75% of their corresponding source water concentrations suggesting that atenolol may not be efficiently removed by chlorine, but is well-removed by ozone.

Occurrence of Pharmaceuticals and EDCs in Distribution Systems. Compounds were detected less frequently in distribution system (tap) waters as compared to source or finished waters (Supporting Information Table S4). Thirteen of the 15 distribution systems contained detectable concentrations of at least one target compound. No detectable concentrations of pharmaceuticals or EDCs were measured in DWTP-11 and DWTP-14, which were two DWTPs withdrawing water from reservoirs with no direct input of wastewater and where no recreational use is permitted. Risperidone and norfluoxetine were each measured in one distribution system sample, though they were not measured in any source or finished water samples. The reason for these detections is not known, though it is important to note that both concentrations were just above their respective MRLs. The three compounds which were detected in greater than half of distribution system waters were atrazine, phenytoin, and meprobamate. The frequencies of detection and median concentrations of these three compounds, as well as carbamazepine, TCEP, and TCPP did not vary significantly between the finished water samples and the distribution system samples. Their persistence in distribution system water illustrates that longer contact times with secondary disinfectants did not play a significant role in removing or lowering the concentrations of these refractory compounds and is consistent with their resistance to chlorine oxidation (Table 3).

Indicator Compounds. The relative occurrence of certain compounds, combined with their behavior through different water treatment technologies, can provide an abbreviated list of indicator compounds that reflect the potential for contamination by other compounds as well as the efficacy of a given type of treatment. Table 4 lists six potential indicator compounds divided into three groups based on their likelihood of being removed by (1) both chlorine and ozone, (2) ozone only, or (3) neither chlorine nor ozone. These indicator compounds were chosen because they were both frequently detected compounds in this and an earlier study (Supporting Information Table S1) and exhibited removal

TABLE 4. Six Frequently Detected Indicator Compounds, Their Removal during Chlorine or Ozone Oxidation, And the Relative Number of Pharmaceuticals and EDCs Removed by Chlorine or Ozone[a]

	removal by	
	chlorine	ozone
group 1		
estrone	good	good
trimethoprim	good	good
group 2		
DEET	poor	good
atenolol[b]	poor	good
group 3		
atrazine	poor	poor
meprobamate	poor	poor
number of pharmaceuticals and EDCs >50% removed by each process[c]		
	16 of 36	25 of 29

[a] see Table 3 for removal efficiencies for each compound. [b] No literature removal efficiencies have been published for atenolol. Its behavior during chlorine or ozone oxidation is inferred from this study. [c] Data adapted from Snyder et al. (*19*).

trends reflective of process performance. Table 4 also presents the relative number of pharmaceuticals and EDCs which are >50% removed by either chlorine or ozone oxidation (*19*). Since the group 1 compounds (estrone and trimethoprim) are readily removed by chlorine and ozone, their presence would indicate a lack of sufficient chlorine or ozone treatment and the greatest potential for contamination by other pharmaceuticals and EDCs that are also easily removed by chlorine or ozone. The group 2 compounds (atenolol and DEET) are not readily removed by chlorine, but are well removed by ozone. The presence of the group 2 compounds (but not group 1 compounds) may indicate the potential for the presence of a more refractory suite of contaminants: the 20 of 36 pharmaceuticals and EDCs not removed by chlorine under simulated drinking water treatment conditions (*19*). Similarly, if group 2 compounds are found downstream of ozonation, it would indicate problems with the ozone process or a potential breach leading to an additional source of contamination by other compounds. Finally, the presence of group 3 compounds coupled with the absence of group 1 or 2 compounds would indicate that the water is likely free of most other organic contaminants and that the ozone process is functioning efficiently. Only 4 of 29 pharmaceuticals and EDCs are not removed by ozone under simulated drinking water treatment conditions (*19*).

Twenty-Two Month Monitoring Program at DWTP-6. Concentrations of 47 pharmaceuticals and EDCs in the source and finished water of DWTP-6, measured over a 22-month period, are presented in Figure 1 (all raw data are available in the Supporting Information Tables S5 and S6). Butylated hydroxy toluene (BHT), TCEP, TCPP, and nonylphenol are not included in this interpretation because their markedly higher MRLs combined with sporadic detection masked the trends of the compounds that were more routinely detected at lower concentrations. Monthly summed concentrations of detected compounds as well as the number of individual compounds detected are presented for both source water and finished waters between March 2006 and December 2007. The summed concentrations varied in source water by approximately a factor of 2: between a collective low of 37 ng/L measured in October 2006, and a high of 80 ng/L measured in November 2007. The summed concentrations were much lower in finished water, and varied by approximately a factor of two: between a collective low of 5.8 ng/L measured in September 2007, and a high of 13 ng/L measured in May 2006 and November 2007. The number of compounds detected always decreased, from 8 to 10 in source water, to 2 to 4 in finished water. In each month, atrazine and meprobamate were detected in finished water and comprised most of the total summed concentrations.

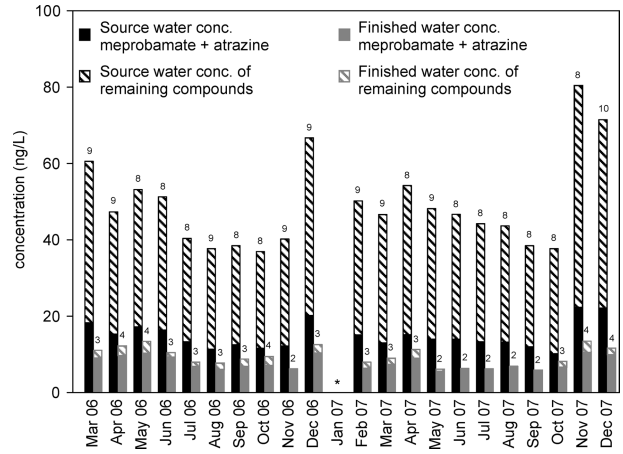

FIGURE 1. Summed concentrations of 47 pharmaceuticals and EDCs detected in source and finished water at DWTP-6 over a 22 month period highlighting the relative contribution from the group 3 indicator compounds (meprobamate and atrazine) compared to the remaining detected pharmaceuticals and EDCs. Numbers above bars represent number of compounds detected. *No data were collected in January 2007.

Figure 1 also illustrates one application of the suggested indicator compounds. The summed concentrations show the contribution from atrazine and meprobamate (i.e., the group 3 compounds) compared to the contribution from all the remaining detected compounds in source and finished water. In source water, atrazine and meprobamate compromise approximately one-third of the summed concentrations and represent two of the 8−10 compounds detected. Following treatment with ozone, atrazine and meprobamate compromise most, if not all, of the summed concentrations and represent two of the 2−4 compounds detected. The detection of atrazine and meprobamate in finished water, combined with the nondetection of group 1 and group 2 compounds (Supporting Information Table S6), suggests that ozonation was functioning properly and that the water was not contaminated with pharmaceuticals and EDCs which are removed by chlorine or ozone oxidation. Thus, the application of an indicator compound "litmus test" for the potential presence or absence of other compounds may be appropriate for use by DWTPs using similar treatment processes.

Acknowledgments

We thank Spencer Porter and Peggy Roefer of the Southern Nevada Water Authority for their help with data collection and interpretation, as well as Erin Snyder from Total Environmental Solutions, Inc. for her invaluable input into this manuscript. This work was funded by the Awwa Research Foundation (project no. 3085) and the WateReuse Foundation (project no. 04-003).

Supporting Information Available

A detailed description of the compound selection criteria, sample collection, and analytical methods. Results from an earlier study of pharmaceutical and EDC occurrence in DWTPs is presented along with all raw data. This material

is available free of charge via the Internet at http://pubs.acs.org.

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ES801845A