

The Occurrence and Fate of Pharmaceuticals, Personal Care Products and Endocrine Disrupting Compounds in a Municipal Water Use Cycle:

A Case Study in the City of Ann Arbor

November 2004

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Abstract

A characterization of the occurrence and fate of a 22 compound target list of pharmaceuticals, personal care products and endocrine disrupting compounds (PPCPs and EDCs) has been performed at various locations within the City of Ann Arbor's (Ann Arbor) water use cycle. Monitoring occurred at four locations within the water use cycle:

- Surface/source water
- Drinking water
- Wastewater influent
- Wastewater effluent

Laboratory analysis indicated the following number amount of target compounds identified in grab samples collected from each monitoring station over the four sampling events:

- 10 of 22 compounds detected in source water (Huron River)
- 4 of 22 compounds detected in finished drinking water
- 17 of 22 compounds detected in wastewater influent
- 15 of 22 compounds detected in treated wastewater effluent

Results of this study indicate a reduction in the concentrations of certain compounds based on samples collected before and after source water and wastewater treatment processes. Collected data indicates variability in the occurrence of PPCPs and EDCs in treated and untreated water and wastewater. Additionally, characterization of this variability and comparison to other source water supplies and treatment processes in Michigan has been identified as an area of additional future study.

INTRODUCTION

Research reviewed over the course of this study indicates that there has been an increase in studies over the past two decades characterizing the occurrence of endocrine disrupting compounds (EDCs), pharmaceuticals and personal care products (PPCPs) in water use cycles in the United States and Europe. PPCPs are often described as a grouping of chemical substances that range from prescription drugs to fragrances and cosmetics. The American Water Works Association (AWWA) defines EDCs as chemicals that interfere with the normal function of the endocrine system. The endocrine system includes endocrine glands and the hormones produced from these glands. Examples of these glands include the pituitary, thyroid, and pancreas. The group of EDCs contains a wide range of compounds such as steroids, pesticides, inorganics, and industrial chemicals.

Compared to established laboratory methods for the analysis of traditional organic compounds, common laboratory protocol for analyzing PPCPs and EDCs are still being developed. As a result, several different analytical methods for characterizing PPCP/EDC compounds in water have been performed in recent studies. In natural waters, solid phase extraction is used along with gas chromatography (GC) paired with mass spectrometry (MS), liquid chromatography (LC) coupled with MS, immunoassays, or a combination of techniques (Snyder, 2003). Choosing between GC and LC analyses is generally based on the physiochemical qualities of the target analyte. Many PPCPs are polar in nature and are not suitable for GC analysis without performing additional preparation and extraction. Therefore, LC analysis, instead of GC analysis, is usually applied when targeting more polar compounds (Boyd, 2003). The ability to analyze samples for pharmaceuticals at low analytical detection limits has improved over time (Daughton, 1999).

Currently, other researchers are evaluating the environmental effects of human and aquatic exposure to PPCPs and EDCs. Additionally, studies completed over the past few decades have recognized that the potential exists for PPCPs to enter the environment from multiple routes, such as, wastewater treatment discharge, industrial discharge, runoff from confined animal feeding operations, and treated sludge applied to agricultural land. (Daughton and Ternes, 1999). PPCPs may enter the treatment process in a reduced form (after passing through body) or by direct discharge of discarded PPCPs.

Points of PPCP and EDC entry into the environment include:

1. Discharge from Wastewater treatment processes such as treatment plant or septic systems,
2. Regulated and unregulated industrial discharges to surface and groundwater,
3. Leaking or overflowing animal waste storage from confined animal feeding operations,
4. Land application of treated animal waste from certain animal feeding operations.

Studies on this topic include the 1999-2000 United States Geological Survey (USGS) National Reconnaissance. The USGS National Reconnaissance was a comprehensive study that characterized the occurrence of PPCPs and EDCs in various surface water resources nationwide. The study reported that water samples collected from 80% of 139 streams monitored in 30 states found one or more of the study's 95 target analytical compounds (including pharmaceuticals, hormones, and other wastewater compounds). The

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sampling sites were selected in areas prone to contamination from agricultural, industrial and metropolitan wastewater (Koplin, 2002).

The purpose of the study reported herein was to evaluate the occurrence and fate of certain PPCPs and EDCs at key locations within the City of Ann Arbor's water use cycle. Specifically, data was obtained by performing laboratory analysis of manually collected water samples for a target compound list of pharmaceuticals, personal care products, and endocrine disruptors. The data were used to characterize the occurrence, fate, and transport of the compounds in the water cycle at four locations during four discreet sampling events. This report documents the field and laboratory methods used to complete the analysis of the target compound list. Additionally, this report describes the water use cycle and summarizes the results of the analytical laboratory reports.

The occurrence of PPCPs and EDCs in the Huron River is of interest to the City based on their reliance on the Huron River for the majority of its community water supply. Approximately 80% of the City's community water supply is drawn from the Huron River (Figure 1). Additionally, MDEQ recognizes the need for information regarding certain classes of substances, including PPCPs and EDCs. The collection of basic occurrence data will assist in developing an understanding of the effect(s), if any, PPCPs and EDCs have on the quality of Michigan's water resource (communication, MDEQ).



Figure 1. Huron River Upstream of the City's Water Intake.

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The target compound list developed for this study was primarily based on three criteria:

1. Compounds identified in the 1999-2000 USGS National Reconnaissance (Koplin, 2002),
2. Ability to complete analysis using defined laboratory methods, and
3. Frequency of compound occurrence in surface and wastewater in the United States and Europe as reported in reviewed literature.

The target compounds for this study are listed in Table 1.

Table 1. Target Compound List

PPCPS & EDCs	Use/Origin	Analytical Method
Antibiotics		
Sulfadimethoxine	human/veterinary antibiotic	LC/MS/MS
Sulfamethazine	human/veterinary antibiotic	LC/MS/MS
Sulfamethoxazole	human antibiotic	LC/MS/MS
Sulfathiazole	human/veterinary antibiotic	LC/MS/MS
Lincomycin	human/veterinary antibiotic	LC/MS/MS
Tylosin	veterinary antibiotic	LC/MS/MS
Trimethoprim	human antibiotic	LC/MS/MS
Analgesics		
Acetaminophen	pain reliever	LC/MS/MS
Ibuprofen	pain reliever	LC/MS/MS
Antiepileptic		
Carbamazepine	antiepileptic/antimanic	LC/MS/MS
Miscellaneous		
Caffeine	stimulant	GC/MS
Cotinine	nicotine metabolite	GC/MS
1,4 Dioxane	solvent stabilizer	GC/MS
Hormones and Sterols		
Testosterone	hormone	GC/MS
Ergosterol	steroidal hormone	GC/MS
Stigmasterol	plant steroid	GC/MS
Sitosterol	plant steroid	GC/MS
Stigmastanol	plant steroid	GC/MS
Progesterone	steroidal hormone	GC/MS
Coprostanol	fecal steroid	GC/MS
Cholesterol	plant/animal steroid	GC/MS
Dihydrocholesterol	plant/animal steroid	GC/MS

SITE CHARACTERISTICS AND SAMPLING PROCEDURES

Four water-sampling events were conducted at four key locations throughout the City's water use cycle:

1. Raw source water intake from the Huron River
2. Finished drinking water from plant tap
3. Raw municipal wastewater prior to treatment
4. Treated municipal wastewater prior to discharge to the Huron River

Raw source water intake from the Huron River

The surface water body characterized for this study was the Huron River, which meanders through several counties in southeastern Michigan. The river flows from Oakland County's Huron Swamp approximately 125 miles to Lake Erie. Land use bordering the Huron River upstream of Ann Arbor's intake is a blend of agricultural, residential, commercial and industrial. Ann Arbor is located within the Huron River watershed. The Michigan Department of Environmental Quality (MDEQ) completed a Source Water Assessment (SWA) of Ann Arbor's Huron River intake in 2004. A map of the City of Ann Arbor's Huron River Source Water Area is illustrated in Figure 2. MDEQ reported soil permeability in the SWA ranges from less than 0.06 in/hr (very slow), to more than 20 in/hr (very rapid).

The 2004 MDEQ study concluded the SWA for Ann Arbor contains an area of about 760 square miles.

Sample Collection

Ann Arbor Water Department personnel, using methods approved by the Michigan Department of Environmental Quality, conducted water sampling for this study. As recommended by the EPA, tobacco, caffeine, and other common products that could affect sample integrity were avoided prior to sampling.

For each of the four sampling events, a grab sample was collected at each of the four sampling stations. Figure 7 illustrates the typical collection of a sample from the wastewater plant. Samples were collected in 1 Liter, amber glass bottles. A total sample volume of 3 liters was collected from each sampling location. One field/trip blank was prepared in the field using high purity ionized water. Collected samples were preserved in ice and shipped overnight (within 24 hours) to the University of Iowa Laboratory. Each location was sampled in February, April, June, and August of 2004.



Figure 7. Sample Collection at the Wastewater Plant.

LABORATORY ANALYTICAL METHODS

Laboratory analysis for each of the target compounds was performed by the University of Iowa Hygienics Laboratory with the exception of 1,4 Dioxane, which was performed by Ann Arbor Technical Services, Inc. The University of Iowa Hygienics Laboratory used 3 liters of sample volume for each analysis. Ann Arbor Technical Services, Inc. used 1 liter of sample volume for each analysis.

Based on the differing families of compounds, two different analytical methods were utilized by the University of Iowa. The first method used was Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) analyses; standard operating procedure UHL-H-020 "Determination of Pharmaceuticals and Antibiotics in Water by High Performance Liquid Chromatography with Tandem Quadruple Mass Spectrometric Detection" was followed (UHL-H-020). The system was mass calibrated with a mixture of polyethylene glycols at least once every six months. The MS system was optimized by infusion of the test analyte into the system while adjustments are made on instrument parameters, so that the best signal response was obtained.

The second method was Gas Chromatography/Mass Spectrometry (GC/MS) analysis for aqueous samples; EPA preparative method 3510 and EPA determinative method 8270 (EPA Test Methods for Evaluating Solid Waste, Physical/Chemical Methods, SW-846) was extended to determine sterols/hormones and two non-prescription drugs using two independent procedures. The GC/MS system was 'tuned' on a daily basis using standard EPA tuning techniques and acceptance criteria; Decafluorotriphenylphosphine was used as the tuning compound. The instrument analytical response was calibrated daily to ensure accurate quantitation.

Samples were stored in a refrigerator while awaiting extraction or analysis with a maximum storage time of 35 days. The temperature of the refrigerator was between 3° and 7° Celsius. The temperature of the refrigerator was verified daily and recorded.

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The LC/MS/MS analytes included sulfadimethoxine, sulfathiazole, sulfamethoxazole, sulfamethazine, tylosin, lincomycin, carbamazepine, trimethoprim, acetaminophen, and ibuprofen. Solid phase extraction was used to isolate and concentrate the analytes from water samples. Analysis was performed by reversed phase high performance liquid chromatography with tandem mass spectrometric detection. An electrospray interface was used to generate ions for detection.

The sterols/hormones determined by GC/MS included coprostanol, cholesterol, dihydrocholesterol (cholestanol), stigmasterol, sitosterol, stigmastanol, testosterone, equilenin, and progesterone. Non-prescription drugs, caffeine, and cotinine (metabolite of nicotine) were determined by GC/MS. A separatory funnel extraction was performed on each sample using methylene chloride as the organic solvent. The sample extracts were dried by passing through sodium sulfate. For the sterols/hormones a derivatization step was employed whereby the trimethylsilyl (TMS) derivative was formed by adding bis(trimethylsilyl)-trifluoroacetamide (BSTFA) plus 1% trimethylchlorosilane (TMCS) to the extract and maintaining the temperature at 70 °C for one hour.

Specifications for data reduction, validation, and reporting were addressed in SOP UHL-H-020 for the LC/MS/MS analyses. In brief, analytes were qualitatively identified by the unique ion pairs, which were monitored with a chromatographic retention time that varied no more than $\pm 2\%$ of the average retention time for calibration standards. Quantification of analytes was performed by external calibration using solutions containing all of the tested analytes in varying concentrations. Calibration standards were analyzed for each set of samples with a new external calibration response curve generated for quantifying results. In general, if a linear curve fit was used, the linear regression correlation coefficient criteria was greater than 0.995. LC/MS/MS analyses used a second order curve (parabolic) fit and compared the calculated value of each calibration standard with its true value. In general, the lowest calibration point was required to be $\pm 30\%$ of true value and all other calibration points' $\pm 10\%$ of true value. The GC/MS data was quantified by injecting varying concentrations of each analyte and then calculating a response factor that was subsequently used to determine the concentration of the analytes in the water samples. Analytes with a response greater than the highest calibration standard concentration were appropriately diluted and reanalyzed. Analytes with a response less than the lowest calibration standard was reported as "less than." For many analytes, a confirmation ion pair was monitored in addition to the primary, or quantitative, ion pair. For those analytes where both a quantitative and confirmatory ion pair could be monitored, the presence of an analyte was considered confirmed and reportable only if both the quantitative and confirmatory ion pairs were observed at levels greater than the lowest calibration standard and when the determined concentration for the confirmatory ion pair was $\pm 30\%$ of the determined concentration for the quantitative ion pair.

Sample extracts for GC/MS determinations were quantitatively measured using the internal standard method of quantitation. Perylene-d12 or acenaphthene-d10 was used as the internal standard. Cholesterol-d6 was used as a surrogate (recovery check) standard for the sterols extraction while p-terphenyl-d14 was used to monitor efficiency of the caffeine/cotinine extraction. The mass spectrometer was configured to operate in selected ion monitoring mode and collected data for at least three ions for each target compound. Retention times and ion ratios observed in samples were compared to those in reference standards to evaluate results. Sterols/hormones with a response in samples less than the lowest calibration standard were reported as "less than." Caffeine/cotinine with a response in samples less than the lowest calibration standard were reported as "estimated" if identification criteria were met.

Analysis for 1,4 dioxane used a Purge and Trap, Gas Chromatography/Mass Spectrometry Detection procedure. The testing method reference USEPA, 1987, Method 1624 (modified, 40 CFR Part 136 Appendix A). The method detection limit was 0.001 mg/L. Data reduction included all activities that convert instrument responses into reportable results, and included mathematical calculations, compound identification, and summary statistics.

RESULTS AND DISCUSSION

Laboratory analysis results have been grouped as follows:

Drinking Water

- Occurrence in source water
- Occurrence in finished drinking water
- Water treatment compound reduction

Wastewater

- Occurrence in wastewater Influent
- Occurrence in wastewater effluent
- Wastewater treatment compound reduction

Sampling results are summarized in Tables 2 through 5 and illustrated in Figure 8 and 9. The results of laboratory analysis for estriol and ergosterol are not being reported as the University of Iowa Hygienics Laboratory experienced poor analyte recovery from spiked samples. As such, the laboratory deemed this data unreliable. The observed recovery percentages for estriol and ergosterol averaged 14.8% and 23.0%, respectively, for the four sampling events. This may be due to inefficient partitioning in the extraction process. The data for estriol and ergosterol is presented but not included in the calculations. Therefore, sample mean and standard deviation is calculated from 22 of the initial 24 target compounds is reported in this study.

Review of the data illustrates that during the first three (February, April and June 2004) sampling events, acetaminophen was detected in wastewater influent samples at concentrations exceeding any other detectable target compound concentration. Acetaminophen was also detected in the first three source water sampling events. However, acetaminophen was not detected in wastewater or source water samples collected in the last sampling event (August 2004). Review of the acetaminophen laboratory analysis data from the August 2004 sampling event indicates that both the agent spike and the matrix spike for the wastewater influent sample reported acceptable 89% and 88% recovery, respectively. Additionally, the August 2004 sample hold time prior to extraction and analysis was consistent with the first three sampling events. This indicates that compound degradation during the sample holding period, if any, was similar to previous sampling events. Acetaminophen is often used in pain relievers. As such, the sudden reduction in detected concentrations may be the result of a spring to fall seasonal reduction in the use of pain relievers. Additionally, the result may be a reflection of reduced University related population in the city during spring/summer periods.

Occurrence in Source Water

Laboratory analysis reported that 10 of the 22 target compounds were detected in source water from the Huron River (Table 2/Figure 8 & 9). The compounds detected in the source water intake cover included antibiotics, analgesics, antiepileptics, stimulants and steroids.

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The highest concentrations of PPCPs were detected in February. PPCP concentrations generally decreased during each successive sampling event. Both ibuprofen and caffeine were detected during only one (February) sampling event. This may be a reflection of seasonal cold/flu cycles, or a reflection of reduced spring/summer city population as the result of University schedules.

Table 2. Analyte Concentrations Detected in Source Water - Huron River (ug/l)

Analyte	February	April	June	August	Mean	Standard
					Concentration	Deviation
					µg/l	µg/l
Antibiotics						
Sulfadimethoxine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethazine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethoxazole	0.019	0.012	0.0037	0.0068	0.010	0.007
Sulfathiazole	<0.0010	<0.0010	<0.0010	<0.0010		
Lincomycin	<0.0010	<0.0010	<0.0010	<0.0010		
Tylosin	<0.0010	<0.0010	<0.0010	<0.0010		
Trimethoprim	0.0024	0.0020	<0.0010	<0.0020	0.0015	0.001
Analgesics						
Acetaminophen	0.025	0.0087	0.0038	<0.0020	0.010	0.011
Ibuprofen	0.0071	<0.0020	<0.0020	<0.0020	0.0025	0.003
Antiepileptics						
Carbamazepine	0.016	0.0080	0.0047	0.0068	0.009	0.005
Miscellaneous						
Caffeine	0.057	<0.040	<0.040	<0.040	0.029	0.019
Cotinine	<0.040	<0.040	<0.040	<0.040		
1,4 Dioxane	<1	<1	<1.0	<1.0		
Steroids and Hormones						
Testosterone	<0.200	<0.200	<0.200	<0.200		
*Equilenin	<0.050	<0.050	<0.050	<0.050		
*Estriol	<0.200	<0.200	<0.200	<0.200		
Ergosterol	<1.000	<1.000	<1.000	<1.000		
Stigmasterol	0.320	0.340	0.200	0.190	0.263	0.078
Sitosterol	2.800	1.200	0.410	0.260	1.168	1.164
Stigmastanol	<0.200	<0.200	<0.200	<0.200		
Progesterone	<0.200	<0.200	<0.200	<0.200		
Coprostanol	<0.100	<0.100	<0.100	<0.100		
Cholesterol	0.580	1.100	1.200	0.430	0.828	0.380
Dihydrocholesterol	<0.100	0.140	0.110	<0.100	0.088	0.217

*Data not used in calculations due to poor recoveries

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Occurrence in Finished Drinking Water

Laboratory analysis reported that 4 of the 22 target compounds were detected in the finished drinking water (Table 3/Figure 8 & 9).

Drinking water analysis was based on finished water prior to leaving the Treatment Plant. As described in the description of the treatment process, groundwater is blended with river source water. The blending ratio varies, but is approximately 80% surface water and 20% groundwater.

Table 3. Analyte Concentrations Detected in Drinking Water (ug/l)

Analyte	February	April	June	August	Mean	Standard
					Concentration µg/l	Deviation µg/l
Antibiotics						
Sulfadimethoxine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethazine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethoxazole	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfathiazole	<0.0010	<0.0010	<0.0010	<0.0010		
Lincomycin	<0.0010	<0.0010	<0.0010	<0.0010		
Tylosin	<0.0010	<0.0010	<0.0010	<0.0010		
Trimethoprim	<0.0010	<0.0010	<0.0010	<0.0020		
Analgesics						
Acetaminophen	<0.0020	<0.0020	<0.0020	<0.0020		
Ibuprofen	0.0030	0.0022	<0.0020	<0.0020	0.0018	0.001
Antiepileptics						
Carbamazepine	<0.0010	<0.0010	<0.0010	<0.0010		
Miscellaneous						
Caffeine	<0.040	<0.040	<0.040	<0.040		
Cotinine	<0.040	<0.040	<0.040	<0.040		
1,4 Dioxane	<1	<1	<1.000	<1.000		
Steroids and Hormones						
Testosterone	<0.200	<0.200	<0.200	<0.200		
Equilenin	<0.050	<0.050	<0.050	<0.050		
*Estriol	<0.200	<0.200	<0.200	<0.200		
*Ergosterol	<1.000	<1.000	<1.000	<1.000		
Stigmasterol	0.160	0.160	<0.100	<0.100	0.105	0.035
Sitosterol	1.400	1.500	0.250	<0.100	0.800	0.740
Stigmastanol	<0.200	<0.200	<0.200	<0.200		
Progesterone	<0.200	<0.200	<0.200	<0.200		
Coprostanol	<0.100	<0.100	<0.100	<0.100		
Cholesterol	0.330	0.560	1.500	0.170	0.640	0.595
Dihydrocholesterol	<0.100	<0.100	<0.100	<0.100		

*Data not used in calculations due to poor recoveries

The February and April analysis of Ibuprofen in the source water intake detected concentrations of 0.0071 µg/l and below detection limit, respectively. The February and April analysis of ibuprofen in the drinking water detected concentrations of 0.0030 µg/l and 0.0022 µg/l (near detection limit of 0.0020 µg/l), respectively. One possible reason for Ibuprofen being detected in the April drinking water sample and not the source water sample is the lag time for water to be processed within the plant, which can vary from hours to a full day. This lag time was not accounted for during the sampling protocol. Other possible reasons include PPCP/EDC concentrations in raw groundwater or minimal effect of the water treatment process on removing Ibuprofen.

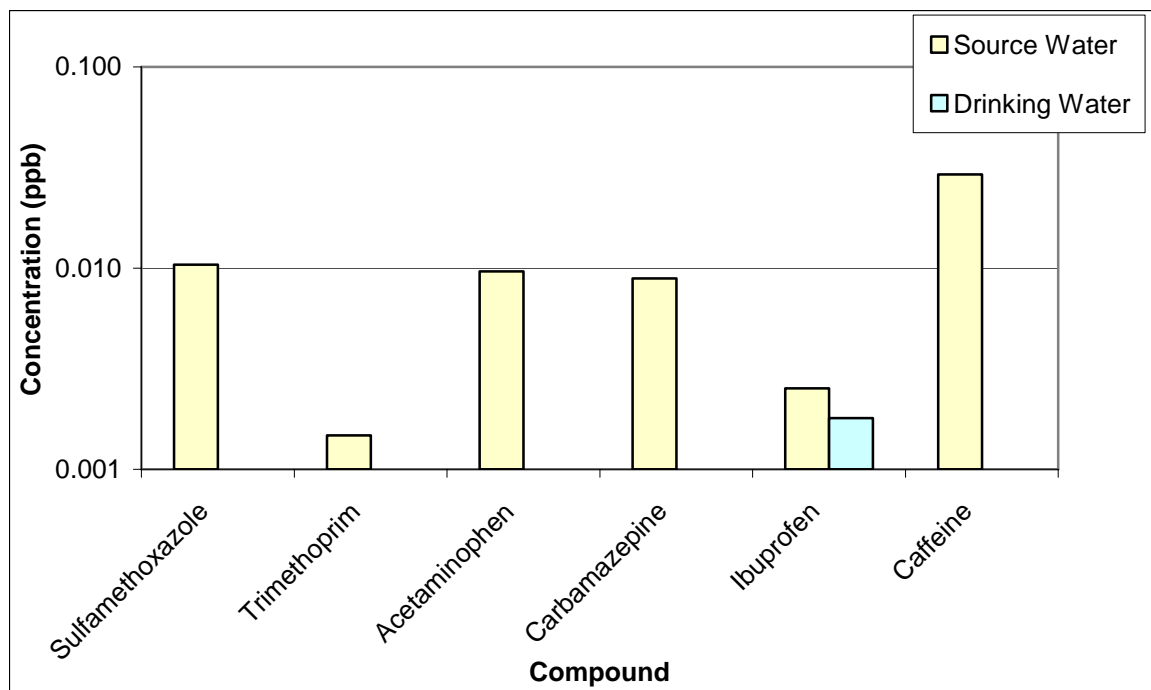


Figure 8. Source Water and Finished Water Mean Concentrations of Detected PPCPs.

It is noted that cholesterol was detected in all four trip and laboratory method blanks. Sitosterol was also detected in the first two sampling event trip blanks and the first and third sampling event's laboratory method blanks. These detections may be the result of low-level contamination of the high purity water used for sample preparation in the laboratory, or possible contamination from the environment and handling. The Ann Arbor Water Treatment Plant provided high purity water for filling trip/field blanks. The University of Iowa provided high purity water for laboratory method blanks. Additional testing to isolate potential sources of the Cholesterol and Sitosterol was not completed as part of this study.

The sterols detected in the drinking water are all naturally occurring compounds (Figure 9). Sitosterol and Stigmasterol are often found in wood pulp. Cholesterol and Dihydrocholesterol are found in both plants and animals.

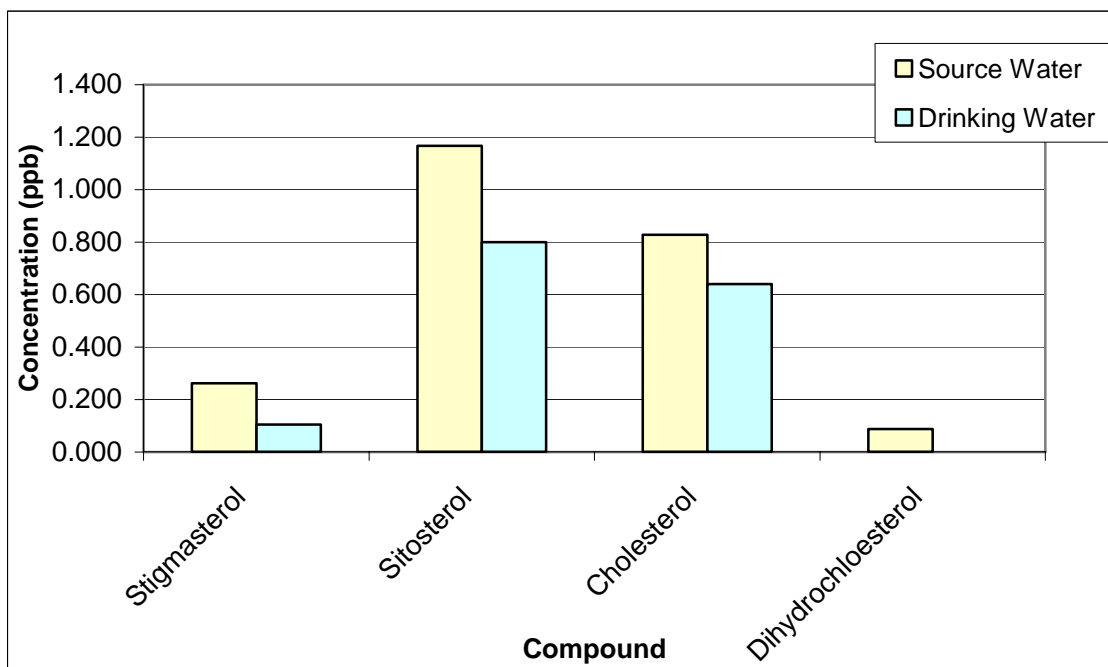


Figure 9. Source Water and Finished Water Mean Concentrations of Detected Steroids

Water Treatment Compound Reduction

Comprehensive, continuous time averaged sampling was beyond the scope of this study. Subsequently, the characterization of compounds removed during the water treatment process was based on comparison of grab samples collected from the source water and the finished drinking water during each of the four sampling events. Compound loadings and subsequently observed removal efficiency will vary based on a number of factors including the time length of a particular loading event and the time required for the treatment plant to fully process the finished drinking water.

Collected data indicates that while detected in source water, sulfamethoxazole, trimethoprim, acetaminophen, carbamazepine, caffeine, and dihydrocholesterol were not detected in the finished drinking water (Figure 8 and 9). The majority of the compounds detected in the source water were not detected in the finished drinking water. Detected concentrations of Ibuprofen, stigmasterol, sitosterol, and cholesterol in the finished water were 29%, 50%, 30%, and 23%, respectively, less than concentrations detected in source water (Figure 10).

Ann Arbor's water treatment process appears to be effective at reducing concentrations in a high percentage of compounds detected in the source water. The removal of the compounds in the water system cannot be correlated to a particular treatment process since individual components of the process were not analyzed. Instead, the removal rates reflect the change of detected compounds in both source water and finished water.

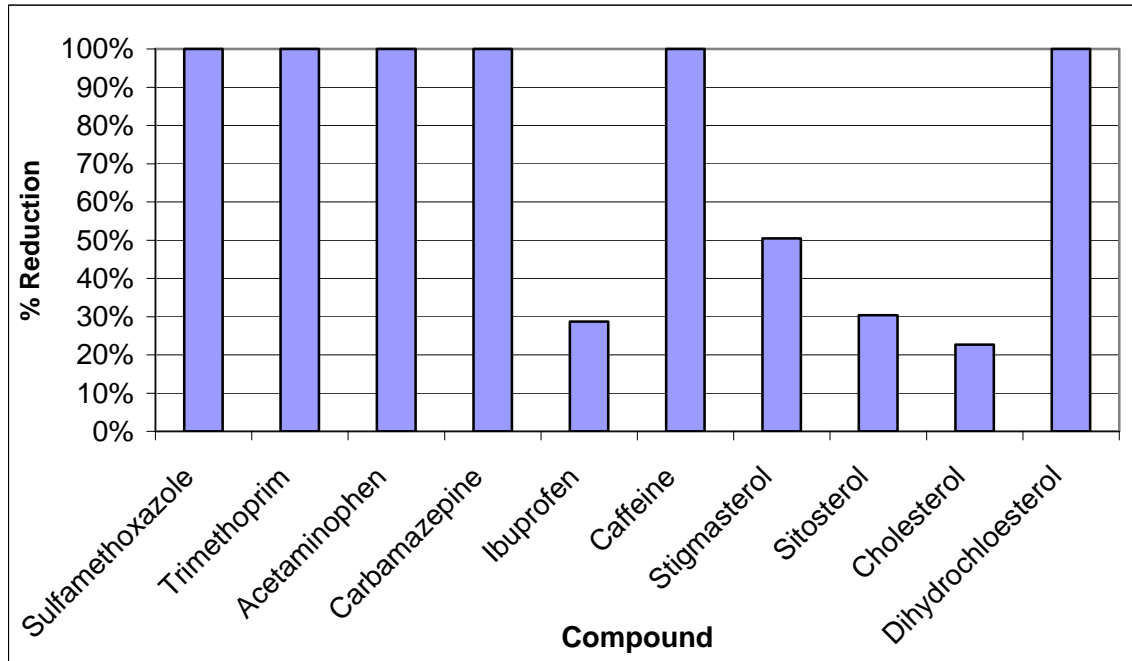


Figure 10. Water Treatment Reduction of Detected Compounds

Occurrence in Wastewater Influent

Laboratory analysis reported that 17 of the 22 target compounds were detected in the wastewater influent (Table 4).

12 of the 17 detected compounds were detected in all 4 sampling events. Sulfadimethoxine was detected during only one (August) sampling event. In August, 1,4 dioxane analysis was not performed for either the wastewater influent or effluent samples.

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Table 4. Analyte Concentrations Detected in Raw Wastewater Influent (ug/l)

Analyte	February	April	June	August	Mean Concentration µg/l	Standard Deviation µg/l
Antibiotics						
Sulfadimethoxine	<0.0010	<0.0010	<0.0010	0.0038	0.0013	0.002
Sulfamethazine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethoxazole	1.2	0.46	0.23	0.87	0.69	0.431
Sulfathiazole	<0.0010	<0.0010	<0.0010	<0.0010		
Lincomycin	0.0063	0.0032	0.002	0.001	0.003	0.002
Tylosin	0.0019	0.0062	<0.0010	<0.0010	0.0023	0.003
Trimethoprim	0.71	0.300	0.24	0.32	0.39	0.214
Analgesics						
Acetaminophen	84	60.	71	<0.0020	53	37.151
Ibuprofen	6.6	9.9	23	7.2	11	7.685
Antiepileptics						
Carbamazepine	0.21	0.23	0.091	0.25	0.19	0.071
Miscellaneous						
Caffeine	30.000	6.000	39.000	40.000	28.750	15.819
Cotinine	<2.000	0.250	<1.600	2.100	1.038	0.776
1,4 Dioxane	3	2	3	NA	3	0.577
Steroids and Hormones						
Testosterone	<2.000	<0.200	<0.200	<0.800		
Equilenin	<0.500	<0.050	<0.050	<0.200		
*Estriol	<2.000	<0.200	<0.200	<0.800		
*Ergosterol	<10.000	<1.000	<5.000	<4.000		
Stigmasterol	35.000	9.500	75.000	29.000	37.125	27.497
Sitosterol	200.000	66.000	480.000	220.000	241.500	173.077
Stigmastanol	28.000	7.700	13.000	33.000	20.425	12.008
Progesterone	<2.000	<0.200	<0.200	<0.800		
Coprostanol	460.000	190.000	1500.000	580.000	682.500	568.880
Cholesterol	360.000	160.000	1200.000	520.000	560.000	451.368
Dihydrocholesterol	70.000	20.000	130.000	50.000	67.500	46.458

NA. Compound not analyzed.

*Data not used in calculations due to poor recoveries

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Occurrence in Wastewater Effluent

Laboratory analysis reported that 15 of the 22 target compounds were detected in the treated wastewater effluent (Table 5/ Figure 11 & 12).

Each of the samples detected was reported in at least 2 sampling events. The April sampling reported 15 analytes and the August sampling reported 11 analytes. Acetaminophen was not detected in all but the August sample and 1,4 Dioxane was not sampled for in August.

Table 5. Analyte Concentrations Detected in Treated Wastewater Effluent (ug/l)

Analyte	February	April	June	August	Mean Concentration µg/l	Standard Deviation µg/l
Antibiotics						
Sulfadimethoxine	0.0010	<0.0010	<0.0010	0.0010		
Sulfamethazine	<0.0010	<0.0010	<0.0010	<0.0010		
Sulfamethoxazole	0.86	0.35	0.42	0.60	0.56	0.228
Sulfathiazole	<0.0010	<0.0010	<0.0010	<0.0010		
Lincomycin	0.0089	0.0044	0.0016	0.0015	0.004	0.003
Tylosin	<0.0010	0.0010	0.0023	<0.0010	0.001	0.001
Trimethoprim	0.61	0.44	0.16	0.22	0.36	0.207
Analgesics						
Acetaminophen	0.0051	0.0042	0.0024	<0.0020	0.003	0.002
Ibuprofen	0.020	0.051	0.039	0.011	0.030	0.018
Antiepileptics						
Carbamazepine	0.35	0.34	0.21	0.36	0.32	0.070
Miscellaneous						
Caffeine	0.310	0.120	0.043	0.110	0.146	0.115
Cotinine	<0.200	<0.040	<0.040	<0.040		
1,4 Dioxane	3	1	3	NA	2	1.155
Steroids and Hormones						
Testosterone	<0.200	<0.200	<0.200	<0.200		
Equilenin	<0.050	<0.050	<0.050	<0.050		
Estriol	<0.200	<0.200	<0.200	<0.200		
Ergosterol	<1.000	<1.000	<1.000	<1.000		
Stigmasterol	1.300	9.000	0.470	0.580	2.838	4.125
Sitosterol	4.700	16.000	0.940	1.000	5.660	7.114
Stigmastanol	0.270	0.950	<0.200	<0.200	0.355	0.405
Progesterone	<0.200	<0.200	<0.200	<0.200		
Coprostanol	3.000	6.200	1.400	1.900	3.125	2.156
Cholesterol	3.200	39.000	2.700	3.000	11.975	18.018
Dihydrocholesterol	1.400	6.900	0.600	0.610	2.378	3.038

*Data not used in calculations due to poor recoveries
NA. Compound not analyzed.

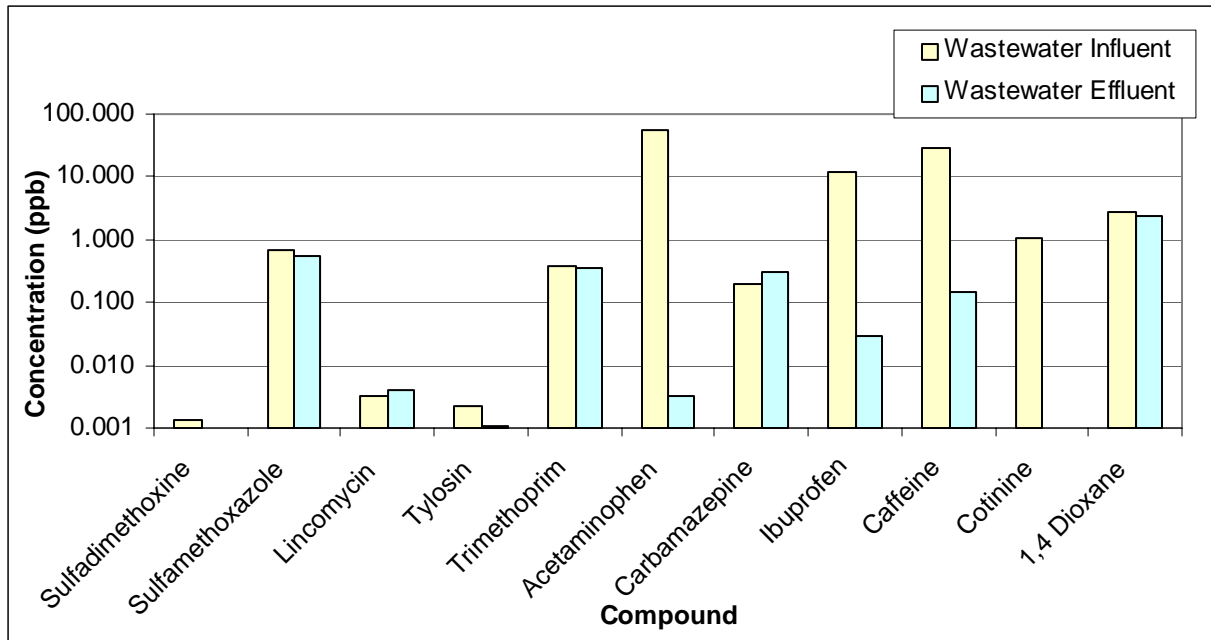


Figure 11. Wastewater Influent and Effluent Mean Concentrations of Detected PPCPs.

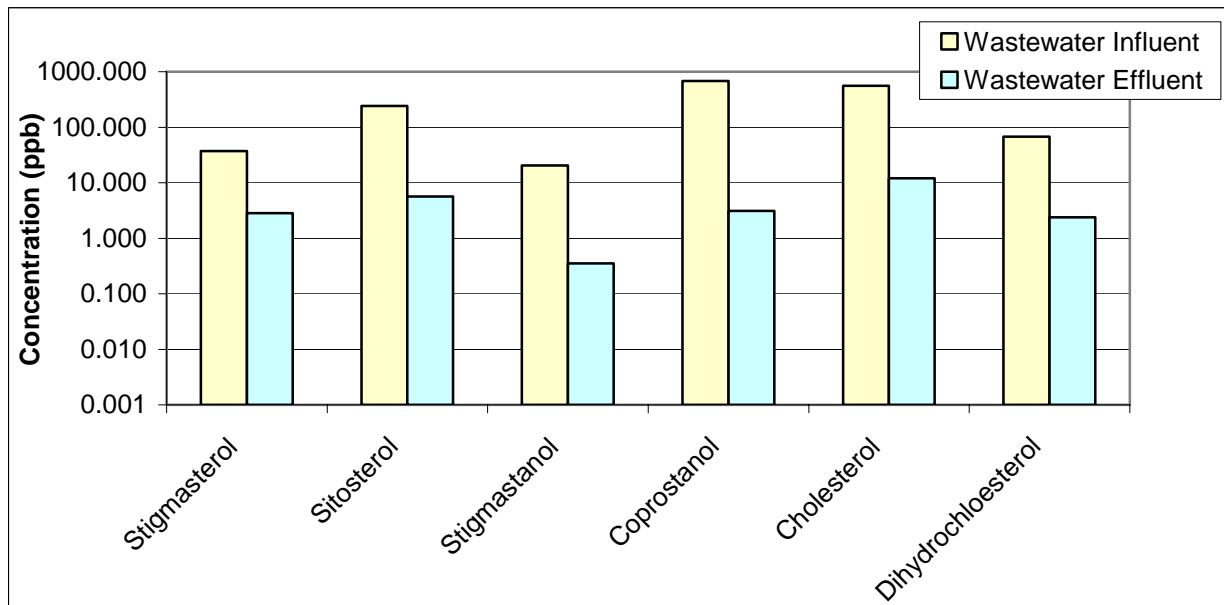


Figure 12. Wastewater Influent and Effluent Mean Concentrations of Detected Hormones and Steroids.

Wastewater Treatment Compound Reduction

As with the water treatment process the characterization of compounds removed during the wastewater process was based on comparison of grab samples collected from the influent and effluent during each of the four sampling events. Compound loadings and subsequently observed removal efficiency will vary based on a number of factors including the time length of a particular loading event and the time required for the treatment plant to fully process the influent.

The wastewater removal rates of the target compound list through the wastewater treatment process ranged from 0% to greater than 99% (Figure 13). The majority of the analytes detected in the influent showed a 90% or greater removal rate. Only trimethoprim, lincomycin, carbamazepine, tylosin, sulfamethoxazole, and 1,4 dioxane showed removal rates below 90%.

11 of the 12 compounds detected in each of the wastewater influent samples were also detected in each wastewater effluent samples.

Ann Arbor's wastewater treatment process appears to be effective at reducing concentrations in a high percentage of compounds detected in the influent. As in the water system the removal of the compounds in the wastewater system cannot be correlated to a particular treatment process since individual components of the process were not analyzed. Instead, the removal rates reflect the change in detected compounds between influent and effluent samples.

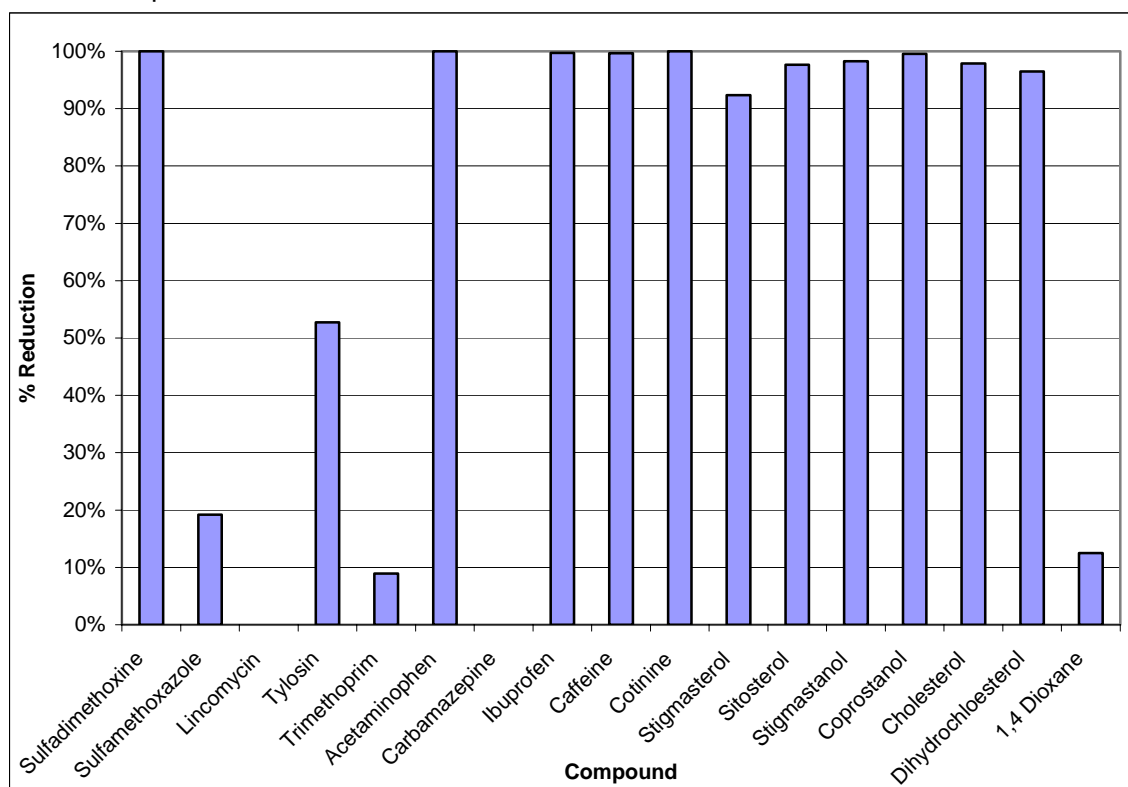


Figure 13. Wastewater Reduction of Detected Compounds.

Conclusion

Analysis of samples collected before and after the water treatment processes indicated a reduction from 10 to 4 target compounds. Additionally, detected concentrations of the 4 remaining compounds were reduced by a minimum of 23%.

The compounds sulfamethoxazole, trimethoprim, acetaminophen, carbamazepine, caffeine, and dihydrocholesterol, were detected in source water samples, they were not detected in samples collected after the water treatment process. The majority of the compounds detected in the source water were not detected in the finished drinking water. Data indicated removal rates of less than 50% for Ibuprofen, stigmasterol, sitosterol, and cholesterol in the water treatment process.

Analysis of samples collected before and after the wastewater treatment processes indicated a reduction from 17 to 15 target compounds. Detected concentrations of the 10 of the 15 remaining compounds were reduced by at least 90%. Data indicated no reduction of Carbamazepine or Lincomycin concentrations in samples collected before and after wastewater treatment process.

Data indicated removal rates of less than 50% for Trimethoprim, lincomycin, carbamazepine, tylosin, sulfamethoxazole, and 1,4 dioxane.

Compounds detected during any of the four sampling events are summarized in Table 6. Compounds detected in each of the four sampling events are summarized in Table 7.

Table 6. Compounds Detected

Monitoring Location	Compounds Detected During the 4 Sampling Events	Percent of 22 Compounds Detected During the 4 Sampling Events
Source Water	10	45.5%
Treated Water	4	18.2%
Wastewater Influent	17	77.3%
Wastewater Effluent	15	68.2%

Table 7. Compounds Detected in All Four Sampling Events

Monitoring Location	Compounds Detected in all 4 Sampling Events	Percent of 22 Compounds Detected in all 4 Sampling Events
Source Water	5	22.7%
Treated Water	1	4.5%
Wastewater Influent	11	50%
Wastewater Effluent	11	50%

Sample concentration standard deviation was calculated for each of the four sampling locations. Concentrations detected at the wastewater influent reported the greatest standard deviation relative to mean concentrations.

The detection of certain PPCP and EDC compounds in various locations of the Ann Arbor water use cycle are an indication of the resilience of these compounds in the environment. Overall, data indicated Ann Arbor's water treatment plant reduced detected concentrations of the target compounds that were identified in samples of source water from the Huron River. Similarly, data indicated Ann Arbor's wastewater treatment plant reduced detected concentrations of the target compounds that were identified in samples of the City's wastewater influent.

The selected list of 22 target compounds represents a small subset of the PPCP/EDC related compounds currently being used in the United States. Although the selected target compound list for this study is small, other PPCP/EDC compounds are likely present in surface waters in both Michigan and the United States.

This work has identified other areas of additional research needs, including:

- Characterization of upstream and downstream surface water quality of large and small municipal wastewater systems
- Characterization of PPCP/EDCs in surface water sediment
- Characterization of PPCP/EDC removal efficiencies for various source water types and treatment systems
- Development of PPCP/EDC concentration trends based on season, source water type, etc.
- Human and Environmental impact of widely detected PPCP/EDCs

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LITERATURE REVIEWED AND REFERENCED

Dana W. Kolpin, Edward T. Furlong, Michael T. Meyer, E. Michael Thurman, Steven D. Zaugg, Larry B. Barber, Herbert T. Buxton, Environmental Science & Technology, *Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance*, Vol. 36, No. 6, 2002, pages 1202-1211

Christian G. Daughton and Thomas A. Ternes, Environmental Sciences Division, U.S. Environmental Protection Agency, *Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change?* Environmental Health Perspectives Volume 107, Supplement 6, December 1999, pages 1-56

Thomas A. Ternes, Water Res., 1998 Elsevier Science Ltd., *Occurrence of Drugs in German Sewage Treatment Plants and Rivers*, Vol. 32, No. 11, 1998, pages 3245-3260

Shane A. Snyder, Paul Westerhoff, Yeomin Yoon, and David L. Sedlak, Environmental Engineering Science, *Pharmaceuticals, Personal Care Products, and Endocrine Disruptors in Water: Implications for the Water Industry*, Volume 20, Number 5, 2003, pages 449-469

Glen R. Boyd, Helge Reemtsma, Deborah A. Grimm, Siddhartha Mitra, The Science of the Total Environment 311, *Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario, Canada*, 2003 Elsevier Science B.V., pages 135-149

A. Jos, G. Repetto, J.C. Rios, M.J. Hazen, M.L. Molero, A. del Peso, M. Salguero, P. Fernandez-Freire, J.M. Perez-Martin, A. Camean, *Toxicology in Vitro* 17, *Ecotoxicological evaluation of carbamazepine using six different model systems with eighteen endpoints*, 2003, pages 525-532

Jorg E. Drewes, Thomas Heberer, Tanja Rauch, and Kirsten Reddersen, *Ground Water Monitoring & Remediation* 23, *Fate of Pharmaceuticals During Ground Water Discharge*, No. 3/Summer 2003/ pages 64-72

Dr. Shane Snyder, Southern Nevada Water Authority, *Endocrine Disruptors and Pharmaceutically Active Compounds: U.S. Regulations and Research*, pages 1-10

Guang-Gui Ying, Rai Kookana and TD Waite, Australian Water Association, *Australian Water Conservation and Reuse Research Program*, January 2004, pages 1-35

Shane Snyder, Paul Westerhoff, Rengo Song, Bruno Levine, Bruce Long, AWWARF Project #2758, *Evaluation of Conventional and Advanced Treatment Processes to Remove Endocrine Disruptors and Pharmaceutically Active Compounds*, pages 1-28

Christian G. Daughton, *Environmental Health Perspectives*, Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition While Promoting Human Health, Volume 111, Number 5, May 2003, pages 757-785

A.I. Schafer and T.D. Waite, Centre for Water and Waste Technology, Civil & Environmental Engineering, The University of New South Wales, Sydney, Australia, *Removal of Endocrine Disruptors in Advance Treatment – The Australian Approach*, pages 37-51

Kuniko Mitamura and Kazutake Shimada, *Chromatography, Derivatization in Liquid Chromatography/Mass Spectrometric Analysis of Neurosteroids, Vol. 22, No. 1 (2001)*

TNO Nutrition and Food Research, *Polymer Analysis, 2001/01/29/voe194e*

Watershed Management Initiative, *Endocrine Disrupting Compounds and Potential Impact on Water Use in the Santa Clara Valley Watershed, Information Sheet, February 2003*

The American Council on Science and Health, *Endocrine Disrupters: A Scientific Perspective, July 1999*

U.S. Environmental Protection Agency, *National Exposure Research Laboratory Environmental Sciences, pages 1-26*

Bryan W. Brooks, Christy M. Foran, Sean M. Richards, James Weston, Philip K. Turner, Jacob J. Stanley, Keith R. Solomon, Marc Slattery, Thomas W. La Point, 2003 Elsevier Science Ireland Ltd, *Toxicology Letters 142 (2003), Aquatic ecotoxicology of fluoxetine, pages 169-183*

Christy M. Foran, James Weston, Marc Slattery, Bryan W. Brooks, and Duane B. Huggett, *Archives of Environmental Contamination and Toxicology, Reproductive Assessment of Japanese Medaka (Oryzias latipes) Following a Four Week Fluoxetine (SSRI) Exposure, 2004, pages 1-26*

Brooks BW, Foran CM, Weston J. Peterson BN, La Point TW and DB Huggett, *Environmental Contamination and Technology (2003), Linkages Between Population Demographics and Municipal Effluent Estrogenicity, 71: 504-511*

Mitch Mitchell, Baylor University, News & Events, *Something Fishy, pages 1-2*

Noreen Parks, Baylor University, News & Events, *Fish on Prozac, page 1*

Judy Long, Baylor University, News & Events, *Baylor Toxicologist Identifies Pharmaceutical Contaminants In Texas Waters, Fish, pages 1-2*

Dr. Bryan Brooks, Department of Environmental Studies, *Municipal effluent estrogenicity in the Guadalajara and Lake Chapala region of Mexico*

Duane B. Huggett, Christy M. Foran, Bryan W. Brooks, Jim Weston, Bethany Peterson, K. Erica Marsha, Thomas W. La Point, and Daniel Schlenk, *Toxicological Sciences 72, Comparison of in Vitro and in Vivo Bioassays for Estrogenicity in Effluent from North American Municipal Wastewater Facilities, 2003, pages 77-83*

D.B. Huggett, I.A. Khan, C.M. Foran, D. Schlenk, *Environmental Pollution, Article in Press, Determination of beta-adrenergic receptor blocking pharmaceuticals in United States wastewater effluent, January 2002, Version 7.51e, pages 1-7*

Christian G. Daughton, Ph.D., *J. Am. Soc. Mass Spectrom: "Account and Perspective", "Emerging" Pollutants, and Communicating the Science of Environmental Chemistry and Mass Spectrometry, 2001, 12(10), 1067-1076, pages 1-15*

**The Occurrence and Fate of Pharmaceuticals, Personal Care Products and Endocrine Disrupting Compounds in a Municipal Water Use Cycle:
A Case Study in the City of Ann Arbor
November 2004**

Audra Morse, Ph.D., Andrew Jackson, Ph.D., P.E., *Fate of a representative pharmaceutical in the environment*, May, 2003, pages 1-41

Environmental Engineering Science, Mary Ann Liebert, Inc., *Emerging Contaminants in Water*, Volume 20, Number 4, 2003, pages 387-388

C.G. Daughton, U.S. Environmental Protection Agency, National Exposure Research Laboratory Environmental Sciences, *PPCPs as Environmental Pollutants*, June 2002; updated July 2002, pages 1-6

Christian G. Daughton, Ph.D., Chief, Environmental Chemistry Branch, Environmental Sciences Division, National Exposure Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, *Non-Regulated Contaminants: Emerging Research, Existing and Future Pollutants in Water Supplies, Old Pollutants, New Concerns – New Pollutants, Unknown Issues*, October 16, 2003, pages 1-10