Pharmaceutical Project Report

A SURVEY OF THE NEW YORK CITY WATERSHED FOR THE PRESENCE OF PHARMACEUTICALS

Lloyd Wilson[1], Patrick Palmer[1], Patrick O'Keefe[2], Thomas King[2], Robert Briggs[2], and Robert Sheridan[2]

[1]Bureau of Water Supply Protection, Center for Environmental Health, New York State Department of Health, Troy, NY 12180
[2]Biggs Laboratory, Wadsworth Center, New York State Department of Health, Albany, NY 12201

June 13, 2006

Table of Contents

List of Figures

List of Tables

Executive Summary

In response to a commitment made when the New York City Watershed Agreement was signed, the New York State Department of Health (NYS DOH) conducted a survey to determine if pharmaceuticals were present in any of the reservoirs of the New York City Watershed. The survey addressed concerns raised in recent scientific literature about the potential for contamination of surface waters with pharmaceuticals. This issue is not unique to New York; it has been studied in other waters of North America (Seiler et al., 1999; Kolpin et al., 2002; Stackelberg et al., 2004), South America (Stumpf et al., 1999), and Europe (Ternes, 1998; Buser et al., 1999; McArdell et al., 2003). The U.S. Environmental Protection Agency (EPA) and the State of New York funded the NYS DOH survey.

In four seasonal sampling events (summer, fall, winter, and spring) between August 2003 and May 2004, 368 samples and 56 field blanks were collected in the New York City Watershed. The samples were comprised of surface water from 8 main sites covering the 3 water supply systems and treated effluent from 4 wastewater treatment plants (WWTPs). Eleven pharmaceuticals were targeted for analysis. The analysis focused on pharmaceuticals that may be found in surface waters at detectable levels, considering available scientific data, prescription and sales information, prescribed daily dose, and estimated environmental fate. We selected the following eleven compounds: amoxicillin, atenolol, caffeine, cephalexin, estrone, 17α-ethinylestradiol, 17β-estradiol, ibuprofen, sulfamethoxazole, trimethoprim, and valproic acid. Carbamazepine was later added, following its detection in some pilot study samples (June 2003). Detection limits ranged from 4 – 502 nanograms per liter (ng/L, equivalent to part per trillion, ppt).

Pharmaceuticals were consistently detected in the effluent of the four-wastewater treatment plants and in a small number of surface water samples of the New York City Watershed. The WWTPs differed in the type and concentration of analytes in the effluent. Although two of the eleven analytes were detected in a small number of the surface water samples, the measured concentrations were well below those that may be expected to have any effect on human health.

Six of the analytes (amoxicillin, cephalexin, 17α-ethinylestradiol, 17β-estradiol, sulfamethoxazole, and valproic acid) were not detected in any sample, while estrone was detected only once. The remaining analytes were detected in most of the WWTP samples, and several reservoir samples. In the WWTPs, atenolol was found most frequently above the detection limit (94%), followed by trimethoprim (83%), carbamazepine (71%), ibuprofen (61%) and caffeine (49%). In fact, carbamazepine was present but less than the detection limit in the remaining 29% of WWTP samples. In the reservoir samples, ibuprofen and caffeine were found above the detection limit in 2.5% and 2.9% of the 240 reservoir samples, respectively.

All of the samples from the wastewater treatment plants (WWTP) contained at least one analyte. Differences in the effluent were found to exist between the four plants. In addition to the pharmaceutical analysis, a subset of the effluent samples during the Pilot Study phase of the project were analyzed for volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs) using EPA Methods 502.2 and 625. Only a few VOCs (acetone, MTBE, chloroform) were detected. Using Method 625, only one target analyte was detected in the WWTP effluent samples, and a number

of non-target SVOCs were tentatively identified. Some of these tentatively identified compounds included: acetaminophen, camphor (decongestant/analgesic), carbamazepine (anticonvulsant), carisoprodol (muscle relaxant), cholesterol, clindomycin (antibacterial), DEET, galoxolide (fragrance), KP-140 (de-airing/antifoam agent), menthol, primidone (anticonvulsant), and valium (antianxiety). None of the listed compounds were detected in the surface water samples or the laboratory blanks.

1.0 Introduction

1.1 Statement of Issue

In response to a commitment made when the New York City Watershed Agreement was signed, the New York State Department of Health (NYS DOH) conducted a survey to determine if pharmaceuticals are present in the New York City source waters. This survey addresses concerns raised in recent scientific literature about the potential for pharmaceuticals to contaminate surface waters. This issue is not unique to New York; it has been studied in other waters of North America (Seiler et al., 1999; Kolpin et al., 2002; Stackelberg et al., 2004), South America (Stumpf et al., 1999), and Europe (Ternes, 1998; Buser et al., 1999; McArdell et al., 2003). However, the New York City Watershed is unique: it is the largest engineered surface water storage and supply source in the world. It serves about 1.2 billion gallons of water daily to approximately 8 million residents of NYC, and 1 million residents in four other southern New York counties (Orange, Putnam, Ulster, and Westchester). This represents almost half of New York State's population. In addition, there are 114 wastewater treatment plants that discharge treated effluent into the watershed. NYC does not filter their drinking water, but they do chlorinate for disinfecting, fluoridate, and add phosphoric acid and sodium hydroxide for corrosion and pH control. Therefore, it provides a good model to investigate whether pharmaceutical compounds are being discharged from treatment plants, if they are present at the reservoir keypoints, and if they are present in water prior to chlorination and distribution.

1.2 Brief review of pharmaceuticals use

Pharmaceutical use in the United States is tracked mainly by two measures (sales and units sold) and two categories (brand name and generic). Data of this type are compiled by a number of private industry groups, including the health care information company NDCHealth Corporation. Summaries of these data are available on their website (http://www.ndchealth.com) and others (www.drugtopics.com).

For 2004, the top brand name drug was Lipitor ($7.1 billion in sales and 69.8 million units) and the top generic drug was hydrocodone/acetaminophen ($1.0 billion and 93.7 million units). Almost 21 metric tons of Lipitor and 2800 metric tons (total) of hydrocodone/acetaminophen were purchased by consumers in the US. Table 2 describes the products sold with the top ten greatest numbers of prescriptions. Table 3 provides the same information except that it is specific to the chemicals investigated in our study.

Comparison of these tables shows that we selected chemicals in high use, including two of the top ten prescribed pharmaceutical products (atenolol and amoxicillin, with an estimated consumption of 66 and 414 metric tons, respectively).

Table 1. 2004 Top 10 Products by Total Prescription (Rx) Count[a]

Rank	Product	Type	Total Rx Count (in millions)	Total Rx Count % Change Prior Year	Avg Dosage[b] (mg/day)	Metric Tons purchased[c]
1	Hydrocodone w/APAP	Generic	92.7	8.2	10 & 1000	28 & 2781
2	Lipitor	Brand	69.8	6.5	10	21
3	Lisinopril	Generic	46.2	17.5	10	14
4	Atenolol[d]	Generic	44.2	2.9	50	66
5	Synthroid	Brand	44.1	-6.7	0.256	0.3
6	Amoxicillin[d]	Generic	41.4	10.5	1000	414
7	Hydrochlorothiazide	Generic	41.3	14.8	25	31
8	Zithromax	Brand	37.2	-6.0	250	47
9	Furosemide	Generic	36.5	3.2	20	22
10	Norvasc	Brand	34.7	4.2	10	10

[a]Modified from NDCHealth Corp. Reflects prescription data for retail, mail order, and institutional pharmacy channels. Information based on NDCHealth proprietary methodologies.
(http://www.ndchealth.com/press_center/uspharmaindustrydata/2004top10productsbytotalprescription.htm)
[b,c]Average doses and tons purchased were calculated using defined daily dose from www.rxlist.com and 30-day dosing period, except Amoxicillin and Zithromax (10- and 5-day dosing periods, respectively).
[d]Atenolol and amoxicillin were investigated in the NYSDOH survey.

Table 2. Total Prescription (Rx) Count[a] of the Study Analytes

Rank	Product	Type	Total Rx Count (in millions)	Total Rx Count % Change Prior Year	Avg Dosage[b] (mg/day)	Metric Tons purchased[c] (estimated)
1	Atenolol	Generic/Beta Blocker	44.2	2.9	50	66
2	Amoxicillin	Generic/antibiotic	41.4	10.5	1000	414
10	Cephalexin	Generic/antibiotic	23.7	-0.2	1000	237
14	Ibuprofen	Generic/pain relief	25.2	0.7	1600	565[f]
26[d]	Sulfamethoxazole	Generic/antibiotic	13.6	3.3	800	109
26[d]	Trimethoprim	Generic/antibiotic	13.6	3.3	160	22
86, 134	Sodium Valproate[e]	Brand/anti-epileptic	8.2	-4.0	1000	246
125	Carbamazepine	Generic/anticonvulsant	2.7	-4.1	400	32.4
var.	17α-Ethinylestradiol	Generic/steroid	41.6[g]	various	various	0.04

[a]*Modified* from NDCHealth Corp. Information based on NDCHealth proprietary methodologies. Reflects prescription data for retail, mail order, and institutional pharmacy channels. Available at: www.drugtopics.com and http://www.ndchealth.com/press_center/uspharmaindustrydata/2004top10productsbytotalprescription.htm.
[b,c]Average doses and tons purchased were calculated using information from www.rxlist.com and www.pdrhealth.com assuming one antibiotic prescription covers a 10-day dosing period; one ibuprofen prescription covers 14 days; one 17α-ethinylestradiol covers a 28-days, other drugs assume one prescription covers a 30-day dosing period.
[d]Sulfamethoxazole and Trimethoprim are generally prescribed in combination. The count given is for the combined prescriptions.
[e]Prescriptions listed are combined for sodium valproate (Depakote, 5.0 million, -14.5%; Depakote ER, 3.2 million, 15.3%).
[e]Ibuprofen metric tons purchased does not include over-the-counter sales.
[g]17α-ethinylestradiol prescriptions are combined for 13 generic labels. Metric Tons Purchased considered 0.035mg as DDD.
Caffeine was not included, as it is not a prescribed drug. The natural hormones Estrone and 17β-Estradiol are not generally prescribed (aside from perhaps in hormone replacement therapy) and as such, no prescription information could be located.

It is expected that as the population of the United States continues to age, pharmaceutical use will continue to grow. Indeed, U.S. spending for prescription drugs is projected to increase by 10.1 percent through 2011 (Heffler et al, 2005). According to the National Association of Chain Drug Stores,

Americans filled over 3.2 billion prescriptions in 2003, an increase of over 1 billion since 1995 (NACDS, 2005). These figures do not include the much larger over-the-counter (OTC) drug market. OTC drugs are those which can be purchased without a prescription: such as aspirin, Claritin (loratidine), ibuprofen, pseudoephedrine, and Prilosec (omeprazole), among others. Clearly, with the aging of the population and continually increasing pharmaceutical sales, increases in the amount of pharmaceuticals entering the waste stream are probable for the foreseeable future.

1.3 Brief review of pharmaceuticals in environment

As shown in the examples above, pharmaceuticals are used in many tons per year. Applied doses of pharmaceuticals are either excreted from the body unchanged, conjugated, or metabolized. These excreted forms enter the waste stream, which in many cases end up at WWTPs. Depending on the removal efficiency of the treatment technique(s) used at a particular plant for a particular drug, measurable concentrations can be found in the effluent, and potentially in the water body receiving the effluent. The potential for a properly used drug to enter the environment depends on factors including but not limited to like the amount consumed, absorption and metabolism in the body, and the rates of chemical, microbial, and/or photo degradation of the compounds in the environment (Metcalfe et al, 2003).

Findings of pharmaceuticals in the environment date back to the early 1970s, including the discovery of clofibric acid (a blood lipid regulator) in the effluent of a Kansas City, Missouri sewage treatment plant (Hignite and Azarnoff, 1977). Despite this, it was not until the 1990s that researchers in the US and Europe began to actively investigate these compounds. Some of the first prominent pharmaceutical detections were found by German and Swiss researchers looking into pesticide contamination of European surface water bodies (Heberer and Stan, 1997; Buser et al., 1998). Their work turned up clofibric acid, as did the work of another German researcher who was specifically looking for pharmaceutical compounds (Ternes, 1998). That same year, Halling-Sørenson et al. (1998) published a comprehensive review of the research to date on the environmental occurrence and fate of these compounds. The topic found its way into more mainstream media following an article in *Science News* (Raloff, 1998) which described the findings of the German and Swiss researchers.

More recently, the United States Geological Survey (USGS) published data on the occurrence of pharmaceuticals and other compounds in streams across the U.S. (Kolpin et al, 2002). However, at the time of our study design and implementation, no researchers in the US had investigated the presence of pharmaceuticals in surface water sources used for drinking water, and that remained the case until the USGS published additional work in mid-2004.

To date, pharmaceuticals have been found in wastewater treatment plant effluents, surface water, ground water, and drinking water. Representatives of most drug classes have been documented, including analgesics, antibiotics, antiepileptics, antihypertensives, antiseptics, beta-blocker heart drugs, contraceptives, hormones, lipid-lowering drugs, psychotherapeutics, and x-ray contrast media. Laboratories are continually updating and developing analytical methods to find a larger group of analytes and at lower concentrations. Detection limits for most compounds are now measured in the low-nanogram per liter (ng/L) range, or parts per trillion (ppt).

2.0 Study Background

2.1 Description of NYC Watershed

The NYC Watershed is made up of three water supply systems: Croton, Delaware, and Catskill (Figure 1). The watersheds of the three systems cover an area of almost 2,000 square miles, approximately the size of the State of Delaware. The reservoirs have a combined storage capacity of 550 billion gallons. The water flows to New York City through aqueducts. The Croton system has 12 reservoirs and 3 controlled lakes. These water bodies are located in Dutchess, Putnam, and Westchester Counties. The largest of these is the New Croton Reservoir, which has a capacity of 19 billion gallons. The Croton system normally supplies 10 percent of the NYC's drinking water. The Catskill system includes two reservoirs (Schoharie and Ashokan) and supplies up to 40 percent of the City's daily needs. This watershed is located in parts of Greene, Schoharie, and Ulster Counties. Southwest of the Catskill watershed is the Delaware system, located in parts of Delaware, Sullivan, and Ulster Counties. The Delaware system includes four reservoirs: Cannonsville, Pepacton, Neversink, and Rondout, with capacities of 95.7, 140, 34.9, and 49.6 billion gallons, respectively. These provide 50 percent of the NYC's daily water needs. Water from both the Catskill and Delaware systems usually passes through the Kensico Reservoir, in Westchester County. The Kensico Reservoir has a capacity of 30.6 billion gallons (http://www.ci.nyc.ny.us/html/dep/watershed/html/reservoirs.html).

2.2. Study Goals

The main study goal is to provide an initial evaluation as to whether pharmaceuticals are in the New York City Watershed and have the potential to enter the New York City Water Supply distribution system. To achieve this goal we collected samples from locations in each of the three water sources (Croton, Catskill, Delaware) and from the outlet of Kensico Reservoir, which is just prior to entry into the NYC distribution system. Another goal of the study included evaluating the input of pharmaceuticals into the watershed by sampling effluent from four different wastewater treatment plants (WWTP). The study also was designed to describe both seasonal or day of the week differences, and possibly, if there were significant concentrations found in the input to reservoirs, describing the outflow concentrations to evaluate the processing occurring in a reservoir.

2.3 Sample collection

At all sites, samples were collected for seven days in a row during each of the four seasons. Reservoir locations were sampled prior to WWTP effluent samples to minimize the potential for cross-contamination. On the first, third, fifth, and seventh days of each sampling event, a duplicate (consecutive) sample was collected. This duplicate sample was collected at least once at each location. We originally planned to collect this QA/QC sample by splitting the sampling stream, but we were unable to find a field-capable device that could accurately and feasibly split the sample without contamination or absorption of some target analytes. Therefore, the duplicate sample was collected immediately following the regular sample, and is referred to as a duplicate sample throughout this paper. All samples were analyzed at the NYS DOH Wadsworth Center laboratories.

2.4 Description of Sampling Locations

Table 3 lists the 12 primary sampling locations for the study. Six locations are on the east side of the Hudson River and six on the west side of the Hudson River. On each side of the Hudson two WWTP were also sampled, with the four remaining locations on each side being surface waters. At least one sample location from each of the three main sources of water (Catskill, Delaware, and Croton) was selected as well as the input and output of two main reservoirs, Kensico and Rondout.

Table 3. NYC Watershed Sampling Locations.

West of the Hudson River (WOH)	East of the Hudson River (EOH)
Neversink Aqueduct at the Central Hudson Gas & Electric Building *Backup location: Intake of the Neversink Aqueduct at the Neversink Reservoir Gate House	Shaft 18 of the Delaware Aqueduct (DEL18)
Outlet of the West Delaware Aqueduct at the Rondout Reservoir (WDA) *Backup location: Intake of the WDA at the Cannonsville Reservoir Gate House	Shaft 17 of the Delaware Aqueduct (DEL17)
Outlet of the East Delaware Aqueduct at the Rondout Reservoir (EDA) *Backup location: Intake of the EDA at the Pepacton Reservoir Gate House	Catskill Aqueduct Alum Plant (CATALUM) *Backup location: Catskill Lower Effluent Chamber
Intake of the Delaware Aqueduct at the Rondout Chamber	Croton Lake Gate House (CROGH)
Walton WWTP	Yorktown Heights WWTP
Margaretville WWTP	Carmel SD#2 WWTP

Note: The four substitute sampling sites were used when a main site was inaccessible or sample collection was not possible. The primary reason for use of substitute locations was when an aqueduct was not flowing (WOH sites) and building maintenance (EOH site). WOH aqueducts were shut down for periodic maintenance, to maintain water levels in the various reservoirs, or due to water quality concerns in the originating reservoir. During our study, the reservoir system operated near, at, and sometimes over its capacity. To minimize overflowing at the Rondout Reservoir, the East Delaware Aqueduct (EDA), West Delaware Aqueduct (WDA), and Neversink Aqueduct were all shut down during the course of the study. The WDA was also shut down during warmer periods due to water quality concerns in the Cannonsville Reservoir. During these periods, samples were collected at the originating reservoir. During normal operation, samples were collected at the EDA and WDA termination points at the Rondout Reservoir, and at the NYCDEP sampling location on the Neversink Aqueduct. Periodic maintenance activities at the Catskill Aqueduct's Alum Plant (CATALUM) forced us to collect these samples further down the aqueduct at the Lower Effluent Chamber (CATLEFF or LEC). On the days we sampled, there was no diversion of the Catskill Aqueduct into Kensico Reservoir, so the water that we collected at the LEC should have been representative of what would have been collected at CATALUM.

Alternate locations were needed when either access was not allowed due to construction or when certain aqueducts were taken off line to manage the water resource. We collected samples of water exiting the Cannonsville, Neversink, Pepacton, Rondout, New Croton, and Kensico Reservoirs, and water entering the Kensico Reservoir via the Delaware and Catskill Aqueducts. The water leaving the Kensico Reservoir at the DEL 18 location is just prior to the water heading into the City's distribution system. The effluents at four WWTPs were collected to give us information about possible sources of pharmaceuticals in the watershed. These plants were in Carmel (Putnam County), Yorktown Heights (Westchester County), Margaretville (Delaware County), and Walton (Delaware County). A map of the sampling locations is provided in Figure 1).

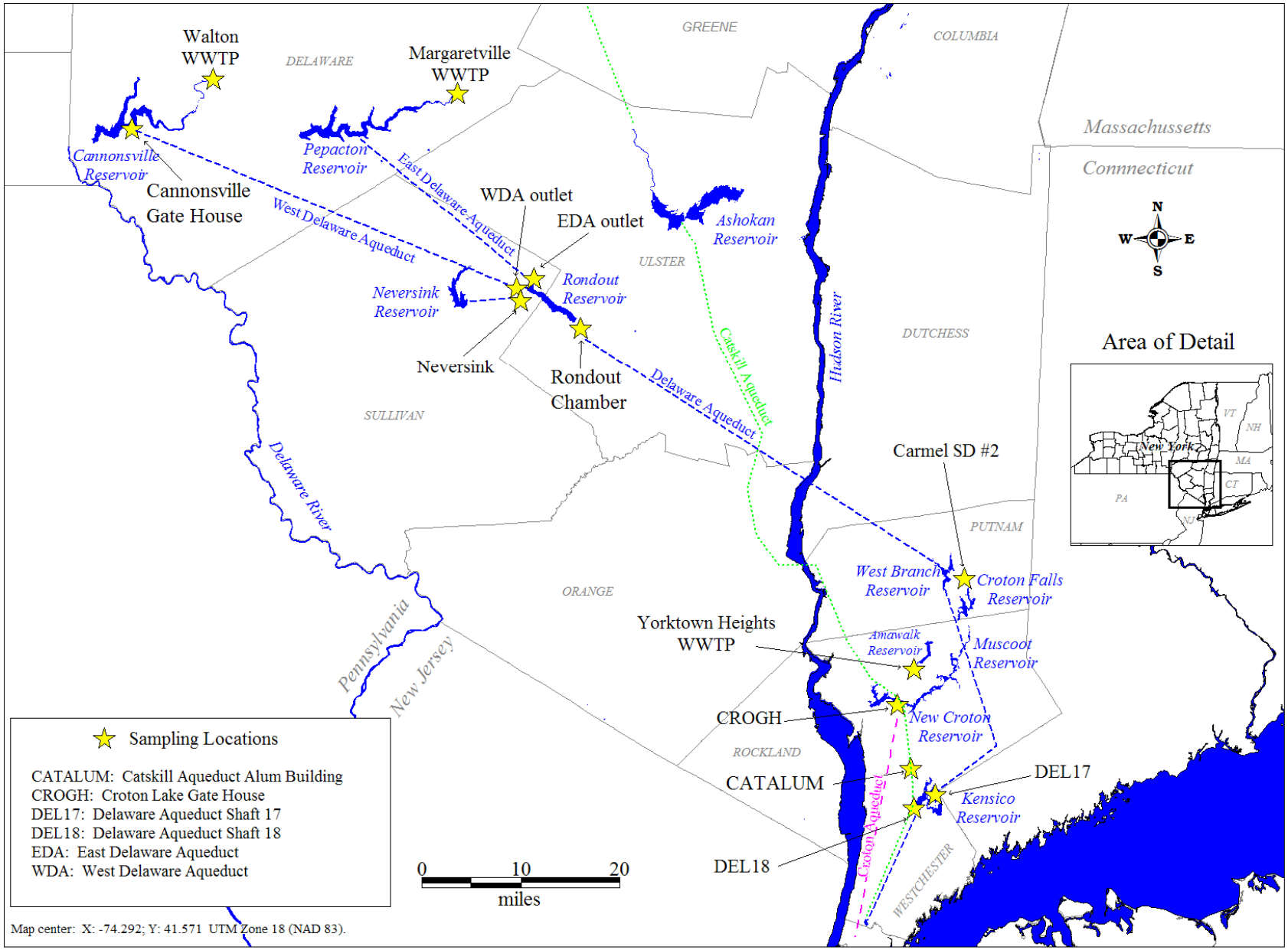


Figure 1. Map of WWTP and Reservoir Sampling Locations, August 2003 - May 2004.

2.5 Description of the Waste Water Treatment Plants

The four WWTPs in the study serve varied populations and utilize varied treatment techniques. The Carmel and Yorktown Heights plants are located in the Croton Watershed. Effluent from Carmel is discharged into a stream that flows into the Middle Branch Reservoir, while effluent from Yorktown Heights is discharged into waters that flow into the Muscoot Reservoir. The Margaretville and Walton plants are located in the Delaware Watershed. Effluent from these plants is discharged into waters that flow into the Pepacton and Cannonsville Reservoirs, respectively. Information on the plants' treatment techniques and populations served is in Table 4.

Table 4: Characteristics of WWTPs and the Populations Served[a].

	Carmel SD #2	**Yorktown Heights**	**Margaretville**	**Walton**
Year Built	1965	1961	1998	1978
Year Updated	1999	1973	-	2002
Operator	ST Environmental	Yorktown Heights (T)	NYCDEP	Walton (T)
Biotreatments Used	conventional activated sludge; step aeration activated sludge; SC	SC[b]; trickling filter	rotating biological contactor; SC	extended aeration
Filters	FSR[c]	intermittent sand filters; FSR	microfiltration – membrane; FSR	microfiltration-CBUDS[d]
Additional Treatment	PA[e]	chemical coagulation and settling; PA; PR[f]	breakpoint chlorination; chemical coagulation and settling; NR[g]; PR	nutrient feed - ammonia; PR
Design Flow (MGD)	0.35	1.5	0.4	1.17
Receiving Water	Michael's Brook	Hallock's Mill Brook	Delaware River – West Branch	Delaware River – East Branch
Population Served (approx.)	3,000	10,000	800	3,500
Population Type	suburban	suburban	rural	rural
Significant Sources	pharmaceutical lab	none known	hospital	nursing home, health care facilities

[a]From NYSDEC, 2004.
[b]SC: secondary clarifier
[c]FSR: rapid sand high rate filters
[d]CBUDS: continuous backwash-upflow, dual-sand filtration
[e]PA: post aeration
[f]PR: phosphorus removal
[g]NR: nitrogen removal

2.6 Selection of analytes

Analytes were selected to maximize our likelihood of finding them in the WWTP effluent and/or the environment. Factors considered were the following: number of prescriptions written per year, amount of the drug in a daily dose, information on drug absorption and metabolism in humans, environmental degradation, and previous research. We selected drugs that were widely prescribed, have a large daily dose (with the estrogens being an exception), are not rapidly metabolized by the body, or those less

prone to degradation in conventional wastewater treatment plants and the environment. Caffeine was also included because it is an established marker for human waste. The laboratory method was developed specifically for the eleven selected compounds. Included in the selected compounds are those that had been found by other researchers prior to our selection (caffeine, carbamazepine, sulfamethoxazole, trimethoprim, the estrogens), those found by researchers during our study (atenolol), and drugs that have not been found in the environment (amoxicillin, cephalexin, valproic acid). Analyte structures can be found in the Appendix 1.

3.0 Methodology/Analytical

The acid/neutral compounds (17α-ethinyl estradiol, 17β-estradiol, estrone, ibuprofen, and valproic acid) and the basic compounds (amoxicillin, atenolol, caffeine, cephalexin, sulfamethoxazole, and trimethoprim) were extracted from separate water subsamples and analyzed by LC/MS. A Method Detection Limit (MDL) study was done as part of the QA/QC program required by the US EPA and is Appendix 1. The United States Environmental Protection Agency approved the MDL study in May 2003. The samples were extracted on the day following collection and final concentration and analysis was completed by August 2003. In addition to the field blank, an internal Quality Control/Quality Assurance (QA/QC) sample was included with the batch of twelve samples undergoing extraction each day. This QA/QC sample was selected randomly from a sample group consisting of: distilled deionized water (DDI) blanks, matrix water blanks, and spikes at the MDL and three times (3x) the MDL in both DDI water and matrix water. The matrix water was collected from the East Branch of the Delaware River, at a location upstream of the Margaretville Wastewater Treatment Plant (WWTP).

3.1 Chemicals and Reagents

Amoxicillin, 17α-ethinylestradiol, 17β-estradiol, atenolol, caffeine, cefadroxil, cephalexin, estrone, ibuprofen, sulfamethoxazole, trimethoprim, valproic acid, deuterium dioxide, 4-methylmorpholine, and D_2SO_4 were purchased from Sigma Chemical (St. Louis, MO, USA). Caffeine (trimethyl-$^{13}C_3$), 17β-estradiol (2,4,16,16'-d_4), isovanillic acid (ring-$^{13}C_6$), phenacetin (ethoxy-1-^{13}C), sulfamethazine (phenyl-$^{13}C_6$), valproic acid (1,2,3,3'-$^{13}C_4$), and vanillic acid (carboxyl-^{13}C) were purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Practolol was purchased from Tocris (Ellisville, MO, USA). Dr. Chuck Litterst from the Division of AIDS (National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA donated Tetroxoprim). The d_4-ibuprofen was synthesized using D_2SO_4 and ibuprofen. The following chemicals and materials were also used: acetone, acetonitrile, ethyl acetate, and methanol, all HPLC grade (Burdick & Jackson from VWR Scientific, West Chester, PA, USA); 88% formic acid, and 100-200 micrometer (μm) silica gel (Mallinckrodt Baker Inc., Paris, KY, USA); 37-53 μm silica gel and QM-A glass microfiber filter paper (Whatman, Maidstone, UK); ammonium formate (Anachemia Chemicals, Rouses Point, NY, USA); dimethyldichlorosilane (Supelco, Bellefonte, PA, USA); Empore™ SDB-XC 47-millimeter (mm) poly(styrenedivinylbenzene) extraction discs, and Empore™ Filter Aid 400 (3M, St. Paul, MN, USA); Carboprep 200 extraction cartridges, 200 m^2/g carbon surface area, and 500 milligram (mg) bed weight (Restek, Bellefonte, PA, USA).

3.2 Solid-Phase Extraction

Acid/Neutral Analytes

Water samples (2-liter [L]) were adjusted to pH 2.5 using 3.4 ml 88% formic acid and spiked with 20 µL of a mixture of internal standards (d_4-ibuprofen, 17β-estradiol [2,4,16,16'-d_4], and valproic acid [1,2,3,3'-$^{13}C_4$]) in methanol, with each standard at 10 nanograms per microliter (ng/µL). Individual samples were extracted using a Teflon housing containing in sequence, from top-to-bottom: glass microfiber filter paper, a 1-centimeter (cm) layer of Filter Aid 400, glass microfiber filter paper, an SDB-XC extraction disk and a fine mesh nylon screen followed by a wide mesh nylon screen. The assembly was then placed on a Speedisk Expanded Extraction Station (Mallinckrodt Baker, Paris, KY, US). The disc was conditioned with 15 milliliters (mL) of acetone, 15 mL of methanol and 20 mL of pH 2.5 distilled deionized (DDI) water. The sample was passed through the disc under vacuum at a flow rate of < 100 mL/min.

After the disc had been dried for about 3 min on high vacuum the Filter Aid 400 and filter paper were removed, and the disc was then dried for an additional 5 min. Next, the disc was transferred to a Baker spe 24G Column Processor (Mallinckrodt Baker Inc., Paris, KY, USA) and 3 aliquots of 4 mL of pH 8.5 methanol (4-methylmorpholine /methanol, l1:1000, v/v) and 3 aliquots of 4 mL of acetone were used to elute the target compounds from the disc into a scintillation vial. A Turbovap II (Zymark, Hopkinton, MA, USA), was used for concentrating samples to 150 µL. The water bath temperature was 40°C, and the nitrogen flow rate was 26 psi. After the addition of 50 µL of DDI water the sample was concentrated to a final volume of 100 µL.

Basic/Amphoteric Analytes

For these analytes, all glassware had to be silanized. The manufacturer silanized the inserts and microvials, and all other glassware was silanized in the laboratory. The silanizing was performed by rinsing with a solution of 10% dimethlydichlorosilane in toluene, followed by two rinses with toluene and then two rinses with methanol. Since it was impractical to segregate glassware, the silanized glassware was also used in the analysis of the acid/neutral compounds.

Carboprep cartridges were placed on a Baker SPE 24G Column Processor and conditioned with 5 mL of pH 2.5 DDI water, followed by 5 mL of DDI water. Samples (1 L) were spiked with 25 µL of an internal standard mixture in methanol which contained cefadroxil, ampicillin, caffeine (trimethyl-$^{13}C_3$), practolol, sulfamethazine (phenyl-$^{13}C_6$), and tetroxoprim at concentrations varying from 1 - 400 ng/µL. The samples were then loaded onto the cartridges through Teflon tubing and the vacuum was adjusted to produce a steady flow rate of about 15 mL/min. After loading, the cartridges were dried under high vacuum for 10 min. The target compounds were eluted from the cartridges, with 2 aliquots of 5 mL of pH 2.9 methanol (90 µL formic acid/100 ml methanol), 2 aliquots of 5 mL of methylene chloride/methanol (80:20, v/v), and 6 aliquots of 5 mL of acetone.

Using the Turbovap II, samples were concentrated to 200 µL and then 500 µL of DDI water was added. When a final concentration of 475 µL was reached, samples were spiked with 25 µL of a 10ng/µL methanol solution of the recovery standard, phenacetin (ethoxy-1-^{13}C), and transferred into a micro-vial for analysis.

3.3 Chromatographic conditions

Chromatography was performed using an Agilent 1100 series high performance liquid chromatography instrument (Agilent Technologies, Palo Alto, CA, USA). The injection volumes were 10 μL for the acidic analytes and 15 μL for the basic analytes. The acidic analytes were separated on a LUNA C18 LC column (150 x 2.0 mm I.D., particle size 3μm; Phenomex, Torrance, CA, USA) at a 0.2 mL/min flow rate with a mobile phase of acetonitrile and a basic buffer of 10mM N-methylmorpholine (pH 9.4). The gradient was from 15% organic phase to 95% organic phase in 19 min. A post run time of 15 min was used in order to insure system equilibration. The basic analytes were separated on an Allure Pentafluoropropyl LC column (150 x 3.2 mm I.D., particle size 5 μm; Restek, Bellefonte, PA, USA) at a 0.5 mL/min flow rate with a mobile phase of acetonitrile and an acidic buffer of 8.7 millimolar (mM) ammonium formate and 10 mM formic acid (pH 3.5). The gradient was from 15% organic phase to 95% organic phase in 14 min. A post-run time of 15 min was used

3.4 Mass spectrometry

A Finnegan LCQ Classic quadrupole ion trap mass spectrometer (MS) (Thermo Finnigan, San Jose, CA, USA), was used as a detector. The ionization was performed by ESI, producing negative molecular ions from the acidic analytes and positive molecular ions from the basic analytes. A single ion monitoring method was used for all of the analytes except for amoxicillin and cephalexin, for which an MS/MS method was used. The Xcalibur software package (Thermo Finnigan, San Jose, CA, USA), was used to control both the high-pressure liquid chromatography (HPLC) and MS. The ESI source parameter settings were: spray voltage: 4.5 kV, nitrogen sheath gas flow rate: 67 au, capillary voltage –33 V and capillary temperature: 200^{o}C.

3.4 Data Processing

Calibration Curves

Calibration curves were constructed to determine the response factor of each analyte relative to the response factor of its internal standard (shown below as Int. Std.). A typical curve is shown in Figure 2 for caffeine and caffeine (trimethyl-$^{13}C_3$). Six calibration solutions were used with analyte concentrations ranging from the limit of detection (LOD) value to 10x LOD and a fixed internal standard concentration that varied from 4 - 6x LOD, depending on the analyte. Each solution was analyzed in triplicate and the average values are presented in Figure 2. The relative response factor (RRF) was determined from the slope of the regression line, which can be rearranged to the following equation:

$$\mathrm{RRF} = \frac{\mathrm{Analyte\,area}}{\mathrm{Analyte\,conc.}} \times \frac{\mathrm{Int.\,Std.\,conc.}}{\mathrm{Int.\,Std.\,area}} \qquad (1)$$

The calibration curves for the internal standards relative to the recovery standards (shown below as Rec. Std.) were constructed in a similar manner by substituting in Figure 2 internal standard data for analyte data and recovery standard data for internal standard data. The RRFs for the internal standards and recovery standards were calculated from the slopes of these curves in a manner similar to that described above for the analytes and internal standards:

$$RRF_{rec} = \frac{\text{Int. Std. area}}{\text{Int. Std. conc.}} \times \frac{\text{Rec. Std. conc.}}{\text{Rec. Std. area}} \qquad (2)$$

Analyte Concentrations and Internal Standard Recoveries

The concentrations of individual analytes were determined by the following equation:

$$C_A = \frac{\text{Analyte area}}{\text{Int. Std. area}} \times \frac{C_{int}}{RRF} \qquad (3)$$

where C_A = analyte concentration (ng/L) and C_{int} = internal standard concentration (ng/L). Recoveries of internal standards were determined by the following equation:

$$\text{Recovery}(\%) = \frac{\text{Int. Std. area}}{\text{Rec. Std. area}} \times \frac{C_{rec}}{RRF_{rec}} \times \frac{100}{C_{int}} \qquad (4)$$

where C_{rec} = recovery standard concentration (ng/L).

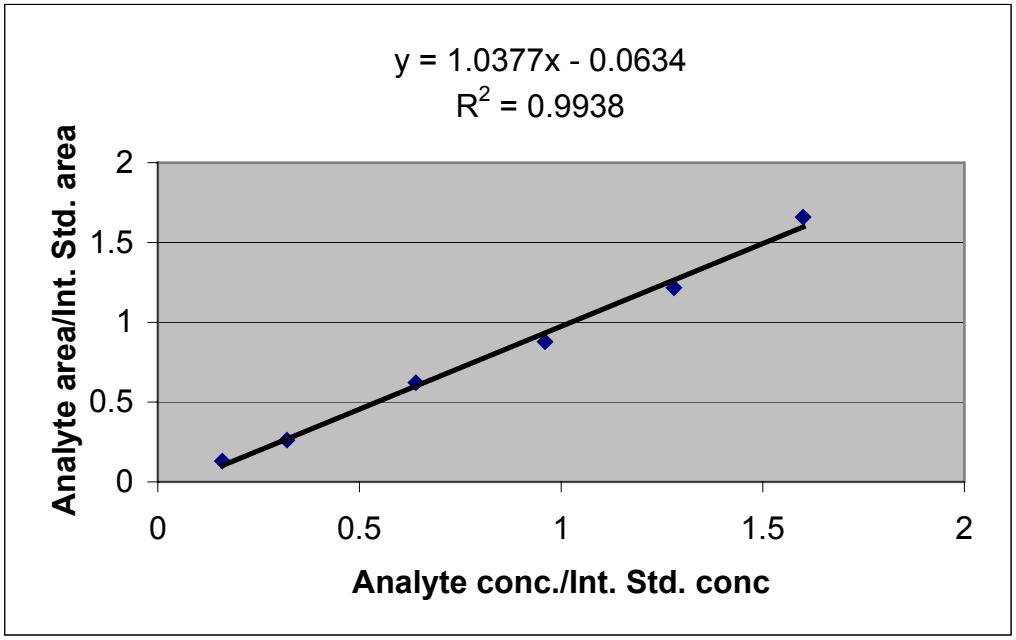


Figure 2. Calibration Curve for Caffeine and the Labeled Internal Standard, (trimethyl-$^{13}C_3$) Caffeine.

3.5 Quality Assurance/Quality Control (QA/QC)

The sample set for QA/QC consisted of field blanks, field sample duplicates, laboratory blanks (distilled deionized water [DDI] and river water [riv]), and laboratory spikes (DDI and riv). There were 56 field blanks (14 per seasonal sampling event or one per sampling day) and they consisted of 4-L volumes of DDI water taken to the point of sampling after which they were transported back to the laboratory with

the field samples. A total of 42 laboratory blanks were also analyzed with the field samples, some of which were prepared from DDI water and others from riv water. Only one sample from this total group of 98 blank samples showed evidence of contamination with a study analyte. This was a field blank from the Winter 2004 sampling event and it was found that the sample contained trimethoprim at the MDL for this compound (4 ng/L).

Internal standard-corrected recovery data from the analysis of samples spiked with the basic/amphoteric analytes are shown in Table 5. The penicillin antibiotics amoxicillin and cephalexin proved to be difficult to extract from water samples. In many of the spiked samples we failed to detect these two compounds. In those samples where the penicillins were detected, there was an extremely wide range in the recovery data. Since it is recognized that the β-lactam ring in penicillins is very unstable in the presence of certain solvents such as methanol, these compounds are generally not included in monitoring surveys of pharmaceuticals in water supplies. The other four analytes were detected in the majority of the spiked samples. However in one sample there was no signal for atenolol and there were no signals for sulfamethoxazole in four samples. With the exception of three samples the recovery values for caffeine were close to 100%. The recovery values for atenolol, sulfamethoxazole, and trimethoprim often exceeded 100% and in the most extreme case a recovery of 1,210% was found for atenolol in a lodspike. These results can be explained by the structures of the internal standards. The caffeine internal standard was a ^{13}C-labeled analog of caffeine and therefore this internal standard had the same chemical and physical properties as "native" caffeine prepared from the most abundant natural isotope of carbon, ^{12}C. Labeled analogs were not available for atenolol, sulfamethoxazole, and trimethoprim and for these compounds we selected surrogates as internal standards. While these surrogates had structures closely related to the structures of the three analytes there could have been differences in recovery and/or response in the LC/MS instrument between an analyte and it's surrogate.

Internal standard-corrected recovery data for the acid/neutral analytes are shown in Table 6. Three internal standards were used in the analysis of this group of analytes, the ^{13}C-labeled analog of valproic acid and the deuterated analogs of ibuprofen and β-estradiol. In contrast to the basic/amphoteric compounds, where we had to rely on surrogates as internal standards for several compounds, in the case of the acid/neutral analytes, we had labeled analogs for all the analytes although one labeled analog had to serve as an internal standard for the three estrogens. Therefore it was not surprising to find that, in general, the recoveries were considerably closer to 100% than the recoveries found for the basic/amphoteric compounds.

The recovery standards, phenacetin (ethoxy-1-^{13}C) and isovanillic acid (ring-$^{13}C_6$), were added respectively to the basic/amphoteric and acid/neutral extracts just prior to analysis on the LC/MS system. It was intended that these recovery standards should be used to obtain the absolute recoveries of the internal standards added to the water samples prior to extraction. The absolute recoveries obtained in this manner proved to be erratic and unreliable, probably as a consequence of the differences between the structures of the recovery standards and the internal standards.

As an alternative approach to obtaining data on the efficiency of the sample preparation procedure, QA/QC samples were prepared with the analytes added to the water samples prior to extraction and the

Table 5. Recovery (%, internal-standard-corrected) of Basic/Amphoteric Analytes from Spiked Distilled Deionized Water (DDI) and Spiked River Water (riv).

Spike Level[a]	**Amoxicillin**	**Caffeine**	**Cephalexin**	**Atenolol**	**Sulfamethoxazole**	**Trimethoprim**
Summer 2003						
DDI 5x lodspike	0	92	0	102	0	143
DDI 5x lodspike	0	179	0	86	0	137
DDI 5x lodspike	0	119	0	173	16	134
Riv 5x lodspike	27	94	379	366	8.2	126
Riv 5x lodspike	47	128	345	453	101	128
Fall 2003						
Riv 3x lodspike	0	200	374	343	72	191
DDI 3x lodspike	0	86	572	168	101	235
DDI 3x lodspike	0	206	474	0	53	187
Riv 8x lodspike		106	129	140	180	148
Riv 8x lodspike	48	96	109	196	331	99
Winter 2004						
DDI lodspike	0	118	0	1210	40	178
DDI lodspike	0	122	0	151	154	179
Riv lodspike	802	98	0	238	0	266
DDI 2x lodspike	0	84	0	73	106	142
Riv 5x lodspike	73	122	155	117	378	244
riv 5x lodspike	0	108	NR[b]	126	NR	178
Spring 2004						
DDI lodspike	11	150	0	268	49	129
DDI lodspike	18	127	0	229	96	169
DDI 10x lodspike	0	94	0	243	44	137
DDI 10x lodspike	21	92	0	165	54	135
riv 10x lodspike	16	96	0	170	32	148
riv 10x lodspike	34	95	0	185	40	165

[a] lod = limit-of-detection (367, 80, 502, 9.0, 111 and 4.0 ng/L respectively for amoxicillin, caffeine, cephalexin, atenolol, sulfamethoxazole and trimethoprim). [b] NR = not reportable (see footnote b of table 2 for explanation).

Table 6. Recovery (%, internal-standard corrected) of Acid/Neutral Analytes from Spiked Distilled Deionized Water (DDI) and Spiked River Water (riv).

Spike Level[a]	Valproic Acid	Ibuprofen	Estrone	17β-estradiol	17α-ethynl-estradiol
Summer 2003					
DDI 5x lodspike	281	315	94	123	91
DDI 5x lodspike	319	125	85	106	66
DDI 5x lodspike	179	121	98	120	76
riv 5x lodspike	212	170	62	60	67
riv 5x lodspike	NR[b]	NR	69	44	52
Fall 2003					
riv 3x lodspike	147	455	0	79	0
DDI 3x lodspike	0	162	111	96	85
DDI 3x lodspike	42	178	78	79	79
riv 8x lodspike	122	72	16	101	44
riv 8x lodspike	144	70	79	81	57
Winter 2004					
DDI lodspike	196	70	38	58	40
DDI lodspike	126	57	47	65	45
riv lodspike	184	54	47	70	63
DDI 2x lodspike	103	45	31	50	29
riv 5x lodspike	101	30	31	43	25
riv 5x lodspike	120	16	32	43	22
Spring 2004					
DDI lodspike	0	85	57	52	43
DDI lodspike	80	103	67	60	41
DDI 10x lodspike	62	201	134	164	174
riv 10x lodspike	71	227	109	174	190
riv 10x lodspike	127	182	125	156	135
riv 10x lodspike	158	170	122	164	141

[a] lod = limit of detection (199, 20, 40, 30, 40, and 39, respectively, for valproic acid, ibuprofen, estrone, 17β-estradiol, and 17α-ethynlestradiol).
[b] NR = not reportable, as a consequence of interference and background noise.

internal standards were then added to the extracts prior to injection into the LC/MS system. Absolute recovery data obtained in this manner for the basic/amphoteric and acid/neutral compounds are presented in Tables 7 and 8 respectively. With the exception of the penicillins, the absolute recoveries for the basic/amphoteric compounds were generally in the range of 30% to 100% although there were some recovery values outside this range (Table 7). The penicillins, which as previously discussed are difficult to analyze, were not detected in most samples. The absolute recovery values for the acid/neutral compounds (Table 8) were in the range of 4.5% to 34%, which was considerably lower than

the absolute recovery values obtained for the basic/amphoteric compounds. The differences in recovery values between the two groups of compounds can be explained by differences in the complexity of the sample preparation procedures used for each group of compounds. The basic/amphoteric compounds were extracted from water using a graphitized carbon cartridge and the concentrated extracts were then analyzed by LC/MS. The acid/neutral compounds were extracted with a disk containing styrene-divinyl benzene as an adsorbent and the extracts were then solvent-exchanged for cleanup on a silica gel micro column prior to analysis by LC/MS. The cleanup step was required for the removal of background interference from WWTP effluent samples and from certain keypoint samples. However the silica gel cleanup step resulted in reduced absolute recoveries. It should be understood that with the internal-standard-corrected procedure we use to determine concentration levels accurate results can be obtained when absolute recoveries are low.

Although carbamazepine was not designated as an analyte in the original sampling and analysis protocol it was later included as an analyte since it is very resistant to degradation or removal by solids during the sewage treatment process. It was found that it could be extracted with the basic/amphoteric analytes and then it could be analyzed by LC/MS using the acid/neutral protocol. Only the WWTP effluents were analyzed for carbamazepine during the Summer 2003 and Fall 2003 sampling events and during this time period there was no carbamazepine internal standard available for spiking. Consequently we were unable to prepare spiked QA/QC samples for these two sampling events and the carbamazepine results from the field samples can only be considered as estimates. A deuterium-labeled carbamazepine standard was acquired prior to the Winter 2004 and Spring 2004 sampling events and results from spiked QA/QC samples included in these two sampling are shown in Table 9. Recoveries close to 100% were obtained for all samples (internal-standard-corrected and absolute recoveries).

Precision data for the field samples were obtained by collecting duplicate field samples during each sampling event. While these samples are referred to as “duplicates” they are actually samples taken sequentially, since it was not feasible to split the 4-L samples. Eight duplicates were collected for each of the four sampling events: four duplicate East-of-the-Hudson River and four duplicates West-of-the-Hudson River. However, positive signals were not obtained from a number samples, and the analytes which were detected varied between sampling locations for each sampling event. Linear regression results for all the samples for which duplicate data were available are shown in Figure 3. In the case of ibuprofen there were extremely large differences in duplicate results from samples collected at two time points from the Yorktown WWTP effluent during Summer 2003 (11, 100, and 22.6 ng/L from one collection and 154 and 17.7 ng/L from another collection). At this stage of the project, we did not have a complete understanding of the absolute recovery problems for the acid/neutral compounds.

Consequently, the spike levels for the acid/neutral internal standards were too low. Since no signals were found for these compounds, we had to use external standards to determine the ibuprofen concentrations in the four samples. Data from the duplicates have been omitted from Figure 3 in view of the potential errors associated with external standard quantitation of samples with low recoveries. For the remaining samples containing ibuprofen and for all the positive samples for the other analytes the slopes of the regression lines were very close to the theoretical value of 1.00 (0.88 – 1.06) and the correlation coefficients were in the range of 0.90 to 0.98. When the results were expressed as relative percent differences (RPDs), the average RPDs were 33, 29, 35, 33, and 18% for ibuprofen, caffeine, atenolol, trimethoprim, and carbamazepine respectively.

Table 7. Absolute Recoveries (%) of Basic/Amphoteric Analytes from Spiked River Water.

	Fall 2003	**Winter 2004**		**Spring 2004**	
Spike Level[a]	5x lodspike	3x lodspike	3x lodspike	3x lodspike	3x lodspike
Spike Type[b]	Internal	Native	Native	Native	Native
Amoxicillin		94	69		13
Cefadroxil	31				
Caffeine		77	99	105	69
13c-Caffeine	83				
Cephalexin		0	112		
Ampicillin	48				
Atenolol		84	51	165	223
Practolol	48				
Sulfamethoxazole		106	164	72	73
13c-Sulfamethazine	104				
Trimethoprim		30	32	30	49
Tetroxoprim	11				

[a] lod = limit-of-detection (values shown in Table 1).
[b] Internal = Internal standards added at the point-of-extraction and native (unlabeled) standards added at the point-of-injection; Native = Native standards added at the point-of-extraction and internal standards added at the point-of-injection.

Table 8. Absolute Recoveries (%) of Acid/Neutral Analytes from Spiked River Water.

	Fall 2003	**Winter 2004**		**Spring 2004**	
Spike Level[a]	5x lodspike	3x lodspike	3x lodspike	3x lodspike	3x lodspike
Spike Type[b]	Internal	Native	Native	Native	Native
Valproic Acid		12	34	25	14
13-Valproic Acid	28				
Ibuprofen		3.8	8.2	19	18
d-Ibuprofen	17				
Estrone		5.7	6.9	11	14
17β-estradiol		7.9	10	11	14
17α-ethynyl estradiol		4.5	9.1	8.2	11
13c-17β-estradiol	38				

[a] lod = limit-of-detection (values shown in Table 2).
[b] Internal = Internal standards added at the point-of-extraction and native (unlabeled) standards added at the point-of-injection; Native = Native standards added at the point-of-extraction and internal standards added at the point-of-injection.

Table 9. Recovery (internal-standard-corrected) and Absolute Recovery of Carbamazepine from Spiked Distilled Deionized Water (DDI) and Spiked River Water (riv).

Spike Level[a]	% Recovery	% Absolute Recovery
Winter 2004		
riv 5x lodspike	115	
riv 5x lodspike	122	
riv 5x lodspike	116	
riv 5x lodspike	124	
Spring 2004		
DDI lodspike	93	
DDI 10x lodspike	159	
DDI 10x lodspike	82	
riv 10x lodspike	107	
riv 10x lodspike	110	
riv 3x lodspike		91
riv 3x lodspike		97

[a] lod = limit of detection (100 ng/L)

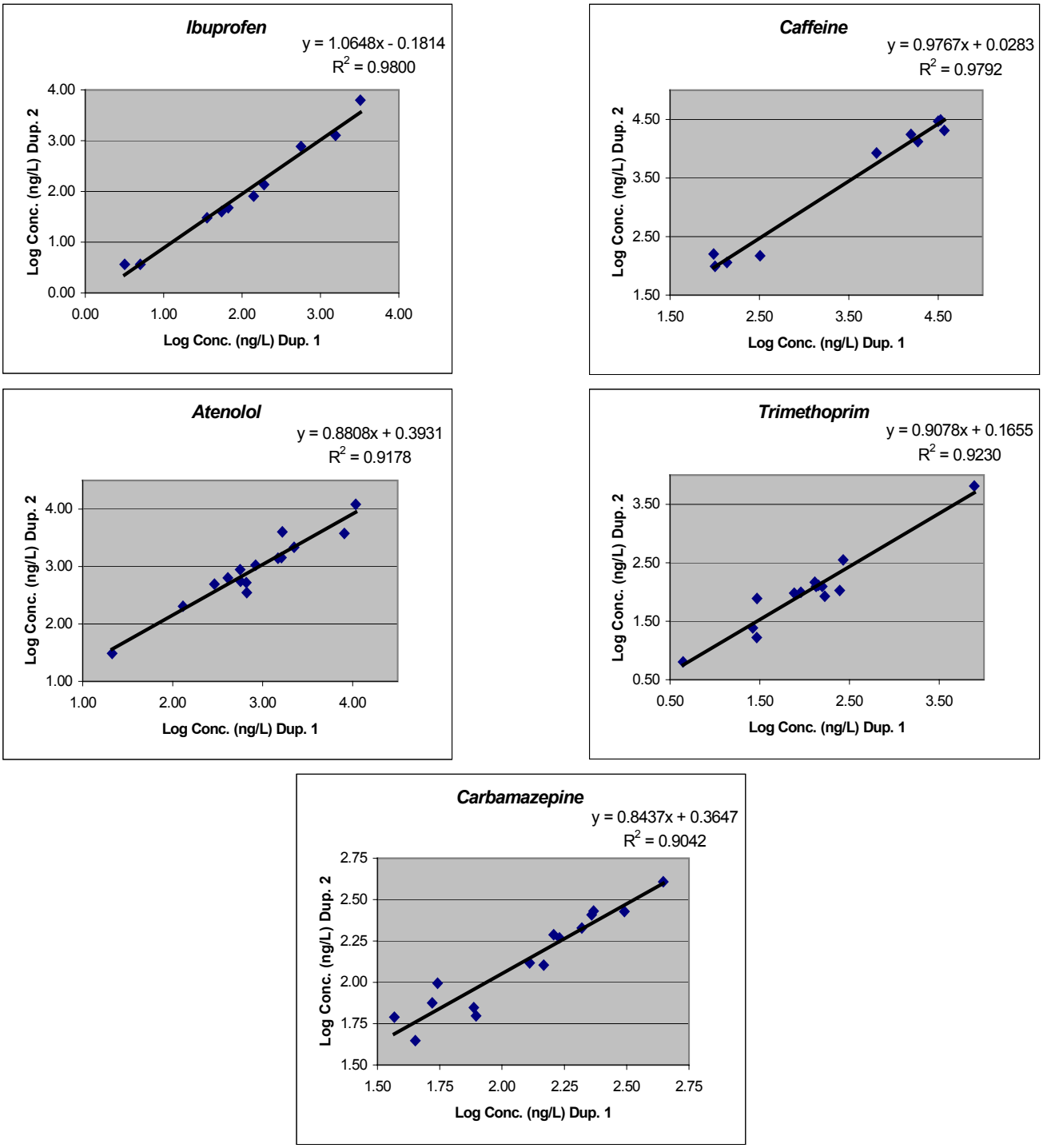


Figure 3. Regression Plots of Results from Field Duplicates Spring 2004.

4.0 Results

A total of 368 samples were collected over the four seasonal sampling events (Table 10). The samples and duplicates were, in general, spread equally across the four seasons and between sites. Duplicates were collected on days 1, 3, 5, and 7 of each sampling week, and at least two duplicates were collected at every location during the course of the study.

Table 10. Number of Samples Collected Per Site by Season.

Sampling Sites	Summer 2003	Fall 2003	Winter 2004	Spring 2004	Total
East of Hudson Locations					
DEL 18[a]	7[h]	7	8	8	30
DEL 17[b]	7	7	8	8	30
CATALUM[c] (CATLEFF)[d,e]	7(1)[e]	8	7	8(1)	30
Croton Lake Gate House	7	8	7	8	30
Yorktown WWTP	11	8	8	7	34
Carmel WWTP	7	8	8	7	30
West of Hudson Locations					
Neversink Aqueduct (Neversink Gate House)	8	8	7(6)	7	30
WDA Outlet (Cannonsville Gate House)[f]	8(8)	8(8)	7	7(3)	30
EDA Outlet (Pepacton Gate House)[g]	7	7(5)	8	8	30
Rondout Chamber	7	7	8	8	30
Walton WWTP	8	8	8	8	32
Margaretville WWTP	8	8	8	8	32
Total Number of Samples	92	92	92	92	368

[a] DEL 18: Shaft 18 of the Delaware Aqueduct.
[b] DEL 17: Shaft 17 of the Delaware Aqueduct.
[c] CATALUM: Catskill Aqueduct Alum Plant.
[d] CATLEFF: Catskill Aqueduct Lower Effluent Chamber
[e] Location in parentheses is the backup sampling location
[f] WDA: West Delaware Aqueduct
[g] EDA: East Delaware Aqueduct
[h] The number of samples includes duplicates (the number of duplicates can be determined by subtracting 7).

Table 11 is a summary of the frequency that each targeted analyte was detected for all samples collected from a given location. It shows that several different pharmaceuticals were frequently detected in the WWTP effluent. In fact, every sample collected from the WWTP contained some of the targeted analytes. The same pharmaceuticals were not found in surface water samples with a few infrequent exceptions in samples from East of the Hudson locations. Ibuprofen and caffeine were detected in a low percentage (either 17 or 7) from three of the East of the Hudson River sampling points. Because there were few detections of the targeted samples from key locations, most of the data analysis in this report is for samples collected from the WWTP.

Table 11. Frequency of Analyte Detection.

Sample Location	Atenolol (9 ng/L)[h]	Caffeine (80 ng/L)	Carbamazepine (100 ng/L)	Ibuprofen (20 ng/L)	Trimethoprim (4 ng/L)	Estrone (30 ng/L)	Amoxicillin (367 ng/L)	Cephalexin (502 ng/L)	17β-Estradiol (40 ng/L)	17α-Ethinylestradiol (39 ng/L)	Sulfamethoxazole (111 ng/L)	Valproic acid (199 ng/L)
East of Hudson Locations												
DEL 18[a]	0	0	0	7	0	0	0	0	0	0	0	0
DEL 17[b]	0	0	0	0	0	0	0	0	0	0	0	0
CATALUM[c] (CATLEFF)[d,e]	0	7	0	7	0	0	0	0	0	0	0	0
Croton Lake Gate House	0	17	0	7	0	0	0	0	0	0	0	0
Yorktown WWTP	100	100	50	97	100	0	0	0	0	0	0	0
Carmel WWTP	93	20	75	10	70	3	0	0	0	0	0	0
West of Hudson Locations												
Neversink Aqueduct (Neversink Gate House)	0	0	0	0	0	0	0	0	0	0	0	0
WDA Outlet[f] (Cannonsville Gate House)	0	0	0	0	0	0	0	0	0	0	0	0
EDA Outlet[g] (Pepacton Gate House)	0	0	0	0	0	0	0	0	0	0	0	0
Rondout Chamber	0	0	0	0	0	0	0	0	0	0	0	0
Walton WWTP	78	22	66	56	72	0	0	0	0	0	0	0
Margaretville WWTP	100	40	94	72	97	0	0	0	0	0	0	0

[a] DEL 18: Shaft 18 of the Delaware Aqueduct.
[b] DEL 17: Shaft 17 of the Delaware Aqueduct.
[c] CATALUM: Catskill Aqueduct Alum Plant.
[d] CATLEFF: Catskill Aqueduct Lower Effluent Chamber
[e] Location in parentheses is the backup sampling location
[f] WDA: West Delaware Aqueduct
[g] EDA: East Delaware Aqueduct
[h] number in parentheses is the detection limit

4.1 Wastewater Treatment Plant Results

A summary of the data for the five pharmaceuticals (atenolol, caffeine, carbamazepine, ibuprofen, and trimethoprim) that were frequently found in samples from each of the WWTP is provided in Table 12. One analyte, estrone, was found in one sample from the Carmel WWTP at a concentration of 56 ng/l. The other six analytes listed in Table that were not found in any samples are not listed in Table 12. The mean caffeine concentration is an order of magnitude greater than the mean concentration of any of the other analytes, however, subsequent analysis will show this is because of the results from the Yorktown WWTP.

Table 12. Pharmaceuticals in WWTP Effluents (ng/L).

	atenolol	caffeine	carbamazepine	estrone (E1)	ibuprofen	trimethoprim
N	127	127	124	127	127	127
Detection Limit (ng/L)	9.0	80.0	100.0	30.0	20.0	4.0
Detections	119	59	88	1	77	108
Mean	1587	12707	211	56	1198	762
Standard Error	241	1594	11	*na*	295	364
Median	576	13400	190	*na*	85	112
Standard Deviation	2632	12244	99	*na*	2588	3783
Minimum	<9.0	<80.0	<100.0	*na*	<20.0	<4.0
90th Percentile	4410	29920	335	*na*	4650	357
Maximum	14200	37200	551	*na*	14600	37000

na: not applicable

Although five analytes in Table 12 are common to all four WWTP, the concentrations found between the WWTP show differences (Figure 4). Figure 4 shows the concentrations for each analyte each plant allowing for comparison between plants and between analytes. Most notably, caffeine was found at a concentration an order of magnitude higher in the Yorktown WWTP effluent compared to samples from the other three WWTP. Carbamazepine concentrations were very similar between the WTTP, and showed the lowest variability in results for each of the individual plants. The other analytes showed substantial variation and differences in mean concentrations detected in the effluent from each of the plants. Each analyte listed in Table 12 and Figure 4 are further discussed in the below.

Atenolol
This analyte was detected more times than any of the other analytes (119 of the 128 total samples). The frequency of detection by site was: Yorktown, 100%; Margaretville, 100%; Carmel, 93%; and Walton, 78%. Concentrations were generally highest at Yorktown (median: 1415 ng/L), while the maximum concentration was detected at Carmel (2257 ng/L).

Caffeine
The mean concentration of caffeine was higher than any other analyte (Table 12). Figure 4 also shows how much this mean was driven by the results for the Yorktown samples. It was detected in every sample from the Yorktown WWTP, but the next highest frequency was 44% at Margaretville. The Yorktown caffeine levels were higher than any other chemicals detected by an order of magnitude, if not more.

Carbamazepine
This compound was not part of the original group of target analytes, but it appeared so frequently in the pilot study samples, we included it in the analysis for the remainder of the study. It wasfound in 88% of the samples at remarkably similar concentrations between WWTP.

Estrogens
Of the three estrogens in our study, there was only one detection (estrone; 56 ng/L at Carmel WWTP). This is surprising, given that the detection limits were initially believed to be at or slightly above environmentally relevant concentrations.

Ibuprofen
As with some of the other analytes, Yorktown had much higher concentrations of ibuprofen that the other three locations (median: 1045 ng/L; max: 14600 ng/L), and in fact, it was present in every sample (though below the detection limit in one sample). Detection frequencies ranged from 97% (Yorktown) to 10% (Carmel).

Trimethoprim
Trimethoprim was detected at every WWTP and with relatively high frequencies. At Carmel, we found a very high concentration in one sample of 37000 ng/L, though the second highest concentration at Carmel was 8090 ng/L. It is unclear if this high concentration is related to the pharmaceutical plant that discharges to the sewers served by this facility. Although the company that owns the plant is known to sell this compound, it has not been confirmed if that location does indeed manufacture trimethoprim.

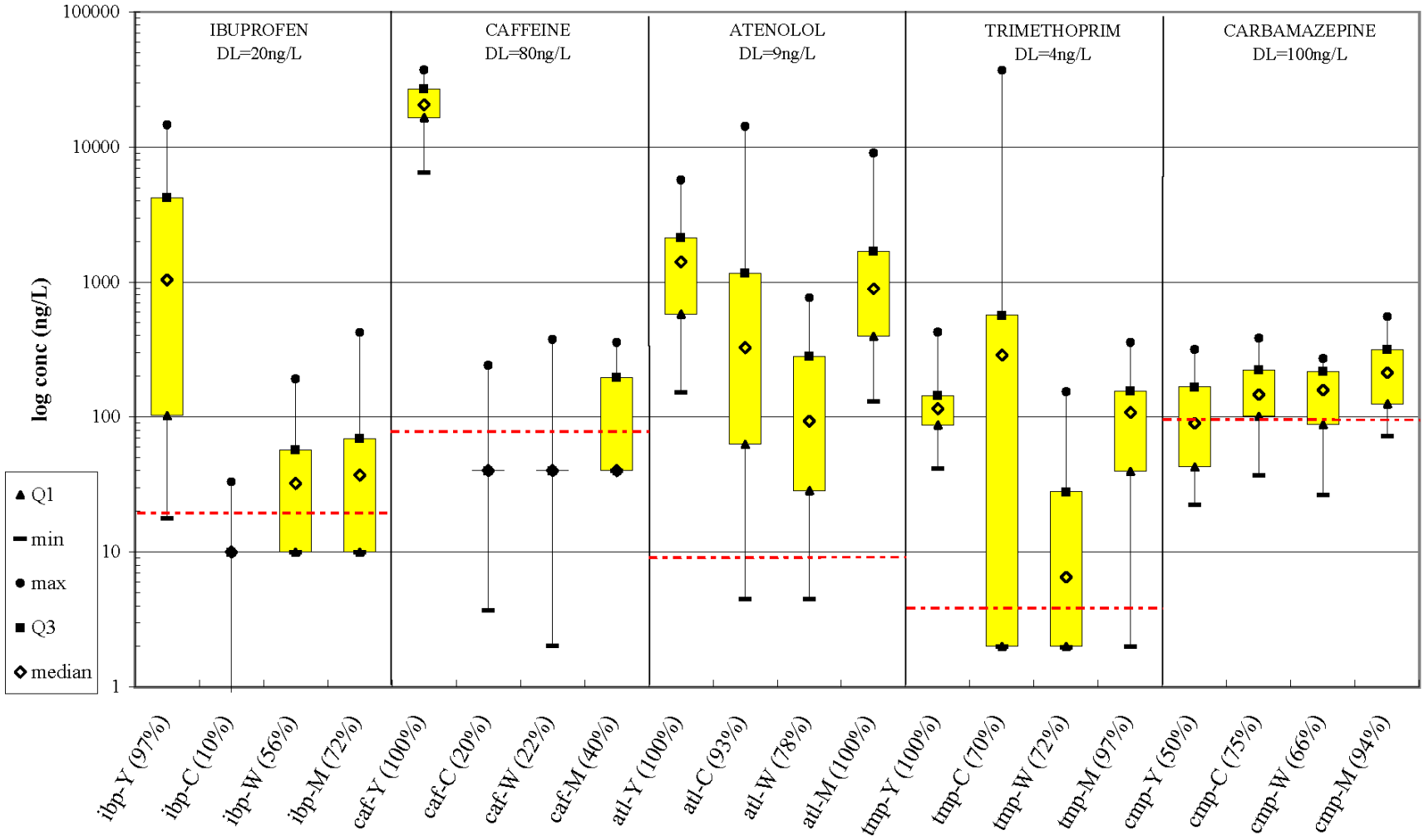


Figure 4. Log Concentrations (ng/L) of Target Analytes in Wastewater Treatment Plant Effluents.

Note: Dashed line indicates the analyte detection limit. The analytes shown are atenolol (atl) caffeine (caf), carbamazepine (cmp), ibuprofen (ibp), and trimethoprim. WWTPs are Yorktown (Y), Carmel (C), Walton (W), and Margaretville (M). This figure includes estimated values for some compounds detected at concentrations below the detection limit and when a compound was not found above the detection limit, a value of half the detection limit was used as the estimated concentration. In parentheses are the frequencies of detection. Q1: 1st quartile; min: minimum; max: maximum; Q3: 3rd quartile.

4.2 Results by season

An evaluation of the seasonal trend was done by comparing the median concentration found at a WWTP per sampling event and is presented in Figure 5. Review of this information shows that, at most locations, median atenolol concentrations varied seasonally at the WWTPs. Trimethoprim also showed large seasonal variations at some WWTP, whereas caffeine and carbamazepine showed little variation.

Atenolol
Atenolol concentrations peaked in winter at all four of the WWTPs and with the exception of samples from the summer at Walton, it was found in every sample. At Yorktown, atenolol was detected in every sample, and the median winter concentration (3925 ng/L) was over an order of magnitude higher than the spring sampling (272 ng/L). This was similar to the pattern seen at Margaretville: atenolol was detected in every sample, and the winter median (5240 ng/L) was much higher than the spring median (200 ng/L). At Carmel, the winter median (10700 ng/L) was more than a 2-log increase over the summer low.

Caffeine
The concentrations of caffeine detected at Yorktown were generally at least 100 times higher than what was found at the other WWTPs. In the summer, Yorktown had the highest median caffeine concentration (29600 ng/L), which was more than twice that of the winter median. Seasonal medians at the other three WWTPs ranged from below the detection limit of 80 ng/L up to the summer median of 250 ng/L seen at Margaretville (where it was detected in all eight summer samples). Caffeine was not detected at Carmel, Margaretville, or Walton during the spring sampling period, nor was it detected at Carmel during the summer. The summer sampling at Walton had one caffeine detection, though it was found in all samples from the other three seasons.

Carbamazepine
All samples from the WWTPs showed the presence of carbamazepine, though in some cases the concentration was less than the 100 ng/L detection limit. Generally, the seasonal medians were quite similar, especially compared to the wide variations seen with the other analytes. Seasonal medians at Yorktown ranged from 30 – 181 ng/L, Carmel ranged from 82 – 268 ng/L, Walton ranged from 70 – 220 ng/L, and Margaretville ranged from 120 – 455 ng/L. All plants had their highest medians in the winter and lower medians in the summer and fall.

Ibuprofen
Ibuprofen was present in all samples from Yorktown, though in one sample it was 18 ng/L, which was slightly below the 20 ng/L detection limit. The peak median concentration (5340 ng/L), which occurred in the spring, was over two orders of magnitude higher than the low median, which occurred in the summer. Much like caffeine, ibuprofen concentrations were generally higher at Yorktown than at the other three WWTPs. At Margaretville, ibuprofen was detected in all samples from the summer and spring, though the detected concentrations in the summer (37 – 422 ng/L) showed a much wider range than in the spring (35 – 76 ng/L). At Carmel, ibuprofen was not found above the detection limit until the spring sampling, though it was present in one summer sample.

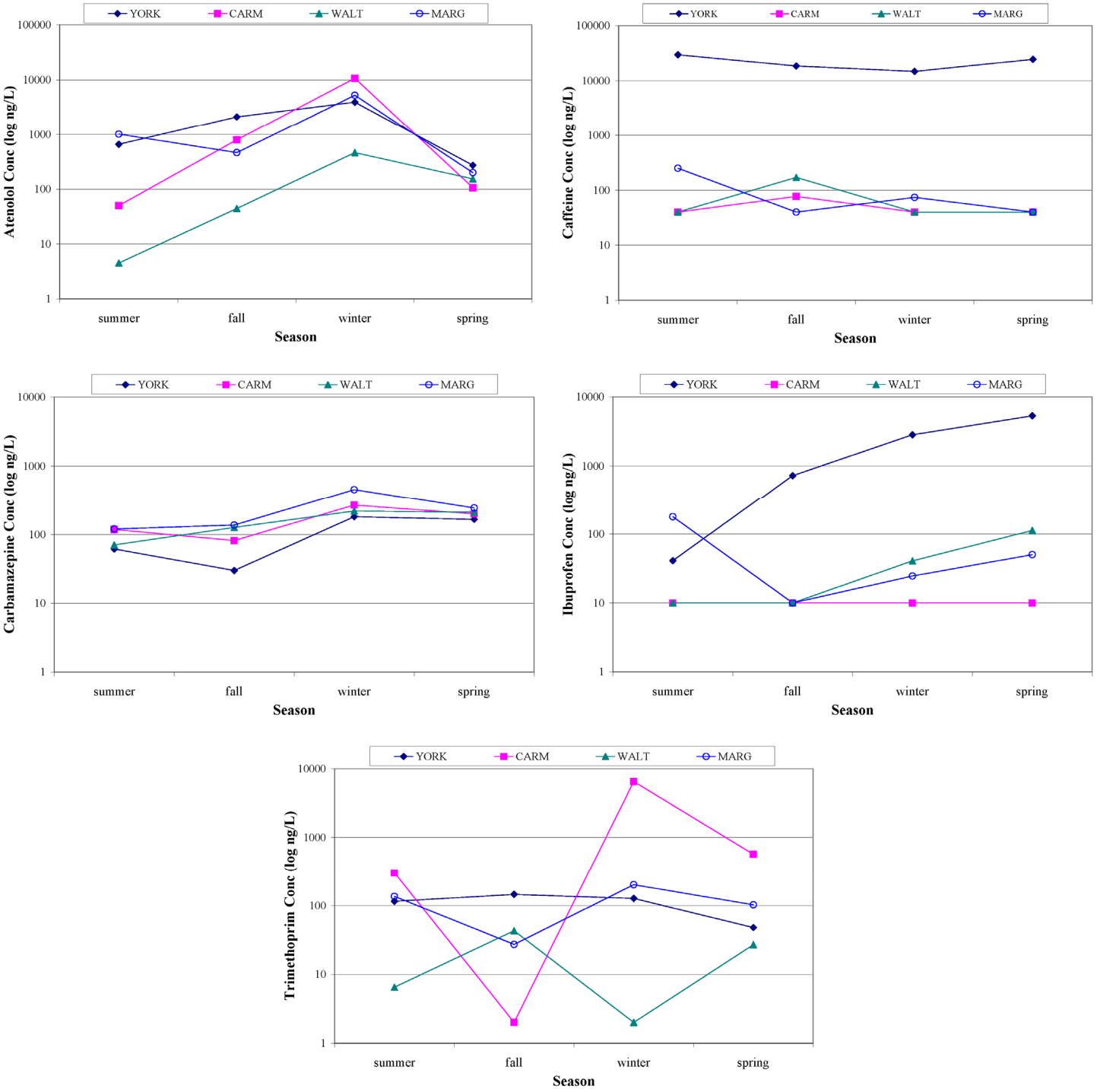


Figure 5. The Median Seasonal Concentrations (ng/L) of the Five Frequently Found Pharmaceuticals in the WWTP Effluents. Note that the y-axis scale for the atenolol and caffeine graphs differ from the others. Medians were calculated from the seven consecutive daily samples collected each season, along with any available duplicates. (Detection limits are: 9 ng/L for atenolol, 80 ng/L for caffeine, 100 ng/L for carbamazepine, 20 ng/L for ibuprofen and 4 ng/L for trimethoprim.)

Trimethoprim
At Yorktown and Margaretville, median concentrations for trimethoprim were similar over the four seasons (48 – 146 ng/L and 27 – 201 ng/L, respectively). Winter and spring samples from Carmel had the highest median concentrations of any location (6490 ng/L and 566 ng/L, respectively). However, trimethoprim was not detected there in the fall, whereas Walton had its highest seasonal median in the fall (43 ng/L), but no detectable concentrations of trimethoprim in the winter samples.

4.3 Results by day

The design of the study also allows for comparison of the concentrations found by day of the week (Figure 6; note differences in scale on the figures below). Although the data are limited (each day of the week average is in most cases comprised of just four samples), concentrations across the seven-day week were generally consistent. Atenolol, caffeine, carbamazepine, and ibuprofen concentrations were consistent at the four treatment plants for the week, as was ibuprofen at all locations except Yorktown (which showed a Saturday decline). Trimethoprim concentrations were more varied, with concentrations at Carmel peaking on Saturdays, but over two orders of magnitude lower on Wednesdays.

4.4 Results from reservoir samples

Caffeine was detected in 7 of the 240 samples collected from the reservoirs, while ibuprofen was detected in 6 samples. Five of the caffeine detections and two of the ibuprofen detections were from the CROGH location. CATALUM had the remaining two caffeine detections (177 ng/L and 103 ng/L), which occurred in the summer and fall.

In addition, CATALUM and DEL18 had two detections of ibuprofen. While CATALUM's detections were around the 20-ng/L detection limit (20 ng/L and 33 ng/L), DEL18 had detections on consecutive days of 932 ng/L and 372 ng/L. The former value is larger than that seen at three of the four WWTPs.

4.5 Evaluation of Measured Water Quality Parameters

Atenolol showed a highly significant ($p=0.001$, Table 13) negative correlation with temperature at all locations. Carbamazepine showed highly significant negative correlations with temperature at all locations but Walton. Also showing significant correlations with temperature were caffeine at Yorktown and ibuprofen at Margaretville. These correlations may point to the importance of biodegradation processes within the WWTPs, as temperature and biological activity are directly related. Carbamazepine also showed negative correlations with oxidation-reduction potential (ORP), but again, not at Walton. Carbamazepine also showed significant correlations with salinity and conductivity at Yorktown. Ibuprofen showed significant correlations with temperature and dissolved oxygen (DO) at Margaretville, and ORP at Walton. Caffeine had significant correlations with ORP at Margaretville and temperature at Yorktown. In addition to the temperature correlations seen with atenolol, there were also significant correlations with DO at Walton and Carmel. Only one significant correlation was found for trimethoprim, which was highly correlated with salinity at Carmel. None of the analytes showed significant correlation with pH at the $p=0.001$ level, though ibuprofen did show correlation with pH at the $p=0.01$ level.

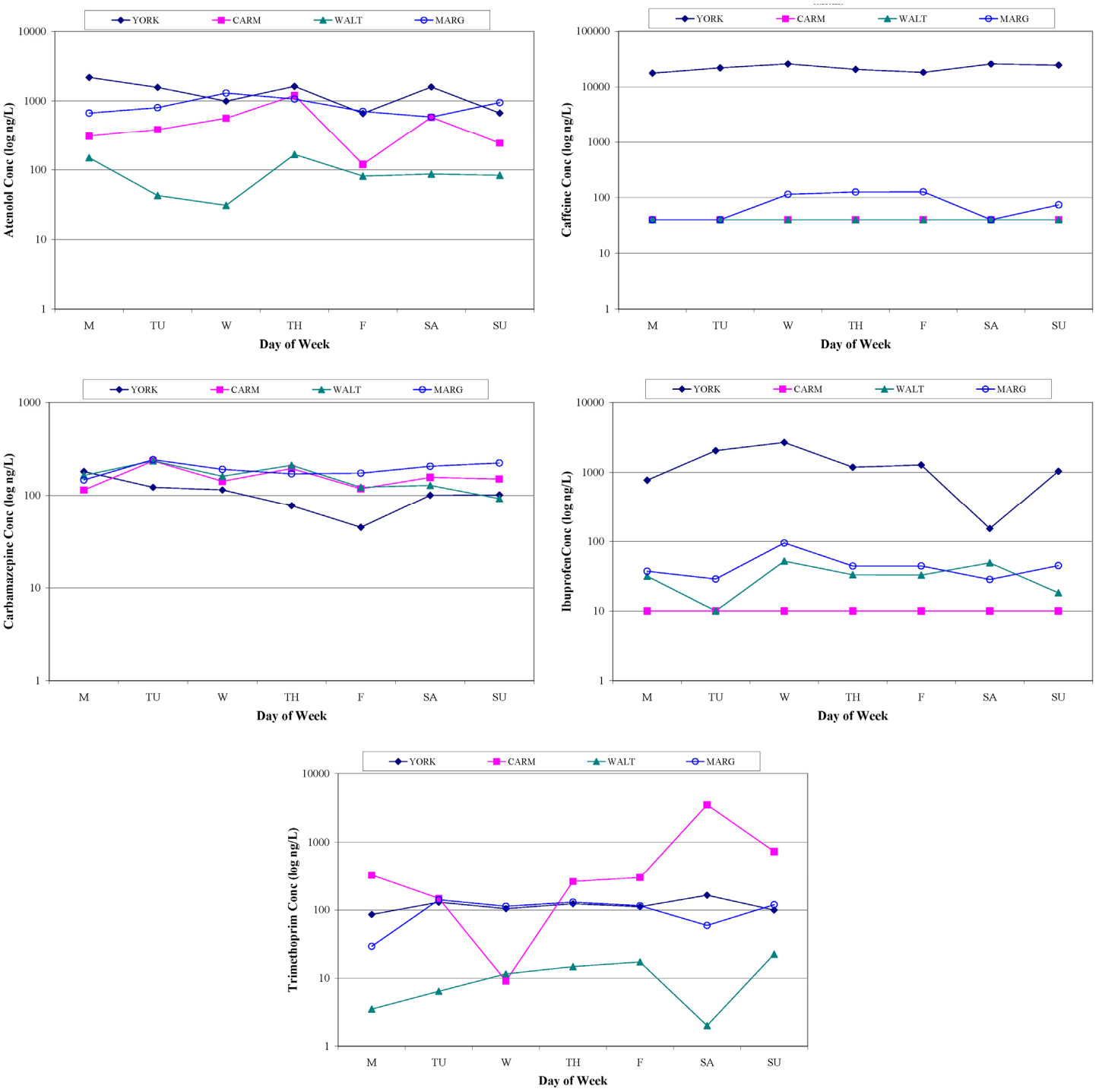


Figure 6. The Median Daily Concentrations (ng/L) of the Five Frequently Found Pharmaceuticals in the WWTP Effluents. Note that the y-axis scale for differ between some graphs. Medians were calculated from the four samples on that day of the week, along with any available duplicates (Detection limits are: 9 ng/l for atenolol, 80 ng/l for caffeine, 100 ng/l for carbamazepine, 20 ng/l for ibuprofen and 4 ng/l for trimethoprim.

Table 13. Simple Linear Correlation (Pearson R) of WWTP results and Water Quality Parameters.

	Analyte				
	atenolol	caffeine	carbamazepine	ibuprofen	trimethoprim
Yorktown					
temp	***-0.55****	***0.59****	***-0.78****	-0.28	-0.10
conductivity	0.18	-0.12	***0.59****	0.26	-0.18
DO[a]	-0.37	0.23	0.18	0.16	-0.33
pH	0.14	0.21	-0.14	0.00	-0.19
salinity	0.19	-0.16	***0.57****	0.26	-0.13
ORP[b]	0.07	0.11	***-0.68****	-0.51	0.09
Carmel					
temp	***-0.69****	-0.02	***-0.67****	-0.04	-0.20
conductivity	**-0.47**	0.00	-0.25	0.32	**0.51**
DO	***0.55****	**-0.46**	***0.77****	0.25	0.21
pH	0.03	0.02	-0.01	**0.47**	-0.30
salinity	-0.44	-0.01	-0.25	0.28	***0.57****
ORP	-0.37	0.13	***-0.65****	-0.15	-0.32
Walton					
temp	***-0.71****	-0.09	-0.24	0.21	-0.03
conductivity	0.23	-0.04	-0.06	0.10	-0.01
DO	***0.60****	-0.02	0.19	0.06	-0.03
pH	-0.12	-0.18	0.29	**0.52**	-0.15
salinity	0.21	-0.04	-0.08	0.13	0.01
ORP	-0.41	0.23	**-0.52**	***-0.67****	0.08
Margaretville					
temp	***-0.61****	0.39	***-0.67****	***0.55****	-0.12
conductivity	**0.52**	0.17	**0.45**	0.20	0.31
DO	0.01	-0.13	0.12	***-0.61****	0.03
pH	0.04	-0.25	0.13	0.03	-0.08
salinity	**0.52**	0.18	0.43	0.20	0.30
ORP	-0.10	***0.63*****	***-0.57****	0.36	-0.05

[a]DO: dissolved oxygen [b]ORP: oxidation-reduction potential
*Bolded values are significant at the p=0.01 level. Bolded and italicized values are significant at the p=0.001 level.

5.0 Discussion

5.1 QA/QC

The QA/QC data showed that we had little cross contamination (i.e. blanks were blank) and that duplicate analyses were mostly in agreement. The QA/QC work, in particular the spike samples, showed that recoveries

for the acid/neutral compounds were generally poor. However, the use of internal standards allowed for accurate quantification in this study. The recoveries for the basic compounds were acceptable.

5.2 WWTP results

Amoxicillin, cephalexin, 17α-ethinylestradiol, 17β-estradiol, sulfamethoxazole, and valproic acid were not detected in any WWTP sample, while estrone was detected once. The remaining 5 analytes were detected in most of the WWTP samples. Atenolol was found most frequently above the detection limit (94%), followed by trimethoprim (83%), carbamazepine (71%), ibuprofen (61%) and caffeine (49%). In fact, carbamazepine was present but less than the detection limit in the remaining 29% of WWTP samples.

A study of European WWTPs showed poor removal (<10%) of atenolol, carbamazepine, and trimethoprim using activated sludge (Paxéus, 2004). Italian WWTPs were not found to remove carbamazepine, while for atenolol, removal was higher in the summer than in the winter (55% vs 10%) (Castiglioni et al., 2006). Another study found measurable concentrations (ranging from 3 – 241 ng/L) in two Italian rivers (Calamari et al., 2003). Other beta-blockers, like bisprolol, metoprolol, nadolol, and propanolol have been detected in effluents and surface waters (Ternes et al., 1998; Huggett et al., 2003; Fono and Sedlak, 2005).

The caffeine results from Yorktown are interesting, as this compound was detected in every sample (range: 6490 – 37200 ng/L). In fact, the minimum concentration measured was twenty times higher than the maximum concentration detected at the other three WWTPs. It is expected that most treatment facilities substantially reduce influent concentrations of caffeine (Heberer, 2002b). If our data represent only the small residual following caffeine's degradation, it may indicate very substantial input of caffeine to the plant, or perhaps more likely, that the plant's treatment poorly degrades caffeine (as well as some of the other analytes). If the plant is operating similar to the Berlin WWTPs Heberer and Redderson (2001) reported on, there would be about 99.9% degradation of the caffeine from the influent to the effluent. Using the average caffeine concentration of 21431 ng/l found at Yorktown, this suggests that the influent to this facility contained over 21,000,000 ng/L (or 21 mg/L) during our sampling period. For comparison, brewed decaffeinated coffee has an approximate caffeine concentration of 28 mg/L and caffeinated sodas generally contain 95 – 104 mg/L of caffeine (American Beverage Association, 2005).

While the caffeine concentrations found at Yorktown were very high compared to the other plants in the study, they are at the low end of the range found by Weigel et al. (2004). These authors detected caffeine in wastewater effluent in the range 20,000 – 293,000 ng/L. Perhaps more interesting, these authors also detected concentrations of caffeine in sea water ranging from 7 – 87 ng/L in the Tromosø Sound on the Northern Coast of Norway.

It is important to note that none of the WWTPs in our study employed a biological nitrification process. This process has been shown in laboratory reactor experiments to significantly degrade trimethoprim during treatment, while other traditional process, like activated sludge, were not effective (Perez et al., 2005; Paxéus, 2004). The absence of biological nitrification processes at the WWTPs in our study (along with the low 4-ng/L detection limit) may help explain why 83% of the WWTP effluent samples had detectable trimethoprim concentrations.

Research into the removal efficiency of current wastewater treatment techniques for these compounds will be of use, especially in areas that utilize water resources without the benefit of significant dilution that NYC's

reservoir system affords. As discussed by Perez et al. (2005), common WWTP retention times of 8 – 12 hours do not provide enough time to complete elimination reactions for the antimicrobials. This would suggest that increased retention times in the treatment phase, combined with some type of detention pond, might further reduce the effluent concentrations of some compounds. However, work by Joss et al. (2005) showed only minor correlation between hydraulic retention time and compound removal efficiencies. Huber et al. (2005) suggest chlorine dioxide as a potential oxidizing agent for sulfonamide and macrolide antibiotics and estrogens, although they acknowledge reactions with ozone generally result in the shortest half-lives and cover the largest number of compounds. Recent work at Italian WWTPs by Castiglioni et al. (2006) developed winter and summer removal rates for over two dozen pharmaceuticals, including atenolol, ibuprofen, and sulfamethoxazole.

The ibuprofen concentrations seen at Yorktown are higher than what was found recently in samples from Canadian WWTPs (<25 ng/L by Miao et al., 2002; and 100 – 300 ng/L by Stumpf et al., 1999) and some Norwegian WWTPs (20 – 680 ng/L; Weigel et al., 2004), but closer to those found in Swiss WWTPs (ND - ~1300 ng/L; Tixier et al., 2003). WWTPs have been shown to remove ibuprofen efficiently, in some cases upwards of 90% removal (Joss et al., 2005), though this is considered dependent on the efficiency of the activated sludge process (Paxéus, 2004). Yorktown does not have activated sludge process, while Carmel (which had the fewest detections), does utilize this treatment technique.

Batch-scale photodegradation experiments using river water indicate that ibuprofen may have an environmental half life of 15 hours, while the half-lives of E1, E2 and EE2 are 2 – 3 hours (Yu-Chen Lin and Reinhard, 2005). The same study demonstrated rapid biological degradation of E2 to E1, and that little or no photodegradation of ibuprofen actually occurs, so the 15-hour half-life for ibuprofen is not from photodegradation. Multiple fate processes work on pharmaceuticals in the environment, which, in addition to dilution, may help explain the sporadic detections in the reservoir data.

The combination of short half lives for the estrogens, their predicted removal rates during wastewater treatment processes, small daily dose, and our detection limits (30 – 40 ng/L) may explain why we only detected E1 in one effluent sample, and E2 and EE2 not at all. At the start of the study we considered our detection limits sufficiently low to allow us to identify any potential problems based on a comparison of our detection limits and values reported in the literature. For example, in the USGS stream survey (Kolpin et al., 2002), the reported median values for 17α-ethinyl estradiol (73 ng/L), 17β-estradiol (9 ng/L), and estrone (27 ng/L) were similar to our detection limits for those compounds (39 ng/L, 40 ng/L, and 30 ng/L, respectively). Based on these data and others, we are expected to detect these analytes with a frequency similar to the USGS data (7% – 16%), especially in the WWTP effluent. However, in contrast to the USGS stream data, Heberer (2002a) suggested that WWTP effluent concentrations of EE2 should generally be less than 3 ng/L.

Using a method developed by Johnson et al. (2000) to estimate input concentrations of these estrogens, we should expect to find them at the following concentrations:

$$[\mathrm{E1}] = P/114F$$
$$[\mathrm{E2}] = P/263F$$
$$[\mathrm{EE2}] = P/1428F$$

where P is the population served by the plant and F is the flow rate of the plant. As we only have access to the effluent flow data, we will assume that it is equal to the input flow.

Using the removal rates suggested by Johnson et al. (2000) of 74%, 88%, and 85%, respectively, we would expect concentrations below our detection limits (as shown in Table 14).

Table 14. Predicted Effluent Concentrations of Estrogens (ng/L).

	estrone (E1)	17β–estradiol (E2)	17α-ethinylestradiol (EE2)
Detection Limit	30.0	40.0	39.0
Yorktown	0.8	4.1	0.2
Carmel	0.5	2.5	0.1
Walton	0.4	1.9	0.1
Margaretville	0.5	2.5	0.1

While Johnson et al. (2000) note that their estimated values proved accurate (+/- 50%) for the majority of samples, our predicted values could be off by a factor of 100 in many cases and we still would not have detected these estrogens.

Although we failed to detect some analytes that may be efficiently removed through treatment or environmental processes, we did detect carbamazepine at all four WWTPs. It has been documented that carbamazepine is resistant to degradation. One study found only an 8% difference between influent concentrations and effluent concentrations (Heberer and Reddersen, 2001), while another (Castiglioni et al. 2006) found no removal. What did surprise us was that this compound was identified in every WWTP sample, though it could be quantified in only 71% of the samples. The lowest estimated concentration was 22 ng/L. However, this compound was not detected in any reservoir sample, indicating some degradation or removal process may be at work. It is either diluted in surface waters to such an extent as to make it unidentifiable, environmental processes degrade it to an unrecognizable metabolite, or perhaps it partitions to sediment following discharge from the WWTP into surface waters.

5.3 Reservoir samples

In the reservoir samples, ibuprofen and caffeine were found above the detection limit in six (2.5%) and seven (2.9%) samples, respectively, of the 240 reservoir samples. However, it is unclear as to whether these compounds were actually present in the reservoir water or their detection was due to a sampling or sample analysis artifact. In one case, ibuprofen was detected in a DEL 18 sample at a concentration (932 ng/L) which was above those found in most WWTP effluent samples. None of the sixteen duplicate samples collected from the reservoir locations had detections of any analyte. Unfortunately, duplicate samples were not collected from these locations on the days when caffeine or ibuprofen were detected. However, during the pilot study, all samples were collected in duplicate. Of the four samples with detections of caffeine or ibuprofen, the corresponding duplicates showed nothing. This suggests these results may be an artifact of sampling or analysis, though it is strange that we did not find similar contamination in samples from the WOH locations, and that we did not detected caffeine and ibuprofen together in any reservoir sample. Accordingly, it may also suggest that there was a sampling issue that was present in the EOH that was not present in the WHO.

Ibuprofen contamination of a sample in the field is not as easily explained as caffeine contamination. Generally, ibuprofen is consumed in pill form, while caffeine is generally consumed in beverages. None of the sampling personnel reported using ibuprofen prior to or during sampling events, while if caffeine was

consumed, it was done a few hours prior to sampling events or after the daily sampling had concluded. Although we took measures to reduce the potential for introduction of these analytes by the sampling team, we can not rule the sampling team out as a potential source.

The results could be showing that caffeine and ibuprofen are intermittently distributed in the reservoir samples, given that, as seen in the Pilot Study (Appendix 3), caffeine and ibuprofen were detected in samples from the EOH reservoirs but not in samples from the WOH reservoirs. It is possible that these molecules may have adhered to particles. This may explain the caffeine concentrations found in some reservoirs, as the samples for the basic/amphoteric analytes were not filtered prior to loading onto the Carboprep cartridges, but it would not explain the ibuprofen detections, as the acid/neutral analytes were filtered.

5.4 Seasonal Variation

Aside from the behavior of atenolol, there were few consistent seasonal trends we could identify. At all locations, atenolol concentrations peaked in winter, with concentrations dropping off in the spring; at Carmel, this drop in concentration was almost 99%. Recent research indicates that WWTPs are less effective at removing atenolol in the winter than they are in the summer (Castiglioni et al. 2006). Caffeine had similar seasonal concentrations at Carmel and Margaretville, but at Yorktown and Walton, peaks were seen in the summer and fall, respectively. For carbamazepine, concentrations at all WWTPs were similar generally similar over the seasons, though they were higher in winter and spring. For ibuprofen, concentrations in Walton and Yorktown peaked in the spring, the few detections at Carmel were in the spring, and Margaretville peaked in the summer. Lower concentrations were seen in the fall. Finally, trimethoprim concentrations were similar over the seasons at Yorktown and Margaretville. Carmel peaked in the spring, and Walton peaked in the fall.

It is likely that the differences seen for some of the analytes (i.e. having a maximum and minimum during the same season at different plants) may be accounted for partially by the operational differences in the WWTPs, and/or the differences in populations from which the plants receive waste. However, this does not explain the variation seen at individual plants. For example, at Carmel, very high levels of trimethoprim were seen in the winter and spring samples, yet this compound was not detected in the fall samples, while moderate concentrations were seen in the summer. These variations could be explained by the presence of a pharmaceutical plant in the service area of the Carmel plant. Although it has not been confirmed, the possibility exists that this plant was manufacturing or packaging trimethoprim during the seasons we detected it in the effluent, but not in the fall.

5.5 Daily Variation

Little variation was seen in daily mean concentrations at the WWTPs. Most compounds at most locations were consistent over the 7-day period. Atenolol concentrations at Carmel dropped off almost 1-log from Thursday to Friday (with Thursday being the week's peak and Friday the week's trough). Ibuprofen at Margaretville was lower on the weekend than during the week. Trimethoprim peaked at Carmel on Saturday and dropped lower on Sunday, whereas at Walton, Saturday was the low point and concentrations recovered on Sunday. We are currently unable to explain these patterns.

5.6 Health significance

The New York State Sanitary Code (10 NYCRR, Part 5) establishes drinking water standards. The analytes in this survey are unspecified organic contaminants (UOC), which have a maximum contaminant level (MCL) standard of 50 micrograms per liter (μg/L, equivalent to parts per billion, ppb). None of the detections in the reservoir samples approaches this standard. There is limited information available to assess the potential for adverse effects in humans from long-term exposure to low levels of most pharmaceuticals in drinking water. Most adverse effect information for human drugs comes from reports of side effects during therapeutic use and from high-dose studies in laboratory animals. Using such existing data, preliminary estimates can be made of drinking water levels that would not be expected to have a significant increased risk of adverse effects over a lifetime of exposure. For caffeine and ibuprofen, no significant long-term adverse effects are expected at drinking water levels several hundred times higher than the highest levels of these analytes detected in the reservoir samples. For caffeine, the amount detected in one reservoir sample represents a daily drinking water exposure level that is thousands of times less than consuming either one cup of coffee (65 – 175 mg per 7 ounces) or some sodas (30 – 55 mg per 12 ounces) (Barone and Roberts, 1996).

Overall, the results from the reservoir samples indicate that the eleven analytes were not detected in most samples, even though very sensitive analytical methods were used. The few observed detections were not found in consecutive samples at any location, and were at levels well below those that would be considered to present a potential health concern from long-term exposure.

5.7 Environmental significance

The results show that selected surface waters do not have consistently detectable concentrations of the analytes. However, all WWTP effluent samples contained detectable concentrations of at least one analyte, but the actual fate of those compounds in the Watershed is unknown. None of our sampling points in the surface waters were near the point of effluent discharge. It is possible that the water column in these areas would contain detectable pharmaceutical concentrations. The WWTP results suggest that organisms living near these discharge points experience chronic exposure to low levels of the pharmaceuticals.

If the WWTPs are indeed providing a constant source of pharmaceuticals to the environment, it is possible that the sediments near these outfalls may act as a sink for some or all of these contaminants, potentially at measurable concentrations. However, we did not collect sediment samples in our study, as the design was focused on assessing the potential for these contaminants to reach the NYC distribution system via the water column. A different design would be used to evaluate the potential ecological effects.

5.8 Comparison to Pilot Study

During the June 2003 Pilot Study, duplicate samples were collected for three consecutive days at all of the locations used for the 2003-2004 study (Appendix 3). The main findings from the Pilot Study are consistent with those in this report. There was good agreement between duplicate results, except for a few results for caffeine, ibuprofen, and trimethoprim in surface water samples from EOH locations. The corresponding duplicates for these positive samples showed no agreement. As expected, all WWTP effluents were shown to

contain pharmaceuticals. Based on the results from the Pilot Study, carbamazepine was added to our targeted analyte list, as it was consistently found in the WWTP effluent samples.

The Pilot Study also looked at semi-volatile organic compounds and volatile organic compounds using traditional USEPA methods. That additional work was done for the full seasonal sampling reported here. Through those analyses, the presence of other pharmaceuticals was detected in the WWTP effluent. Those results are described in the Pilot Study report in Appendix 3.

6.0 Conclusions

Pharmaceuticals were consistently detected in the effluent of four wastewater treatment plants within the New York City Watershed. The type and concentration of analytes in the effluents differed between the plants. None of the analytes were detected in the surface waters of the West of Hudson Watershed, but there were a small number of unexplained detections in surface water samples from the East of Hudson Watershed.

Two compounds, caffeine and ibuprofen, were found infrequently in several East of Hudson reservoir samples. Their presence was not confirmed in the corresponding duplicates, which suggests they are sampling or analysis artifacts. The amount of caffeine found was thousands of times lower than what is in a cup of coffee and the amount of ibuprofen was also thousands of time less than what is found in over-the-counter medicine. The measured concentrations were well below those that may be expected to have any effect on human health. None of the other pharmaceuticals we tested for were found in the surface water samples. Possible explanations include dilution, transformation (breakdown), volatilization, and sedimentation. However, this study was not designed to determine the fate of the pharmaceuticals found in the WWTP effluent

It is expected that investigation of other wastewater treatment plants in the NYC watershed would show that their effluents are also a source of pharmaceuticals to surface waters.

As analytical methodologies and detection limits improve, these and other compounds will be found with increasing frequency in other surface waters and potable drinking water (as recently evidenced by Stackelberg et al., 2004). This is especially true given the forecasts for increasing pharmaceutical use as the age distribution of the U.S. population shifts toward elderly.

Municipalities that are considering (or have already implemented) recycling of treated wastewater need to be aware of the compounds present in the wastewater as well as their expected environmental fate. Although most water recycling is for non-potable purposes, such as irrigation on golf courses, other uses can affect potable water supplies. These projects include recharging ground water aquifers and augmenting surface water reservoirs with recycled water.

Estimates of the expected estrogen concentration in the wastewater effluent suggest that our detection limits were too high to determine their presence. In contrast, several researchers have reported finding these compounds in surface water at concentrations above our analytical detection limits.

7.0 Recommendations

The environmental fate of pharmaceutical compounds discharged to surface waters by the WWTPs should be investigated. As we have discussed, six analytes were detected in the WWTP effluents, but only two (caffeine

and ibuprofen) were detected in the reservoir samples, and even then, infrequently. One explanation for this is the tremendous amount of dilution for all pollutants (including wastewater) that occurs in the NYC reservoir system. If dilution were the explanation, it would be prudent to investigate other source water scenarios where the drinking water is drawn from a smaller source water volume and/or where treated effluent accounts for a larger proportion of the source water. Of the four WWTPs studied, any of them would be reasonable to use as a source of pharmaceuticals to help determine environmental fate

Although we have found some interesting differences between the investigated WWTPs, as well as daily and seasonal variations at the WWTPs themselves, we do not have a detailed characterization of the influents. In addition, we do not have detailed demographic information on the populations served by the WWTPs including their use of pharmaceuticals. These pieces of information would be crucial if a cradle-to-grave model of pharmaceuticals in the waste stream were to be developed.

Work on the analytical methods for some of the investigated compounds and/or other novel compounds should continue. Although we achieved exceptionally low detection limits for trimethoprim (4 ng/L) and atenolol (9 ng/L), the detection limits for other compounds were much higher, like amoxicillin (367 ng/L) and cephalexin (502 ng/L). A specific area of method development based on our work would be recovery of the analytes from the sample.

8.0 Acknowledgements

This work was funded by the USEPA under a New York City Watershed Protection Grant from the Safe Drinking Water Act. The grant was administered by the NYS Department of Environmental Conservation. We would like to thank the following people for their assistance in the design and implementation of this project: Ken Markussen, NYSDEC; Charles Cutietta-Olson, NYC Department of Environmental Protection; Patrick Phillips, USGS; and Dennis McChesney, USEPA. We would also like to thank Kirsten Lewis and her staff at the NYCDEP Grahamsville Laboratory, as well as Kimberley Mazor and other NYSDOH staff for their assistance during the sample collection phase.

9.0 REFERENCES

American Beverage Association. Caffeine Content of Beverages. Accessed August 3, 2005 at: http://www.ameribev.org/health/caffeinecontent.asp

Barone, J.J., Roberts, H.R. Caffeine consumption. *Food and Chemical Toxicology*, **1996**, *34*, 119-129.

Buser, H., Muller, M.D., Theobald, N. Occurrence of the pharmaceutical drug clofibric acid and the herbicide mecoprop in various Swiss lakes and in the North Sea. *Environmental Science & Technology,* **1998,** *32,*188.

Buser, H.-R., Poiger, T., Muller, M.D. Occurrence and environmental behavior of the chiral pharmaceutical drug ibuprofen in surface waters and in wastewater. *Environmental Science & Technology,* **1999,** *33*, 2529-2535.

Calamari, D., Zuccato, E., Castiglioni, S., Bagnati, R., Fanelli, R. Strategic survey of therapeutic drugs in the Rivers Po and Lambro in Northern Italy. *Environmental Science & Technology,* **2003**, *37*, 1241-1248.

Castiglioni, S., Bagnati, R., Fanelli, R., Pomati, F., Calamari, D., Zuccato, E. Removal of pharmaceuticals in sewage treatment plants in Italy. *Environmental Science & Technology,* **2006**, *40*, 357-363.

Fonon, L.J., Sedlak, D.L. Use of the chiral pharmaceutical propanolol to identify sewage discharges into surface waters. *Environmental Science & Technology,* **2005**, *39*, 9244-9252.

Halling-Sørenson, B., Nors Nielsen, S., Lanzky, P.F., Ingerslev, F., Holten Lützhøft, H.C., Jergensen, S.E.. Occurrence fate and effects of pharmaceutical substances in the environment - a review. *Chemosphere,* **1998,** *36*(2), 357–393.

Heberer, T., Stan, H.J. Determination of clofibric acid and N-(phenylsulfonyl)-sarcosine in sewage, river and drinking water. *International Journal of Environmental Analytical Chemistry,* **1997,** *67*(1-4), 113-123.

Heberer, T., Reddersen, K. Occurrence and fate of pharmaceutical residues in the aquatic system of Berlin as an example for urban ecosystems. In: *Proceedings of the Second International Conference on Pharmaceuticals and Endocrine Disrupting Chemicals in Water*. October 9-11, 2001, Minneapolis, Minnesota: National Ground Water Association.

Heberer, T. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. *Toxicology Letters*, **2002a**, *131*, 5-17.

Heberer, T. Tracking persistent pharmaceutical residues from municipal sewage to drinking water. *Journal of Hydrology*, **2002b**, *266*, 175-189.

Heffler, S., Smith, S., Keehan, S., Borger, C., Clemens, M.K., Truffer, C. U.S. Health Spending Projections for 2004-2014. *Health Affairs*, **2005,** W5-74 – W5-85. Web exclusive. Accessed May 10, 2005 at www.healthaffairs.org).

Hignite, C., and Azarnoff, D.L. Drugs and drug metabolites as environmental contaminants: Chlorophenoxyisobutyrate and salicylic acid in sewage water effluent. *Life Sciences*, **1977**, *20* (2), 337-341.

Huber, M.M.; Korhonen, S.; Ternes, T.A.; von Gunten, U. Oxidation of pharmaceuticals during water treatment with chlorine dioxide. *Water Research*, **2005**, *39*, 3607-3617.

Huggett, D.B., Khan, I.A., Foran, C.M., Schlenk, D. Determination of beta-andrenergic receptor blocking pharmaceuticals in United States wastewater effluent. *Environmental Pollution*, **121**, 199-205.

Joss, A.; Keller, E.; Alder, A.C.; Gobel, A.; McArdell, C.S. Ternes, T.; Siegrist, H. Removal of pharmaceuticals and fragrances in biological wastewater treatment. *Water Research*, **2005**, *39*, 3139-3152.

Kolpin, D.W., Furlong, E.T., Meyer, M.T., Thurman, E.M., Zaugg, S.D., Barber, L.B., Buxton, H.T. Pharmaceuticals, hormones, and other wastewater contaminants in U.S. streams, 1999-2000 – a national reconnaissance. *Environmental Science & Technology,* **2002**, *36*, 1202-1211.

McArdell, C.S., Molnar, E., Suter, M. J.-F., Giger, W. Occurrence and fate of macrolide antibiotics in wastewater treatment plants and in the Glatt Valley Watershed, Switzerland. *Environmental Science & Technology,* **2003**, *37*, 5479-5486.

Metcalfe, C.D., Koenig, B.G., Bennie, D.T., Servos, M., Ternes, T.A., Hirsch, R. Occurrence of neutral and acidic drugs in the effluents of Canadian sewage treatment plants. *Environmental Toxicology and Chemistry*, **2003**, *22*(12), 2872–2880.

Miao, X.-S., Koenig, B.G., Metcalfe, C.D. Analysis of acidic drugs in the effluents of sewage treatment plants using liquid chromatography–electrospray ionization tandem mass spectrometry *Journal of Chromatography A*, **2002**, *952*, 139–147

National Association of Chain Drug Stores. Table no. 122. Retail Prescription Drug Sales: 1995 to 2003. *Statistical Abstract of the United States: 2004-2005* (p. 96). Washington, D.C.: U.S. Census Bureau. Available at: http://www.census.gov/prod/www/statistical-abstract-04.html

NDCHealth Corporation. 2004 Top 10 Products by Total Prescription Count. Accessed May 9, 2005, at: http://www.ndchealth.com/press_center/uspharmaindustrydata/2004top10productsbytotalprescription.htm

New York State Department of Environmental Conservation. *Descriptive Data of Municipal Wastewater Treatment Plants in New York State*. **2004**. Albany, New York: NYSDEC.

Paxéus, N. Removal of selected non-steroidal anti-inflammatory drugs (NSAIDs), gemfibrozil, carbamazepine, β-blockers, trimethoprim, and triclosan in conventional wastewater treatment plants in five EU countries and their discharge to the aquatic environment. *Water Science & Technology*, **2004**, *50*(5), 253–260.

Physician's Desk Reference. 2005. Published by Thomson Health Care. Available at: www.pdrhealth.com.

Perez, S., Eichhorn, P., Aga, D.S. Evaluating the biodegradability of sulfamethazine, sulfamethoxazole, sulfathiazole, and trimethoprim at different stages of sewage treatment. *Environmental Toxicology and Chemistry*, **2005**, *24*, 1361-1367.

Raloff, J. Drugged waters - Does it matter that pharmaceuticals are turning up in water supplies? *Science News,* **1998,** *153*, 187-189.

Seiler, R.L., Zaugg, S.D., Thomas, J.M., Howcroft, D.L. Caffeine and pharmaceuticals as indicators of waste water contamination in wells. *Ground Water,* **1999**, *37*, 405-410.

Stackelberg, P.E., Furlong, E. T., Meyer, M.T., Zaugg, S.D. Henderson, A.K., Reissman, D.B. Persistence of pharmaceutical compounds and other organic wastewater contaminants in a conventional drinking-water treatment plant. *Science of the Total Environment,* **2004**, *329*, 99–113.

Stumpf, M., Ternes, T.A., Wilken, R.-D., Rodrigues, S.V., Baumann, W. Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil. *Science of the Total Environment,* **1999**, *225*, 135-141.

Ternes, T.A. Occurrence of drugs in German sewage treatment plants and rivers. *Water Research*, **1998**, *32*, 3245–3260.

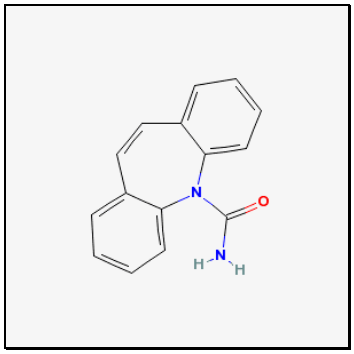
Tixier, C., Singer, H.P., Oellers, S., Muller, S.R. Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters. *Environmental Science and Technology*, **2003**, *37*, 1061-1068

Weigel, S., Berger, U., Jensen, E., Kallenborn, R., Thoresen, H., Hühnerfuss, H. Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsø/Norway with emphasis on ibuprofen and its metabolites. *Chemosphere*, **2004**, *56*, 583-592.

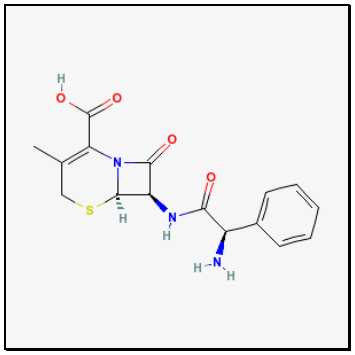
Yu-Chen Lin, A., Reinhard, M. Photodegradation of common environmental pharmaceuticals and estrogens in river water. *Environmental Toxicology and Chemistry*, **2005**, *24*, 1303-1309.

APPENDIX 1.
Chemical Structures of the Targeted Analytes.

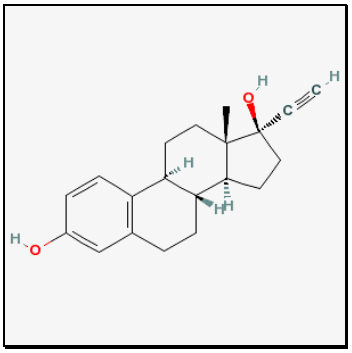
amoxicillin
CAS#: 26787-78-0



atenolol
CAS#: 29122-68-7



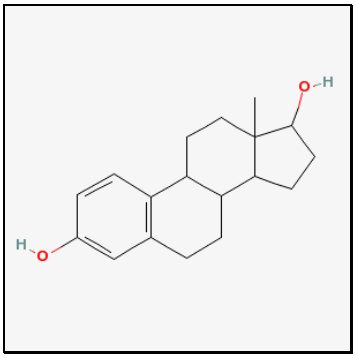
caffeine
CAS#: 58-08-2

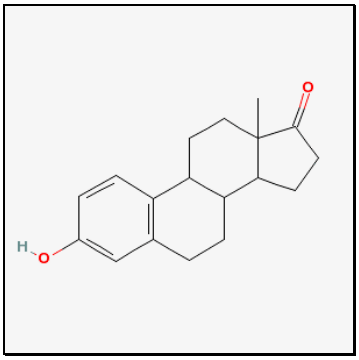


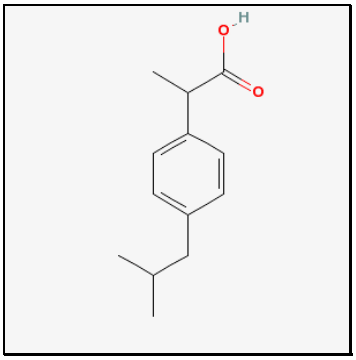
carbamazepine
CAS#: 298-46-4

cephalexin
CAS#: 15686-71-2

17α-ethinylestradiol
CAS#: 53-63-6



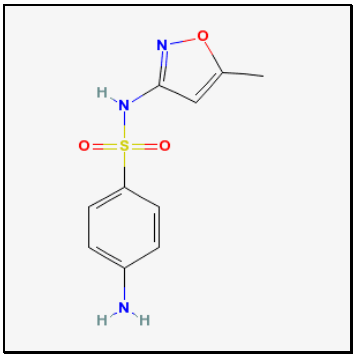


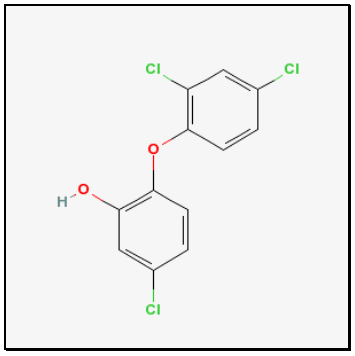


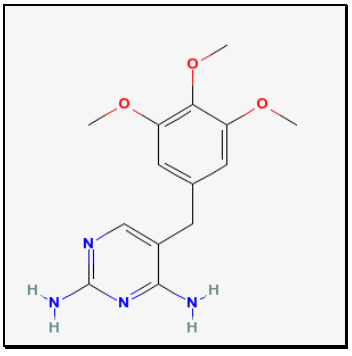
17β-estradiol
CAS#: 50-28-2

estrone
CAS#: 53-16-7

ibuprofen
CAS#: 15687-27-1





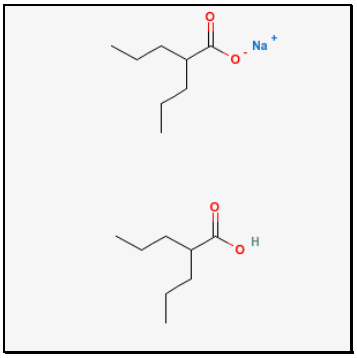


sulfamethoxazole

triclosan

trimethoprim

CAS#: 723-46-6 CAS#: 3380-34-5 CAS#: 738-70-5



valproic acid
CAS#: 99-66-1

Note: Structures available at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pccompound

APPENDIX 2.

Analyte Data for Each WWTP by Season (concentrations in ng/L)

Non-detects and values below the detection limit were assigned a value of one-half the detection limit.

Table A2-1. Ibuprofen (detection limit: 20 ng/L).

Location	Measure	Overall	Summer	Fall	Winter	Spring
Yorktown	samples	34	11	8	8	7
	detects	34	11	8	8	7
	minimum	18 PL	18 PL	158	79	4130
	median	1045	41	729	2845	5340
	mean	2598	1302	681	2873	6513
	maximum	14600	11100	1180	6520	14600
	90th	6359	1560	1075	6373	9668
Carmel	samples	30	7	8	8	7
	detects	5	1	0	0	4
	minimum	1 PL	11 PL	-	-	1 PL
	median	24	11 PL	-	-	25
	mean	19	11 PL	-	-	21
	maximum	33	11 PL	-	-	33
	90th	30	11 PL	-	-	31
Walton	samples	32	8	8	8	8
	detects	18	1	1	8	8
	minimum	26	52	57	26	53
	median	56	52	57	41	112
	mean	80	52	57	52	114
	maximum	191	52	57	136	191
	90th	144	52	57	80	169
Margaretville	samples	32	8	8	8	8
	detects	23	8	2	5	8
	minimum	22	37	32	22	35
	median	53	178	32	37	50
	mean	105	208	32	51	53
	maximum	422	422	32	114	76
	90th	325	391	32	91	70

Table A2-2. Caffeine (detection limit: 80 ng/L).

Location	Measure	Overall	Summer	Fall	Winter	Spring
Yorktown	Samples	34	11	8	8	7
	Detects	34	11	8	8	7
	Minimum	6490	13300	14400	6490	18600
	Median	20600	29600	18500	14750	24500
	Mean	21899	27355	20050	14556	23829
	Maximum	37200	37200	32600	24900	27300
	90^{th}	32330	33800	27000	20210	27060
Carmel	Samples	30	7	8	8	7
	Detects	7	0	4	3	0
	Minimum	4 PL	0	114	4 PL	-
	Median	120	-	173	98	-
	Mean	132	-	175	74	-
	Maximum	240	-	240	120	-
	90^{th}	221	-	231	116	-
Walton	Samples	32	8	8	8	8
	Detects	9	1	6	2	0
	Minimum	2 PL	111	97	2 PL	-
	Median	159	111	216	10	-
	Mean	165	111	225	10	-
	Maximum	373	111	373	18	-
	90^{th}	307	111	332	16	-
Margaretville	Samples	32	8	8	8	8
	Detects	13	8	1	4	0
	Minimum	108	117	214	108	-
	Median	215	250	214	176	-
	Mean	225	244	214	189	-
	Maximum	355	355	214	295	-
	90^{th}	323	333	214	274	-

Table A2-3. Atenolol (concentrations in ng/L).

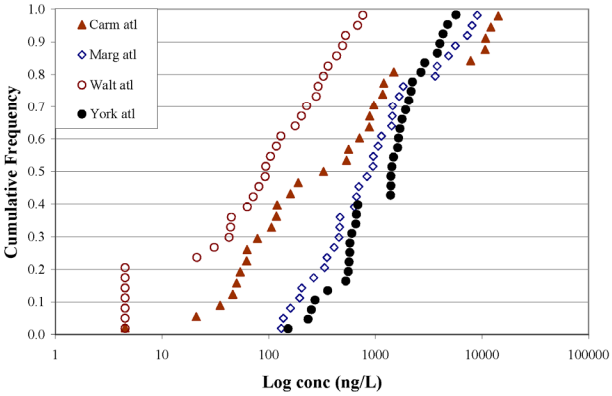
Location	Measure	Overall	Summer	Fall	Winter	Spring
Yorktown	Samples	34	11	8	8	7
	Detects	34	11	8	8	7
	Minimum	152	528	686	1400	152
	Median	1415	656	2115	3925	272
	Mean	1681	982	2045	3435	358
	Maximum	5710	1620	2910	5710	664
	90^{th}	3967	1480	2749	5052	612
Carmel	Samples	30	7	8	8	7
	Detects	28	6	8	7	7
	Minimum	21	35	326	1170	21
	Median	431	52	794	10700	106
	Mean	2337	61	758	8326	105
	Maximum	14200	118	1200	14200	189
	90^{th}	10730	90	1038	12940	172
Walton	Samples	32	8	8	8	8
	Detects	25	1	8	8	8
	Minimum	21	72	21	291	93
	Median	130	72	44	464	154
	Mean	228	72	53	484	166
	Maximum	763	72	94	763	279
	90^{th}	512	72	85	706	243
Margaretville	Samples	32	8	8	8	8
	Detects	32	8	8	8	8
	Minimum	131	700	334	1670	131
	Median	893	1008	465	5240	200
	Mean	1894	1063	751	5496	267
	Maximum	9040	1440	1820	9040	635
	90^{th}	5552	1426	1561	8368	478

Table A2-4. Trimethoprim (concentrations in ng/L).

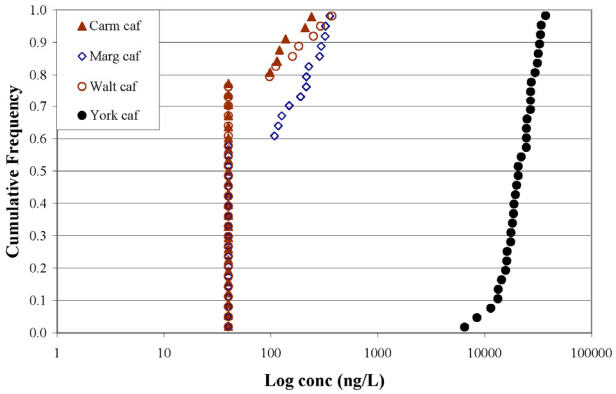
Location	Measure	Overall	Summer	Fall	Winter	Spring
Yorktown	Samples	34	11	8	8	7
	Detects	34	11	8	8	7
	Minimum	42	77	85	106	42
	Median	115	115	146	127	48
	Mean	126	112	174	146	72
	Maximum	424	147	424	246	154
	90^{th}	184	137	276	208	111
Carmel	Samples	30	7	8	8	7
	Detects	21	7	0	7	7
	Minimum	9	260	-	131	9
	Median	332	300	-	6490	566
	Mean	3502	302	-	4267	5937
	Maximum	37000	361	-	8090	37000
	90th	7780	344	-	7904	16480
Walton	Samples	32	8	8	8	8
	Detects	23	8	6	3	6
	Minimum	2	4	13	2	24
	Median	13	7	67	3	32
	Mean	31	7	75	3	32
	Maximum	153	12	153	4	41
	90th	73	8	137	3	40
Margaretville	Samples	32	8	8	8	8
	Detects	31	8	7	8	8
	Minimum	14	86	14	14	24
	Median	112	136	29	201	103
	Mean	121	139	53	190	94
	Maximum	355	175	155	355	157
	90th	270	175	114	341	135

Table A2-5. Carbamazepine (concentrations in ng/L).

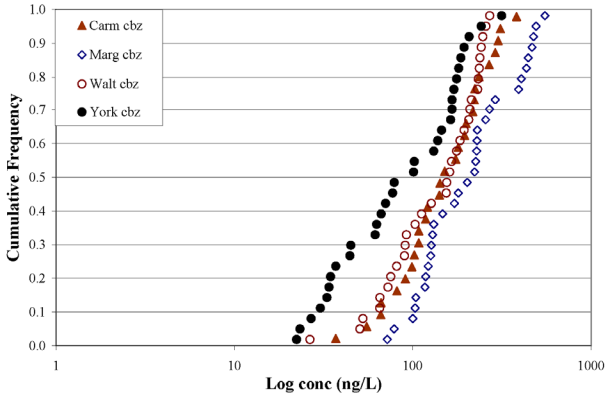
Location	Measure	Overall	Summer	Fall	Winter	Spring
Yorktown	Samples	32	11	6	8	7
	Detects	32	11	6	8	7
	Minimum	22	30	22	138	102
	Median	90	62	30	181	166
	Mean	110	55	40	200	155
	Maximum	315	79	101	315	194
	90th	193	77	67	264	186
Carmel	Samples	30	7	8	8	7
	Detects	28	7	7	7	7
	Minimum	37	66	37	180	121
	Median	147	118	82	268	199
	Mean	167	118	77	270	203
	Maximum	382	151	108	382	290
	90th	293	146	102	339	250
Margaretville	Samples	32	8	8	8	8
	Detects	32	8	8	8	8
	Minimum	72	100	72	228	180
	Median	212	120	137	455	243
	Mean	239	118	140	432	264
	Maximum	551	131	222	551	434
	90th	464	130	208	509	333
Walton	Samples	32	8	8	8	8
	Detects	32	8	8	8	8
	Minimum	27	27	51	112	127
	Median	158	70	127	220	211
	Mean	152	70	138	203	199
	Maximum	270	103	257	270	242
	90th	242	94	213	254	239



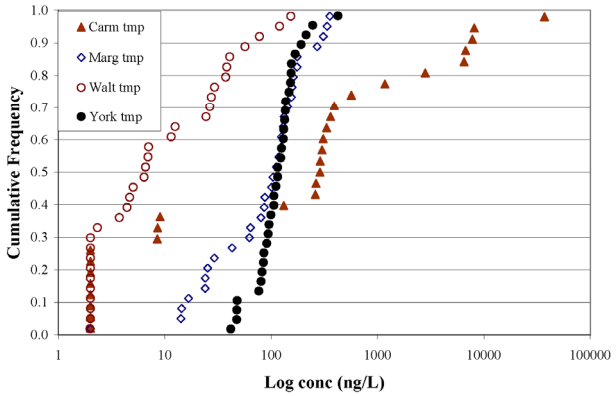
A. Atenolol



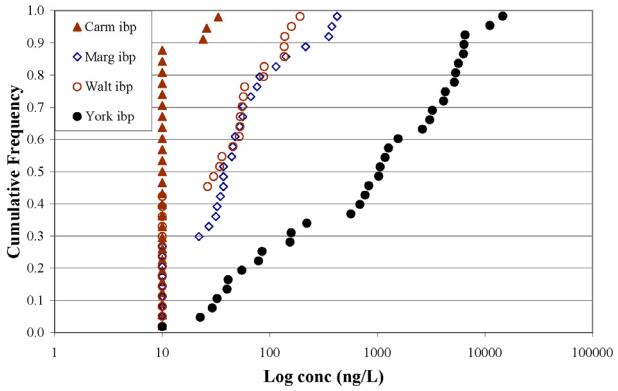
B. Caffeine



C. Carbamazepine



D. Trimethoprim



E. Ibuprofen

Figure A2-1. Cumulative Frequency Graphs of Detected Log Concentrations for Selected Analytes in WWTP effluents (detection limits in parentheses): A. Atenolol (10 ng/L); B. Caffeine (80 ng/L); C. Carbamazepine (100 ng/L); D. Trimethoprim, (4 ng/L); E. Ibuprofen (20 ng/L). Nondetects were assigned a value of half the detection limit. WWTPS: Carmel (▲), Margaretville (◇), Walton (○), Yorktown (●).

Appendix 3. Method Detection Limit Study

Appendix 4. Pilot Study Report

Appendix 5. Quality Assurance Project Plan

P:\Sections\Source Water\Pharmaceutical project\Documents\Pharm Final Rpt 060806.doc

Appendix 3. Method Detection Limit Study

New York State Department of Health
Wadsworth Center
Addendum to the Quality Assurance Project Plan for the Survey of the New York City Watershed for the Presence of Pharmaceuticals

Validation Data for Methods Involved in the Isolation and Analysis of the Selected Pharmaceutical Compounds

April 7, 2003

INTRODUCTION

The validation study was carried out by spiking seven replicate water samples with the appropriate compounds at concentrations which, based on signal-noise considerations, were judged to be approximately four times greater than the method detection limit (MDL). The MDL was then calculated at the 99 percent confidence level using the standard deviations of the analyte concentrations and the appropriate value of Students t (40 CFR-Chapter 1-Part 136). The water samples were obtained from a location upstream of the Margaretville Waste Water Treatment Plant sampling site. Analyte background signals were found only for sulfamethoxazole and trimethoprim. The background signals for these two compounds were less than ten percent of the spiking levels. The accuracy of the method was evaluated by comparing the experimentally determined analyte concentrations with the spiked concentrations. Analyte concentrations were determined by adding internal standards directly to the water samples at the same time as the analytes were added. After analysis, the analyte concentrations were determined by an isotope ratio calculation using the signals from the analyte and internal standard ions together with a response factor of the internal standard relative to the analyte. Absolute recoveries of the internal standards were determined by using recovery standards added prior to sample injection.

EXPERIMENTAL METHODS

Chemicals and Reagents

Amoxicillin, 17α-ethinylestradiol, 17β-estradiol, atenolol, cefadroxil, cephalexin, estrone, ibuprofen, sulfamethoxazole, trimethoprim, deuterium dioxide, and d_2-sulfuric acid were purchased from Sigma Chemical (St. Louis, MO, USA). Caffeine (trimethyl-$^{13}C_3$), 17β-estradiol (2,4,16,16'-d_4), isovanillic acid (ring-$^{13}C_6$), phenacetin (ethoxy-1-^{13}C), sulfamethazine (phenyl-$^{13}C_6$), valproic acid (1,2,3,3'-$^{13}C_4$), and vanillic acid (carboxyl-^{13}C) were purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Valproic acid, caffeine, and 4-methylmorpholine were purchased from Aldrich Chemical (Milwaukee, WI, USA). Practolol was purchased from Tocris (Ellisville, MO, USA). Tetroxoprim was donated by Dr. Chuck Litterst from the Division of Aids (National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA). The d_4-ibuprofen was synthesized from ibuprofen using d_2-sulfuric acid and D_2O.[1] Acetone, acetonitrile, ethyl acetate, methanol, and toluene, all HPLC-grade, were purchased from Burdick & Jackson (VWR Scientific, West Chester, PA, USA). The 88%

formic acid and the 100-200 μm mesh silica gel were purchased from Mallinckrodt Baker (Paris, Kentucky, USA). The ammonium formate was purchased from Anachemia Chemicals (Rouses Point, NY, USA). The silanizing agent, dimethyldichlorosilane, was purchased from Supelco (Bellefonte, PA, USA). The 47-mm SDB-XC discs and the Filter Aid 400 were purchased from Empore (St. Paul, MN, USA). The SDB-XC consists of poly(styrenedivinylbenzene) and has a thickness of 0.5 mm. The Carboprep 200 cartridges, with a carbon surface area of 200 m^2/g and a bed weight of 500 mg, were purchased from Restek (Bellefonte, PA, USA). The 37-53 μm mesh silica gel was purchased from Whatman (Maidstone, England).

Extraction Procedure

I. Acid/Neutral Analytes

The 2-L sample is adjusted to pH 2.5 using 88% formic acid. The SDB-XC disc is placed in a plastic housing with a piece of Whatman glass microfibre filter paper on top. Three centimeters of Empore Filter Aid 400 are added on top of the filter paper and another piece of filter paper is placed on top of the filter aid to prevent the filter aid from scattering. A Teflon gasket is placed on top of the disc, to ensure a tight seal. The disc is then placed into the J.T. Baker Speedisk Expanded Extraction Station (Mallinkrodt Baker, Paris, Kentucky, USA). The disc is conditioned with 15 ml of acetone, 15 ml of methanol, and 20 ml of pH 2.5 DDI water. The sample is then loaded onto the disc at a flow rate less than 100 ml/min by vacuum.

The disc is dried for about 3 min by high vacuum. The filter aid and filter paper are removed, and the disc is placed in a clean housing to eliminate any trapped water. The disc is then dried for 5 min by high vacuum. Next, the disc is transferred to a J.T. Baker Vacuum Manifold for elution into a scintillation vial. Three 4-ml aliquots of pH 8.5 methanol and three 4-ml aliquots of acetone are used to elute the target compounds from the disc. The sample is transferred into a Zymark tube for concentration. Lastly, the disc and plastic housing are rinsed with acetone into the Zymark tube.

A Turbovap II (Zymark, Hopkinton, MA), is used for sample concentration in both methods. The water bath temperature is 40°C and the nitrogen flow rate is 26 psi. The sample is concentrated to 150 μl, followed by the addition of 50 μl of DDI water. A final concentration of 100 μl is used for the cleanup step.

A silica gel mixture is used in the cleanup step. The silica gel is made with equal parts of 37-53 μm and 100-200 μm mesh silica gel mixed with DDI water. Two grams of this silica gel mixture are sandwiched between Pyrex glass wool in an Eppendorf autopipet tip (Eppendorf, Hamburg, Germany). The silica gel is conditioned with three 2-ml aliquots of ethyl acetate/toluene (50:50). The 100-μl sample is then loaded onto the silica gel. Next, the target compounds are eluted from the silica gel, by air pressure, with five 2-ml aliquots of toluene/ethyl acetate (85:15). The sample is concentrated to 200 μl, then 200 μl of DDI water are added. When a final volume of 200 μl is reached, the sample is transferred into a microvial insert for injection.

II. Basic/Amphoteric Analytes

In this method, all of the glassware used is silanized. The manufacturer silanized the inserts and microvials, and all other glassware is silanized in the lab. The silanizing is performed by rinsing with a solution of 10% dimethlydichlorosilane in toluene, followed by two rinses with toluene and two rinses with methanol.

The Carboprep cartridge is placed on a J.T. Baker vacuum manifold, and conditioned with 5 ml of pH 2.5 DDI water and 5 ml of pH unadjusted DDI water. The sample is loaded onto the cartridges using Teflon tubing. The vacuum is adjusted to produce a steady drip rate of about 15 ml/min. After loading, the cartridge is dried under high vacuum for 10 min. The target compounds are eluted from the cartridge into a Zymark tube with two 5-ml aliquots of pH 2.9 methanol, two 5-ml aliquots of methylene chloride/methanol (80:20), and six 5-ml aliquots of acetone.

Using the Turbovap II, the sample is then concentrated to 200 µl, followed by the addition of 500 µl of DDI water. When the final concentration of 500 µl is reached, the sample is transferred into a microvial insert for injection.

Chromatographic conditions

Chromatographic separations are carried out with an Agilent 1100 series high performance liquid chromatography instrument (HPLC) (Agilent Technologies, Palo Alto, CA, USA). The injection volumes are 10 mL for the basic analytes and 20 mL for the acidic analytes.

For the basic analytes, a mobile phase of acetonitrile and an acidic buffer of 8.7-mM ammonium formate and 10-mM formic acid (pH 3.5) are used. The gradient is from 15% organic phase to 95% organic phase in 14 min. A post run time of 6 min is used.

For the acidic analytes, a mobile phase of acetonitrile and a basic buffer of 10-mM N-methylmorpholine (pH 9.4) are used. The gradient is from 15% organic phase to 95% organic phase in 19 min. A post run time of 10 min is used.

The basic analytes are separated on an Allure Pentafluoropropyl LC column (150 x 3.2 mm I.D., particle size 5 mm; Restek, Bellefonte, PA, USA) at a 0.5 ml/min flow rate. The acidic analytes are separated on a LUNA C18 LC column (150 x 2.0 mm I.D., particle size 3 mm; Phenomex, Torrance, CA, USA) at a 0.2 ml/min flow rate.

Mass Spectrometry

An LCQ Classic quadrupole ion trap mass spectrometer (Thermo Finnigan, San Jose, CA, USA), is used as a detector. The ionization is performed by electrospray, which is used to produce negative molecular ions from the acidic analytes and positive molecular ions from the basic analytes. A single ion monitoring method is used for all of the analytes, except for amoxicillin and cephexalin, where a MS/MS method is used. An Xcalibur software package (Thermo Finnigan, San Jose, CA, USA), is used to control both the HPLC and MS.

The ESI source parameter settings are as follows: spray voltage, 4.5 kV; nitrogen sheath gas flow rate, 67 arbitrary units (au); capillary voltage, –33 V; and capillary temperature, 200°C.

Table 1. Ion Monitoring Parameters

Analytes (Internal Stds) **(Recovery Stds)**	SIM Mass	MS/MS Precursor	MS/MS Product	MS/MS Collisional Energy	Isolation Window
Amoxicillin		365.9	348.8	20%	5.0
(Cefadroxil)		365.9	346.7	20%	5.0
Caffeine	195.1				5.0
($^{13}C_3$-Caffeine)	198.2				5.0
Cephalexin		348.8	157.9	20%	5.0
(Ampicillin)		348.8	160.0	20%	5.0
Atenolol	267.1				4.0
(Practolol)	267.1				4.0
Sulfamethoxazole	254.0				5.0
($^{13}C_6$-Sulfamethazine)	285.1				5.0
Trimethoprim	291.2				4.0
(Tetroxoprim)	335.0				4.0
($^{13}C_1$-Phenacetin)	181.2				1.0
Valproic Acid	143.2				2.0
($^{13}C_4$-Valproic Acid)	147.2				2.0
Ibuprofen	204.9				2.0
(d_4-Ibuprofen)	208.1				2.0
17β-Estradiol	271.4				1.5
17α-Ethinyl Estradiol	295.5				2.0
Estrone	269.4				1.5
($^{13}C_2$-17β-Estradiol)	275.5				2.0
($^{13}C_6$-Vanillic Acid)	168.0				3.0

RESULTS AND DISCUSSION

The MDL values are shown in Tables 2 and 3 for the acid/neutral and the basic/amphoteric compounds, respectively. Seven of the eleven compounds selected for the New York City watershed survey were also included in a recent survey by the United States Geological Survey (USGS) of 139 streams in the US for the presence of 95 organic wastewater contaminants.[2] The MDL values for these seven analytes can be compared to the reporting levels (RLs) used as a measure of the detection limit in the stream survey. (It should be noted that the RL values were obtained by a variety of procedures, like instrument response and published

values, which were modified to take account of the experience of the analyst with the compounds, known interferences, and known recovery problems. Therefore, every RL value may not have been obtained as rigorously as the MDL values in the current validation study.) The MDL values can also be compared with the median and maximum concentrations found in the stream survey. These three comparisons provide a good measure of the adequacy of the methods for detecting the selected pharmaceuticals in the NYC watershed.

Of the four acid/neutral compounds which were common to both studies, ibuprofen had the lowest MDL (20 ng/L), which was comparable to the RL value found in the stream survey (18 ng/L), and considerably lower than the median (200 ng/L) and maximum values (1 μg/L) found by USGS. The three steroids, estrone, 17β-estradiol, and 17α-ethinyl estradiol, had MDL values of 30, 40, and 39 ng/L, respectively. In the USGS study, these steroids, together with fifteen other steroidal compounds, were analyzed by gas chromatography/mass spectrometry (GC/MS) methods; the RL values were all at 5 ng /L. The median and maximum values were 27 ng/L and 112 ng/L for estrone, 9.0 and 93 ng/L for 17β-estradiol, and 73 and 831 ng/L for 17α-ethinyl estradiol. Therefore, while the RL values were approximately six to eight times lower than the MDL values, the LC/MS method used in our study would have been capable of determining the median levels for estrone and 17α-ethinyl estradiol. In the case of 17β-estradiol, the LC/MS method would only have been capable of detecting the maximum concentration found in the USGS study. The remaining compound in the acid/neutral group, valproic acid, was not included in the USGS study. The MDL for this compound was relatively high (199 ng/L), as there was a closely eluting compound with a response at the same mass as the vaplroic acid $(M - 1)^-$ ion, which resulted in background interference. The interference may have been present in some of the solvents or reagents used in the sample preparation process, as it was also present in DDI water blanks.

Three of the basic/amphoteric group of compounds (caffeine, sulfamethoxazole, and trimethoprim) were also analyzed in the USGS study. Caffeine and sulfamethoxazole had MDLs of 77 ng/L and 111 ng/L, respectively, which were close to the median levels (81 ng/L and 151 ng/L) found for the same compounds in the stream survey. On the other hand, trimethoprim had a much lower MDL (4 ng/L), which was close to the RL value in the USGS study. The other three basic/amphoteric compounds, atenolol, amoxicillin, and cephalexin, had MDL values of 9.0, 367 and 502 ng/L, respectively. The low MDL for atenolol is close to the limit of detection (LOD) of 2.4 ng/L reported for the same compound in a monitoring program of pharmaceuticals in groundwater in Baden-Württemberg, Germany.[3] Atenolol was not found in any of the samples analyzed in the German study, but several other β-blockers (metoprolol, bisoprolol, and sotalol) were found in at least one sample at concentrations exceeding 10 ng/L. However, prior to starting the validation study, we did identify atenolol (393 ng/L), in addition to caffeine (125 ng/L) and trimethoprim (26 ng/L), in the effluent from a sewage treatment plant downstream from the water collection site.

Amoxicillin, but not cephalexin, was also analyzed in the groundwater monitoring study with an LOD of 4.6 ng/L. This low limit of detection was achieved by carrying out MS/MS analysis using an LC/triple quadrupole MS system. We also carried out MS/MS analysis for amoxicillin and cephalexin, but the ion trap MS appears to be a less sensitive instrument than a triple quadrupole MS; consequently, we had much higher limits of detection for the β-lactam

antibiotics. However, there were no reports of any β-lactam antibiotics being found in any of the USGS groundwater samples.

Table 4 presents data showing the agreement between the spiked concentrations for the MDL determinations and the concentrations found after analysis. The agreement with the mean analytical concentrations was excellent for six of the compounds (17β-estradiol, amoxicillin, caffeine, cephalexin, atenolol, and sulfamethoxazole), varying from -1.6% to +15%. Mean analytical results for ibuprofen, estrone, 17α-ethinyl estradiol, and trimethoprim differed from the spiked levels by -44%, -27%, -25%, and +35%. This indicates less agreement, but it is within the acceptable limits for this project. The mean analytical result for valproic acid differed by +132% as a result of the interference problems discussed previously. The data were obtained using internal standards added to the water samples prior to extraction. Therefore, these compounds were subject to all the recovery losses encountered by the analytes during the sample preparation process. It was found that the presence of matrix had differing effects on the response factors of the analytes and the surrogate internal standards, so the response factors had to be determined using cleaned-up river water rather than DDI water.

While internal standard recovery values were not required for determining analyte concentrations, they do provide information on the efficiency of the sample preparation process. These data were obtained by adding recovery standards to the extracts just prior to analysis (Table 5). For this study, the mean recovery values ranged from 36% for ^{13}C-17β-estradiol to 81% for ^{13}C-caffeine. Some of the standard deviations were large. To a considerable extent, this reflects the inherent variability associated with using a single recovery standard to determine the recovery of several internal standards. It should be emphasized that these recovery values do not enter into the calculations used to determine the analyte concentrations.

In summary, MDL values for the seven pharmaceuticals in our study which were also included in the USGS study ranged, with one exception, from the detection limits to the median concentrations found in the latter study. The one exception, 17β-estradiol, had a detection limit which was only about half the maximum concentration found in the USGS study. Currently, we are carrying out experiments to develop a considerably more sensitive technique to determine concentrations of all the acid/neutral compounds. In this procedure, the analytes will be converted to pentaflurobenzyl ethers or esters, and analyzed by negative chemical ionization (NCI) GC/MS. Of the four compounds selected for our study which were not included in the USGS study, atenolol had the lowest MDL (9.0 ng/L). This was the second lowest MDL for the entire validation study, and was comparable to the detection limit found for the same compound in a groundwater monitoring study conducted in Germany.[3] The three other compounds (valproic acid, amoxicillin, and cephalexin) had MDL values of 199, 367, and 502 ng/L, respectively. The GC/MS method described above should provide an improved MDL for valproic acid, and we hope to obtain increased sensitivity for the two β-lactam antibiotics when a new LC/triple quadrupole MS becomes operational in the laboratory in the near future. This instrument should also allow us to obtain confirmatory MS/MS data for the other analytes.

REFERENCES

1. Leis, H.J., Leis, M., and Windischofer, W. **1996**. Stable isotope labeling and determination of ketoprofen in human plasma and urine by gas chromatography/negative chemical ionization mass spectrometry. *J. Mass Spectrometry*. **31**:486-492.

2. Kolpin et al. **2002**. Pharmaceuticals, hormones and other organic wastewater contaminants in U.S. streams, 1999-2000: a national reconnaissance. *Environ. Sci. Technol.* **36**: 1202-1211.

3. Sacher, F., Lange, F.T., Brauch, H.-J., and Blankenhorn, I. **2001**. Pharmaceuticals in groundwaters. Analytical methods and results of a monitoring program in Baden-Württemberg, Germany. *J. Chromatogr. A* **938**: 199-210.

Table 2. MDL Determinations for Acidic/Neutral Compounds in NYC Water Supply Monitoring Project

(All analytes and internal standards spiked at 100 ng/L)

Analytes (Internal Standards)	Analyte Determinations in Replicates (ng/L) 1	2	3	4	5	6	7	Mean	Standard Deviation	MDL (3.14*SD)
Valproic acid (^{13}C-Valproic acid)	216	183	227	368	197	238	192	232	63	199
Ibuprofen (d_4-Ibuprofen)	53	49	51	68	60	57	56	56	6.4	20
Estrone (^{13}C-17β-Estradiol)	59	77	64	79	88	73	73	73	9.6	30
17β-Estradiol (^{13}C-17β-Estradiol)	96	87	90	122	100	86	89	96	13	40
17α-Ethinyl estradiol (^{13}C-17β-Estradiol)	69	61	64	97	82	80	73	75	12	39

Table 3. MDL Determinations for Basic/Amphoteric Compounds in NYC Water Supply Monitoring Project

Analytes (Internal Standards)	Spiking Conc (ng/L)	Analyte Determinations in Replicates (ng/L)							Mean		Standard Deviation		MDL
		1	2	3	4	5	6	7	%Rec	(ng/L)	%Rec	(ng/L)	(3.14*SD)
Amoxicillin (Cefadroxil)	1000	765	900	905	810	890	845	1130	89	892	12	117	367
Caffeine ($^{13}C_3$-caffeine)	500	515	475	500	520	463	510	460	98	492	5.1	25	80
Cephalexin (Ampicillin)	1000	800	750	1185	720	815	855	965	87	870	16	160	502
Atenolol (Practolol)	50	47	53	44	49	50	47	47	96	48	5.7	2.9	9.0
Sulfamethoxazole ($^{13}C_6$-sulfamethazine)	250	308	310	270	287	331	222	278	115	287	14	35	111
Trimethoprim (Tetroxoprim)	25	33.4	34.4	36.4	33.4	33.4	32.4	33.4	135	34	5.1	1.3	4.0

Table 4. Agreement Between Spiked and Analytical Results from NYC Water Supply Monitoring Project				
Analyte	Spiked Conc (ng/L)	Mean Analytical Concentrations (ng/L, 7 replicates)	% Difference Between Mean & Spiked Conc.	Range of % Differences Between Replicates and Spiked Conc.
Valproic acid	100	232	+132	+83 to +268
Ibuprofen	100	56	-44	-51 to -32
Estrone	100	73	-27	-41 to -12
17β-Estradiol	100	96	-4	-14 to +22
17α-Ethinyl estradiol	100	75	-25	-39 to -3
Amoxicillin	1000	892	-11	-24 to +13
Caffeine	500	492	-2	-8 to +4
Cephalexin	1000	870	-13	-28 to +19
Atenolol	50	48	-4	-12 to +6
Sulfamethoxazole	250	287	+15	-11 to +32
Trimethoprim	25	34	36	+30 to +46

The percent difference between the mean and spiked concentrations was calculated using the following formula and rounded to the nearest whole number: [(mean conc/spiked conc)- 1] x 100 = % difference

Table 5. Absolute Recovery of Internal Standards Using Recovery Standards										
Internal Standards (Recovery Standards)	Spiked Conc (ng/L)	Replicate Results (ng/L)							Mean %Rec	Standard Deviation %Rec
		1	2	3	4	5	6	7		
^{13}C-Valproic acid ($^{13}C_6$-Vanillic acid)	100	151	114	106	21	27	43	16	68	54
d_4-Ibuprofen ($^{13}C_6$-vanillic acid)	100	107	57	115	15	25	33	42	56	40
^{13}C-17β-Estradiol ($^{13}C_6$-Vanillic acid)	100	41	58	56	32	28	13	24	36	17
Cefadroxil ($^{13}C_1$-Phenacetin)	5000	2465	3930	2390	2835	3255	2430	1275	53	16
$^{13}C_3$-Caffeine ($^{13}C_1$-Phenacetin)	500	245	515	385	420	495	435	345	81	18
Ampicillin ($^{13}C_1$-Phenacetin)	500	185	395	185	315	220	220	120	47	18
Practolol ($^{13}C_1$-Phenacetin)	50	28	43	32	33	34	34	32	67	9.1
$^{13}C_6$-Sulfamethazine ($^{13}C_1$-Phenacetin)	100	37	50	41	42	41	41	38	41	4.2
Tetroxoprim ($^{13}C_1$-Phenacetin)	25	8	13	9	10	10	10	9	39	6.3

Appendix 4. Pilot Study Report

Survey of the New York City Watershed for the Presence of Pharmaceuticals
Pilot Study Progress Report

Patrick Palmer[1], Patrick O'Keefe[2], Lloyd Wilson[1], Robert Sheridan[2], and Thomas King[2]

[1]Center for Environmental Health, New York State Department of Health, Troy, NY 12180
[2]Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, NY 12201

Introduction

The New York State Department of Health is conducting a survey to determine if a select list of pharmaceuticals and hormones can be detected at keypoints in the New York City Watershed. The results are intended to address concerns documented in recent scientific and popular literature regarding the potential for contamination of surface waters by such chemicals.[1-3] The pilot study is the first of five sampling events for the survey. Its purpose was to identify any problems in the pharmaceutical analytical methodology, and, in particular, to determine the extent of agreement between results from samples collected in duplicate on the same day at each sampling site. There were eleven compounds targeted in the pharmaceutical analysis: four antibiotics (amoxicillin, cephalexin, sulfamethoxazole, and trimethoprim); three estrogens (17α-ethinylestradiol, 17β-estradiol, and estrone), an anti-epileptic/anti-psychotic (valproic acid), a beta-blocker (atenolol), an anti-inflammatory (ibuprofen), and caffeine.

The pilot study was conducted on June 10-12, 2003, at six sites East of the Hudson River (EOH) and June 24-26, 2003, at seven sites West of the Hudson River (WOH). Sampling locations are shown in Figure 1 and listed in Table 1. At each site, two 4-L grab samples were collected in succession, yielding 72 samples over both sampling periods. Water was also collected for volatile and semi-volatile organic compound analysis. All samples were stored on ice until delivery to the Wadsworth Center at the end of the field day, where they were kept in a walk-in cooler until extraction by laboratory staff. A daily field blank was used for pharmaceutical samples, and daily trip blanks were used for volatile organic compound samples. Water quality parameters (conductivity, dissolved oxygen, oxidative-reductive potential, pH, and temperature) were measured at each location during the collection using a YSI 600QS-05.

Complications at two of the sites forced us to sample at backup locations. The CATALUM site (EOH) was not accessible during the pilot study, as the building was undergoing an asbestos removal project. Since the aqueduct was being diverted around the Kensico Reservoir on those days, samples were collected further down the aqueduct at the CATLEFF location. During the first two days of the WOH sampling, the West Delaware Aqueduct (WDA), which transports water from the Cannonsville Reservoir to the Rondout Reservoir, was not operating. Samples on these two days were instead collected at the elevation taps at the Cannonsville/WDA Intake Chamber. This same water would have been flowing into the WDA had it been operating. The WDA was in operation on the third day, so that day's samples were collected at the Rondout Reservoir outlet of the aqueduct, as originally scheduled. Two bottles from the first day broke during transport to the laboratory, resulting in only one pharmaceutical sample being analyzed from two EOH sites (CROGH and DEL 17).

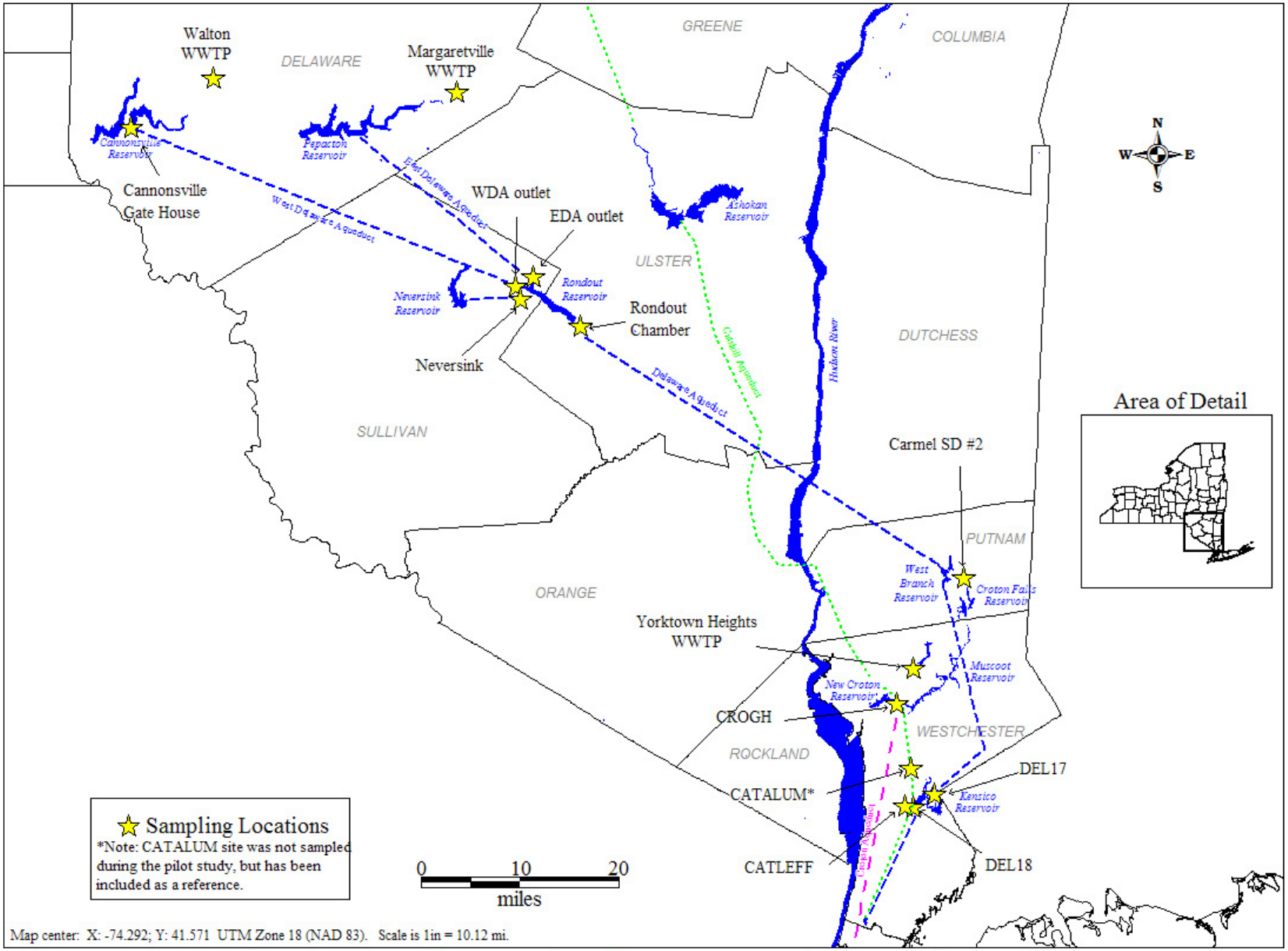


Figure 1. Sampling Locations for NYSDOH Pharmaceutical Study

Table 1. Sampling Locations for the Pilot Study.

West of the Hudson River (WOH)	East of the Hudson River (EOH)
Neversink Aqueduct at the Central Hudson Gas & Electric Building	Shaft 18 of the Delaware Aqueduct (DEL18)
Outlet of the West Delaware Aqueduct at the Rondout Reservoir (WDA)	Shaft 17 of the Delaware Aqueduct (DEL17)
Outlet of the East Delaware Aqueduct at the Rondout Reservoir (EDA)	Catskill Aqueduct Lower Effluent Chamber (CATLEFF)*
Intake of the Delaware Aqueduct at the Rondout Chamber	Croton Lake Gate House (CROGH)
Intake of the WDA at the Cannonsville Reservoir Gate House	Yorktown Heights WWTP
Walton WWTP	Carmel SD#2 WWTP
Margaretville WWTP	*CATLEFF was used in place of the Alum Building on the Catskill Aqueduct (CATALUM) due to asbestos remediation at the latter.

Analytical Methods

The acid/neutral compounds (17α-ethinyl estradiol, 17β-estradiol, estrone, ibuprofen, and valproic acid) and the basic compounds (amoxicillin, atenolol, caffeine, cephalexin, sulfamethoxazole, and trimethoprim) were extracted from separate water subsamples and analyzed by LC/MS as described in the Method Detection Limit (MDL) study. The MDL study was approved by the United States Environmental Protection Agency in May 2003 (see Appendix 1). The samples were extracted on the day following collection, and final concentration and analysis was completed by August 2003. In addition to the field blank, an internal Quality Control/Quality Assurance (QA/QC) sample was included with the batch of twelve samples undergoing extraction each day. This QA/QC sample was selected randomly from a sample group consisting of: distilled deionized water (DDI) blanks, matrix water blanks, and spikes at the MDL and three times (3x) the MDL in both DDI water and matrix water. The matrix water was collected from the East Branch of the Delaware River, at a location upstream of the Margaretville Wastewater Treatment Plant (WWTP).

Results

(a) Field and Laboratory Blanks Caffeine was detected in a matrix blank at a concentration of 91 ng/L, a result that was minimally higher than the MDL value of 80 ng/L. However, this analyte was not detected at the MDL in any of the six field blanks or in a DDI water blank. Trimethoprim, the analyte with the lowest MDL (4 ng/L), was detected in the matrix blank and two field blanks at concentrations below the MDL (2.1, 1.8, and 3.1 ng/L, respectively). No blanks had signals at the MDL for the other nine analytes.

(b) Spiked Samples The acidic/neutral group of analytes was recovered from both DDI water and matrix water spikes at concentrations close to 100% of the spike value, with only valproic acid giving an excessively high recovery. The interference observed coeluting with valproic acid at m/z=143 skewed the spike recovery for both DDI water and matrix water (Table 2). Similar results

were observed during validation, resulting in high variability for valproic acid spike recoveries, thereby giving rise to a high MDL. An alternate detection method or confirmation by a second chromatographic system may be necessary for confident detection of this compound.

All six basic/amphoteric analytes were seen in each spike, including the two β-lactam antibiotics, amoxicillin and cephalexin. Accurate quantification of some analytes was difficult. Since the LCQ LC/MS ion-trap instrument used in this project tends to have a small linear dynamic range for certain compounds, careful examination of calibration curves can reveal potential problems in quantification. Most of the six analytes in this group gave calibration curves with obvious quadratic trends. We had hoped to avoid this effect by limiting the range of standards to one order of magnitude; however, even this relatively short range proved to be too wide for linear response. Therefore, the number of curve points had to be reduced and restricted to the range close to that of the unknown. By doing this, the curve had a linear trend and was restricted to the range of interest. The calibration curves were adjusted in this way for quantification of spike results (Table 2). Figures 2A and 2B show the full curves and the truncated curves for trimethoprim. Amoxicillin was problematic, giving a low recovery for the matrix 3x MDL spike and non-detects for the DDI spike. Cephalexin and sulfamethoxazole gave higher than expected recoveries for both matrix spikes, although they seemed consistently high. However, none of the analytes that gave problematic spike results were detected in samples.

(c) Environmental Samples WWTP effluent samples accounted for the majority of detections with most of these samples containing detectable concentrations of at least three analytes. As expected, the variety of sample types resulted in the co-extraction of chromatographic interference, making the identification of all analytes difficult in every sample. Furthermore, the high concentration of several analytes necessitated sample dilution to such an extent that the respective internal standard was not identifiable. At this point, the calibration curve was extended, or external standard quantification was used. As previously mentioned, many of these samples contained analytes in such high concentrations that dilutions of up to 120x were needed. When the diluted sample was re-analyzed, the respective internal standard was not seen. This was the case with caffeine in all samples from the Yorktown WWTP. All samples from Yorktown contained atenolol and trimethoprim in concentrations requiring five-fold dilutions (Table 3a). When these dilutions were reanalyzed, the respective internal standards were still detectable and were used for quantification. In the case of ibuprofen, the calibration curve was extended in order to bring the initial sample injections into quantification range. This eliminated the need for dilution and re-analysis. The slope of the extended calibration line was very close to the slope of a calibration line constructed with the higher concentration data points (Figures 3A and 3B), but the original calibration line had a slope which was a factor of two lower (Figure 3C). For the sample Yorktown-1, the ibuprofen internal standard was not seen, but the native ibuprofen was detected. For this situation, external standard quantification was used and the results are not corrected for recovery. All other ibuprofen detects were quantified using internal standards.

For the basic compounds (atenolol, caffeine, and trimethoprim), duplicate results did not differ by more than 30%, with the exception of caffeine in samples 1 and 2 from the Carmel WWTP, where there was a 61% difference in results. Caffeine was not detected in any of the samples from the Walton WWTP, and was detected in only one sample from the Margaretville WWTP. In general, these two WWTPs, which are located in rural areas, had much lower concentrations of the basic analytes than the Carmel and Yorktown Heights WWTPs, which are located in large suburban communities.

The agreement between duplicate results was poor for ibuprofen, the only acid/neutral analyte detected in the study. We believe the reason for this is that the extractions were carried out using a single-use SPE disk holder that had been adapted for multiple sample use in our laboratory. It appears that in the case of some water samples from the WWTPs, the water was bypassing the disk, leading to incomplete extraction. On a temporary basis, the problem has been controlled by selecting single-use disk holders where the components of the disk holder fit together tightly. Our machine shop is currently manufacturing disk holders that will provide a permanent solution to the problem.

Traces of ibuprofen were also found in several samples from some of the aqueducts connecting to the reservoirs. Currently, we are carrying out additional analyses by GC/MS to determine if these signals are valid.

VOC and SVOC Analysis

In addition to the pharmaceutical analysis, a subset of samples was analyzed for volatile and semi-volatile organic compounds. Results are shown in Tables 4 and 5. These were collected on two days in the East of Hudson (June 10 and 12, 2003) and three days in the West of Hudson (June 24-26, 2003). The samples were analyzed using USEPA Methods 502.2 (VOCs) and 625 (SVOCs). In general, most analytes were not detected. Acetone was found in both samples from Yorktown (12.0 and 18.0 μg/L). MTBE was found in all three samples from Walton (28.0, 27.0, and 28.0 μg/L), as were chloroform (24.0, 25.0, and 26.0 μg/L) and traces of bromodichloromethane and dibromochloromethane. Traces of these compounds were also were detected in samples from Carmel and Yorktown. The latter three compounds are likely disinfection byproducts from chlorination during the wastewater treatment process. No traces of these compounds were found at Margaretville, where chlorine is no longer used for disinfection (the plant uses ultraviolet disinfection).

Only one compound was found above the detection limit in the standard SVOC analysis. The plasticizer bis(2-ethylhexyl)phthalate, or DEHP, was found in the June 26 sample from the Neversink Aqueduct. However, it also appeared in the corresponding laboratory blank during analysis. A number of compounds not specific to Method 625 were tentatively identified in the SVOC samples. Without having the specific standards for these non-target analytes, uncertainty exists in their identification and estimated concentration. However, the laboratory reported that there is a high probability the identifications are correct. Some of these tentatively identified compounds found in the WWTP effluent samples included: acetaminophen, camphor (decongestant/analgesic), carbamazepine (anticonvulsant), carisoprodol (muscle relaxant), cholesterol, clindomycin (antibacterial), DEET, galoxolide (fragrance), KP-140 (de-airing/antifoam agent), menthol, primidone (anticonvulsant), and valium (antianxiety). None of the listed compounds were detected in the keypoint samples or the laboratory blanks.

For the remainder of the study, VOC and SVOC samples will be collected only at the WWTPs. These analyses had originally been intended for each day of sampling, but it was determined that the laboratory would not be able to process such a large volume of samples within acceptable holding times.

Conclusions and Findings

- The agreement between duplicate field samples for basic compounds was excellent. The differences between duplicate results in some samples for ibuprofen (the only acidic compound identified in the field samples) were attributed to problems with the disk holder during extraction. These problems have now been corrected as described above.

- The concentrations of analytes in some WWTP samples were considerably higher than anticipated. Consequently, sample extracts had to be diluted up to 120x in order to maintain the instrument responses within the established calibration curves. However, we used a relatively low level of internal standard and excessive dilution resulted in the absence of any signal from the internal standards. This necessitated determining the sample concentration using an external standard. In certain instances, the calibration curve was extended to avoid sample dilution. This approach is not recommended, since the ion trap LC/MS has a very limited dynamic range.

- Laboratory spikes were prepared at the MDL and at 3x MDL in DDI water and in matrix water. At both levels and in both media, all the acid/neutral compounds, with the exception of valproic acid, showed excellent recoveries that were close to 100%. The three basic/amphoteric drugs identified in the pilot project (caffeine, atenolol, and trimethoprim) also had recoveries close to 100% for the 3x MDL spikes, although considerably higher recoveries were found in the MDL spikes. The other basic analytes had variable recoveries.

- Ibuprofen, trimethoprim, and caffeine were detected in three, two, and one keypoint samples, respectively. These findings were not confirmed in the corresponding duplicates.

- Daily sample collection at all locations for VOCs and SVOCs produced a significant burden for the laboratory. This had a negative impact on the laboratory's existing workload. It was determined that analysis of seven days of samples from all locations would not be feasible without exceeding sample holding times.

Future Work and Analyses

- In view of the much higher concentrations of caffeine, atenolol, and trimethoprim found in the WWTP samples, we plan to include higher spike concentrations (10x to 100x MDL, depending on the analyte) for the remainder of the study. A higher concentration of internal standard will enable dilutions to be performed without losing the internal standard signal. While we do plan to have duplicates for 10% of the field samples during seasonal sampling, we will also include spike duplicates as an additional measure of precision.

- Valproic acid is subject to interference, and in its place, we may want to analyze another common anti-epileptic drug, carbamazepine.

- Attempts will be made to confirm the pharmaceutical analyte detections in the keypoint samples using other analytical techniques such as GC/MS. Although rigorous steps are taken to control cross contamination from high level samples, we will determine if blanks extracted immediately after high level samples are contaminated with any of the analytes.

- Samples for VOCs and SVOCs will be collected only at the WWTPs, and only for three consecutive days. This will ensure that the laboratory's sample processing capacity is not overwhelmed samples will not exceed holding times.

References

1. Kolpin, D. W.; Furlong, E. T.; Meyer, M. T.; Thurman, E. M.; Zaugg, S. D.; Barber, L. B.; Buxton H. T. Pharmaceuticals, Hormones, and other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance. *Environ Sci Technol* **2002**, *36*, 1202-1211.

2. Daughton, C. G.; Ternes, T. A. Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change? *Environ Health Perspect* **1999**, *107 (suppl 6)*, 907-938.

3. Halting-Sørensen, B.; Nors Nielsen, S.; Lanzky, P. F.; Ingerslev, F.; Holten Lützhøft, H. C.; Jorgensen, S. E. Occurrence, Fate and Effects of Pharmaceutical Substances in the Environment- A Review. *Chemosphere* **1998**, *36 (2),* 357-393.

Table 2. Method Detection Limits and the Percent Recovery of Pharmaceuticals from Spiked Blanks (% recovery)
(*analytes in italics were detected in environmental samples*)

Analyte	Detection Limit (ng/L)	DDI water		Matrix water	
		MDL spike (%)	3x MDL spike (%)	MDL spike (%)	3x MDL spike (%)
amoxicillin	367	ND	ND	93	43
caffeine	80	279	117	261	167
cephalexin	502	101	196	400	409
atenolol	9	174	167	236	105
sulfamethoxazole	111	227	144	201	254
trimethoprim	4	225	112	189	127
valproic acid	199	157	218	150	104
ibuprofen	20	104	73	95	91
estrone	30	85	110	103	102
17β-estradiol	40	111	134	109	104
17α-ethinylestradiol	39	83	124	110	109

Notes
Matrix water was collected upstream of the Margaretville WWTP in the East Branch (Delaware River).
DDI: distilled deionized
MDL: method detection limit
ng/L: nanograms per liter
ND: not detected

Table 3a. Concentrations (ng/L) of Pharmaceuticals Found in Wastewater Treatment Plant Effluents
(analyte detection limit in parentheses)

Location	Date	Amoxicillin (367 ng/L)	Caffeine (80 ng/L)	Cephalexin (502 ng/L)	Atenolol (9 ng/L)	Sulfamethoxazole (111 ng/L)	Trimethoprim (4 ng/L)	Valproic acid (199 ng/L)	Ibuprofen (20 ng/L)	Estrone (30 ng/L)	17β-Estradiol (40 ng/L)	17α-Ethinylestradiol (39 ng/L)
Yorktown	6/10/03	ND	**21000**	ND	**883**	ND	**91**	ND	**338**	ND	ND	ND
		ND	**20200**	ND	**1250**	ND	**93**	ND	**161**	ND	ND	ND
	6/11/03	ND	**17800**	ND	**2140**	ND	**127**	ND	**26**	ND	ND	ND
		ND	**22200**	ND	**1600**	ND	**104**	ND	**127**	ND	ND	ND
	6/12/03	ND	**15800**	ND	**709**	ND	**111**	ND	ND	ND	ND	ND
		ND	**15700**	ND	**757**	ND	**116**	ND	**169**	ND	ND	ND
Carmel	6/10/03	ND	**220**	ND	**264**	ND	**495**	ND	ND	ND	ND	ND
		ND	**563**	ND	**367**	ND	**400**	ND	ND	ND	ND	ND
	6/11/03	ND	**666**	ND	**349**	ND	**383**	ND	ND	ND	ND	ND
		ND	**518**	ND	**267**	ND	**402**	ND	ND	ND	ND	ND
	6/12/03	ND	**443**	ND	**253**	ND	**455**	ND	ND	**31**	ND	ND
		ND	**391**	ND	**214**	ND	**379**	ND	**49**	ND	**48**	ND
Walton	6/24/03	ND	ND	ND	**107**	ND	ND	ND	**26**	ND	ND	ND
		ND	ND	ND	**72**	ND	ND	ND	ND	ND	ND	ND
	6/25/03	ND	ND	ND	**146**	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	**176**	ND	ND	ND	ND	ND	ND	ND
	6/26/03	ND	ND	ND	**177**	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	**154**	ND	ND	ND	**166**	ND	ND	ND
Margaretville	6/24/03	ND	ND	ND	**908**	ND	**70**	ND	**23**	ND	ND	ND
		ND	ND	ND	**824**	ND	**81**	ND	**126**	ND	ND	ND
	6/25/03	ND	ND	ND	**716**	ND	**63**	ND	ND	ND	ND	ND
		ND	**158**	ND	**847**	ND	**69**	ND	**26**	ND	ND	ND
	6/26/03	ND	ND	ND	**524**	ND	**39**	ND	**249**	ND	ND	ND
		ND	ND	ND	**854**	ND	**39**	ND	**79**	ND	ND	ND

Notes
ng/L: nanograms per liter
ND: not detected

Table 3b. Concentrations (ng/L) of Pharmaceuticals Found in East-of-Hudson Reservoir Keypoint Samples
(analyte detection limit in parentheses)

Location	Date	Amoxicillin (367 ng/L)	Caffeine (80 ng/L)	Cephalexin (502 ng/L)	Atenolol (9 ng/L)	Sulfamethoxazole (111 ng/L)	Trimethoprim (4 ng/L)	Valproic acid (199 ng/L)	Ibuprofen (20 ng/L)	Estrone (30 ng/L)	17β-Estradiol (40 ng/L)	17α-Ethinylestradiol (39 ng/L)
DEL18	6/10/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/11/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/12/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CATLEFF	6/10/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/11/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/12/03	ND	ND	ND	ND	ND	**7 SR**	ND	**304 SR**	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DEL17	6/10/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		sample was lost during transport to the laboratory										
	6/11/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/12/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CROGH	6/10/03	samples were lost during transport to the laboratory										
	6/11/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	**184 SR**	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/12/03	ND	ND	ND	ND	ND	ND	ND	**20 SR**	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Notes
DEL18: Shaft 18 of the Delaware Aqueduct at the Kensico Reservoir
CATLEFF: Catskill Aqueduct Lower Effluent Chamber at the Kensico Reservoir
DEL17: Shaft 17 of the Delaware Aqueduct
CROGH: Croton Lake Gate House
ng/L: nanograms per liter
ND: not detected
SR: suspect result

Table 3c. Concentrations (ng/L) of Pharmaceuticals Found in West-of-Hudson Reservoir Keypoint Samples
(analyte detection limit in parentheses)

Location	Date	Amoxicillin (367 ng/L)	Caffeine (80 ng/L)	Cephalexin (502 ng/L)	Atenolol (9 ng/L)	Sulfamethoxazole (111 ng/L)	Trimethoprim (4 ng/L)	Valproic acid (199 ng/L)	Ibuprofen (20 ng/L)	Estrone (30 ng/L)	17β-Estradiol (40 ng/L)	17α-Ethinylestradiol (39 ng/L)
Neversink	6/24/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/25/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/26/03	ND	ND	ND	ND	ND	**50 SR**	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
EDA	6/24/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/25/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/26/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
WDA CANN*	6/24/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/25/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/26/03	ND	ND	ND	ND	ND	ND	ND	**32 SR**	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Rondout	6/24/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/25/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	6/26/03	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Notes
EDA: East Delaware Aqueduct
WDA: West Delaware Aqueduct
CANN: Cannonsville Reservoir
ng/L: nanograms per liter
ND: not detected
SR: suspect result
*For the first two days of the pilot study, samples were collected at the WDA Intake Chamber at the Cannonsville Reservoir. The third day's samples were collected at the WDA outlet at the Rondout Reservoir.

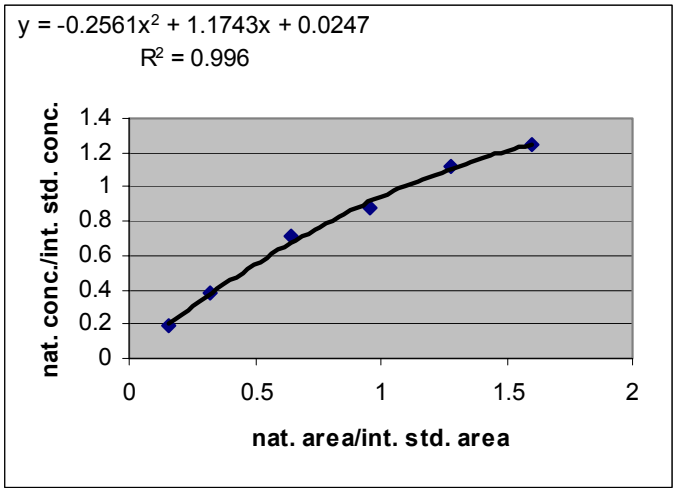


Figure 2A. Trimethoprim Calibration Curve using All Data Points

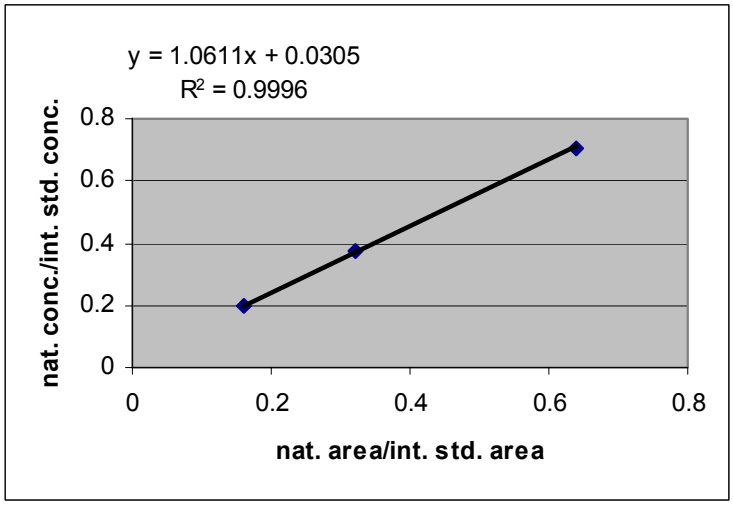


Figure 2B. Trimethoprim Calibration Curve using a Reduced Number of Data Points

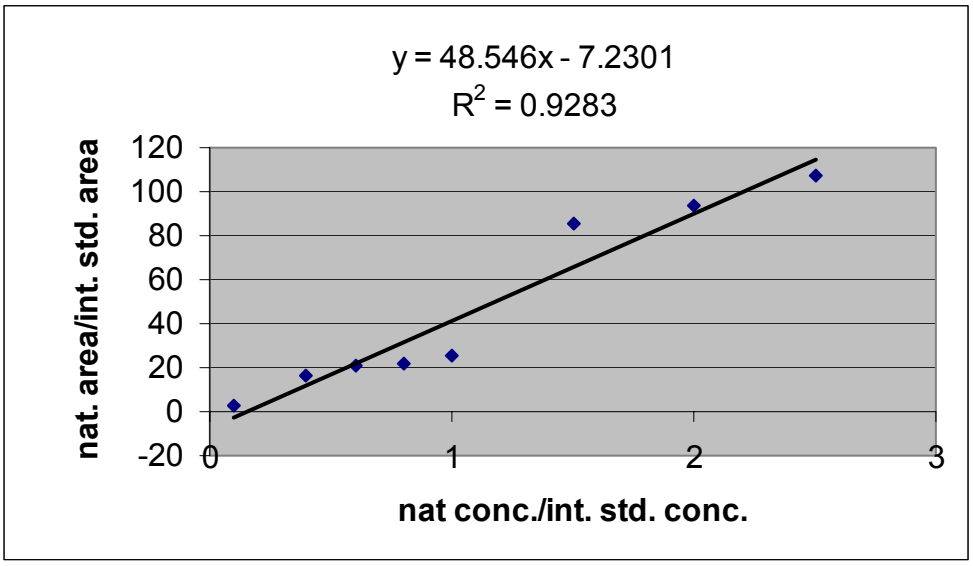


Figure 3A. Extended Calibration Curve for Ibuprofen

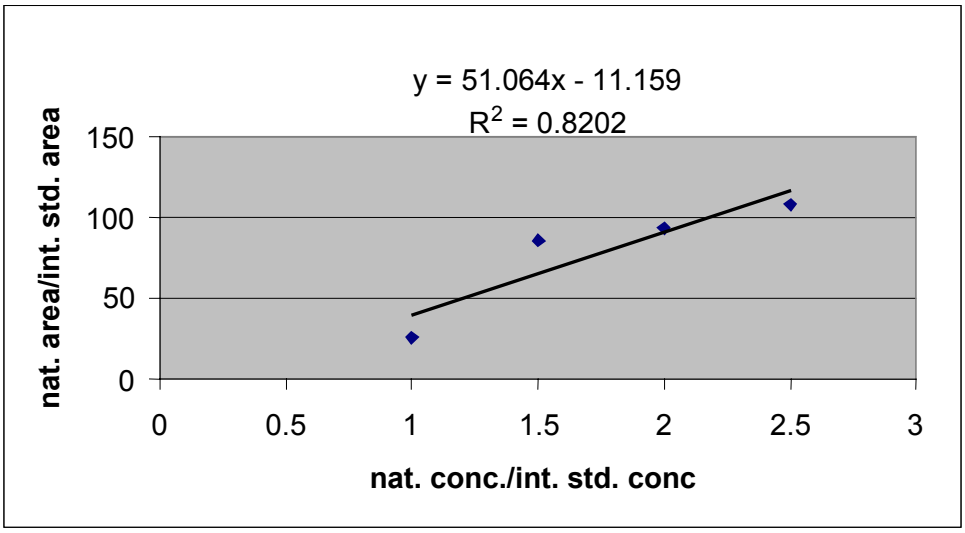


Figure 3B. Calibration Curve for Ibuprofen Using High Concentration Data Points

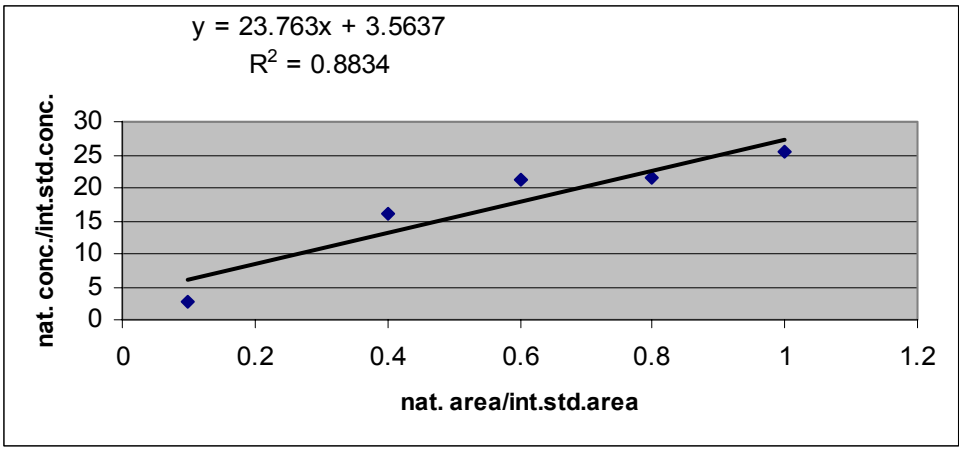


Figure 3C. Calibration Curve for Ibuprofen Using Low Concentration Data

Table 4. Concentrations of Volatile Organic Compounds in Pilot Study Samples (results are in micrograms per liter, ug/L)

	DEL18		CATLEFF		DEL17		CROGH		CARMEL		YORK		blk		Neversink			EDA			Rondout			Cannonsville		WDA	Walton WWTP			Margaretville WWTP		
ANALYTE	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03
dichlorodifluoromethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
chloromethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
vinyl chloride	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
bromomethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
chloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
trichlorofluoromethane	0.1 BJ	<10.0	0.07 BJ	<10.0	0.03 BJ	0.02 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.07 BJ	<10.0	<10.0	0.03 BJ	<10.0	<10.0	<10.0	<10.0	0.02 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,1-dichloroethene	0.2 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,1,2-trichlorotrifluoroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
carbon disulfide	0.1 BJ	<10.0	0.05 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.09 BJ	0.08 BJ	<10.0	0.1 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	0.08 J	<10.0	<10.0	0.09 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
acetone	<10.0	<10.0	3.0 J	<10.0	<10.0	2.0 J	<10.0	<10.0	<10.0	<10.0	**12.0**	**18.0**	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
methyl acetate	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
methylene chloride	<10.0	0.1 BJ	<10.0	0.1 BJ	<10.0	<10.0	0.1 BJ	0.1 BJ	0.5 BJ	0.5 BJ	3 BJ	0.3 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.3 BJ	0.4 BJ	<10.0	0.2 BJ	0.4 BJ	0.3 BJ	0.2 BJ	0.3 BJ	0.3 BJ	0.2 BJ	0.1 BJ	0.08 BJ	0.3 BJ	0.9 BJ
trans-1,2-dichloroethene	<10.0	<10.0	0.07 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.1 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
MTBE	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.2 J	<10.0	2.0 J	3.0 J	0.6 J	1.0 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	**28.0**	**27.0**	**28.0**	<10.0	<10.0	<10.0
1,1-dichloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
cis-1,2-dichloroethene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
2-butanone (MEK)	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
chloroform	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	4.0 J	3.0 J	5.0 J	5.0 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	**24.0**	**25.0**	**26.0**	<10.0	<10.0	<10.0
1,2-dichloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.4 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,1,1-trichloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
cyclohexane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
carbon tetrachloride	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
benzene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
trichloroethene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
methylcyclohexane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,2-dichloropropane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
bromodichloromethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.4 J	0.3 J	0.8 J	0.6 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	5.0 J	6.0 J	6.0 J	<10.0	<10.0	<10.0
cis-1,3-dichloropropene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
trans-1,3-dichloropropene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,1,2-trichloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
dibromochloromethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.08 J	<10.0	0.2 J	0.2 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	1.0 J	1.0 J	1.0 J	<10.0	<10.0	<10.0
bromoform	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.06 J	<10.0	0.1 J	<10.0	<10.0	<10.0
4-methyl-2-pentanone (MIBK	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
toluene	0.09 J	0.1 BJ	0.08 J	<10.0	0.06 J	<10.0	<10.0	<10.0	0.2 J	<10.0	0.8 J	3.0 BJ	0.1 J	0.1 J	<10.0	<10.0	0.2 BJ	<10.0	<10.0	<10.0	0.06 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	0.2 BJ	<10.0	0.08 BJ	<10.0	0.05 BJ	0.1 BJ
tetrachloroethene	0.1 BJ	0.1 BJ	0.1 BJ	0.07 BJ	0.08 BJ	0.03 BJ	0.1 BJ	0.09 BJ	0.5 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.09 BJ	0.09 BJ	0.1 BJ	0.08 J	0.05 BJ	0.1 BJ	0.1 BJ	0.04 BJ	0.1 BJ	0.1 BJ	0.06 BJ	<10.0	0.05 BJ	0.1 BJ	0.07 BJ	0.04 BJ	0.1 BJ
2-hexanone (MBK)	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,2-dibromoethane (EDB)	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
chlorobenzene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
ethylbenzene	0.1 BJ	0.1 BJ	0.06 BJ	0.06 BJ	0.04 BJ	0.05 BJ	0.05 BJ	<10.0	0.05 BJ	<10.0	0.06 BJ	0.2 BJ	0.07 BJ	0.07 BJ	0.1 BJ	0.07 BJ	0.05 BJ	0.05 BJ	0.06 BJ	0.04 BJ	0.09 BJ	0.09 BJ	0.05 BJ	0.2 BJ	0.3 BJ	0.08 BJ	0.09 BJ	0.04 BJ	0.06 BJ	0.04 BJ	0.04 BJ	0.05 BJ
total xylenes	0.3 BJ	0.3 BJ	0.3 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.2 BJ	2.0 BJ	0.4 BJ	0.3 BJ	0.3 BJ	0.3 BJ	0.3 BJ	0.2 BJ	0.1 BJ	0.02 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.7 BJ	1.0 BJ	0.2 BJ	<10.0	0.1 BJ	0.3 BJ	0.1 BJ	0.1 BJ	0.2 BJ
styrene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
isopropylbenzene	0.08 BJ	<10.0	0.05 BJ	<10.0	<10.0	<10.0	0.03 BJ	<10.0	<10.0	<10.0	<10.0	0.2 J	0.08 BJ	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,1,2,2-tetrachloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,3-dichlorobenzene	0.2 BJ	0.2 BJ	0.1 BJ	0.09 BJ	0.1 BJ	0.09 BJ	0.1 BJ	0.06 BJ	0.08 BJ	0.06 BJ	0.08 BJ	0.08 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.09 BJ	0.08 BJ	0.1 BJ	0.1 BJ	0.06 BJ	0.1 BJ	0.07 BJ	0.1 BJ	0.07 BJ	0.08 BJ	0.1 BJ	0.06 BJ	0.07 BJ	0.1 BJ
1,4-dichlorobenzene	0.2 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.09 BJ	0.5 BJ	0.5 BJ	0.3 BJ	0.3 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.08 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.3 BJ	0.2 BJ	0.3 BJ	0.2 BJ	0.2 BJ	0.2 BJ
1,2-dichlorobenzene	0.2 BJ	0.1 BJ	0.08 BJ	0.07 BJ	0.08 BJ	0.06 BJ	0.05 BJ	0.05 BJ	0.08 BJ	0.06 BJ	0.06 BJ	0.07 BJ	0.2 BJ	0.1 BJ	0.1 BJ	0.1 BJ	0.09 BJ	0.1 BJ	0.07 BJ	0.06 BJ	0.08 BJ	0.08 BJ	0.03 BJ	0.07 BJ	0.04 BJ	0.06 BJ	0.07 BJ	0.06 BJ	0.1 BJ	0.05 BJ	0.05 BJ	0.09 BJ
1,2-dibromo-3-chloropropane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0
1,2,4-trichlorobenzene	0.3 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.2 BJ	0.1 BJ	0.09 BJ	0.1 BJ	0.1 BJ	0.09 BJ	0.1 BJ	0.1 BJ	0.4 BJ	0.3 BJ	0.2 BJ	<10.0	0.2 BJ	0.2 BJ	0.1 BJ	0.06 BJ	0.1 BJ	<10.0	0.06 BJ	0.09 BJ	<10.0	0.1 BJ	0.1 BJ	0.06 BJ	0.2 BJ	0.1 BJ	0.08 BJ	0.2 BJ

Notations:
J: estimated value
B: analyte found in assoicated blank as well as sample
BJ: analyte found in associated blank as well as sample AND estimated value

Table 5. Concentrations of Semivolatile Organic Compounds in Pilot Study Samples (results are in micrograms per liter, ug/L)

	DEL18		CATLEFF		DEL17		CROGH		Carmel SD #2		Yorktown WPCP		Neversink			EDA			Rondout			Cannonsville		WDA	Walton WWTP			Margaretville WWTP		
ANALYTE	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/10/03	6/12/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03	6/24/03	6/25/03	6/26/03
phenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.2 J	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
benzaldehyde	<10.0	<10.0	<10.0	0.05 J	<10.0	<10.0	<10.0	<10.0	0.2 J	0.3 J	0.3 J	0.8 J	<9.0	<9.0	<10.0	0.03 J	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.4 J	0.2 J	0.1 J	0.1 J	0.09 J	<10.0
bis(2-chlorethyl)ether	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2-chlorophenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2-methyl phenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.03 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2,2'-oxybis(1-chloropropane)	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
4-methyl phenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.4 J	0.5 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
n-nitrosodi-n-propylamine	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
hexachloroethane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
nitrobenzene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
isophorone	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2-nitrophenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2,4-dimethylphenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.07 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
bis(2-chloroethoxy) methane	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2,4-dichlorophenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.07 J	0.1 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
naphthalene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.03 J	0.1 J	<9.0	<9.0	0.01 BJ	<9.0	0.007 BJ	<10.0	<9.0	<9.0	<10.0	0.009 BJ	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
4-chloroaniline	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
hexachlorobutadiene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
caprolactam	<10.0	0.7 J	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.07 J	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
4-chloro-3-methylphenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2-methylnaphthalene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.02 J	0.04 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
hexachlorocyclopentadiene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2,4,6-trichlorophenol	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.06 J	<10.0	<10.0	0.03 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
1,1'-biphenyl	0.08 BJ	0.06 BJ	0.05 BJ	0.1 BJ	0.07 BJ	0.1 BJ	0.06 BJ	0.09 BJ	0.06 BJ	0.09 BJ	0.07 BJ	0.1 BJ	0.05 BJ	0.05 BJ	0.05 BJ	0.07 BJ	0.05 BJ	0.09 BJ	0.04 BJ	0.05 BJ	0.07 BJ	0.06 BJ	0.04 BJ	0.07 BJ	0.05 BJ	0.03 BJ	0.05 BJ	0.07 BJ	0.05 BJ	0.06 BJ
2,4,5-trichlorophenol	<24.0	<10.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
2-chloronaphthalene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2-nitroaniline	<24.0	<10.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
dimethylphthalate	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	0.07 J	<9.0	<9.0	<10.0
acenaphthylene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
2,6-dinitrotoluene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.5 J	0.4 J	0.7 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.1 BJ	<9.0	0.1 J	<24.0	<24.0	<24.0
3-nitroaniline	<24.0	<10.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
acenaphthene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	0.01 BJ	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.007 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
2,4-dinitrophenol	<24.0	<10.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
4-nitrophenol	<24.0	<10.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
dibenzofuran	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.005 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
2,4-dinitrotoluene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
diethylphthalate	0.06 BJ	0.04 BJ	0.2 BJ	0.09 BJ	0.1 BJ	0.05 BJ	0.3 BJ	0.06 BJ	0.3 BJ	0.1 BJ	0.5 BJ	0.7 BJ	0.06 BJ	0.02 BJ	0.02 BJ	0.03 BJ	0.02 BJ	0.03 BJ	0.03 BJ	0.02 BJ	0.02 BJ	0.1 BJ	0.1 BJ	0.04 BJ	0.04 BJ	0.02 BJ	0.02 BJ	0.02 BJ	0.02 BJ	0.02 BJ
4-chlorophenyl phenyl ether	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
fluorene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
4-nitroaniline	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
2-methyl-4,6-dinitrophenol	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
n-nitrosodiphenylamine	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.3 J	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	0.08 J	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
4-bromophenyl phenyl ether	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
hexachlorobenzene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
atrazine	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	0.07 J	0.05 J	0.05 J
pentachlorophenol	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<25.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<47.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0	<24.0
phenanthrene	0.01 J	<10.0	<10.0	<10.0	<10.0	<10.0	0.02 J	<10.0	<10.0	<10.0	<10.0	0.02 J	<9.0	<9.0	0.007 J	<9.0	0.007 BJ	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
anthracene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.008 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
carbazole	<10.0	<10.0	0.02 J	<10.0	<10.0	<10.0	0.01 J	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.05 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
di-n-butyl phthalate	0.9 BJ	0.2 BJ	0.3 BJ	0.8 BJ	0.6 BJ	0.2 BJ	0.4 BJ	0.2 BJ	0.7 BJ	0.4 BJ	0.4 BJ	0.6 BJ	0.04 BJ	0.06 BJ	0.1 BJ	0.05 BJ	0.01 BJ	0.09 BJ	0.04 BJ	0.09 BJ	0.09 BJ	0.9 BJ	1.0 BJ	0.1 BJ	0.07 BJ	0.1 BJ	0.08 BJ	0.05 BJ	0.07 BJ	0.08 BJ
fluoranthene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.03 J	<9.0	<9.0	0.008 J	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.02 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
pyrene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.03 J	<10.0	<10.0	<10.0	<10.0	0.09 J	<9.0	0.01 BJ	0.03 J	<9.0	<9.0	0.009 J	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	0.02 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
butyl benzyl phthalate	0.2 BJ	0.4 BJ	0.2 BJ	0.2 BJ	0.1 BJ	0.06 BJ	0.7 BJ	0.1 BJ	0.3 BJ	0.2 BJ	9.0 BJ	0.2 BJ	0.03 BJ	0.01 BJ	0.02 BJ	0.05 BJ	0.03 BJ	0.02 BJ	0.01 BJ	0.02 BJ	0.02 BJ	<9.0	0.09 BJ	0.02 BJ	0.03 BJ	0.05 BJ	<10.0	<9.0	0.04 BJ	0.03 BJ
3,3'-dichlorobenzidine	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
benzo(a)anthracene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	0.02 J	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
chrysene	<10.0	<10.0	<10.0	0.01 J	<10.0	<10.0	0.02 J	<10.0	0.04 J	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	0.01 BJ	<9.0	<9.0	<10.0	<9.0	0.01 BJ	<10.0	0.03 BJ	<9.0	<10.0	<9.0	<9.0	<10.0
bis(2-ethylhexyl)phthalate	0.4 BJ	0.3 BJ	0.3 BJ	0.5 BJ	0.4 BJ	0.8 BJ	0.3 BJ	0.7 BJ	0.6 BJ	0.8 BJ	0.4 BJ	8.0 BJ	0.2 BJ	0.1 BJ	**36.0 B**	0.2 BJ	0.4 BJ	0.3 BJ	0.09 BJ	0.5 BJ	0.2 BJ	0.3 BJ	0.6 BJ	0.2 BJ	0.2 BJ	0.3 BJ	0.1 BJ	0.2 BJ	0.6 BJ	0.2 BJ
di-n-octyl phthalate	<10.0	<10.0	<10.0	0.03 BJ	<10.0	0.06 BJ	0.03 J	<10.0	<10.0	0.04 BJ	<10.0	<10.0	<9.0	<9.0	1.0 BJ	<9.0	0.02 BJ	0.01 BJ	<9.0	0.02 BJ	0.01 BJ	<9.0	0.03 BJ	0.006 BJ	0.03 BJ	0.01 BJ	0.004 BJ	0.008 BJ	0.03 BJ	0.01 BJ
benzo(b)fluoranthene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
benzo(k)fluoranthene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
benzo(a)pyrene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
indeno(1,2,3-cd)pyrene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
dibenz(a,h)anthracene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0
benzo(ghi)perylene	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0	<9.0	<19.0	<10.0	<9.0	<9.0	<10.0	<9.0	<9.0	<10.0

Notations:
J: estimated value
B: analyte found in associated blank as well as sample
BJ: analyte found in associated blank as well as sample AND estimated value

Appendix 5. Quality Assurance Project Plan

09/04/2003

1. Title and Approval Page

Survey of the New York City Watershed
For the Presence of Pharmaceuticals

Project Manager Signature:

Signature:_____ Date:_____

Approved by:
Center for Environmental Health
New York State Department of Health:

Signature:_____ Date:_____

Signature:_____ Date:_____

Approved by:
Wadsworth Center
New York State Department of Health:

Signature:_____ Date:_____

Quality Assurance Officer:

Signature:_____ Date:_____

Approved by:
Division of Water, New York State Department of Environmental Conservation:

Signature:_____ Date:_____

Quality Assurance Officer

Signature:_____ Date:_____

2. Project Description

This project is a survey of surface waters in the New York City watershed for the presence of pharmaceutically active compounds. The results are intended to address concerns documented in recent scientific and popular literature regarding the potential for contamination of potable water by these products. We will determine if detectable levels of selected analytes are present at multiple locations in the New York City (NYC) Delaware, Catskill, and Croton water supplies, including the points of intake for NYC's drinking water distribution system, effluents of waste water treatment plants, and inlets and outlets of intermediate reservoirs. There will be five sampling events for this project. The first will be a three-day preliminary sampling at all locations. The remaining events will involve collection of samples in each of the four seasons, with sampling occurring for seven consecutive days at each location.

The most important measure of the project's success is the reliability of our sampling and measurements, so that we can adequately address citizen concerns. We believe completeness is one indication of reliability and our goal is to have 90 percent of our samples to meet quality assurance and quality control objectives. We are working to have no false positives or false negatives, each being equally undesirable, and will consider more than 10 percent unacceptable. (See Section 10 for discussion of potential corrective actions.) We will compare the data to NYS public drinking water standards, which, for unspecified organic compounds, is 50 micrograms per liter (μg/L). (This standard does not apply to wastewater treatment plant effluents, and will therefore only be used as a reference.) For each compound, we will also compare the data to the manufacturer's defined daily dose and the results of other similar research in surface waters. Survey results will be summarized in a report and provided to the US Environmental Protection Agency (USEPA), NYC Department of Environmental Protection (NYC DEP), New York State Department of Environmental Conservation (NYS DEC), local municipalities, and other interested parties.

We believe it is unlikely that we will find any of our analytes at the intakes of NYC's drinking water distribution system because of dilution and degradation in the reservoir system. However, based on published research in this field, and the data gathered in the method validation study (see Addendum), we do expect to detect some analytes in the effluent of the selected wastewater treatment plants (WWTP) at levels below the drinking water standard previously discussed.

3. Technical Design

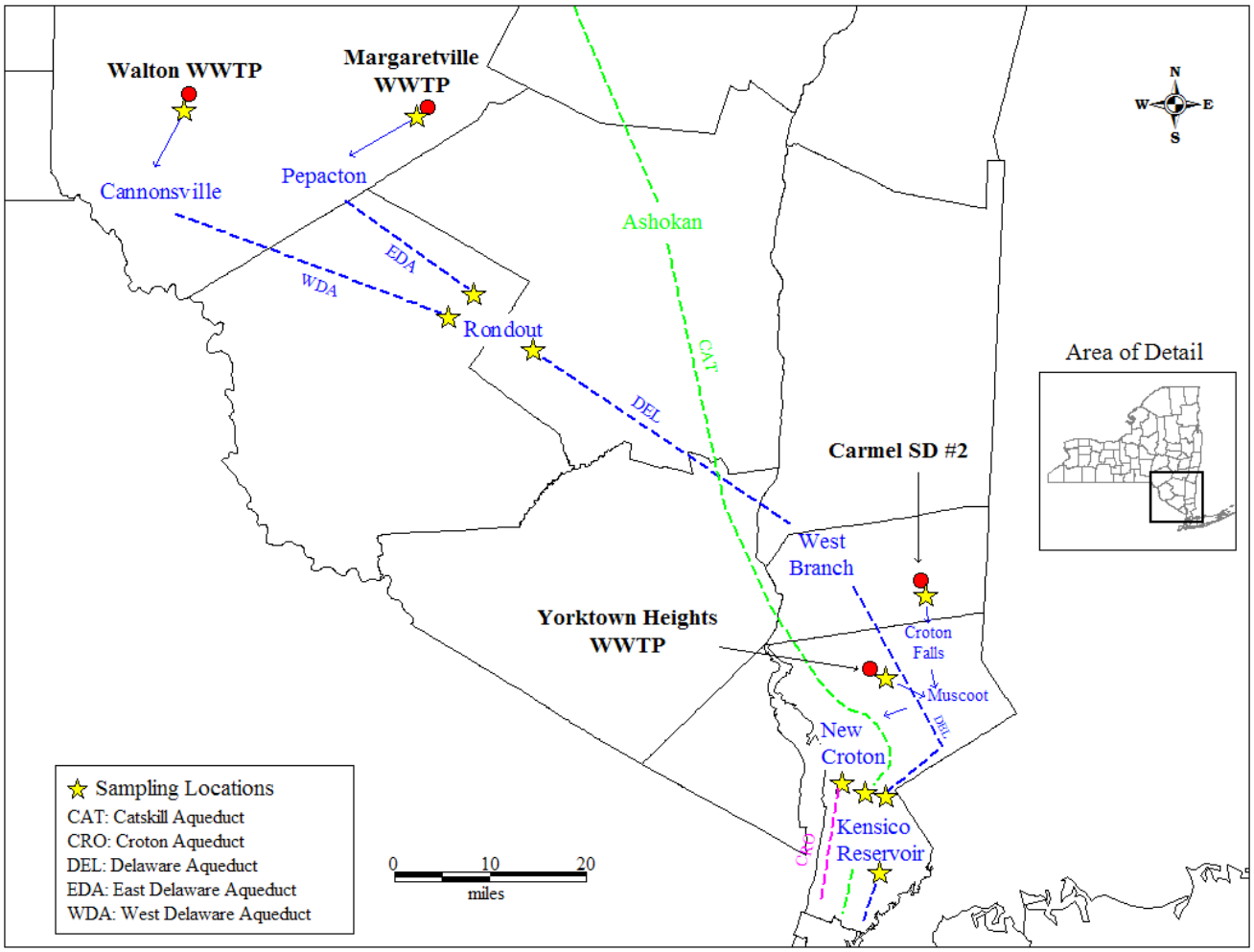
The sampling strategy will evaluate potential sources of pharmaceutically active compounds in the waters of the NYC Delaware, Catskill, and Croton supplies, and test the water as it enters the NYC distribution system. This strategy was chosen so that we can evaluate the potential pharmaceutical input for the watershed and the quality of water entering the distribution system. The compounds we will analyze for are: amoxicillin, atenolol, caffeine, cephalexin, estrone, ibuprofen, 17α-ethinylestradiol, 17β-estradiol, sulfamethoxazole, trimethoprim, and valproic acid (a derivative of Depakote®).

We selected our analytes based on a qualitative assessment of the following: quantity of the pharmaceuticals used; human metabolism of the pharmaceutical; extent of degradation in sewage treatment facilities and environment (½ life); analytical methodology; and what other researchers have found in the environment. We believe we have maximized the possibility of finding pharmaceuticals by selecting those that are consumed in large quantities, are poorly metabolized, have low rates of degradation, and have been found in the environment by other studies. No evaluation is being made of the effect of additives to the water supply (e.g. chlorine) on the target compounds.

Sampling will take place quarterly, to account for possible seasonal variation in pharmaceutical load, types of pharmaceuticals in use (e.g., allergy or cold medications), and the biodegradation efficiency of both

environmental processes and the selected WWTPs (which may fluctuate with temperature and/or water volume).

Figure 1. Sampling Locations for Pharmaceutical Study



Sampling will be conducted at three types of locations in the watershed (Figure 1): WWTPs, inlets and outlets of intermediate reservoirs, and the outlets of the terminal reservoirs (which are also the intakes to the NYC drinking water distribution system). Sample locations at WWTPs were selected to assess input of pharmaceuticals into the watershed. Sampling at both inlets and outlets of a reservoir may allow us to evaluate if they have a significant role in pharmaceutical processing. Finally, samples taken at the intake to the NYC distribution system (where water exits the terminal reservoirs) will show if detectable levels of the analytes enter the potable water supply.

The four WWTP outfalls selected for sampling are listed below, and include facilities in both the East-of-Hudson (EOH) and West-of-Hudson (WOH) watersheds. Treatment plant capacity, customer base (e.g. hospitals), and plant location were considered when selecting potential sampling points. We have targeted WWTPs that treat waste from a hospital (Margaretville and Carmel) and one that treats waste from a dairy facility (Walton).

Our current sampling plan is to divide the water supply system into two sampling areas, due to the impracticality of daily sampling over such a large area. Thus, sampling in the EOH and WOH watersheds will take place during separate weeks. Sampling for the WOH watershed will consist of the following six locations:

1. water flowing through the Neversink Aqueduct at the Central Hudson G & E Building;
2. the outfalls of the East and West Delaware Aqueducts at Rondout Reservoir (from the Pepacton and Cannonsville Reservoirs, respectively);
3. water exiting the Rondout Reservoir (the intake to the Delaware Aqueduct);and
4. the outfalls of two WWTPs (Margaretville and Walton, which discharge into waters that flow into the reservoirs at Pepacton and Cannonsville, respectively).

Sampling for the EOH watershed will consist of the following six locations:

1. the outfalls of two WWTPs (Carmel SD #2 and Yorktown Heights, which discharge into the Croton Falls and Muscoot Reservoirs, respectively;
2. at the CATALUM site on the Catskill Aqueduct;
3. exiting the New Croton Reservoir at the New Croton Lake Gate House (CROGH);\
4. entering the Kensico Reservoir at shaft #17 (DEL 17; from Rondout and West Branch Reservoirs via the Delaware Aqueduct); and
5. exiting the Kensico Reservoir at shaft #18 (DEL 18).

During the preliminary sampling in the WOH watershed, the West Delaware Aqueduct was offline (not flowing into Rondout) for two of the three sampling days. For those two days, samples were collected from the Cannonsville Reservoir effluent chamber. It is anticipated that this situation may happen again during the study for any of the three aqueduct locations. Therefore, if an aqueduct is offline, we will attempt to collect samples from its originating reservoir (either Cannonsville, Pepacton, or Ashokan).

Field blanks will be analyzed for each sampling day. Four liters of distilled deionized water will be carried into the field, transferred into another sample bottle, and transported back to the laboratory. Field blanks will allow us to assess the potential for field and laboratory contamination of samples. Finding analytes in field blanks will suggest that false positive results are possible. During the preliminary sampling, duplicate samples will be collected at each of the 11 sampling locations for 3 days (33 duplicates, 66 samples) to assess reproducibility. During the seasonal sampling events, duplicate samples will be collected on days 1, 3, 5, and 7 (32 duplicates; 16 each for EOH and WOH). The specific EOH and WOH locations for duplicate sampling will be determined with the results of the preliminary study. Preference will be given to sites with good detection of the analytes. In summary, we will collect 33 sets of duplicate samples (66 samples total) in the pilot study, and 32 sets of duplicates (64 samples total) during the four-season survey. (See Table 1 in Section 6 for more on the sampling schedule.)

4. Project Organization and Responsibility

Project Management- Responsible for all aspects of the project including sampling, analysis, reporting (written and public presentations).

Mr. Lloyd R. Wilson, Ph.D.
Section Chief, Special Assessment Section

Bureau of Toxic Substance Assessment
New York State Department of Health
518-402-7810

Oversight of Sample Collection and Field Measurements
Mr. Patrick Palmer
Research Scientist, Special Assessment Section
Bureau of Toxic Substance Assessment
New York State Department of Health
518-402-7810

Field Work
1 person in Dr. Wilson's section (to be hired)

Oversight of Sample Analysis and Reporting
Mr. Patrick O'Keefe, Ph.D.
Principal Investigator, Dioxin Analysis Laboratory
Laboratory of Organic Chemistry
Wadsworth Center
New York State Department of Health
518-473-3378

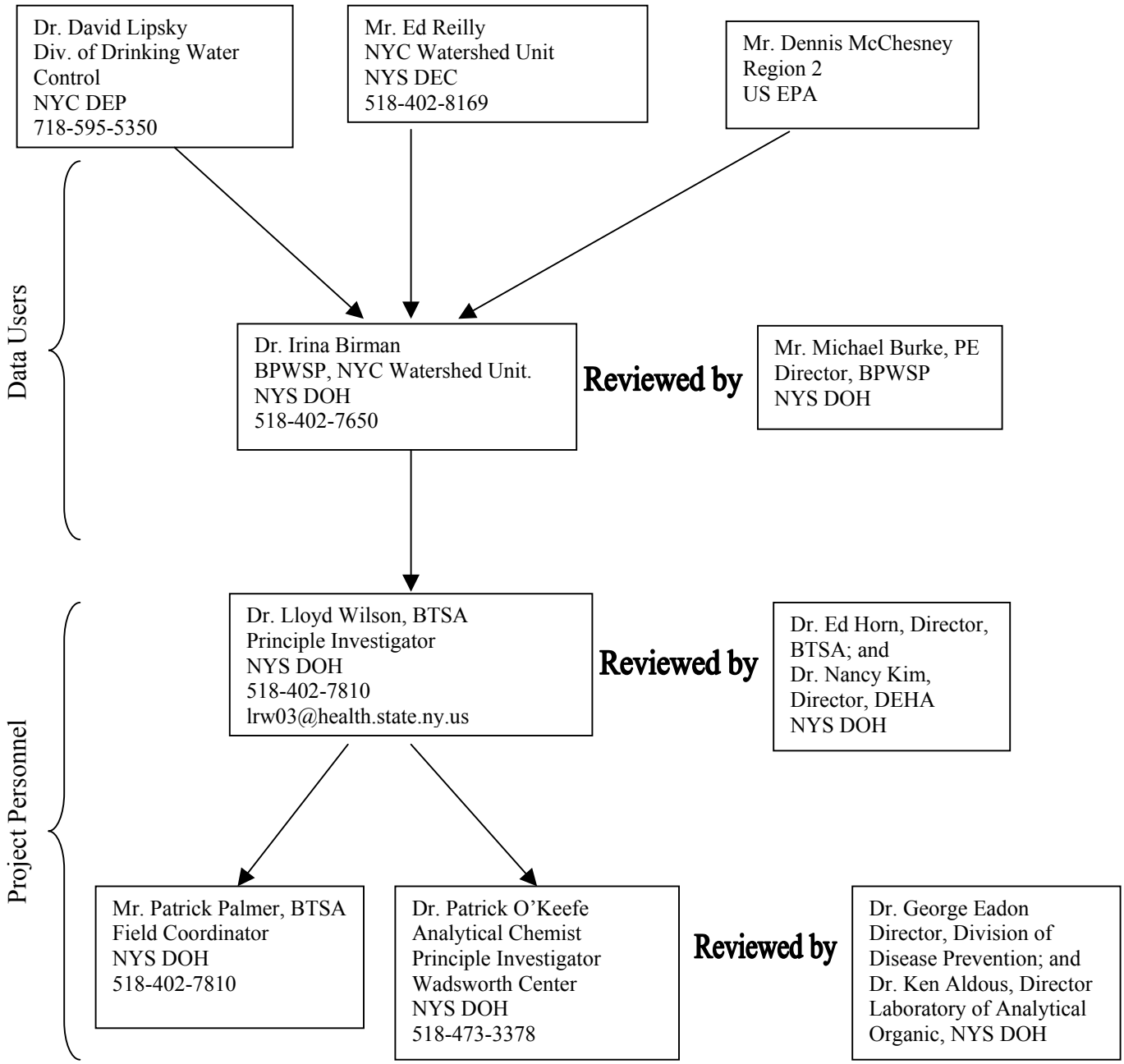
Sample Analysis
Mr. Robert Sheridan
Research Scientist
Mr. Thomas King
Assistant Research Scientist
Laboratory of Organic Chemistry
Wadsworth Center
New York State Department of Health
518-473-3378

The data report users identified below will use the data to assess if pharmaceuticals are a water quality issue for the watershed. Included in this list are NYS personnel who oversee the water quality of the watershed.

Mr. Ed Reilly
Division of Water
New York State Department of Environmental Conservation
518-402-8169

Ms. Irina Birman, Ph.D.
Research Scientist, New York City Watershed Unit
Bureau of Public Water Supply Protection
New York State Department of Health
518-402-7650

Figure 2. Organization Chart for the Pharmaceutical Project



BTSA: Bureau of Toxic Substance Assessment, Division of Environmental Health Assessment, NYS DOH
BPWSP: Bureau of Public Water Supply Protection, NYS DOH
DEHA: Division of Environmental Health Assessment, NYS DOH

5. Special Training Requirements and Responsibility

Our project involves no specific training certification necessary for its completion. However, key personnel involved with this project have strong background in this type of research. Dr. Wilson has over fifteen years of experience in collecting environmental samples, writing reports, and analyzing data. Dr. O'Keefe has over twenty years as a laboratory chief and has been the Wadsworth Center's principle investigator (analytical chemist) of polychlorinated dibenzodioxins (PCDD). He has developed methodologies for air, water, soil, and biological tissue PCDD analysis. The work performed by Dr. O'Keefe has been at the leading edge of PCDD analytical techniques. The instrumentation and analytical techniques used for PCDD are similar to those used in the analysis of pharmaceuticals in surface water and treated wastewater.

Lloyd Wilson and Patrick Palmer - OSHA 40 hour Health and Safety Training for Hazardous Waste Site Investigation Personnel

Lloyd Wilson - 1989 EPA Region 2 Edison training seminar on CERCLA Quality Assurance

6. Project Schedule

Table 1. Project schedule

Date	Event	Number of Samples
October 00 to March 03	Finalize Study Plan, hire staff, finalize analytical methodology, QAPP approval (QAPP submitted doing work requested)	
June 03	Preliminary Sampling/Pilot study EOH* area (6 sites, duplicate sampling x 3 days) WOH area (5 sites, duplicate sampling x 3 days) 1 Field Blank per sampling day	EOH: 36 WOH: 30 Fblank: 6
July 03	Progress report	
August 03	EOH area (6 sites x 7 daily samples per site) EOH duplicate sample - days 1,3,5 and 7 WOH area (5 sites x 7 daily samples per site) WOH duplicate sample - days 1,3,5, and 7 1 Field Blank per sampling day	EOH: 42 EOHDUP: 4 WOH: 35 WOHDUP: 4 Fblank: 14
October 03	EOH area (6 sites x 7 daily samples per site) EOH duplicate sample - days 1,3,5 and 7 WOH area (5 sites x 7 daily samples per site) WOH duplicate sample -days 1,3,5, and 7 1 Field Blank per sampling day	EOH: 42 EOHDUP: 4 WOH: 35 WOHDUP: 4 Fblank: 14
January 04	EOH area (6 sites x 7 daily samples per site) EOH duplicate sample - days 1,3,5 and 7 WOH area (5 sites x 7 daily samples per site) WOH duplicate sample -days 1,3,5, and 7 1 Field Blank per sampling day	EOH: 42 EOHDUP: 4 WOH: 35 WOHDUP: 4 Fblank: 14
March 04	EOH area (6 sites x 7 daily samples per site) EOH duplicate sample - days 1,3,5 and 7 WOH area (5 sites x 7 daily samples per site) WOH duplicate sample -days 1,3,5,and 7 1 Field Blank per day	EOH: 42 EOHDUP: 4 WOH: 35 WOHDUP: 4 Fblank: 14
June 04	Final Data received from laboratory	
September 04	Draft Report	
November 04	Final Report	

*EOH is east of Hudson, WOH is west of Hudson

7. Field Sampling Table or Related Information

Overall Sampling Information for the NYC Watershed Pharmaceuticals in Water Study

Table 2. Description of Samples to Be Collected

Sample Matrix	Sample Type	Total # Samples	Sample Volume	Sample Container	Sample Preservation	Holding Time
Surface Water	Field samples including duplicates	406	4 Liters	Amber Bottle	$\leq 4^{o}C$	48 hr
Distilled Water	QA/QC Field Blanks	62	4 Liters	Amber Bottle	$\leq 4^{o}C$	48 hr

8. Field Sampling Procedures

Field measurements of surface water will be made with a Quanta System (Hydrolab Corporation) for the following parameters: conductivity, dissolved oxygen, pH, redox potential, temperature, and turbidity. The unit will be rinsed with distilled deionized water before taking readings at each sample location. All sensors will be thoroughly cleaned with either soap or rubbing alcohol after each round of sampling (as per manufacturer's instructions). Calibration of equipment will be checked before each round of sampling, and adjusted if necessary. Field performance for temperature and pH will be checked each sampling day using an ice bath and pH buffers. Coordinates of all sampling locations will be obtained with a GPS unit during the preliminary sampling.

Grab samples will be collected in four-liter amber glass containers. (These containers will be solvent cleaned and silanized in the laboratory or by the glassware manufacturer.) Sample collectors will wear disposable, powder-free gloves during all sample collection. No caffeinated beverages will be consumed or stored by field staff in the transport vehicle at any time during this fieldwork. Field staff will not be allowed to collect samples if they are taking any medication containing the survey's analytes. If a staff member has been prescribed any of the analytes, he/she will not be permitted in the field until their medication regimen has ceased.

Where possible, samples will be collected directly into the 4-L bottles. However, at most locations, it is necessary to use a smaller 1-L amber glass bottle as a transfer container. Prior to sample collection, the 1-L transfer and/or 4-L sample bottle(s) will each be rinsed three times with water (~ 0.5 L) from the sampling location. Separate transfer bottles will be used for each location.

Field blanks will be analyzed for each sampling day. Four liters of distilled, deionized water will be transported into the field, transferred into another sample bottle, and transported back to the laboratory. After collection, all containers will be stored on ice until delivery to the lab (at the end of the sampling day). Samples at wastewater treatment plants will be collected after those at the keypoints, and will be stored in separate coolers during transport to minimize any potential contamination. Upon delivery to the lab, samples will be immediately stored in refrigeration (4°C), and extracted within 48 hours of collection.

9. Sample Handling and Custody Requirements

All sample containers will be accompanied by chain of custody, sample collection, and laboratory accession forms. Relevant information about each sample such as location, time, and temperature will be recorded as each sample is collected. Copies of these forms are attached.

10. Analytical Procedures and Method Validation

The eleven compounds selected for the study have a variety of functional groups that respond in different ways to changes in pH. As a result of the presence of carboxylic acid groups, two of the compounds, the anti-convulsant valproic acid and the analgesic ibuprofen, are acidic. The three steroid compounds, estrone, 17β-estradiol, and 17α-ethinyl estradiol, are weaker acids because of the presence of phenolic groups. For the purpose of this study, these three are described as "neutral" compounds. The cardiac β-blocker atenolol, the antibiotics sulfamethoxazole and trimethoprim, and the stimulant caffeine all contain amino groups, and are therefore considered basic. However, the two β-lactam antibiotics, amoxicillin and cephalexin, are amphoteric since they contain both amino and carboxylic acid groups. In addition to these differences in response to pH, there are also considerable differences between the compounds in terms of their solubilities in water and organic solvents. For instance, the steroids are practically insoluble in water but are soluble in both polar (methanol) and moderately polar (methylene chloride) organic solvents. Trimethoprim is slightly soluble in water but is relatively insoluble in methylene chloride. The β-lactam antibiotics present additional challenges to the analytical chemist since the lactam ring can be opened under alkaline conditions in methanol.[1] These compounds are also subject to irreversible adsorption on glass surfaces which have not been deactivated by silanization.[2] As a result of these differences in the properties of the individual compounds, it was necessary to collect two water subsamples in order to extract all the compounds. One subsample was used to extract the acidic/neutral compounds and the other was used to extract the basic/amphoteric compounds.

Solid phase extraction (SPE) was selected as the method of choice for isolating the pharmaceutical compounds from water samples.[3] In this procedure, the water samples are passed through disks or cartridges containing a suitable adsorbent. The analytes are then desorbed using small volumes of organic solvents. In preliminary experiments, a styrene-divinyl benzene disk (Empore SDB-XC) was found to give the best recoveries for the acidic/neutral compounds. Acidifying the water samples to pH 2.5 neutralizes the compounds, allowing for maximum interaction with the reverse-phase adsorbent. By adding the glass particulate product Filter Aid on top of the disk, suspended particles and some of the dissolved organics (humics) will be removed from the water as it is filtered through the disk. The Filter Aid is then removed so that humic acids will not be desorbed with the analytes. Desorption is accomplished with pH 8.5 methanol followed by acetone. The basic methanol ionizes the analytes, making it easier to desorb them from the disk. Additional cleanup of the extracts is accomplished by using water-deactivated silica gel. Previous work has shown that water-deactivated silica gel can be used successfully to cleanup sewage effluents which are subsequently analyzed for estrogens.[4] It was found that the complete group of basic/amphoteric compounds could not be extracted from water with either polymeric adsorbents or cation exchange resins. However, cartridges containing the high-surface area graphitized carbon Carboprep P can be successfully used for isolating all the basic/amphoteric compounds. The environmental pH of the water samples (approximately pH 7) is adequate for adsorption. The basic groups are then ionized for maximum desorption by using pH 2.9 methanol, followed by methylene chloride/methanol and acetone.

The Zymark Turbovap II sample concentrator will be used for all sample concentration steps. This instrument is capable of concentrating six sample extracts simultaneously to final volumes of 100 µl. The internal standards will be added at the beginning of the sample preparation process. Therefore, both the

analytes and the internal standards will experience the same recovery losses at each step in the process. Analog compounds labeled with heavier isotopes (deuterium or ^{13}C atoms) are available as internal standards for valproic acid, ibuprofen, 17β-estradiol, and caffeine. The ^{13}C-17β-estradiol will also be used as an internal standard for the closely related estrogens estrone and 17α-ethinyl estradiol. In the case of the other five compounds, surrogates will be used with structures closely related to the analytes. It has been found that the recovery of each analyte is close to that of its corresponding surrogate.

All the compounds will be analyzed by LC/MS using electrospray as the ionization method. This is the only method capable of providing qualitative and quantitative data for the complete range of compounds included in the study. The amphoteric/basic compounds will be analyzed in the positive ion mode using an acidic buffer. The acid/neutral compounds will be analyzed in the negative ion mode. In this case, a basic buffer will be required in order to form negative ions from the neutral compounds (estrogens). The analyte concentrations will be determined by an isotope ratio calculation using the signals from the analyte and internal standard ions together with a response factor of the internal standard relative to the analyte. Absolute recoveries of the internal standards will be determined by using recovery standards added prior to sample injection. Complete details of all the analytical procedures are provided in the Addendum.

The QA/QC samples will consist of the field blanks and duplicates discussed previously (in Sections 6 and 7) together with the following internal QA/QC samples: method blanks (distilled water), matrix spike duplicates and method blank spikes, duplicate injections of extracts, and calibration standards. Table 3 contains a summary of the analytical QA/QC plan. The field blanks and method blanks will be used respectively to determine if contamination has occurred in the field or in the laboratory environment. The field duplicates will serve to determine the overall precision of the method, including the sampling step, whereas the extract duplicates will provide information on the precision of the analytical step, including sample injection. Matrix spike duplicates have also been included, in the event that the field duplicates do not have positive signals for all the analytes. Finally, the method blank spikes will be used to assess the accuracy of the method. The numbers of field blanks and sample duplicates have been outlined in Sections 6 and 7. The number of internal QA/QC samples, excluding the calibration samples, will be as follows: 10 method blanks, 5 matrix spike duplicates, 5 method blank spikes and 10 extract duplicates.

Table 3: Summary of the QA/QC Plan for Analysis of Selected Pharmaceuticals in the New York City Watershed

Sample Type	Control Element	Acceptance Criterion	Frequency
Study Samples	Limit-of-Detection (LOD)	Reported Level should exceed the experimentally determined Method Detection Limit	All Samples
Field Blanks	Field and/or Laboratory Contamination	Blank Analyte Signal < 20% of Sample Signal	18% of Field Samples
Field Duplicates	Precision	Relative percent difference between duplicates not to exceed ± 30%	10% of Field Samples
Duplicate Spiked Matrix Samples	Precision	Relative percent difference between duplicates not to exceed ± 30%	2% of Field Samples
Extract Duplicates	Instrumental Precision	Relative percent difference between duplicates not to exceed ± 30%	3% of Field Samples
Method Blanks	Laboratory Contamination	Blank Analyte Signal < 20% of Sample Signal	3% of Field Samples
Spiked Method Blanks	Accuracy	Reported values should be within ± 30% of spiked values	2% of Field Samples
Surrogate Standards	Recovery	Recoveries should be in the range of 30% to 120%	All Samples

Five-point calibration curves will be established for each analyte and triplicate analyses will be carried out at each concentration level. The five calibration solutions will contain the analyte at concentrations ranging from 50 ng/ml to 2 μg/ml, and the appropriate internal standard at a fixed concentration of approximately 300 ng/ml. The ratios of the analytical signals from the analyte and the internal standard will be plotted against the concentration ratios of the two compounds. The slope of the curve will be used to obtain a response factor. The curves will be plotted at the beginning of the project, and the mid-point calibration solution will be run on a daily basis when samples are being analyzed. If the response factor determined from the daily check sample deviates by more than ± 20% from the response factor determined from the original calibration curve, corrective action should be taken. This could involve re-tuning the instrument, preparing a new mid-point calibration solution, and, if necessary, preparing another calibration curve. The retention times of the analytes on the LC columns will also be checked for each daily calibration sample. The retention times of the analytes relative to the internal standards should not change by more than ± 20%.

The target detection limit for the analytes was 10 ng/L, which is similar to that reported in a number of other studies. This detection limit is below the level of pharmaceuticals reportedly found in surface waters. In practice, this detection limit was not achieved for all analytes in an initial method detection limit (MDL) study (see attached Addendum for study details). The detection limits found in this study were (from lowest to highest): trimethoprim, 4 ng/L; atenolol 9 ng/L; ibuprofen, 20 ng/L; estrone, 30 ng/L; 17α-ethinyl estradiol, 39 ng/L; 17β-estradiol, 40 ng/L; caffeine, 80 ng/L; sulfamethoxazole, 111 ng/L; valproic acid, 199 ng/L; amoxicillin, 367 ng/L; and cephalexin, 502 ng/L. The acquisition of a new LC/triple quadrupole MS should allow us to achieve lower detection limits, which will be reported in a future MDL study.

As stated earlier, no evaluation is being made of the effect of water supply additives (e.g. chlorine) on the target compounds. In addition, no estimation of original target compound concentrations will be attempted by using metabolites and/or breakdown products, as these are not being investigated.

11. Secondary Data (Non-direct Measurement) Projects

While we are collecting samples for analysis of pharmaceuticals, we will also collect samples for analysis using US EPA method 502.2 (volatiles) and US EPA Method 625 (semi-volatiles). This information will be gathered to identify an atypical event, if one occurs.

To the degree possible, we also want to coordinate our sampling efforts with those of other programs, including, but not limited to, the NYC DEP and the USGS. The NYC DEP collects samples for analysis of organic and inorganic contaminants and bacteriology as part of their routine monitoring program. The USGS collected samples during the summer of 2000 and 2001 at eleven locations in the EOH watershed for analysis of a wide range of compounds, including 7 of our 11 analytes. We hope to coordinate efforts with USGS so that sampling occurs on the same day at locations included in both projects. For example, in August 2003, our fieldwork schedules will likely overlap for some period at the four WWTPs included in our study.

12. Other Data Quality Indicators

12A. Representativeness Our sampling program is biased toward finding pharmaceuticals to determine if they are entering NYC EOH and WOH watersheds, and if they are present at the intakes of the NYC drinking water distribution system. This bias is to ensure we meet the expectations of protecting public health. To best characterize which analytes may be entering the watershed, we will sample the WWTP effluent as it leaves the facility (and before it enters the discharge stream). Measurements of pH, temperature, DO, ORP and conductance will be taken using a Hydrolab Quanta (see Section 14).

Input and output samples at the reservoirs will represent water directly entering and leaving each location. Water leaving the reservoirs may not be from the middle of the reservoir's water column. Depending on water quality measurements, NYC DEP may choose to draw water from the upper or lower depths. Our sample will represent whichever part of the column is actively entering the system. As with the WWTP effluent samples, Hydrolab field measurements will be used to look at the characteristics of the water sampled.

The design of our sampling program also allows for an evaluation of temporal variability on both seasonal and daily scales. We will have four sampling periods, one per season, each of seven consecutive days, so that each day of the week is represented. We anticipate that this scheme will include low and high flow conditions, as well as different types of weather conditions.

12B. Comparability Our pharmaceutical analysis is based on peer reviewed published methodology and developed in consultation with the USGS. There were two qualitative measures used in selecting our list of analytes: (a) the compounds are representative of what other researchers have found in the environment, and (b) the methodology could be feasibly done with existing personnel and equipment. Caffeine and ibuprofen have been included mainly for these reasons, and because caffeine is one of the most commonly detected "pharmaceuticals." Seven of our analytes were included in the target compound list of the USGS sampling program.[3] We hope that by narrowing the list to a relatively few compounds, we can increase sensitivity while still allowing for direct comparison to the USGS data.

12C. Completeness As stated earlier, our intention is for 90% of the collected samples to meet QA/QC goals. If we encounter a situation where a batch of samples, from either a particular week or season, yields

unacceptable results, it may be necessary to conduct additional sampling for replacement. The preliminary study will help us evaluate feasibility of our QA/QC goals.

13A. Peer Review

The final report will be reviewed by experts outside the project team for evaluation of the methodology, results, and conclusions. This will include staff at the NYC DEP and NYS DEC directly involved in protection of the NYC watershed. We also anticipate publishing these results in a peer-reviewed journal.

13B. Peer Involvement

The USGS has been consulted and we will continue to consult with them as we progress with this study. We have consulted with them on all phases of the project and expect to share drafts of our reports. In particular, we have spoken with Mr. Patrick Phillips of the Troy, NY office, and Drs. Mike Meyer and Larry Barber of USGS facilities in Boulder, Colorado.

14. Instrument, Equipment and Supplies Testing Maintenance

The hand-held GPS unit requires no calibration, but will be checked periodically by taking measurements at a geodomic marker. The Hydrolab Quanta unit will be checked with a standard before each day of sampling. Readings will be taken from a standard solution before and after sampling to ensure no loss of accuracy during the sampling period. Maintenance and cleaning of the sensors will be conducted after each week of sampling. Sensors will be cleaned with either soap or rubbing alcohol, and stored wet to prevent damage and drying out. The Quanta was factory-serviced on June 13, 2003. As long as the unit measures the performance standards correctly during the study, any additional manufacturer calibration should not be necessary. Due to the factory servicing of the Quanta, it was necessary to use a different instrument (YSI 600QS-05) to take readings during the pilot sampling.

Table 4. Accuracy of Instrument Measurements

	Hydrolab Quanta	YSI 600QS-05
Temperature:	+/- 0.2 ˚C	+/- 0.15 ˚C
Dissolved Oxygen:	+/- 0.2 mg/l	+/- 0.2 mg/l
Specific Conductance:	+/- 1%	+/- 0.5% or 0.001 mS/cm
pH:	+/- 0.2 units	+/- 0.2 units
ORP:	+/- 25 mV	+/- 20 mV
Depth:	+/- 0.3 m	N/A

The daily calibration procedures described in Section 10 will be used to ensure that the GC/MS and LC/MS instruments are operating under optimum conditions. Poor resolution of analytes and shifts of relative retention times outside the tolerance range will require the replacement of a GC or LC column. Loss of sensitivity and changes in relative response factors of analytes and internal standards are indicative of

contamination problems in the MS instrument, or in the case of GC/MS instruments, the GC injection port. To avoid problems related to contamination, the septa and injection port liners in the GC will be replaced at frequent intervals, and the sources of the MS instruments will be cleaned.

15. Assessments

Prior to study implementation, approval signatures will be obtained from Mr. Lawrence T. Bailey, Quality Assurance Officer for the Division of Water, NYS DEC, and Dr. John Garden II, Quality Assurance Officer for the Wadsworth Center.

A progress report will be submitted following the completion of the pilot study/preliminary sampling. A quarterly report on the status of the project will be circulated to all the individuals listed in Section 4 (Project Organization). The reports will include how many samples were collected, how many were analyzed (and met QA/QC), and a description of the conditions during sampling. The reports will also be shared with the NYS DOH management, including: Dr. Nancy Kim, Director, Division of Environmental Health Assessment; Dr. Edward Horn, Director, Bureau of Toxic Substance Assessment; and Mr. Michael Burke, Director, Bureau of Public Water Supply. All individuals will be briefed on the status of the project on a quarterly basis. Each of the individuals listed here and in Section 4 could stop this project, if needed.

Dr. Ken Aldous, Chief of the Laboratory of Organic Analysis at Wadsworth Center, and Dr. George Eadon, Director of the Division Laboratory for Environmental Disease Prevention at the Wadsworth Center, NYS DOH will be responsible for reviewing all work performed by Dr. Patrick O'Keefe. Either individual could stop the analyses for corrective action.

As stated under the peer review section, we anticipate having Mr. Patrick Phillips of the USGS involved. We will share our report on the pilot study and drafts of our final reports. The NYS DEC project manager and QA officers also will review our documents.

16. Data Review

Dr. Patrick O'Keefe will be responsible for data review. Data will be rejected for an analyte if the reported level is below the MDL value listed in Section 10, the corresponding surrogate recovery is below 30% or exceeds 120%, and the corresponding field blank has more than 20% of the analyte concentration in the sample. If the holding time or temperature specified in Table 2 is exceeded, or data for duplicates or spikes are not within the acceptance limits listed in Table 3, sample results will still be reported. However, these results will be flagged to indicate that they do not meet all QA/QC criteria. Concentrations of analytes will be determined from surrogate standards. Injection standards will be used to correct for recovery losses of surrogate standards.

17. Documentation and Records

Quarterly reports, a progress report following the completion of the pilot/preliminary study, and a final report will be circulated to all the individuals described in Section 4 (Project Organization and Responsibility) and in Section 15 (Assessments). Dr. Wilson, Dr. O'Keefe, and Mr. Palmer will be responsible for writing reports. All data and reports will be stored on the Center for Environmental Health LAN server, and on compact disc (CD) and paper in the Bureau of Toxic Substance Assessment. SAS®, Microsoft Access®,

Excel®, and Word® will be used for data management, statistical analysis, and report writing. Upon delivery to the laboratory, all samples will be assigned a laboratory accession number. These numbers will be logged in the Wadsworth Center's computerized data handling system ELDARS (Electronic Laboratory Data and Reporting System). The data will be retrievable by any of the project personnel and staff in the NYS DOH Bureau of Public Water Supply. Additionally, summary tables that include all of the data, including duplicates and field blanks, will be in the final report. The minimum data required for entry into STORET will be collected for each sample. These records will be kept for a minimum of 10 years.

References

1 Bruno, F., Curini, R., DiCorcia, A., Nazzari, M. and Samperi, R. **2001**. Method development for measuring trace levels of penicillins in aqueous environmental samples. *Rapid Commun. Mass Spectrom.* **15**: 1391-1400.

2. Sörensen, L.M., Rasmussen, B.M., Boison, J.O. and Keng, L. **1997**. Simultaneous determination of six penicillins in cow's milk by a multiresidue high-performance liquid chromatographic method. *J. Chromatogr. B.* **694**: 383-391.

3. Kolpin et al. **2002**. Pharmaceuticals, hormones and other organic wastewater contaminants in U.S. streams, 1999-2000: a national reconnaissance. *Environ. Sci. Technol.* **36**: 1202-1211.

4. Kuch, H. and Ballschmitter. **2000**. Determination of endogenous and exogenous estrogens in effluents from sewage treatment plants at the ng/L-level. *Fresenius J. Anal. Chem.* **366**: 392-395.

Appendix 1. Supplemental information for the analytes

Pharmaceutical	Type	DDD	Reason for testing	Detection Limit
amoxicillin CAS # 26787-78-0	semisynthetic antibiotic	750-1750 mg	>60% excreted unchanged in urine; over 34 mil units sold (2002)**	367 ng/L
atenolol CAS # 29122-68-7	beta-andrenergic receptor blocking agent	50-200 mg	>40% excreted unchanged in urine, >50% excreted unchanged in feces;	9 ng/L
caffeine CAS # 58-08-2	stimulant	230-460 mg per typical coffee drinker	present in coffee, tea, soda, chocolate, and candy; good indicator of human waste stream influence in water bodies	80 ng/L
cephalexin CAS # 23325-78-2	cephalosporin antibiotic	1000-4000 mg	90% excreted unchanged in urine; over 24 mil units sold (2002)	502 ng/L
valproic acid (metabolite of Depakote) CAS # 99-66-1	anticonvulsant/ antiepileptic; also antimigraine	750 mg	3% excreted unchanged, 30-50% as metabolites in urine; over 6 mil units sold (2002); possible links to autism	199 ng/L
17β-estradiol (E_2) CAS # 50-28-2	natural steroid	N/A	inactive metabolite may be changed into active; estrogen in WWTP; persistent in sewage, lake water	40 ng/L
estrone (E_1) CAS # 53-16-7	natural steroid	N/A	inactive metabolite may be changed into active estrogen in WWTP; persistent in sewage, lake water	30 ng/L
17α-ethinylestradiol (EE_2) CAS # 57-63-6	synthetic steroid	0.02-0.05 mg	found in oral contraceptives; persistent in sewage, lake water	39 ng/L
ibuprofen CAS # 15687-27-1	non-steroidal antiinflammatory	800-1600 mg	used in large amounts (over 22 mil prescription units sold in 2002, plus over the counter sales); 1% excreted unchanged in urine; inherently biodegradable in WWTP	20 ng/L
sulfamethoxazole CAS # 723-46-6	antibiotic (combined w/ trimethoprim)	1600 mg	30% excreted in unchanged form, 55% as metabolite; non-degradable in STP, < 25% degraded after 1 yr in surface water; over 13 mil units of the combo sold (2002)	111 ng/L
trimethoprim CAS # 738-70-5	synthetic antibiotic (usually combined w/ sulfamethoxazole)	320 mg (in combo) 200mg (individually)	with sulfamethoxazole combo, 67% excreted unchanged (urine); individually, 40-48% excreted unchanged (urine); over 13 mil units of the combo sold (2002)	4 ng/L

DDD: Defined Daily Dose;

WWTP: Wastewater Treatment Plant

**: Prescription units sold in US, available at *www.drugtopics.com*

Pharmacology and dosage information available at *www.rxlist.com*

Caffeine DDD is shown for coffee, using information from *www.allaboutcoffee.org/id25htm* and Mandel, H.G. (**2002)** Update on caffeine consumption, disposition, and action. *Food Chem Toxicol* . **40**: 1231-1234.

NEW YORK STATE DEPARTMENT OF HEALTH
Wadsworth Center
Albany, NY 12201-0509

Chain of Custody Record

Instructions: This form must be completed for any sample which might be used in enforcement proceedings or litigation.
Transporting Samples: During transport of the sample from sampling site to the laboratory, the chain of custody must be unbroken. Generally this will require the sample be delivered by the sample collector or his designated representative who will sign for the receipt, integrity and transfer of the sample during shipment. If integrity of the sample is questionable, describe problem on the reverse side of this form.

Sample ID (Lab Use Only)	Field Ref#	Coll. Date	Coll. Time	Collection Point	Sample Type
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other
					☐ Water ☐ Air ☐ Soil ☐ Other

Custody of Samples

	Name	Affiliation	Date	Time
1 a. Sample container prepared by			/ /	
b. Sample container prepared by			/ /	
2. Received by			/ /	
3. Received by			/ /	
4. Sample Collected by			/ /	
5. Sample Received by			/ /	
6. Sample Received by			/ /	
7. Sample Received by			/ /	
8. Sample Received by			/ /	
9. Sample Received by			/ /	
10. Sample Received at Lab by			/ /	
11. Sample Accessioned by			/ /	

DOH-3349 (5/95)

NEW YORK STATE DEPARTMENT OF HEALTH
Wadsworth Center, PO Box 509, Albany, NY 12201-0509

Request for Analysis

Lab Use Only
Lab Sample ID _____ Sample Rec'd [Year Month Day Mil Hour] Temp _____ °C
Test Pattern _____ Temp Stat _____ Turb _____

Health Emergency Yes ☐ No ☐ Chain of Custody Form With Sample ☐ Add text: _____

Program Code _____ Program Name _____

Location of Sampling Point Source, Site, Spill, Water System or other ID Number _____

Water System Facility No _____ Sample Point No. _____

Drainage Basin _____ Gazetteer Code _____ County _____ Town _____

Latitude _____ Longitude _____ Lat/Long Data Source _____ Format _____

Altitude or Depth (include units) from Ground _____ from Sea Level _____

Location / Project / Facility Name _____

Exact Description of Site _____

Address of Sampling Point No. & St. _____ City / Town _____ Zip _____

Address for Notification No. & St. _____ City / Town _____ Zip _____

Sampling Information

Grab / Composite Finish [Year Month Day Mil Hour Minute]
Composite Start [ ][ ][ ][ ][ ]

Type of Sample (select from list) [ ][ ] Description _____

Field Measurements
Sample temperature _____ °C 02TEMP
Free Chlorine Residual _____ 24CHLORRES
Total Chlorine Residual _____ 23CHLORRES

Submitted by _____ Sample Collected by _____ Phone Number _____

Report Results to CO ☐ RO ☐ LPHE ☐ FED ☐ INFO ☐ LAB ☐ Special mail code _____

ASP or CLP: Case _____ SDG _____ Customer No. _____

Complaints, Observations, Reasons for Submission ☐ Routine Surveillance

☐ (A) Illness ☐ (D) Color ☐ (G) New Equip. or Proc. ☐ (J) Other
☐ (B) Taste/Odor ☐ (E) Natural ☐ (H) Equipment Failure
☐ (C) Turbidity ☐ (F) Fish Kill ☐ (I) Interruption in Chlorination

Additional information regarding this sample

_____

_____

Field Information

Preservative	Aliquot	Lab Use pH
☐ HCl		
☐ HNO_3		
☐ H_2SO_4		
☐ NaOH		
☐ Thiosulfate		
☐ Ascorbic acid		

Sanitary Bacteriology

Check Water Source
☐ Chlorinated Potable Water
☐ Unchlorinated Potable Water
☐ Bottled Water
☐ Nonpotable Surface Water
☐ Chlorinated Waste Water
☐ Other _____

Microscopic Analysis
☐ Routine Analysis
☐ MPA
☐ Other _____

Organic Chemistry
☐ Chlorinated Insecticides
☐ Nitrogen/Phosphorus Pest
☐ Herbicides
☐ PCBs
☐ Purgeables
☐ Ketone or Ket-Fuel
☐ Semi-Volatiles
☐ THMs
☐ Haloacetic Acids
☐ Other _____

Inorganic Chemistry
☐ Potable Water,
☐ Potable Water, OCSS-I + secondary
☐ Langelier Index
☐ Nitrate
☐ Trace Metals Scan
☐ Trace Metals (specify) _____
☐ Lead
☐ Other _____

Nuclear Chemistry
☐ Routine Surveillance
☐ Other _____

Air Analysis
Canisters
☐ Petroleum H/C
☐ Halogenated H/C
☐ Other _____
Badges
☐ PERC
☐ Other _____
Cartridges
☐ Specify _____
Other _____

DOH-246 (12/2001) WHITE COPY - Laboratory YELLOW COPY - Collector Retains

Pharmaceutical Study
EOH Trip Data Sheet- Water Parameters

Date: _____ Time: _____ Staff initials: ____/_____ Sample # _____

Location (circle one): KENSICO: DEL18 DEL17 CATALUM
CROTON LAKE GATE HOUSE (CROGH)
YORKTOWN HEIGHTS WWTP
CARMEL SD # 2

GPS coordinates:
Latitude (Y): _____ Longitude (X):_____

Describe 24-hour precipitation (if any): _____
Was Quanta checked in lab? Y or N Date: _____ Time: _____
Was instrument cleaned in lab? Y or N Date: _____ Time: _____

Check Quanta readings in standard solution before sampling.
Is sample circulator on? Y or N

	DOH Hydrolab readings:	**NYC DEP readings:**
Water Temp:	_____ °C	_____°C
Specific Conductance:	_____ uS/cm	_____uS/cm
Dissolved O_2:	_____ mg/L	_____ mg/L
	_____ % DO	
pH:	_____	_____
Salinity:	_____ PSS	_____ PSS
ORP:	_____ mV	_____ mV
Turbidity:		_____ NTUs

Rinse instrument sensors with DDI water after parameters have been measured.
Replace storage cup over instrument sensors, and leave some DDI water in cup (to prevent sensor dehydration)

Sampling:
1. If tap is off, turn on and let run for 4 minutes.
2. Rinse 4-liter bottle 3x with water to be sampled.
3. Overfill bottle to minimize air pocket when capped.
4. Label sample with appropriate I.D.
   SAMPLE #: _____
5. Refrigerate sample on ice until laboratory delivery.

Has sample been recorded on chain of custody form? Y or N

Pharmaceutical Study
WOH Trip Data Sheet- Water Parameters

Date: _____ Time: _____ Staff initials: ____/_____ Sample # _____

Location (circle one): NEVERSINK Aqueduct Chamber
RONDOUT: WDA (West Delaware Aqueduct outlet)
EDA (East Delaware Aqueduct outlet)
CHAMBER (Delaware Aqueduct inlet)
WALTON WWTP
MARGARETVILLE WWTP

GPS coordinates:
Latitude (Y): _____ Longitude (X):_____

Describe 24-hour precipitation (if any): _____
Was Quanta checked in lab? Y or N Time: _____ Date: _____
Was instrument cleaned in lab? Y or N Time: _____ Date: _____

Check Quanta readings in standard solution before sampling.
Is sample circulator on? Y or N

	DOH Hydrolab readings:	**NYC DEP readings:**
Water Temp:	_____ °C	_____°C
Specific Conductance:	_____ uS/cm	_____uS/cm
Dissolved O_2:	_____ mg/L	_____ mg/L
	_____ % DO	
pH:	_____	_____
Salinity:	_____ PSS	_____ PSS
ORP:	_____ mV	_____ mV
Turbidity:		_____ NTUs

Rinse instrument sensors with DDI water after parameters have been measured.
Replace storage cup over instrument sensors, and leave some DDI water in cup (to prevent sensor dehydration)

Sampling:
1. If tap is off, turn on and let run for 4 minutes.
2. Rinse 4-liter bottle 3x with water to be sampled.
3. Overfill bottle to minimize air pocket when capped.
4. Label sample with appropriate I.D.
   SAMPLE #: _____
5. Refrigerate sample on ice until laboratory delivery.

Has sample been recorded on chain of custody form? Y or N