Modelling Temporal and Spatial Transportation of Pharmaceuticals, Personal Care Products, and Endocrine Disrupting Compounds in a Canadian Watershed

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Temporal and spatial concentrations of several pharmaceuticals and personal care products (PPCPs), and endocrine disrupting compounds (EDCs) are predicted in the Grand River watershed using a novel version of the PhATE (Pharmaceutical Assessment and Transport Evaluation) model code, which is adapted to explicitly consider Canadian conditions. Specific PPCPs and EDCs previously measured in the Grand River watershed in Ontario, Canada, are selected as the target compounds for this study. Due to observed seasonal variability in climate, hydrology, and pharmaceutical loadings at the case study location, predicting seasonal concentrations of each chemical is expected to improve simulation results and the PhATE model is modified accordingly. In this regard, required seasonal hydrological parameters (i.e. flow rate and velocity) are estimated based on site data. Furthermore, chemical loss parameters (i.e. in-stream decay, human loss, and removal efficiency of treatment plants) are extracted from the literature and then calibrated to observed seasonal behaviour. Calibration parameters for the case study include in-stream decay, human loss, and removal efficiency of three different types of treatment plants. Simulated concentrations are validated by comparing them with measured data at two previously sampled locations in the Grand River. In general, the PhATE model, when modified to account for seasonal variability, accurately simulates pharmaceutical concentrations in the Grand River.

The validated PhATE model is used in a predictive mode to identify streams and stream segments with high potential risk of being exposed to the selected PPCPs and EDCs in the watershed in different seasons. Results suggest that a portion of the Grand River extending from the effluent of Waterloo and Kitchener wastewater treatment plants down to the municipality of Brantford is likely to be at higher risk, relative to other portions of the watershed. Moreover, the potential for PPCP toxicity to aquatic species is assessed using the maximum simulated concentrations for the Grand River watershed. According to regulatory guidelines developed by the European Union (EU), most of PPCPs are predicted to be at concentrations that require further assessment and/or more stringent regulations and restrictions.

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List of Acronyms

PPCP: Pharmaceuticals and Personal Care Product

EDC: Endocrine Disrupting Compound

NP: Nonylphenol

DEET: N,N-diethyl-m-toluamide

DWTP: Drinking Water Treatment Plant

WWTP: Waste Water Treatment Plant

WSC: Water Survey of Canada

GRCA: Grand River Conservation Authority

EU: European Union

PhATE: Pharmaceutical Assessment and Transport Evaluation

GREAT-ER: Geo-referenced Regional Exposure Assessment Tool for European Rivers

OSTRICH: Optimization Software Toolkit for Research Involving Computational Heuristics

PhRMA: Pharmaceutical Research and Manufactures of America

Chapter 1
Introduction

1.1 Background

Pharmaceuticals, personal care products (PPCPs) and endocrine disrupting compounds (EDCs) are chemicals used extensively for day-to-day treatment, prevention, and beautification. They have been identified as significant chemical pollutants in the aquatic environment [1]. Previous studies of various industrialized and industrializing nations have reported detectable amounts of PPCPs and EDCs in surface and ground waters, drinking water, and the effluent of sewage treatment plants [2-7]. Canadian watersheds are similarly affected [5-10], although detected concentrations have generally been low, i.e., between nanograms and micrograms per litre [5, 11, 12]. However, even at low concentrations, the continual discharge of these chemicals into the environment may have adverse health effects on aquatic biota, such as feminization of various species [13, 14]. Therefore, the fate and transport of PPCPs and EDCs in varying environments has emerged as an important research topic [13, 15].

Identification and detection of PPCP and EDC compounds in natural systems requires highly sensitive instruments that consume considerable time and money. Therefore, there has been an increasing interest in the development of models capable of reliably predicting the fate of pharmaceuticals. Reliable models should exhibit the following characteristics: (1) they should adequately replicate historical conditions and/or previously measured concentration data; (2) they should generate informative and well-constrained expressions of predictive uncertainty and/or the likelihood of interesting outcomes and scenarios; and (3) they should provide useful guidance for subsequent data collection and monitoring efforts [16]. In this regard, the GREAT-ER (Geo-referenced Regional Exposure Assessment Tool for European Rivers) and PhATE (Pharmaceutical Assessment and Transport Evaluation) models were developed to estimate the concentrations of aquatic chemicals in the surface waters of Europe and the United States, respectively [17, 18]. These user-friendly models have led to an improved understanding of PPCPs and EDCs in U.S. and European environments [16, 19-21]. However, neither of these geo-referenced water quality models has been previously applied to Canadian watersheds.

1.2 Objectives

The primary objective of this thesis was to predict the concentrations of frequently detected pharmaceuticals and personal care products in a Canadian watershed using the PhATE model. As the inherent seasonality of Canadian environments is substantial, the secondary objective was to modify the PhATE model so that it accommodates various sources of seasonal variability in order to improve the prediction of the pharmaceuticals and personal care products.

Chapter 2
Literature Review

2.1 Sources and Occurrence of Pharmaceuticals in Surface Water

Humans ingest pharmaceuticals and related products almost daily, and a certain fraction of each dosage is excreted (i.e. as feces or urine) due to incomplete metabolism in the human body. This excreted fraction ultimately discharges to surface waters as (potentially treated) anthropogenic waste water [5-7, 15, 22, 23]. In urbanized areas, the primary discharge point is a wastewater treatment plant, which will, in general, discharge a combination of treated and untreated wastewater into the receiving surface water. Consequently, PPCPs and EDCs are discharged to the environment in both unaltered parental and metabolized forms [1, 23-25]. Additional sources of pharmaceutical loading include the disposal of unused and expired pharmaceuticals in the trash and down drains. Overall, wastewater treatment plants are the single largest source of PPCP and EDC loading into surface waters [11, 23, 26-31].

As PPCPs and EDCs pass through a given WWTP (Waste Water Treatment Plant), a certain amount of removal occurs via the combined processes of biodegradation, mineralization, sorption, photo-degradation, and volatilization [6, 10, 31-33]. Of these processes, biotransformation has been recognized as the most significant mechanism, while volatilization and sorption are thought to play relatively minor roles [31].

After discharge into surface waters, the relative influence of the various attenuation processes is not completely understood and is subject to site-specific conditions. For example, photo-degradation can be a potentially significant degradation mechanism during surface water transport [32, 34, 35]. However, it has been suggested that photo-degradation may be less significant in the Grand River due to the high turbidity of these waters [36]. Furthermore, the influence and mechanisms for sorption of PPCPs and EDCs in surface water is at present unclear. In general, these hydrophilic compounds will remain in the aqueous phase and are not likely to have high sorption capacities [37-39]. However, hydrophobic partitioning is not the only critical factor in pharmaceutical sorption – other mechanisms, such as ion exchange, hydrogen bonding, and mineral absorption, can also play a significant role [37].

2.2 Detection of Pharmaceuticals in Canada

The presence of pharmaceuticals and personal care products in Canadian surface waters has been observed by a number of researchers [5-10, 42, 43]. The most frequently detected compounds include ibuprofen, naproxen, sulfachlorpyridazine, gemfibrozil, salicylic acid, carbamazepine, bezafibrate, and diclofenac [5, 6, 8-10]. Observed concentrations of PPCPs and EDCs range from below detection limits to micrograms per litre [6, 8, 10]. In the Grand River watershed, PPCP and EDC concentrations have been detected in the nanogram per litre range [5, 42, 43].

Naproxen and ibuprofen have been detected at the highest concentrations, relative to other pharmaceutical compounds [8, 10]. Yet these compounds are also associated with the highest WWTP reduction, with percent removals ranging from 89% to 99% [6, 10]. Conversely, carbamazepine and indomethacin are the most persistent pharmaceuticals and have very low WWTP removal efficiency [6, 8].

2.3 Seasonal Variability in PPCPs Concentration

Relatively few studies have considered the seasonal variability of PPCP and EDC concentrations in the environment [e.g. 42, 43, 44-46]. Nonetheless, these studies suggest that PPCP and EDC concentrations are influenced by several seasonally varying factors, including chemical consumption, rainfall events, flow rate, and temperature.

Seasonal factors influencing human use of specific PPCPs include elevated consumption of ibuprofen and naproxen during the cold and flu season, and increased usage of DEET during the summer months [42, 44, 45]. In contrast to these over-the-counter remedies, gemfibrozil and carbamazepine are prescribed drugs for treatment of chronic conditions and are therefore consumed at a relatively constant rate throughout the year [44].

High discharge rates associated with spring melt and seasonal rainfall events may reduce the efficiency of treatment plants, resulting in elevated PPCP and EDC loadings in surface water [12, 47]. In contrast, summer time exposure of pharmaceuticals to long periods of sunlight may increase the removal efficiency of some types of treatment (e.g. lagoons) [8].

Although there is some disagreement in the literature (i.e. [10, 44] vs. [47]), there is evidence that the removal efficiency of treatment plants is highly dependent upon temperature

and is likely to be lowest during the winter. Furthermore, in surface waters and other natural systems, temperature can significantly influence biodegradation, photolysis and sorption [48]. For some compounds, such as ibuprofen and naproxen, the different processes are influenced in opposing ways such that the overall degradation behaviour does not vary significantly across seasons [47, 49].

Observational data suggests that different compounds have different timings with respect to the occurrence of peak concentrations in surface waters. Examples of such variability include peak concentrations of: (1) ibuprofen and naproxen in the winter and fall [42, 43]; (2) DEET in the summer [43]; (3) gemfibrozil in spring and summer [42]; (4) lincomycin HCl in spring and fall [42]; and (5) sulfamethoxazole in the summer and fall [42]. Other compounds, including carbamazepine, trimethoprim, NP, and bezafibrate have been observed to have relatively constant (i.e. non-seasonal) concentrations in surface waters [42, 43].

2.4 Modelling of Predicted Environmental Concentrations

As mentioned previously, modelling the transport of pharmaceuticals and personal care products as well as predicting their concentrations in surface waters is critical to understanding the potential impact of these compounds on the environment. For example, the PhATE (Pharmaceutical Assessment and Transport Evaluation) model was developed by the Pharmaceutical Research and Manufactures of America (PhRMA) to simulate concentrations of active pharmaceutical ingredients in eleven watersheds across the United States [17]. Similarly, the GREAT-ER (Geography-Referenced Regional Exposure Assessment Tool for European Rivers) model was developed as a means of predicting the concentrations of aquatic chemicals as well as the distribution of the concentrations of these compounds in European surface waters [18]. These models can be used to estimate the potential risk of aquatic chemicals in the environment at both national and regional scales. Furthermore, the models allow for an assessment of the relative influence of different biotic and abiotic processes on the elimination of PPCP and EDC compounds from surface waters [16, 50]. Lastly, these models can help guide the design of a cost-effective field sampling strategy by highlighting the stream segments with higher potential risk [19, 50].

However, ambiguity in the chemical and physical properties of pharmaceuticals as well as uncertainty in the hydrological characteristics of a given watershed can significantly reduce the predictive capabilities of the PhATE and GREAT-ER models [19-21]. Furthermore, fundamental assumptions made by these models, such as ignoring the release of untreated pharmaceuticals from treatment plants during rain events, can cause systematic bias in model predictions [17]. Similarly, various parameter assumptions (such as constant treatment removal, uniformly distributed pharmaceutical usage, and/or constant and spatially homogeneous first-order decay) can further degrade model predictive capabilities.

The PhATE model was chosen in lieu of the GREAT-ER model because a previous research agreement allowed for convenient access to PhATE modeling code along with extensive documentation, dedicated technical support, and personalized training.

The PhATE model uses simple mass balance equations applied to a given pharmaceutical compound along a given reach or segment of surface water. For each segment, mass enters either from WWTP point-sources along the segment or via inflow from upstream segments. Masses leave a given segment via first-order in-stream decay, flow diversions, or outflow to a downstream segment [17]. The potential mass of PPCPs entering from a given wastewater treatment plant is estimated via average annual human usage of the compounds multiplied by the size of the population served by the wastewater treatment plant. This maximum potential loading is reduced via two loss terms, namely: (1) percent removal by human metabolism; and (2) percent removal within the treatment plant [17]. The PhATE model treats each segment of a given watershed as a plug-flow system, resulting in the following mass-balance equations:

$$M_{WWTP} = P \times M_h \times (1 - L_h) \times (1 - L_{WWTP}) \quad (1)$$

$$C_{PEC} = \frac{[(M_0 \mathrm{e}^{-kt_R}) + \sum(M_i \mathrm{e}^{-kt_i})]}{Q} \quad (2)$$

where P is population served by a given treatment plant or zero if no WWTP is present along a given reach, M_h is annual pharmaceutical usage per capita (kg/person/year), L_h is percent loss of pharmaceuticals by human metabolism (fraction), L_{WWTP} is the percent removal by the treatment plant (fraction), M_{WWTP} is the point-source mass loading to the associated surface water segment (kg/year), C_{PEC} is predicted environmental concentration of the compound (mg/L), M_o is mass

loading from upstream (g/day), K is first-order decay rate constant (day^{-1}), t_R is travel time (day), M_i is point-source mass loading from the i^{th} treatment plant (g/day), t_i is travel time from the *ith* plant to the end of the segment (day), and Q is flow rate (m^3/day).

The input and output data for the model are saved in the Microsoft Access databases. The GIS software is also used to manage the hydrological data for the watershed when graphical results need to be shown.

It is worth noting that the in-stream decay in PhATE is such a single rate constant that reflect the total sum of relevant factors like biodegradation, volatilization, sorption to the sediment, photodegradation, etc. Also, it is assumed that the entire amount of a compound produced by manufacturers in a year is consumed by humans and enters into the surface water only via treatment facilities.

The PhATE model is also summarized in Table 2-1 along with the GREAT-ER model. As indicated in Table 2-1, there are many similarities between the two models and study results are likely applicable to both models.

Table 2-1: Comparison of the Features and Capabilities of the PhATE and GREAT-ER models

	PhATE	GREAT-ER
Watersheds applied	On 11 Watersheds in the US	On 16 European Watersheds
Assumptions	Uses steady-state deterministic mass balance equations	
Segmentation	Only the rivers that receive mass of the chemical compounds from upstream or WWTPs are considered in the model and segmented with relatively constant characteristics	All rivers in the watershed are considered in the model and segmented with relatively constant characteristics
Mixing in the system	Rivers are considered as plug flow, and lake and reservoirs are considered as completely mixed tanks	
Basic Input Parameters	Usage per capita, in-stream first-order loss, human loss, removal efficiency for each WWTP treatment type loss.	
Parameters Distribution	Not directly supported	Distribution of the parameters can be specified by the user ((i.e. normal, logarithmic or uniform))
Hydrological Regime	Deterministic(mean flow and low flow)	Stochastic (Monte-Carlo to generate variation in flow and velocity)
Data Storage	MS Access, GIS	GIS and DBF
Adding New Watershed	Requires several changes in MS Access	Requires full GIS functionality including ARC/INFO

2.5 Toxicity of Pharmaceuticals to Aquatic Organisms

Because of the physio-chemical properties of PPCPs, they have the potential to adversely affect aquatic life via both acute and chronic effects [51-54]. However, it is likely that chronic effects present the more significant health risk [54, 55]. In this regard, understanding the full impact of long-term exposure to mixtures of PPCPs and their degradation products is the focus on ongoing research [51, 56, 57]. The toxicity of chemicals is typically measured in terms of an "Effect Concentration" (EC), where EC50 refers to the concentration at which 50% of dosed organisms die or are adversely impaired; and the Lowest Observed Effect Concentration (LOEC) is the minimum dosage at which any adverse effect is observed. Several studies have suggested Effect Concentrations for various PPCPs and with respect to various aquatic species [51-53, 56-60] – relevant summary information is provided in Table 2-2. Ibuprofen and carbamazepine are associated with the lowest Effect Concentration values – just 10 ng/L of these compounds can alter the behaviour of certain aquatic species [60].

Table 2-2: Toxicity of PPCPs on Aquatic Species

Compound	Species	Toxicological endpoint	Effect Concentration	Reference
ibuprofen	Fish , Japanese medaka	-	1-100 μg/L	[56]
ibuprofen	Gammarus pulex	-	10 ng/L	[60]
ibuprofen	H. attenuate	LOEC	1 mg/L	[54]
naproxen	H. attenuate	EC50	2.6 mg/L	[54]
naproxen	C. dubia	EC50	0.33 mg/L	[61]
carbamazepine	H. attenuate	EC50	3.76 mg/L	[54]
carbamazepine	Gammarus pulex	-	10 ng/L	[60]
carbamazepine	Daphnia pulex	-	1 μg/L	[59]
gemfibrozil	H. attenuate	LOCE	1 mg/L	[54]
gemfibrozil	H. attenuate	EC50	1.76 mg/L	[54]
gemfibrozil	C.dubia	EC50	0.53 mg/L	[61]
bezafibrate	H. attenuate	LOEC	1 mg/L	[54]
bezafibrate	C.dubia	LOEC	0.047 mg/L	[61]
nonylphenol	Fish, rainbow trout	EC50	0.22 mg/L	[52]
sulfamethoxazole	C. dubia	EC50	0.21 mg/L	[61]
sulfamethoxazole	Algae P. subcapitata	EC50	0.52 mg/L	[61]
sulfamethoxazole	Daphnia	-	1-10 μg/L	[51]
trimethoprim	Daphnia	-	1-10 μg/L	[51]

Chapter 3
Methodology and Case Study

The PhATE model was adapted to account for Canadian conditions and applied to the Grand River watershed in Ontario, Canada. The basic PhATE model was modified so that various physical, chemical, and hydrological factors were allowed to vary with the seasons (i.e., spring, summer, fall, and winter). Seasonal hydrological parameters were estimated directly using flow rate values reported by the Grand River Conservation Authority (GRCA) and the Water Survey of Canada (WSC). Physical and chemical parameters were extracted from the literature and subsequently calibrated to a split-sample subset of available observation data for the Grand River watershed. Observation data not used for calibration served as the basis for subsequent model validation, which verified the ability of a calibrated model to adequately predict PPCP concentrations. In addition, the sensitivity of the model output to various parameters was analyzed in order to identify the most influential parameters for predicting PPCP concentrations.

Following validation of the modified PhATE model, seasonally varying concentrations of PPCPs were predicted for the entire Grand River watershed. This allowed for identification of those portions of the watershed which are likely to contain the highest PPCP concentrations, thereby representing the highest risk areas in terms of negatively impacting aquatic ecosystems. Finally, in order to assess the toxicity potential of the selected compounds, the maximum predicted concentrations of PPCPs throughout the watershed were compared to corresponding minimum effect concentrations reported in the literature.

The organization of the reminder of the thesis is as follows. This chapter introduces the Grand River watershed case study and PPCPs relevant to the Grand River watershed. Also, in this chapter, the feasible ranges for the associated model parameters are presented and each compound is briefly introduced. The estimation of hydrological data for the Grand River watershed is explained in Chapter 4. The numerical experiments including simulation of concentrations of the PPCPs and sensitivity analysis, calibration, and validation of the parameters are presented in Chapter 5. The results of the numerical experiments are reported in Chapter 6. This thesis ends with summary and conclusions in Chapter 7.

3.1 Case Study: Grand River

The Grand River watershed is located in Southwestern Ontario and drains an area of about 6800 km^2 from the highlands of Dufferin County to Port Maitland on Lake Erie [9]. The annual average precipitation throughout the watershed is 750-1000 mm and the average annual temperature is 6.5 ^oC [63]. The Grand River watershed includes the cities of Kitchener, Waterloo, Cambridge, Guelph, and Brantford as well as numerous smaller villages and towns. The watershed receives treated effluent from wastewater treatment plants, which serve about 530,000 residents. Surface waters of the watershed also supply drinking water to portions of various municipalities [66, 67]. A map of the Grand River watershed is given in Figure 3-1.

A total of forty wastewater treatment plants are located in the watershed. Twenty eight are municipal plants that discharge treated effluent into the Grand River and its branches; of these, fifteen are advanced tertiary treatment, nine have secondary treatment, and four are lagoons [64-66]. The location of wastewater and drinking water treatment plants throughout the watershed is shown in Figure 3-2.

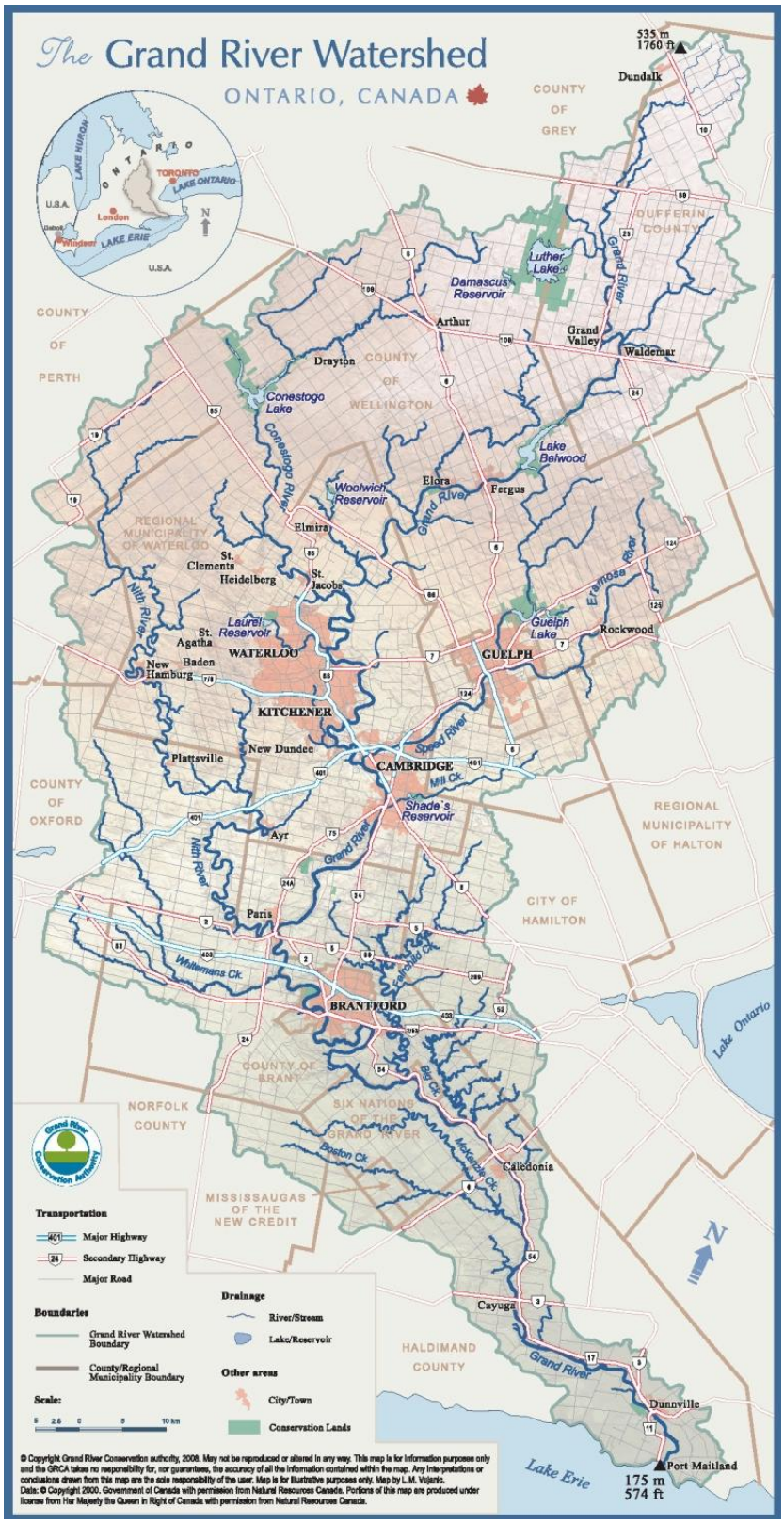


Figure 3-1: A map of the Grand River watershed (courtesy GRCA)

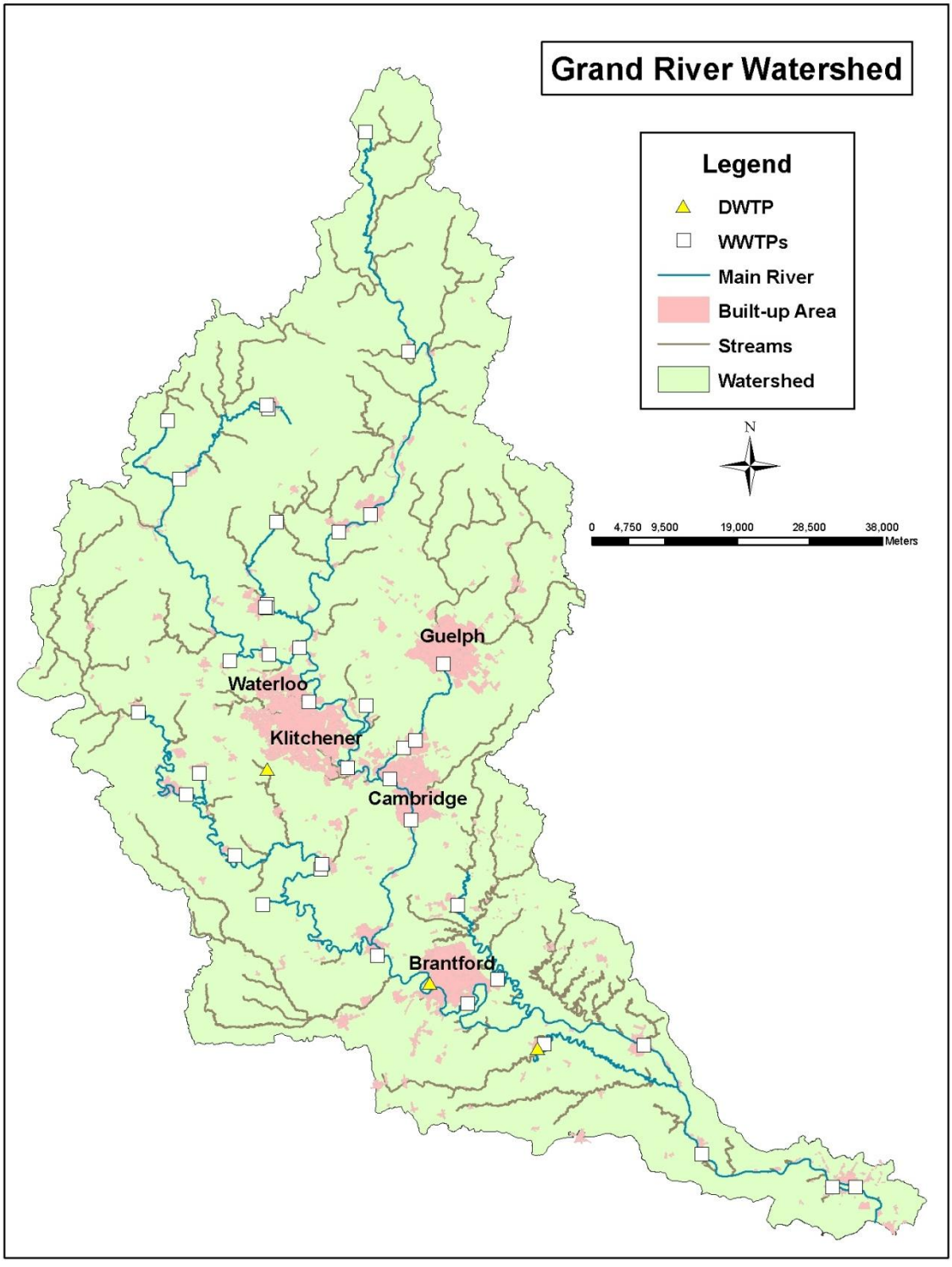


Figure 3-2: Locations of wastewater and drinking water treatment plants in the Grand River Watershed

3.2 Selection of Target Compounds

In this study, the selection of compounds was motivated by the following criteria: (1) the presence of the compounds in Canadian surface waters at relatively high concentrations; (2) high usage of the selected pharmaceuticals by the Canadian population; and (3) the availability of seasonal measured data in the watershed, thereby facilitating a robust assessment of the model. The considered PPCPs and EDCs included: ibuprofen, naproxen, carbamazepine, gemfibrozil, sulfamethoxazole, trimethoprim, bezafibrate, nonylphenol (NP), and N,N-diethyl-m-toluamide (DEET). Table 3-1 displays a list of the selected compounds and some of their general properties including therapeutic classes, molecular weights, octanol-water and sludge-water partitioning coefficients, and pK_a (acid dissociation constant).

Table 3-1: Properties of the selected PPCPs and EDCs

Compound	Therapeutic Class	Molar Mass (g/mol)	Log $K_{o/w}$	K_d (l/kg)	pK_a
Ibuprofen	Anti-inflammatory	206.28 ($C_{13}H_{18}O_2$)	3.5[a]	453.79[a]	4.91
Naproxen	Anti-inflammatory	230.259($C_{14}H_{14}O_3$)	3.18[a]	217.2[a]	4.15
Carbamazepine	Anti-epileptic	236.269($C_{15}H_{12}N_2O$)	2.25[a]	25.52[a]	<2
Gemfibrozil	Lipid regulator	250.333($C_{15}H_{22}O_3$)	4.77[b]	nd[b]	4.7
Sulfamethoxazole	Antibiotic	253.279($C_{10}H_{11}N_3O_3S$)	0.89[b]	2.86[b]	5.7
Trimethoprim	Antibiotic	290.32($C_{14}H_{18}N_4O_3$)	0.91[b]	1.17[b]	7.3
Bezafibrate	Lipid regulator	361.819($C_{19}H_{20}C_lNO_4$)	4.25[c]	2551.8[a]	3.6
NP	Nonionic detergent metabolite	220.35($C_{15}H_{24}O$)	4.48[d]	4333.6[a]	10.7
DEET	Insect repellant	191.27($C_{12}H_{17}NO$)	2.02[e]	15[a]	<2

a. [37]; b. [67]; c. [68]; d. [69]; e. [70]

3.2.1 Chemical and Physical Analysis of the Compounds

Nearly 65 publications were reviewed to determine various properties of the selected PPCPs and EDCs. Interestingly, the available literature suggests significant variability in the removal of PPCPs and EDCs by treatment plants. This variation is attributed to the use of different treatment processes, variability in the functioning of same or similar processes, and differences in wastewater composition (e.g. industrial vs. municipal wastewaters) [12, 29]. For this study, and as summarized in Table 3-2, parameter ranges were utilized, which spanned all values reported

in the literature. However, removal efficiency of bezafibrate and DEET were not available, and a full range (0 to 100%) was used. Following that each compound of interest is briefly introduced.

Table 3-2: Literature-derived ranges of parameter values for the selected compounds (to be continued)

Compunds	Lagoon R[1] (%)	References	Sec.TP[2] (%)	References	Tert.TP[3] (%)	References
Ibuprofen	77 – 100	[6, 31, 44]	72 – 97	[11, 71-77]	81 – 100	[27, 30, 31, 75, 78, 79,77]
Naproxen	90 – 99.8	[6, 31, 44]	32 – 99	[6, 11, 73-76]	50 – 99.8	[6, 27, 29-31, 75, 77, 79, 80]
Carbamazepine	5 – 51	[6, 31, 44]	0 – 53	[11, 39, 71, 73, 75-77]	0 – 60	[27, 30, 31, 75]
Gemfibrozil	15 – 60	[6, 31, 44]	5 – 81	[11, 74, 75, 77]	55 – 75	[27, 31, 75, 79]
Sulfamethoxazole	17 – 99	[44, 77]	9 – 99.8	[71, 73, 77, 81, 82]	1 – 99	[27, 30, 81]
Trimethoprim	65 – 99	[77]	0 – 100	[20, 73, 75, 77, 81, 83-	0 – 99.6	[20, 27, 30, 75, 78, 81]
Bezafibrate	0 – 100*	Not-available	0 – 100	[20, 71, 73]	15 – 93	[29]
NP	0 – 64	[87, 88]	60 – 97	[28, 88-90]	42 – 97	[27, 28, 30, 88]
DEET	0 – 100*	Not-available	0 – 95	[90-92]	45 – 95	[91]

[1]Removal efficiency by lagoon, [2]Secondary treatment plant removal efficiency, [3]Tertiary treatment plant removal efficiency

Table 3-2: Literature-derived ranges of parameter values for the selected compounds (Continued)

Compunds	In stream Loss (1/day)	References	Human Loss (%)	References
Ibuprofen	0.022 – 1.124	[12, 32, 36, 77, 79, 93, 94]	61 – 92	[11, 95]
Naproxen	0.051 – 11.885	[12, 36, 79, 93, 96-98]	89 – 99	[95, 99]
Carbamazepine	0.0012 – 0.24	[12, 26, 32, 39, 94]	69 – 87	[39, 95]
Gemfibrozil	0.0578 – 1.124	[36, 79, 100]	74 – 94	[95, 101]
Sulfamethoxazole	0.059 – 11.09	[26, 102-104]	80 – 90	[95, 105]
Trimethoprim	0.0396 – 0.24	[104, 106]	50 – 56	[105]
Bezafibrate	0 – 0.161	[93, 98]	49 – 50	[11, 95]
NP	0.007 – 1.44	[89, 107, 108]	-	
DEET	-	Not-available	<20	[109]

Carbamazepine

Carbamazepine is a prescribed drug used in the treatment of epilepsy and bipolar disorder, as well as a wide variety of mental disorders. Between 12 to 31 percent of ingested carbamazepine is not metabolized and is excreted via feces and urine [39, 95]. Carbamazepine has a low octanol-water partition coefficient and is known to be a hydrophilic compound [31, 110]. This compound has low photo- and bio-degradation rates in surface waters, with half-lives of 3-100 days and 24 hours, respectively [26, 32, 94]. Between 10 and 50% removal efficiency during wastewater treatment has been reported for carbamazepine [6, 27, 39, 49, 71, 75], with higher removal rates found in plants that perform tertiary treatment and/or lagoon treatment. The low removal efficiency of carbamazepine is attributed to its low sorption coefficient and low biodegradation capacity [39, 80, 110]. In fact, there have been reported cases of higher carbamazepine concentrations following wastewater treatment [47]. Such behaviour has also been observed with other chemicals, including trimethoprim, sulfamethoxazole, and gemfibrozil [6, 81]. Carbamazepine concentrations exhibit significant seasonal variability in the Grand River watershed, with higher concentrations detected in the summer and fall seasons [42].

Ibuprofen

Ibuprofen is a non-prescription antiphlogistic drug that is used for relieving symptoms of arthritis, primary dysmenorrhea, fever, and pain. Excretion rates for non-metabolized ibuprofen have been estimated to be 7 and 23 percent via urine and feces, respectively [95]. Over 90% removal of ibuprofen via wastewater treatment has been observed in numerous studies [6, 22, 27, 28, 71, 73]. Given sufficient residence time (i.e. at least 6 hours), complete removal can be achieved [22]. In natural waters, additional removal may occur via biodegradation and sedimentation [12, 22]. Some researchers argue that acidic pharmaceuticals like ibuprofen are likely to have low sorption capacity in natural systems [88]. Human consumption of ibuprofen is markedly seasonal, with peak usage occurring in the winter. Additionally, there is evidence that bio- and photo-degradation of ibuprofen in surface waters follows seasonal trends [12, 22, 26, 97, 111].

Naproxen

Naproxen is a non-steroidal anti-inflammatory drug (NSAID) used for the relief of pain, fever, inflammation and stiffness. After ingestion, between 1 and 20% of the drug is excreted via urine and feces [29, 99]. Wastewater treatment removal percentages for naproxen range from 20 to 100% [6, 11, 29-31, 44, 49, 73, 74]. In general, degradation of analgesics like ibuprofen and naproxen in wastewater treatment is primarily from biodegradation; sorption during primary and secondary treatment is insignificant. In natural systems, biodegradation and photolysis are the primary pathways for elimination of naproxen [12, 97], and measured photo-degradation half-lives range from minutes to hours [34, 97, 112], with peak rates occurring in the summer.

Antibiotics

Trimethoprim and sulfamethoxazole are antimicrobial drugs used for the treatment of infectious diseases in humans. By design, such compounds are not readily biodegradable and relatively low (~50%) wastewater treatment removal efficiencies have been reported [28, 102, 106]. However, there is evidence of photo-degradation being an important removal process [113, 114] that exhibits significant pH sensitivity [103, 115] and seasonal variation.

Fibrates

Bezafibrate and gemfibrozil are lipid regulator pharmaceuticals used for the treatment of patients who have mixed or combined hyperlipidaemia, a common complication of diabetes [116]. Almost 50% of ingested gemfibrozil is partially metabolized an excreted as glucuronides [27]. Removal of these compounds via wastewater treatment is very low (~10%) and requires significant residence time (i.e. several hundred hours) [116]. While adsorption, biodegradation, and hydrolysis of gemfibrozil in natural systems is relatively limited, biodegradation of bezafibrate can be significant, with reported half-life values ranging from 4.3 to 8.4 days depending on flow velocity [93]. This velocity dependence results in an indirect seasonal dependence because distinct seasonal flow patterns have been observed in Canadian surface waters.

NP

Nonylphenol (NP) and its ethoxylates (NPEs) are widely used surfactants found in soaps, detergents, and similar cleaning products. More than half of NP found in the environment is a

result of individual consumer use of products containing NP. Concern about the endocrine disrupting properties of NP led Environment Canada to introduce national regulations and restrictions on the manufacture and importation of NP/NPEs. Consequently, annual NP production has reduced from 3.35 million kg in 2003 to 1.03 million kg in 2006. Removal efficiency of NP in wastewater treatment plants can be between 60 and 97%, depending on the type of treatment [27, 28, 30, 88, 89]. Nonetheless, concentrations of NP in the microgram per litre range have been observed in various surface waters [4, 43, 89]. Although biodegradation rates for NP in natural systems tend to be low (0.007 to 0.051 day^{-1}) [107, 108], photo-degradation can be considerable (1.2 to 1.7 day^{-1}) [89].

DEET

N,*N*-diethyl-*m*-toluamide (DEET) is an active ingredient of most commercial insect repellents marketed in North America. Approximately 80% of DEET that is applied to the human body is ultimately discharged to a wastewater system [109]. However, little is known about removal of DEET via wastewater treatment or natural processes. For example, a wide range (i.e. between 10 and 90%) of removal efficiencies has been reported for wastewater treatment of DEET [90-92]. Furthermore, mechanisms and rates of elimination of this compound in surface waters have not been reported.

3.2.2 Measured PPCPs and EDCs Data in Grand River

Previously collected seasonal concentrations of PPCPs and EDCs served as the observational data sets utilized in this study for model calibration and validation [42, 43]. One of the data sets was collected in the Grand River near Mannheim from 2006 to 2008 [43], while the other data set was collected in the Grand River near Mannheim and Holmedale from 2005 to 2006 [42]. The average seasonal concentrations of each chemical for these data sets is given in Table 3-3 and Table 3-4. The actual daily reported data is given in Appendix A (reproduced, with permission, from [42, 43]).

Table 3-3: Average seasonal concentrations of PPCPs and EDCs in the Grand River near Manheim (from [43] data set)

Seasons	DEET	ibuprofen	NP	naproxen	Carbamazepine
Fall 2006	37.0	9.0	3.5	15.0	11.5
Winter 2006-7	16.2	96.0	18.6	123.5	28.7
Spring 2007	50.5	66.6	12.2	65.5	17.7
Summer 2007	99.9	8.3	20.9	23.7	33.8
Fall 2007	58.1	39.4	37.8	54.2	30.5
Winter 2007-8	33.2	50.9	33.5	66.5	14.9
Spring 2008	32.9	17.3	12.6	36.2	12.1
Summer 2008	127.4	7.3	2.6	30.0	21.0

Table 3-4: Average seasonal concentration of PPCPs and EDCs in two Grand River locations (from [42] data set)

Seasons		Ibuprofen	Naproxen	Carbamazepine	Gemfibrozil	Bezafibrate	Sulfamethoxazole	Trimethoprim
Winter 2005-6	Mannheim	23.3	20.4	7.3	1.3	2.5	10	4.0
Spring 2005-6		14.4	28.7	7.4	1.5	2.5	10	3.1
Summer2005		12.0	36.5	24.1	2.5	2.5	10	5.4
Fall2005		28.4	20.6	20.3	2.1	3.4	19.7	7.3
Winter 2005-6	Holmedale	29.1	10.6	15.0	2.4	5.8	10	5.0
Spring 2005-6		22.2	10.9	16.5	3.5	6.1	15.8	4.2
Summer2005		6.5	22.4	370.1	3.2	2.5	23.0	4.3
Fall2005		17.9	32.1	42	3.6	6.6	32.0	4.4

Chapter 4
Hydrological Data Estimation

4.1 GIS Data Collection

The Grand River Conservation Authority (GRCA) provided Geographic Information System (GIS) data for the Grand River watershed. Relevant data sets were available from the Map Library of the University of Waterloo as well as the GRCA website (www.grandriver.ca). The GIS data included information on virtual drainage, sewage treatment plants, water flow stations, dams, and sub-catchments. The virtual drainage for the watershed provided not only the drainage network but also the *Strahler* stream ordering (explained in Section 4.4) of the various stream segments. Information on sewage treatment plants consisted of the location of the plants as well as the population being served by each plant.

Following established guidelines [117], only surface waters receiving treated waste water, either from a treatment plant or from upstream flow, were included in the PhATE model of the Grand River watershed. These 'primary' rivers were divided into 84 segments using virtual drainage data. Segmentation was based on the following criteria proposed by BASINS (Better Assessment Science Integrating point and Nonpoint Sources) [118]: (1) any significant differences in flow rate, channel slope, roughness, or channel geometry; and (2) the presence of dams or other obstructions.

Water Flow Stations

Numerous flow monitoring stations are located in the Grand River watershed, including 25 stations operated by the WSC (Water Survey of Canada) and 30 operated by the GRCA (Grand River Conservation Authority). Historical flow data from each WSC station was retrieved from the Environment Canada website (www.ec.gc.ca/rhc-wsc). However, historical data from the GRCA stations was unavailable, with the exception of the data at Doon Station, which was provided by Dwight Boyd of the GRCA (personal comm.). The locations of the WSC and GRCA monitoring stations are indicated in Figure 4-1. Station names and corresponding geographical coordinates and record lengths are provided in Appendix B. Data reported for two of the monitoring stations (i.e. 2GA027, with only four years of record, and 2GA042, a seasonal

monitoring station) was deemed insufficient and these stations were therefore not utilized in this study.

Flow data measured at the WSC stations was used to estimate the hydrological data required by PhATE in the remaining un-gauged streams of the watershed (i.e. mean and low flow values and mean and low velocities for each stream segment). As can be seen from Figure 4-1, the flow stations are well-distributed throughout the watershed and this allowed for adequate interpolation of un-gauged areas.

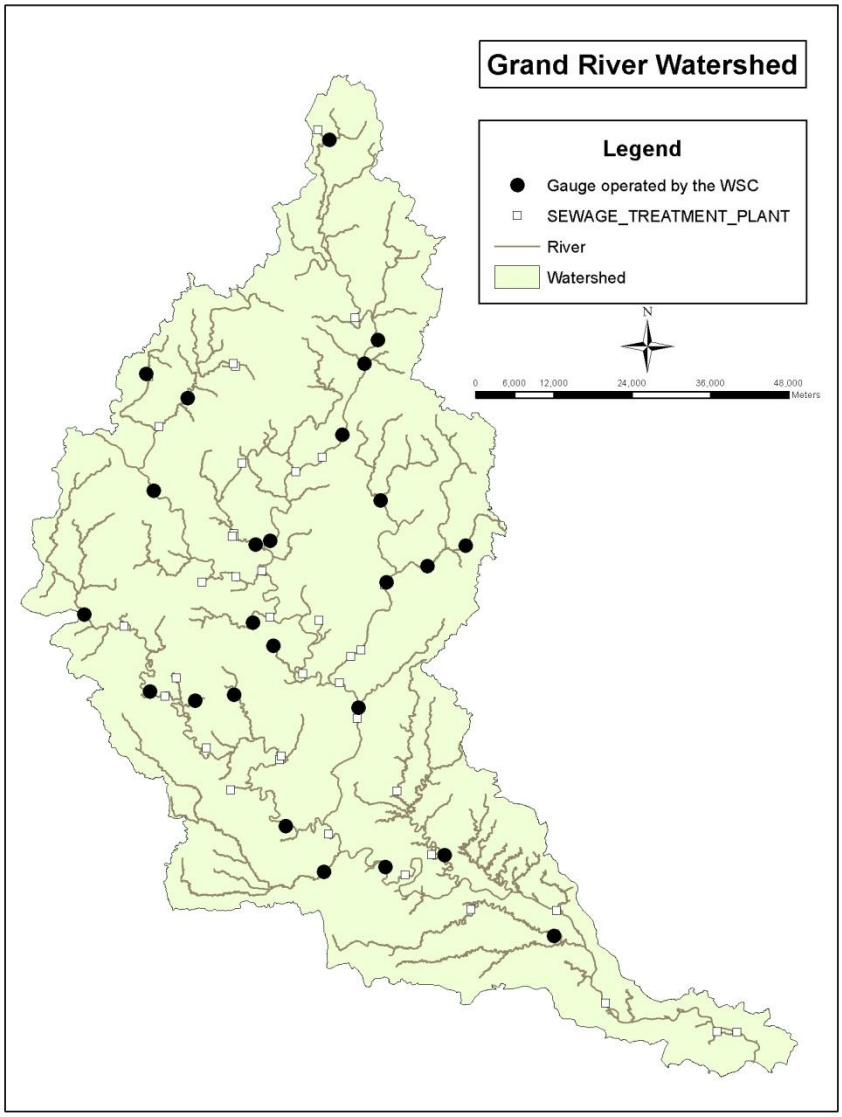


Figure 4-1: Location of the WSC and GRCA monitoring stations in the Grand River watershed

4.2 Average and Low Annual Flow Rate

Flow rates for each stream segment of the watershed were not readily accessible; therefore, it was essential to estimate the flow for the entire steam segments in the watershed. Drainage area, precipitation, and temperature are the most important variables for estimating average annual flow [119]. Of these variables, drainage area is recognized as the most influential factor [120]. To illustrate the strong relationship between flow and drainage area in the Grand River watershed, the *average annual flow* obtained from the WSC stations is plotted in Figure 4-2 versus the corresponding drainage area, determined using the geospatial processing features of ArcGIS. As shown in Figure 4-2, there is an excellent linear relationship between these two variables. Two linear regressions were utilized - one regression for segments with a drainage area greater than 1,200 km^2 and another regression for stations associated with a drainage area of less than 1,200 km^2.

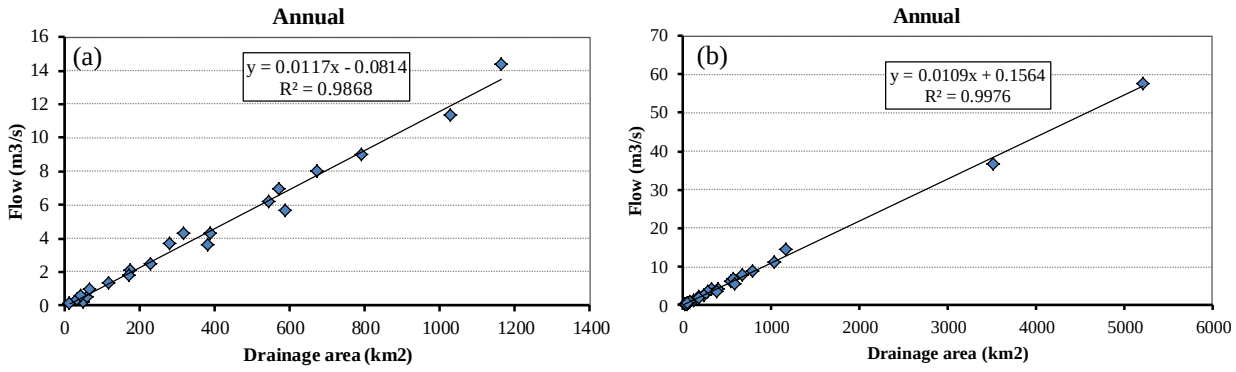


Figure 4-2: The relationship between average annual flow and drainage area in the Grand River watershed (a) for segments with drainage area less than 1,200 km^2 (b) for segments with drainage area greater than 1,200km^2

The relationship between *low annual flow* and drainage area is shown in Figure 4-3 (see next page). The R-squared values for this relationship were not as robust as for the average annual flow, but were deemed to be suitable for estimating low flow in un-gauged stream segments. Using the regression lines given in Figure 4-2 and Figure 4-3, annual average flow and annual low flow values were estimated for each segment in the watershed as a function of the corresponding drainage area.

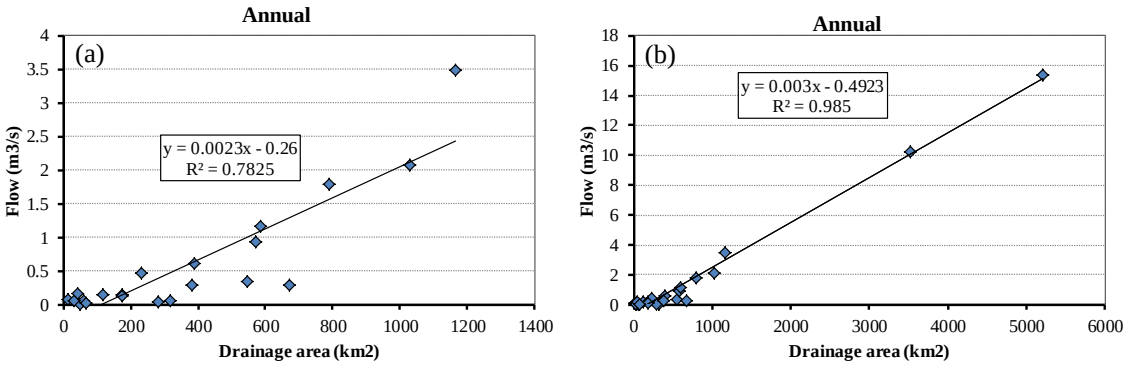


Figure 4-3: The relationship between low annual flow and drainage area in the Grand River watershed (a) for segments with drainage area less than 1,200 km^2 (b)for segments with drainage area greater than 1,200 km^2

4.3 Seasonal Flow

As described previously, one of the objectives of this research was to apply the PhATE model in a manner that accounts for the inherent seasonal variability of Canadian environments. As a result, it was necessary to develop additional *seasonal* (i.e. spring, summer, fall, and winter) estimates of average and low flow values for each stream segment. This process, known as *hydrological seasoning*, is described in the following sub-section.

4.3.1 Hydrological Seasoning

Before estimating seasonal flows, it was necessary to first define each hydrological season. In this regard, a hydrological season was defined as three continuous months of relatively similar flow rates. To more readily discern these seasons from the available data, the average daily flow of each station was standardized to have a mean of zero and variance of one, using the following equation.

$$Standardized\ Flow = (Average\ Daily\ Flow - Average\ Annual\ Flow)/STDEV \qquad (3)$$

Standardized flow values for the considered WSC stations are plotted in Figure 4-4. As shown, the lowest flow values occur from June to November, moderate flow values occur from December to February, and the highest flow values occur from March to May. Consistent with these observed trends, hydrological seasons were defined as follows: winter – December,

January, and February; spring – March, April, and May; summer – June, July, and August; and fall – September, October, and November.

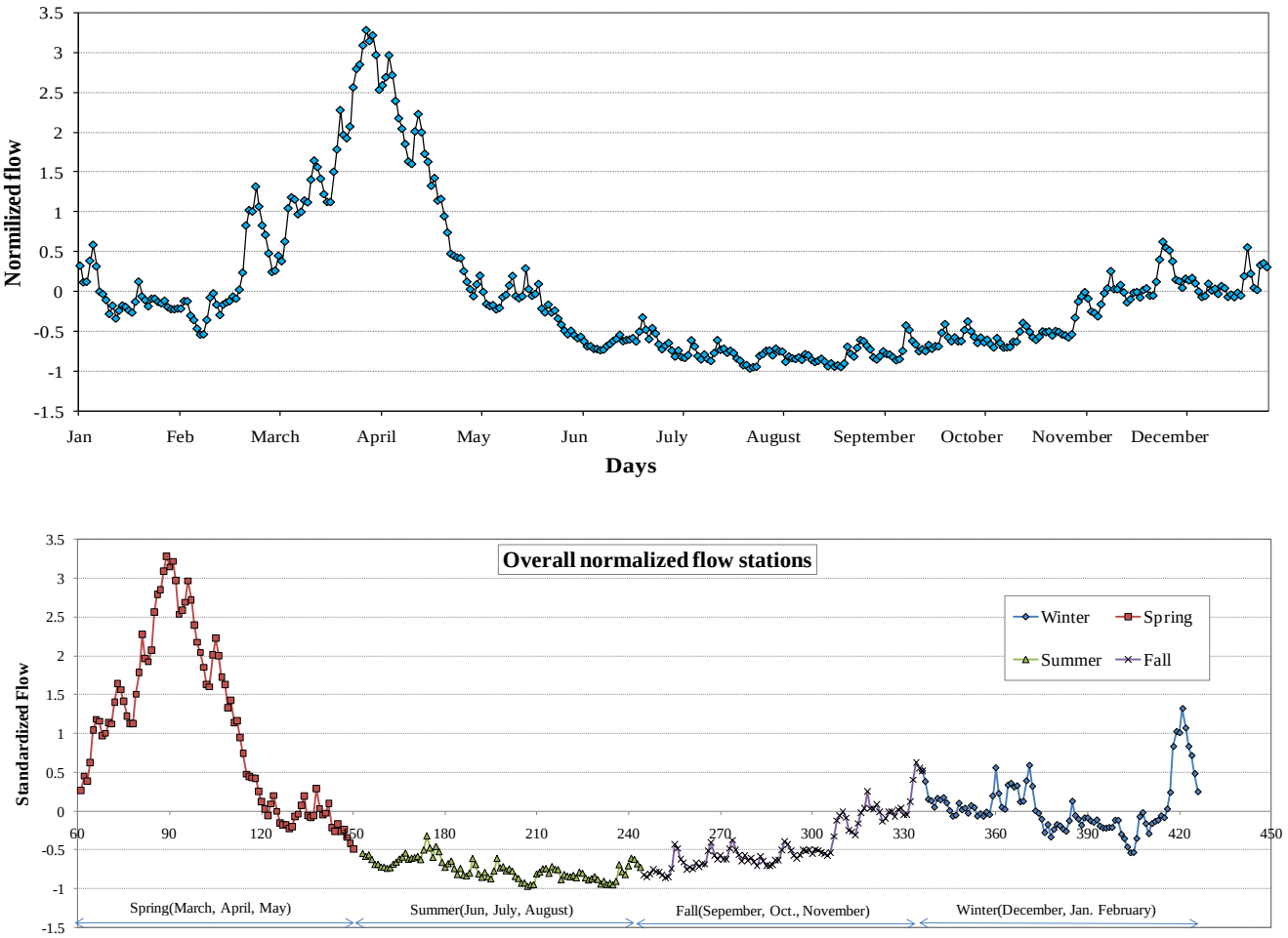


Figure 4-4: Determination of hydrological seasons using standardized flow values averaged over all WSC stations (top pane – raw standardized data record; bottom pane – time-shifted record with seasonal delineation)

4.3.2 Average Seasonal Flow

Similar to the estimation of average annual flow, average seasonal flow for each monitoring station was plotted against the corresponding drainage area, where average seasonal flows were determined by averaging daily flow data for a given hydrological season (see previous section). As was done for average annual flow, two linear regressions were calculated, corresponding to drainage areas greater than and less than 1,200 km^2. To address observed flow trends in the summer and fall, an additional linear regression was calculated using data for stations with a drainage area of less than 200 km^2. The resulting seasonal relationships between flow and drainage area, along with corresponding R-squared values, are given in Table 4-1 and graphs of each corresponding regression are provided in Appendix C. As shown in Table 4-1, drainage area is highly correlated with average seasonal flow and the regressions yielded R^2 values ranging from 0.78 to 0.99.

Table 4-1: Linear relationship between average seasonal flow rate (Q) and drainage area (DA), with corresponding R-squared values

Season	For segments with DA>1200 km^2	For segments with DA<1200 km2	For segments with DA<200 km2
Winter	Q = 0.0106 DA + 0.304 R^2 = 0.9916	Q = 0.0116 DA + 0.0442 R^2 = 0.9784	-
Spring	Q = 0.0203 DA + 0.2999 R^2 = 0.9975	Q = 0.0211 DA + 0.012 R^2 = 0.9688	-
Summer	Q = 0.0056 DA - 0.1916 R^2 = 0.9866	Q = 0.0058 DA - 0.2491 R^2 = 0.8744	Q = 0.0035 DA + 0.0939 R^2 = 0.7769
Fall	Q = 0.0071 DA + 0.2132 R^2 = 0.9887	Q = 0.0082 DA - 0.1328 R^2 = 0.9283	Q = 0.0068 DA + 0.0321 R^2 = 0.8777

4.3.3 Low Seasonal Flow

A variety of definitions and procedures for determining low flow have been proposed [121]. For example, low flow in the United States is generally indicated by either a “7Q10” or “7Q2” value, defined as the lowest average flow occurring over a seven day period with a ten (7Q10) or two (7Q2) year return interval. Alternatively, low flow can be defined as flow having an exceedance probability of some given percentage (e.g. 95% or 90%). In this study, low seasonal flow was defined according to a 95% exceedance probability – meaning that 5% of recorded flow values

for a given season would be less than or equal to the low flow value and the remaining 95% of recorded values would be greater than the low flow value.

After defining low flow values for each season at the WSC stations, the procedure for determining low seasonal flow values for un-gauged segments was analogous to the procedure for estimating of the average seasonal flow. Linear regression equations relating low seasonal flow and drainage area are given in Table 4-2 and further details are provided in Appendix C. As shown in Table 4-2, the R-squared values ranged from 0.69 to 0.99 and stations with a drainage area greater than 1,200 km^2 exhibit a relatively stronger correlation between flow and drainage area. For segments with a small drainage area, the liner regressions given in Table 4-2 sometimes yielded negative flow values – in such cases, the minimum measured flow value was utilized instead.

Table 4-2: Linear relationship between seasonal low flow rate (Q) and drainage area (DA), with corresponding the R-squared values

Season	For segments with DA>1200 km^2	For segments with DA<1200 km2
Winter	Q = 0.0027 DA - 0.3203 R^2 = 0.9883	Q = 0.0022 DA - 0.1138 R^2 = 0.874
Spring	Q = 0.0045 DA - 0.573 R^2 = 0.9849	Q = 0.0031 DA - 0.11 R^2 = 0.8227
Summer	Q = 0.0031 DA - 0.4475 R^2 = 0.9747	Q = 0.0028 DA - 0.3352 R^2 = 0.6916
Fall	Q = 0.0027 DA - 0.4499 R^2 = 0.9844	Q = 0.0021 DA - 0.2446 R^2 = 0.7749

4.4 Velocity

Along with stream flow, the PhATE model requires information about average and low flow velocities for each stream segment in order to generate the travel time of the compounds in the surface water (see equation (2) in section 2.4). For this study, velocity information was inferred using available flow data paired with relevant morphologic features of a given stream segment.

Average Velocity

The width (*W*), depth (*D*) and velocity (*V*) of a given stream segment have been shown to be logarithmically related to stream flow (*Q*) [122] as given in the following equations:

$$W = aQ^b \quad (4)$$

$$D = cQ^f \quad (5)$$

$$V = kQ^m \quad (6)$$

where *a*, *c*, *k* and *b*, *f*, *m* are hydrological coefficients such that $a \times c \times k = 1$ and $b + f + m = 1$.

Previous studies of the morphologic features of rivers in Southern Ontario have included portions of the Grand River watershed [123]. Table 4-3 summarizes the results of these studies, and includes location information (in terms of station identifier) along with the estimated values for *Manning's n* friction factor and hydrological coefficients given in eqns. 4-6.

To apply equations 4-6 to all segments in the watershed, each stream was classified according to its *Strahler* stream order. The *Strahler* stream order approach classifies a given stream segment based on the number of connecting upstream and downstream branches – when streams with the same order intersect, the order of the corresponding downstream segment is increased [124]. The *Strahler* stream order ranges from one (for head water segments) to seven at the most downstream pour-point of the Grand River watershed. *Strahler* stream orders for the Grand River watershed are given in Table 4-3.

Stream segments were divided into two categories according to stream order: (1) stream order < 4; and (2) stream order > 3. For stream order < 4, velocity relationships developed for station numbers 24-26 were applied. For stream order > 3, velocity relationships developed for station numbers 7, 17, and 29 were applied and averaged into a final velocity estimate.

Table 4-3: the relationships between discharge and velocity, area, depth, and with reported by Annable 1996

Station No.	Manning 'n'	V(m/s)	A(m^2)	D(m)	W(m)	STRAHLER
7	0.033	$0.3428Q^{0.3820}$	$2.9140Q^{0.6159}$	$0.2896Q^{0.4046}$	$11.7838Q^{0.2263}$	5
17	0.033	$0.2301Q^{0.5669}$	$4.3366Q^{0.4325}$	$0.2231Q^{0.4821}$	$14.4259Q^{0.0888}$	5
22	0.042	-	-	-	-	3
24	0.035	$0.2126Q^{0.1665}$	-	-	-	3
25	0.046	$0.2126Q^{0.1665}$	$4.7132Q^{0.8351}$	$0.1161Q^{0.45}$	$13.5511Q^{0.3214}$	1
26	0.032	$0.2126Q^{0.1665}$	$4.7280Q^{0.8705}$	$0.1161Q^{0.45}$	$13.5511Q^{0.3214}$	3
29	0.031	$0.4531Q^{0.2902}$	$2.2021Q^{0.7083}$	$0.2931Q^{0.4407}$	$8.4262Q^{0.2265}$	5
39	0.031	-	-	-	-	

Low Flow Velocity

The corresponding velocity in low flow conditions for each stream segment were calculated using the following equation [125]:

$$Low\ Flow\ Velocity = (Mean\ Flow\ Velocity)\left(\frac{Low\ Flow}{Mean\ Flow}\right)^{0.43}$$

Chapter 5
Numerical Experiments

5.1 PhATE Simulation (Uncalibrated)

As discussed previously, reliably predicting the concentration of pharmaceuticals in surface water depends on an adequate assignment of several hydrological and chemical parameters. In this study, these required parameters for the PhATE model were classified as being either *prescribed* or *estimated* parameters. Prescribed parameters included flow and velocity of stream segments and annual per capita pharmaceutical usage. Values for these parameters were derived from data that was readily available for the Grand River watershed and/or Canada. Conversely, appropriate values of estimated parameters (i.e. removal efficiencies of lagoons and secondary and tertiary treatment plants, in-stream loss, and human loss) for the given case study were not readily available. Thus, an initial survey of the literature was performed in order to establish a reasonable range of expected values for these parameters. Subsequent sensitivity analysis explored the influence of these parameters on model outputs, and various trial-and-error and automated calibration efforts adapted the parameter values to obtain model results that best matched observed behaviour in the Grand River watershed.

Exploring whether the use of seasonal parameters could improve PhATE predictions was an important objective of the research. As mentioned in Chapter 4 (Hydrological Data Estimation), seasonal low and mean flow and corresponding seasonal velocities were developed for each segment of the watershed using available data. These seasonal hydrologic parameters were incorporated into four Access database input files, corresponding to one input file per season. Also included in each input file were corresponding seasonal estimates of pharmaceutical loading and various loss parameters (see Table 5-1). Both the loss and loading parameters varied according to the type of pharmaceutical compound considered for a given simulation.

While an initial set of baseline (i.e. uncalibrated) simulations utilized the parameter values given in Table 5-1, subsequent numerical experiments (i.e. manual calibration, sensitivity analysis, and automated calibration) adjusted the various seasonal loss and loading terms in a systematic manner. The methodology and rationale for these additional experiments are described in the following sections.

Table 5-1: Seasonal removal efficiency of treatment plants and in-stream decay for the selected chemicals (values estimated based on a combination of literature review and expert judgment)

compound		Removal by Lagoon (%)	Removal by Secondary TP (%)	Removal by Tertiary TP (%)	In-Stream Loss (day^{-1})
Ibuprofen	Winter	99	78	87	0.139
	Spring	88	86	92	0.062
	Summer	77	90	90	0.288
	Fall	94	90	91	0.078
Naproxen	Winter	99	62	79	2.66
	Spring	95	73	79	2.66
	Summer	90	74	90	4.62
	Fall	99	69	87	1.39
Carbamazepine	Winter	21	4	4	0.001
	Spring	29	4	17	0.082
	Summer	28	21	17	0.072
	Fall	18	11	53	0.009
Gemfibrozil	Winter	99	78	87	0.139
	Spring	88	86	92	0.062
	Summer	77	90	90	0.288
	Fall	94	90	91	0.078
Sulfamethoxazole	Winter	58	39	56	1.111
	Spring	70	33	56	1.145
	Summer	58	56	40	2.968
	Fall	58	15	70	1.127
Trimethoprim	Winter	82	42	55	0.109
	Spring	82	38	41	0.109
	Summer	82	51	35	0.109
	Fall	82	42	53	0.109
Bezafibrate	Winter	50	15	58	0.081
	Spring	50	77	58	0.081
	Summer	50	54	58	0.081
	Fall	50	15	58	0.081
NP	Winter	32	79	74	0.031
	Spring	32	79	74	0.208
	Summer	32	79	74	0.734
	Fall	32	79	74	0.031
DEET	Annual	50	37	62	0.791

5.2 Manual Calibration

The uncalibrated PhATE simulations yielded extremely unrealistic predictions for certain compounds (e.g., naproxen) when applied to the Grand River watershed. For these compounds, and for reasons that are described below, using literature and/or engineering judgment was not an effective method for assigning certain parameter values. As a result, such parameters were targeted for manual "trial-and-error" calibration. The manual calibration exercise consisted of a

series of simulations for each compound. These numerical experiments involved manually perturbing selected parameter values and then running the corresponding revised PhATE model. The objective of each manual calibration was two-fold: (1) to achieve a better correspondence between PhATE outputs (i.e. predicted pharmaceutical concentrations in the various stream segments of the Grand River) and previously measured concentrations; and (2) to gain preliminary insights about the influence of individual parameters on model predictions.

To improve the results of the PhATE simulations of NP and DEET in the Grand River watershed, the loading terms for these compounds were selected for manual calibration. These terms were chosen for manual calibration because their usage in the Grand River watershed is not known and uncalibrated values of these terms were assigned using U.S. data for total NP and NPE and for DEET.

For naproxen, the uncalibrated simulation used an average of literature-derived values for assigning treatment plant removals and in-stream loss parameters. However, this approach yielded PhATE predictions which significantly underestimated naproxen concentrations, relative to the measured data – evidently the uncalibrated loss and removal rates were too high. In fact, researchers have suggested that chemical removal in Canadian treatment plants is likely to be lower than in other countries as the result of the generally colder climate [6]. Therefore, manual calibration was applied to these loss terms to explore whether reducing the loss rates to below average values (see Table 5-2) could improve model predictions.

In the Grand River watershed, it is reasonable to expect ibuprofen and naproxen usage to spike in the winter, and DEET usage to peak in the summer [42, 44, 45]. However, quantitative data on seasonal usage of these compounds was not available and as a result the uncalibrated simulations did not consider seasonality. This motivated a series of manual calibration experiments that considered the influence of markedly different seasonal usage of ibuprofen, naproxen, and DEET within the Grand River watershed. For these experiments, the annual usage of each compound was divided among the four seasons and the percentages allocated to each season were manually calibrated. The resulting estimated per capita usage for each compound is given in Table 5-3 along with prescribed annual usage values.

Table 5-2: Low seasonal parameters for naproxen

Compound		Removal by Lagoon (%)	Removal by Secondary TP (%)	Removal by Tertiary TP (%)	In-Stream Loss (day^{-1})
naproxen	Winter	90	32	50	0.060
	Spring	90	42	50	0.060
	Summer	90	37	73	0.040
	Fall	90	32	50	0.051

Table 5-3: Annual and seasonal usage of the selected compounds

Compound	Annual use (kg/person-year)	Winter use (kg/person-year)	Spring use (kg/person-year)	Summer use (kg/person-year)	Fall use (kg/person-year)
Ibuprofen	0.008183	0.015285	0.008838	0.002291	0.006219
Naproxen	0.001825	0.002628	0.002482	0.000730	0.001460
Carbamazepine	0.000727	0.000727			
Gemfibrozil	0.000126	0.000126			
Sulfamethoxazole	0.000684	0.000684			
Trimethoprim	0.000167	0.000167			
Bezafibrate	4.63E-05	4.63E-05			
NP	0.000905	0.000905			
DEET	0.000752	0.000362	0.000724	0.001200	0.000724

5.3 PhATE Parameters Sensitivity Analysis

A sensitivity analysis (SA) was conducted to evaluate the influence of estimated parameters on predicted pharmaceutical concentrations in the surface waters of the Grand River watershed. Sensitivity analysis is a procedure for ranking parameters in terms of their overall influence on model outputs [126]. Different strategies for sensitivity analysis have been proposed [127-130], and this study considered a screening-level global sensitivity analysis technique based on the Taguchi design of experiments (TDOE) approach [131-136].

The Taguchi design of experiments method is a fractional-factorial experimental approach that has been a popular tool for tuning various manufacturing processes [133] and has recently been adapted for performing sensitivity analyses on model parameters [131, 135]. The method requires a series of numerical experiments involving a discrete set of values (levels) for the various uncertain parameters (factors). Instead of evaluating all factor-level combinations, orthogonal arrays are utilized to define an experimental layout that minimizes computational expense while maximizing information gain. To assess the various sensitivities of interest, the experimental results can be analyzed quantitatively or graphically.

For this study, the required TDOE experiments were analyzed using a quantitative analysis of variance (ANOVA) approach [132, ch. 7]. In this regard, parameters that explain a larger percentage of variation are more influential and will have higher TDOE scores. To set up the Taguchi experiments, 4 and 5 levels for each parameter were considered. Given these settings and the number of factors (i.e. 5, the number of estimated parameters) the L_{16} and L_{25} orthogonal arrays were selected for the 4- and 5-level designs, respectively. The results of these SA experiments are discussed in Section 6.2 .

5.4 PhATE Auto Calibration

Automated calibration (also known as parameter estimation) applies an optimization search algorithm to adjust uncertain model parameters in order to obtain the best possible correspondence between model outputs and historical observation data. Numerous local, global, and hybrid search algorithms have been successfully applied to calibrate various environmental models (e.g. see [126] for list of alternatives). Use of an automated calibration algorithm requires definition of an objective function and in this study the conventional weighted sum of squared

residual (WSSR) approach was utilized [137]. The following sub-sections describe the optimization software and algorithms utilized in this research.

OSTRICH

OSTRICH (Optimization Software Tool for Research In Computational Heuristics) is an open-source and model-independent code that implements numerous local, global and hybrid search algorithms, including non-linear regression, particle swarm optimization, and dynamically dimensioned search routines [138]. After linking the OSTRICH toolkit with the PhATE modeling system (see below), the DDS algorithm [139] was utilized for performing automated calibration.

To use OSTRICH, it was first necessary to link it with the desired simulation model (i.e. PhATE). OSTRICH is specifically designed so that it can easily be linked with models that accept and generate text-based input/output files with no user interaction required. However, the PhATE model works *only* through a graphical user interface (GUI) and depends heavily on user-interaction via various button clicks and dialog windows. Furthermore, the PhATE model utilizes the Access Database file format for its output files. As a result, linking OSTRICH with the PhATE model was not trivial. Therefore, Webber Chan, a co-op student from the department of Software Engineering, was tasked with modifying the OSTRICH software to support the Access Database file format. Furthermore, to programmatically manipulate the input of the PhATE model, Mr. Chan made use of AutoHotKey – an open-source utility for windows that can simulate keystrokes and mouse clicks. Appropriate AutoHotKey scripts were created allowing OSTRICH to run the PhATE model without user intervention.

DDS

The Dynamically Dimensioned Search (DDS) algorithm was employed for calibration of the PhATE model [139]. The DDS algorithm focuses on finding “good-enough” global solutions within a specified maximum computational budget. Designed to mimic the trial-and-error approach commonly employed by practitioners, DDS may be viewed as a kind of stochastic direct search procedure (Tolson, personal communication). The algorithm requires no tuning and the search dimension is dynamically refined as optimization proceeds.

Chapter 6
Results and Discussion

6.1 Simulation Results (Uncalibrated)

The cumulative distribution of the measured concentrations was used to show the efficiency of the model to predict a reliable range of concentration for each season. Figure 6-1 shows the predicted concentration (PEC) of ibuprofen, the limit of detection (LOD) and the limit of quantification (LOQ) along with the empirical cumulative distribution function of the measured concentration values. The same plots for the other compounds (i.e. naproxen and carbamazepine, NP and DEET) are presented in Appendix D. In these plots, the measured concentrations below LOQ were assigned the average of LOQ and LOD, and similarly, measured concentrations below LOD were assigned the half the LOD values.

The plots presented in Figure 6-1 and Appendix D demonstrate the following results:

- For ibuprofen and naproxen, about 50% of measured concentrations in summer, spring, and winter fell within the simulated concentrations associated with average seasonal mean flow and average seasonal low flow. However, in the fall, only 20-30% of the measured concentrations fell within the corresponding simulated concentration range.
- Simulated concentrations of carbamazepine showed good agreement with the measured data. Only one measured data point in the spring and one in the summer exceeded the low flow-based simulated concentration. The mean flow concentration in winter and spring was simulated less than the LOQ.
- Conversely, less than 30% of NP measured concentrations were between the simulated concentrations, as the measured data distributed widely.
- For DEET, about 40 to 60 percent of the measured concentrations fell within the simulated concentrations in low and mean flow. A small number of measured concentrations exceeded the low flow simulated concentration in all seasons, with the exception of the measured data in the spring when 20% of the measured data were greater than the simulated concentration associated to low flow.

Overall, approximately fifty percent of the measured concentrations were between the seasonal simulated mean flow concentration and low flow concentration. However, more than 85 percent of the measured concentrations of the compounds were less than or equal to the seasonal simulated low flow concentration. The model tended to over predict concentrations, and where model predictions were poorly matched to the measured data, the misfits tended to be due to the model over-predicting rather than under-predicting. This trend was attributed to the fact that many of the measured concentrations were likely sampled at times when the flow rate was greater than the seasonal average flow.

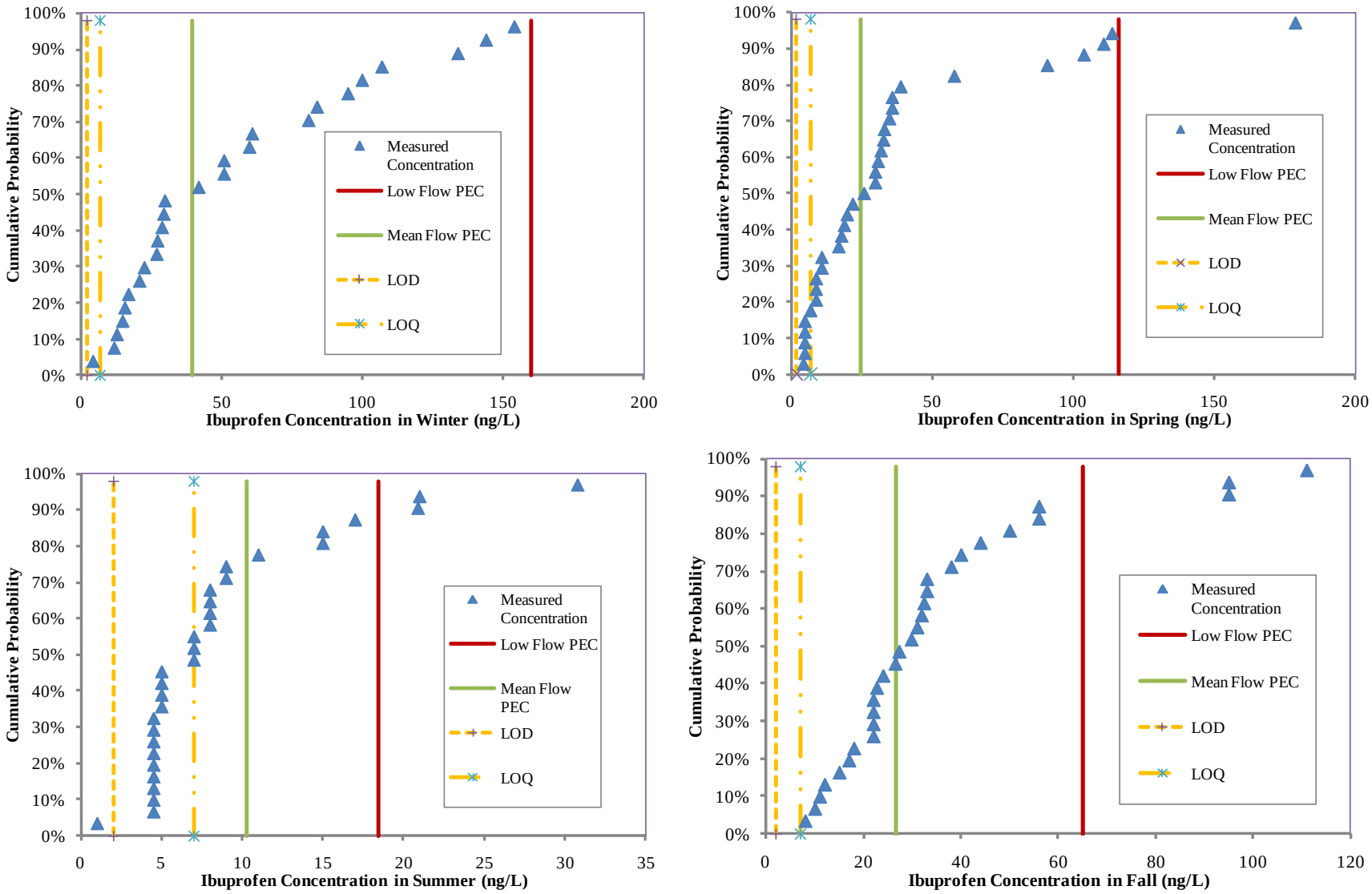


Figure 6-1: Comparing seasonal simulated concentration of ibuprofen and the seasonal cumulative measured data – PEC: predicted concentration, LOD: limit of detection, and LOQ: limit of quantification

6.2 Results of PhATE Parameters Sensitivity Analysis

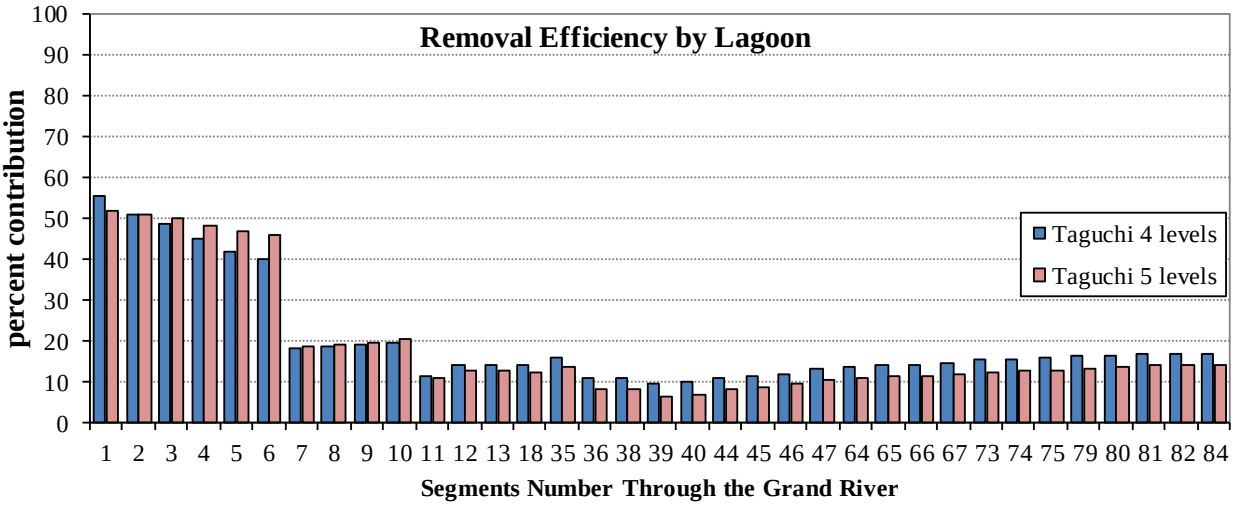
To assess the sensitivity of the selected PPCPs (i.e. ibuprofen, naproxen, carbamazepine, gemfibrozil, sulfamethoxazole, and trimethoprim) concentrations in the surface water to the PhATE model parameters, the sum of squared differences (SSD) and the percent contribution explained by the sum of squared differences were used. The SSD was defined as the summation of squared differences between the average concentrations at different levels and the average overall concentrations. The percent contribution, which is the ratio of each SSD to the total SSD, normalized the magnitude of the variation.

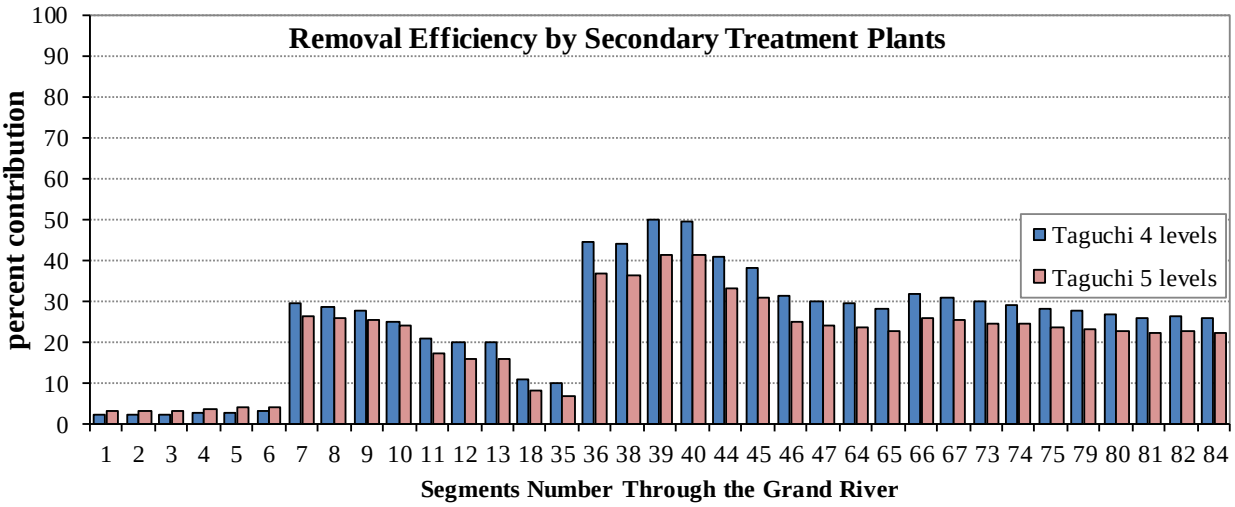
As stated in Section 5.3 , two Taguchi orthogonal array designs, L'_{16} and L'_{25}, were deemed appropriate for sensitivity analysis in this study; therefore, two separate analyses were conducted for ibuprofen to compare them and pick the best one (see Figure 6-2). The comparison showed that, in general, there was an insignificant difference between the two designs; however, using L'_{16} yielded more reasonable results. For example, the results of the L'_{16} experiment were more convenient to show whether the given segment received effluent from a specific type of treatment plant. Therefore, a sensitivity analysis of each compound was conducted by applying the Taguchi method using 4 levels (L'_{16}).

For the selected compounds, the percent contribution values and the sum of squared differences of each parameter on concentrations are shown in histograms along the Grand River segments. The histograms presenting results of the sensitivity analysis for the ibuprofen parameters are shown in Figure 6-2 and Figure 6-3, and the same histograms for the other compounds are presented in Appendix E. Parameters with a larger percent of the overall variation in the concentrations had a more significant influence on model outputs. The results indicated that the upper stream segments of the Grand River were less affected than the downstream segments (from segment 36). The downstream segments of the Grand River receive the effluent of more populated treatment plants (e.g., Waterloo and Kitchener wastewater treatment plants); therefore, parameters are likely to have more considerable influence on the concentrations.

Generally, human loss, which can represent the effect of loading as well, and removal efficiency by secondary treatment plants were recognized as parameters with the most significant

effect on concentrations of PPCPs. Wastewater treatment removal and loading are suggested to have equal effects on all concentrations within the watershed [17]. However, the results of this study showed that the treatment plant closest to a segment usually has a greater effect on the concentration in comparison with the effect of other treatment plants. Nonetheless, the influence of each parameter is highly related to its feasible interval. For example, the concentrations of sulfamethoxazole and naproxen with a high in-stream decay value (i.e. higher than 11 day^{-1}) were considerably affected by in-stream decay rate. This parameter is suggested to have a greater effect on low concentrations and a lower effect on high concentrations, which usually occur in locations close to wastewater treatment plants [17].





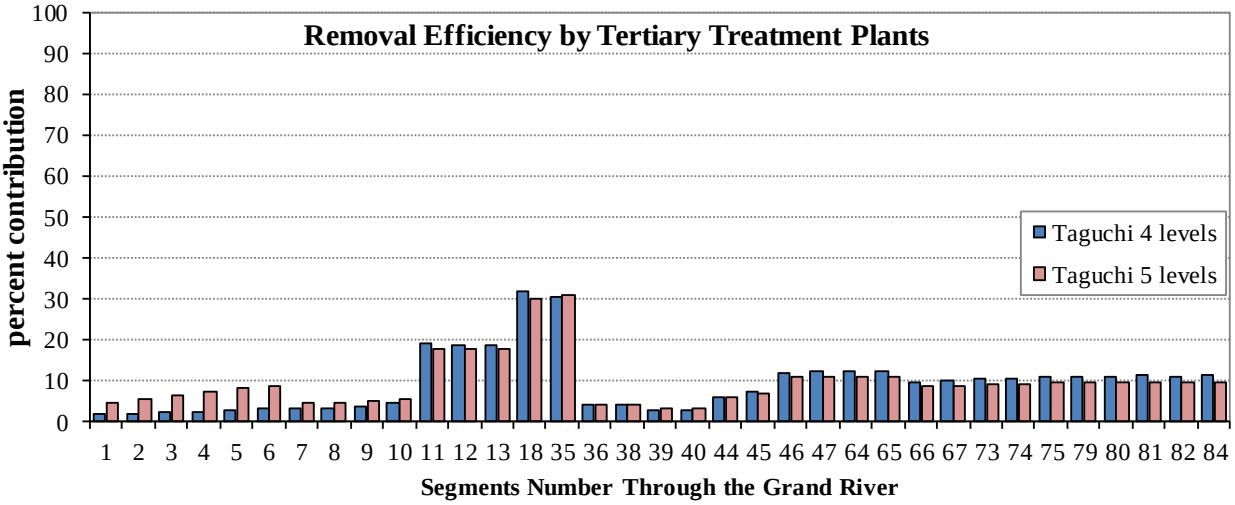


Figure 6-2: The percent contribution of parameters on the concentrations of ibuprofen (to be continued)

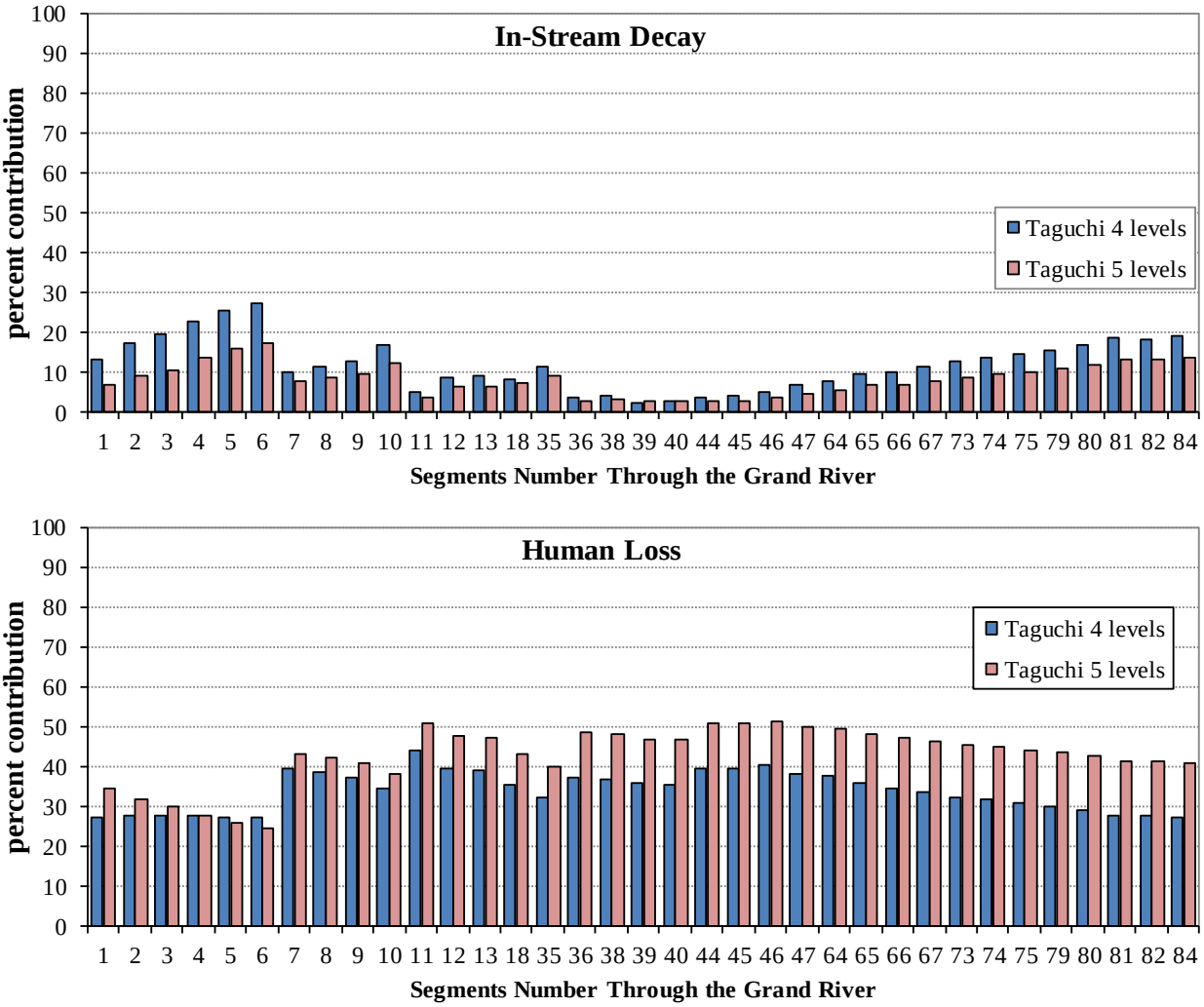


Figure 6-2: The percent contribution of parameters on the concentrations of ibuprofen (continued)

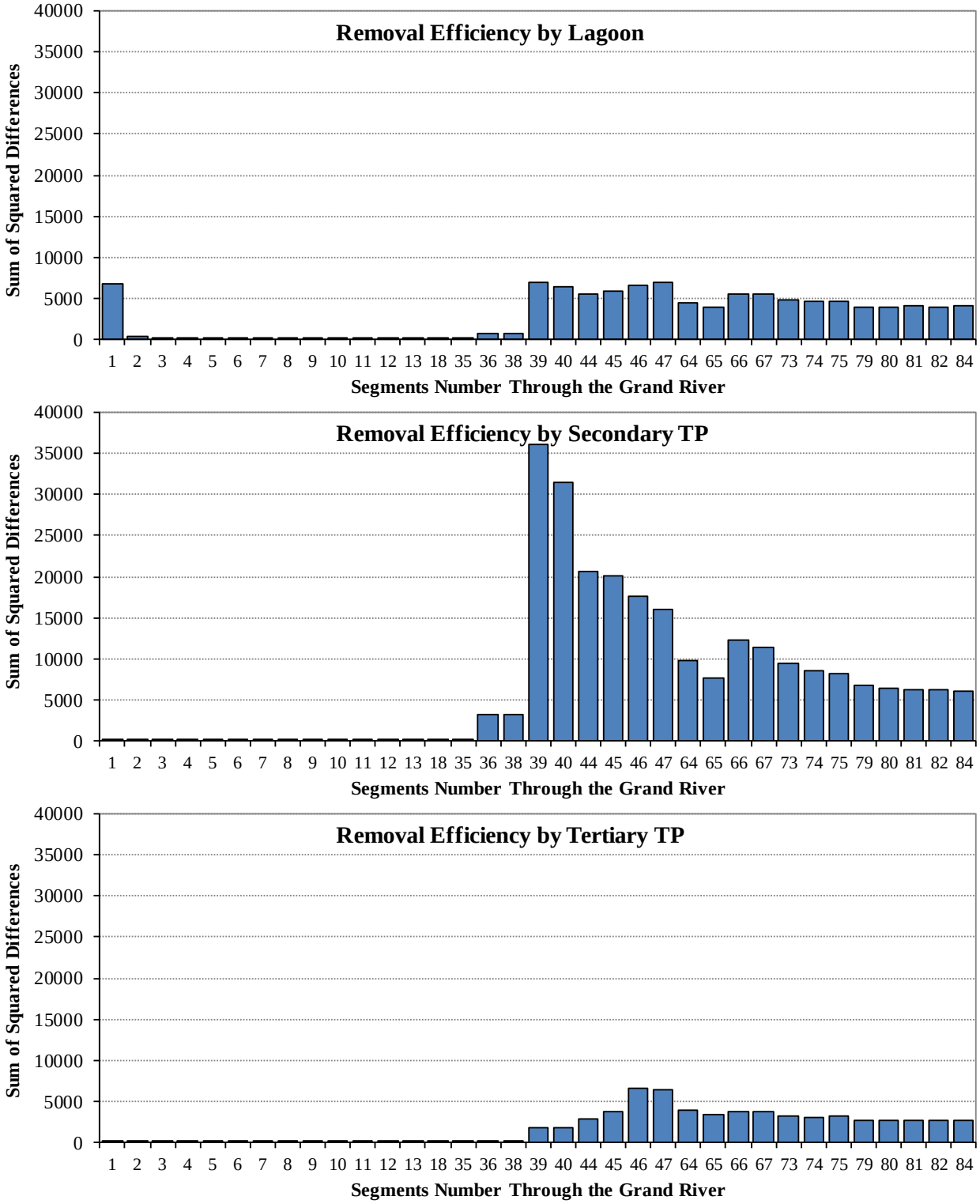


Figure 6-3: The sum of squared differences of ibuprofen concentrations at four different levels (to be continued)

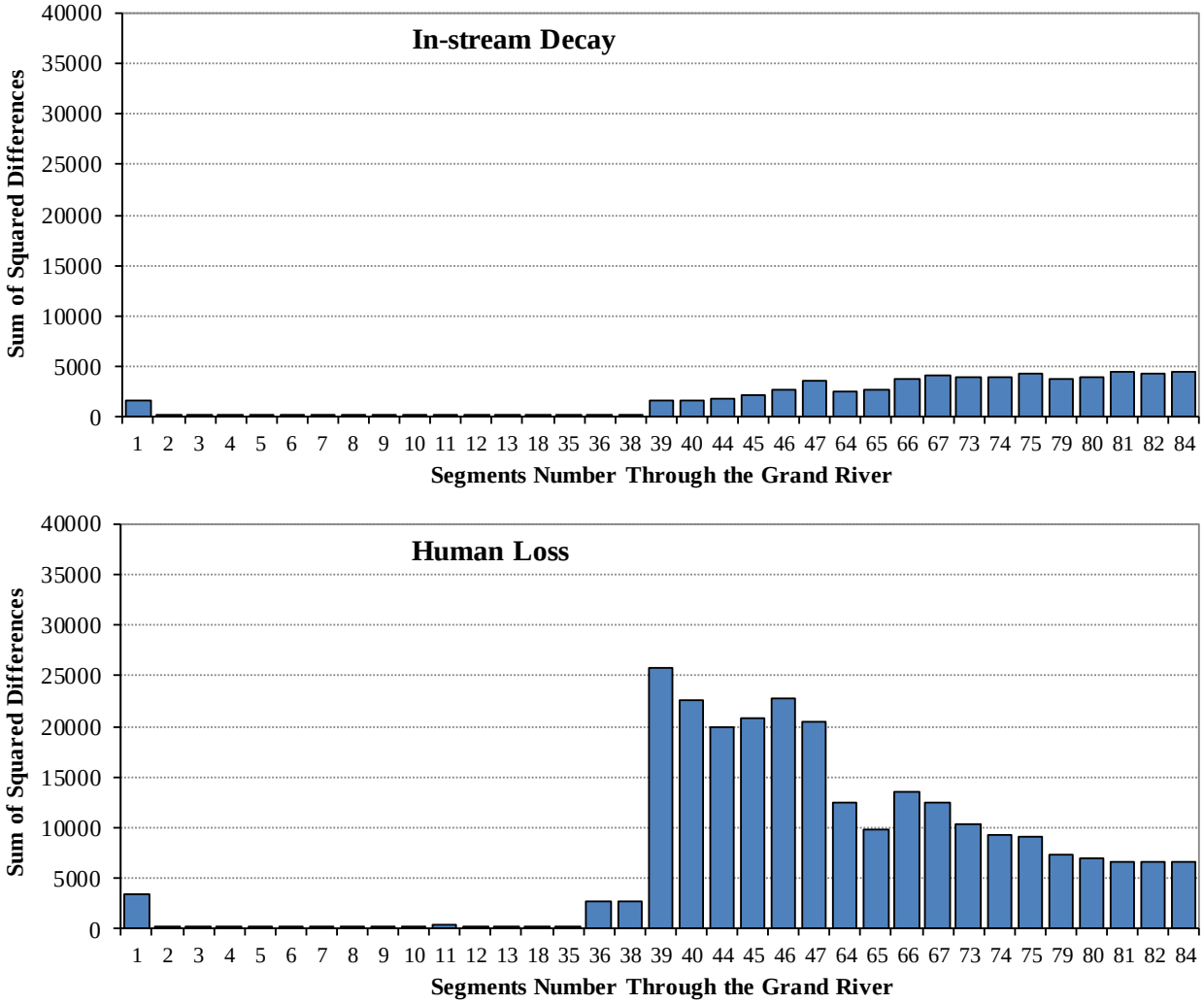


Figure 6-3: The sum of squared differences of ibuprofen concentrations at four different levels (continued)

6.3 Calibration Results

Using the DDS optimization algorithm through the OSTRICH interface, the five PhATE model parameters (i.e., removal efficiency of lagoon, removal efficiencies of secondary and tertiary treatment plants, in-stream decay, and human loss) were seasonally calibrated to obtain model results that best matched to the observed concentrations in the Grand River watershed. Calibration was performed based on the ranges for the parameter values reported in the literature

for each parameter and using the average parameter values as the initial solution. The calibration objective function was defined as minimizing the weighted sum of the squared deviations (errors – SSE) of simulated concentration values from measured data. Equal importance (weights) was assumed for all observations while calibrating for all compounds except for bezafibrate and sulfamethoxazole. For calibration of these two compounds, the measured concentrations above the detection limit received a greater weight (i.e., a weight twice as large as the weight of observations below the detection limit).

Two hundred function evaluations were employed in the auto-calibration process. Each function evaluation consisted of *n* PhATE model runs, where *n* was the number of available observations in each season. For example, for the ibuprofen calibration in winter, each function evaluation consisted of 20 PhATE model runs, one for each of the input files. Approximately 4 seconds was the required time for the PhATE model to run on a desktop computer with an Intel® Core™i3 CPU (520 @ 2.93GHz). Therefore, each function evaluation, e.g., consisting of 20 model runs, required about 80 seconds, and a calibration trial with only 200 function evaluations required up to 4.5 hours. Going beyond 200 function evaluations was out of the available computational budget because there was a considerable number of calibration trials for different seasons for each compound and because it was not possible to work with the computer while running.

The sufficiency of using 200 function evaluations was tested using two calibration trials with higher numbers of function evaluations, one for ibuprofen in winter (with 2000 function evaluations) and another calibration trial for naproxen in fall (with 1400 function evaluations). These experiments showed no significant improvement over the experiments with 200 function evaluations. The uncalibrated value of SSE (objective function value) for ibuprofen was 296340, while after calibration using 200 and 2000 function evaluations, the SSE values reached 6513 and 6034, respectively. For naproxen, calibration did not improve the SSE significantly, as SSE slightly decreased from 15406 uncalibrated to about 11342 and 11237 after calibration with 200 and 1400 function evaluations, respectively. Figure 6-4 and Figure 6-5 also graphically compare the model performance in the uncalibrated and after-calibration phases in the aforementioned experiments.

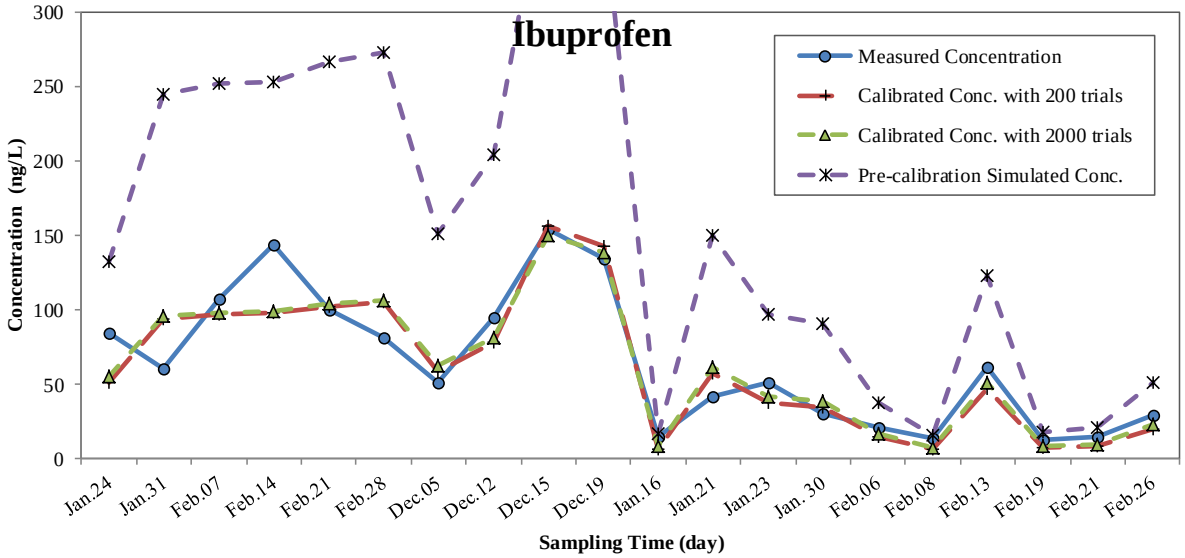


Figure 6-4: Measured and simulated concentrations of ibuprofen in winter at sampling time

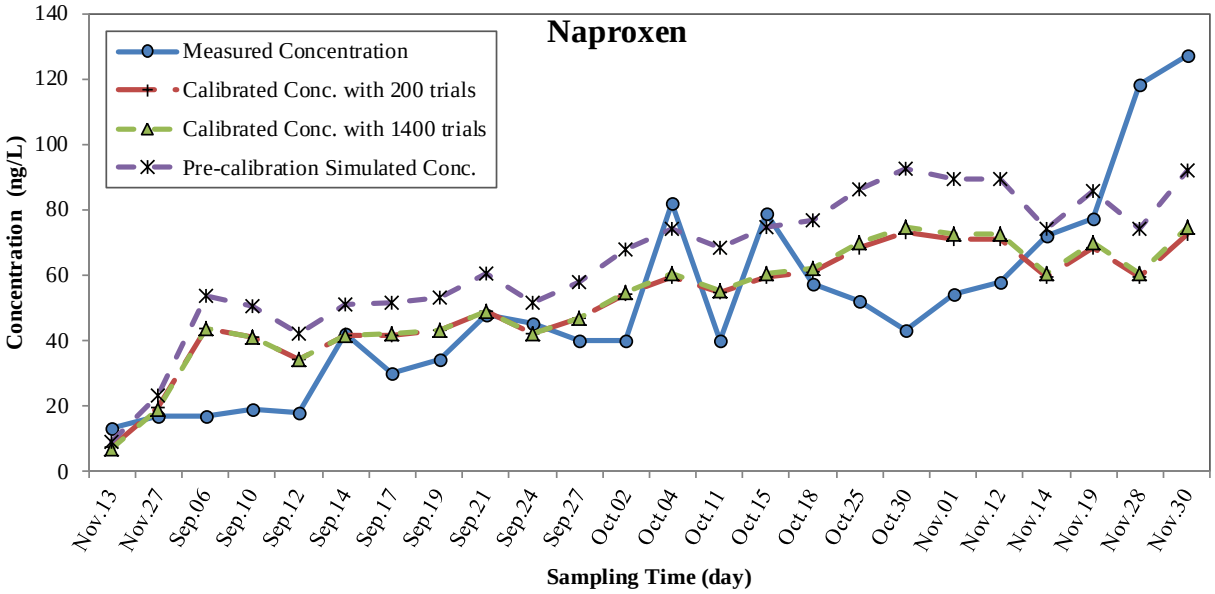


Figure 6-5: Measured and simulated concentrations of naproxen in fall at sampling time

A composite scaled sensitivities (CSS) analysis was also conducted through OSTRICH on the best parameter sets that were found for each compound in each season. The CSS values represent the overall sensitivity of the model expressed by each parameter [137]. A high value of CSS represents a high sensitivity of the model output to the parameter [52, 85]. The CSS depends on the parameter values and might not properly represent the sensitivity of the model to parameters with low values or highly correlated parameters [137]. Table 6-1 shows the CSS and the calibrated parameter values, which were referred to as *the most probable seasonal parameters* of the selected compounds for the case.

According to the CSS values reported in Table 6-1 and similar to the results of the sensitivity analysis in section 6.2 , human loss had the most significant influence on the concentrations of the selected compounds in the surface water. The removal efficiency of the secondary treatment plants was the second most important parameter, especially for ibuprofen, naproxen, and NP. In-stream decay also significantly affected concentrations of naproxen, DEET, trimethoprim.

As shown in Table 6-1, the calibrated human loss values for each compound varied for each season, while human loss is expected to remain constant for all seasons. This variation can be the result of imperfect modelling and calibration and/or seasonality in loading. As explained in Section 5.2 (model parameterization for calibration), loading was fixed in the uncalibrated step for each season; therefore, seasonality in loading can be partially conveyed by seasonality in human loss parameters.

Table 6-1: Calibrated Parameter values and Composite Scaled Sensitivities (numbers in parentheses) (to be continued)

Compound	Season	Parameters				
		Removal by Lagoon (%)	Removal by Secondary TP (%)	Removal by Tertiary TP (%)	In-Stream Loss (day^{-1})	Human Loss (%)
Ibuprofen	winter	78 (9.44)	84 (322.85)	87 (73.85)	0.083 (2.21)	89 (608.38)
	spring	97 (2.45)	86 (196.68)	84 (29.57)	1.093 (9.95)	76 (119.47)
	summer	79 (0.88)	93 (64.69)	82 (19.67)	0.418 (1.1)	83 (36.06)
	fall	98 (13.48)	93 (360.33)	87 (77.24)	0.002 (0.03)	79 (148)
Naproxen	winter	95 (0.36)	32 (42.89)	52 (6.13)	2.150 (46.71)	66 (187.93)
	spring	91 (0.31)	32 (24.24)	52 (4.23)	2.314 (23.37)	66 (107.62)
	summer	90 (0.19)	42 (17.41)	78 (3.61)	1.154 (5.90)	64 (44.58)
	fall	98 (0.89)	33 (24.49)	55 (6.48)	0.663 (9.84)	80 (220.21)
Carbamazepine	winter	49 (0.35)	37 (10.62)	39 (2.29)	0.237 (1.71)	82 (100.39)
	spring	0 (0)	12 (1.87)	68 (2.23)	0.238 (0.91)	83 (74.21)
	summer	33 (0.36)	21 (6.43)	24 (1.62)	0.005 (0.06)	79 (111.42)
	fall	13 (0.09)	21 (6.40)	45 (2.75)	0.238 (2.23)	85 (159.02)

Table 6-1: Calibrated Parameter values and Composite Scaled Sensitivities (numbers in parentheses) (Continued)

Compound	Season	Parameters				
		Removal by Lagoon (%)	Removal by Secondary TP (%)	Removal by Tertiary TP (%)	In-Stream Loss (day^{-1})	Human Loss (%)
DEET	winter	67 (0)	14 (4.14)	54 (0.41)	5.219 (25.60)	1 (0.26)
	spring	2 (0)	0 (0)	45 (1.06)	4.398 (34.52)	0 (0)
	summer	79 (0.04)	21 (27.47)	53 (2.36)	3.288 (60)	1 (1.06)
	fall	29 (0.01)	40 (33.5)	60 (1.46)	4.156 (42.31)	9 (5.07)
NP	winter	63 (0.29)	81 (64.83)	79 (7.54)	1.432 (6.62)	74 (49.47)
	spring	0 (0)	95 (92.47)	82 (10.91)	1.437 (4.22)	47 (7.14)
	summer	44 (0.52)	81 (157.45)	92 (21.61)	1.020 (9.125)	0 (1.52)
	fall	32 (2.07)	89 (198.91)	86 (41.24)	0.120 (2.36)	57 (47.31)
Gemfibrozil	winter	15 (0.01)	45 (1.20)	62 (1.01)	0.290 (0.29)	75 (6.24)
	spring	60 (0.03)	33 (1.05)	55 (1.09)	0.339 (0.41)	75 (9)
	summer	60 (0.01)	18 (0.55)	69 (1.02)	1.095 (1.64)	87 (19.38)
	fall	15 (0.01)	41 (1.57)	75 (1.71)	0.288 (0.46)	87 (18.91)

Table 6-1: Calibrated Parameter values and Composite Scaled Sensitivities (numbers in parentheses) (Continued)

Compound	Season	Parameters				
		Removal by Lagoon (%)	Removal by Secondary TP (%)	Removal by Tertiary TP (%)	In-Stream Loss (day^{-1})	Human Loss (%)
Bezafibrate	winter	2 (0)	0 (0)	16 (0.52)	0.003 (0.01)	40 (4.94)
	spring	0 (0)	1 (0.05)	15 (0.55)	0.046 (0.17)	40 (5.56)
	summer	50 (0.05)	68 (4.58)	68 (2.8)	0.161 (0.38)	45 (3.46)
	fall	33 (0.06)	33 (3.8)	68 (5.12)	0.141 (0.87)	40 (6.76)
Sulfamethoxazole	winter	No Calibration as all the measure data were below the detection limit				
	spring	17 (0.03)	18 (4.78)	22 (3.92)	0.861 (12.89)	80 (142.79)
	summer	21 (0.17)	23 (11.09)	86 (28.06)	0.201 (5.6)	86 (258.00)
	fall	17 (0.07)	20 (10.06)	60 (17.48)	0.683 (19.16)	80 (205.34)
Trimethoprim	winter	65 (0.10)	42 (3.08)	92 (4.31)	0.04 (0.08)	53 (5.25)
	spring	65 (0.01)	65 (6.08)	92 (5.61)	0.039 (0.06)	50 (3.80)
	summer	66 (0.32)	84 (20.53)	93 (14.35)	0.038 (0.13)	53 (5.73)
	fall	65 (0.26)	79 (15.31)	93 (11.36)	0.04 (0.12)	56 (6.36)

To visually compare the performance of the PhATE model before and after calibration, the simulated concentrations are shown versus the corresponding measured data in Figure 6-6 to Figure 6-14. Evidently from the figures, the PhATE model was capable of predicting the variation in concentrations of PPCPs and EDCs, when actual flows were used, and calibration resulted in a significantly better estimation (compared to uncalibrated) of the concentrations in the Grand River watershed. The PhATE model simulation had better results while simulating ibuprofen, naproxen, carbamazepine, and gemfibrozil compared to other compounds. The estimated R-squared values for these drugs ranged from 0.48 for ibuprofen to 0.69 for gemfibrozil.

In April 2008, when there was a peak in the measured concentrations, the model simulation failed to reasonably predict the measured concentrations of ibuprofen, naproxen, and carbamazepine (showed in Figure 6-6 to Figure 6-14). The assessment of the flow regime also showed that there was a large peak in the flow rate in April 2008, suggesting a higher amount of treatment bypass in the watershed or lower efficiency of the treatment plants at that time.

Evaluation of the calibration results for compounds that were frequently measured below the detection limit (e.g., 70% of NP concentrations were reported below the detection limit) was challenging. The concentrations reported for observations below detection limit were assumed to be equal to the detection limit for the calibration purpose. As shown in Figure 6-10, the simulated concentrations of NP did not fit the measured data well, so the calibrated parameters in Table 6-1 might be unreliable. The occasional jumps (peaks) from below detection limit to considerable values may suggest the pulse-type release of this industrial compound into the environment. It must be mentioned that NP (an endocrine disrupting compound) and DEET (a personal care product) have different pathways of entering into the environment other than pharmaceuticals. Also, there is an uncertainty in the mass loading of these compounds which results in uncertainties in their predictions.

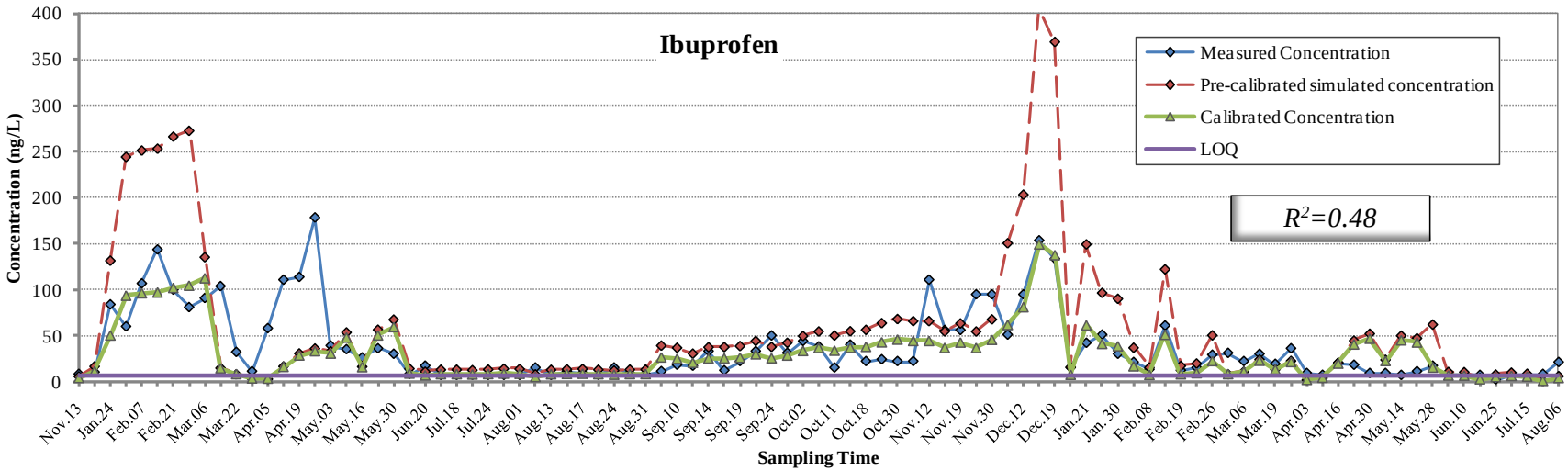


Figure 6-6: Simulated concentrations of ibuprofen before and after calibration compared to its measured concentrations

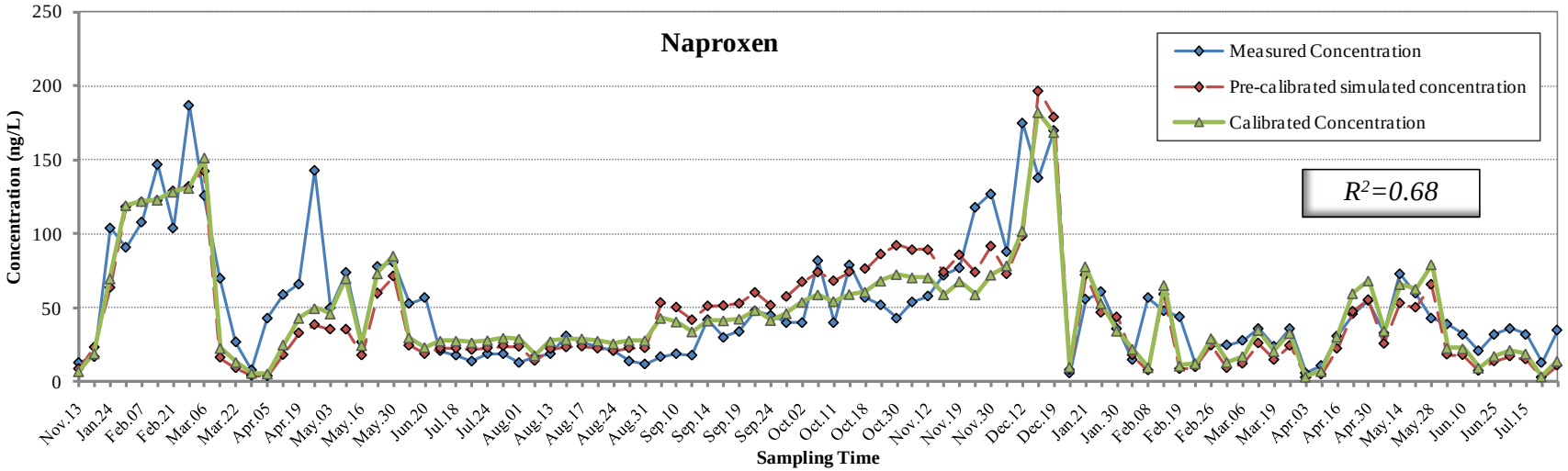


Figure 6-7: Simulated concentrations of naproxen before and after calibration compared to its measured concentrations

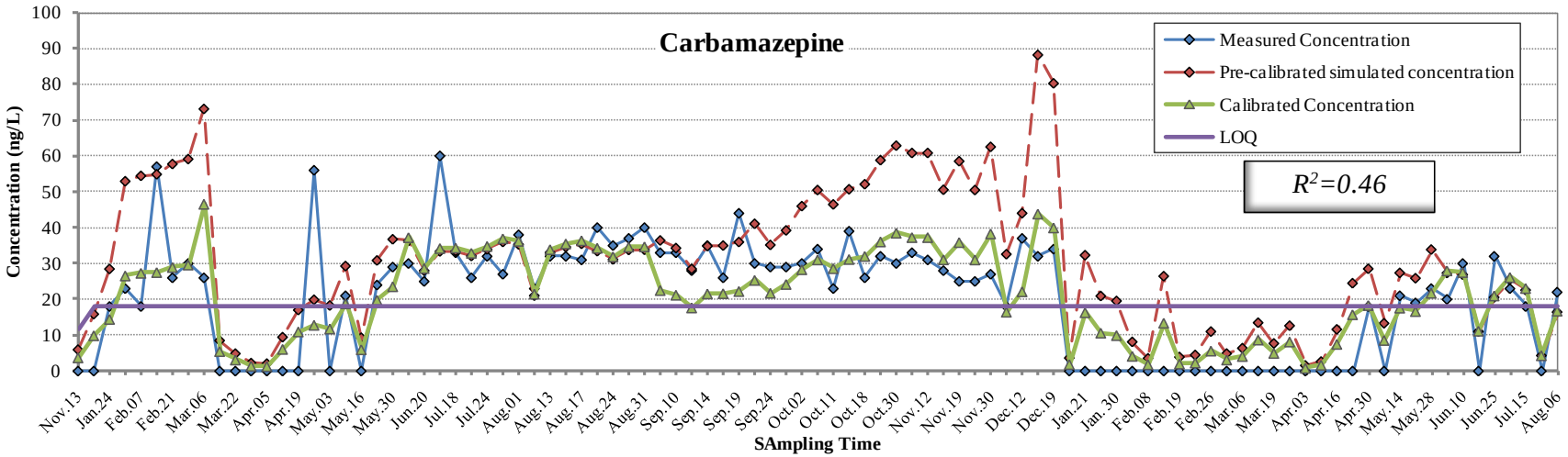


Figure 6-8: Simulated concentrations of carbamazepine before and after calibration compared to its measured concentrations

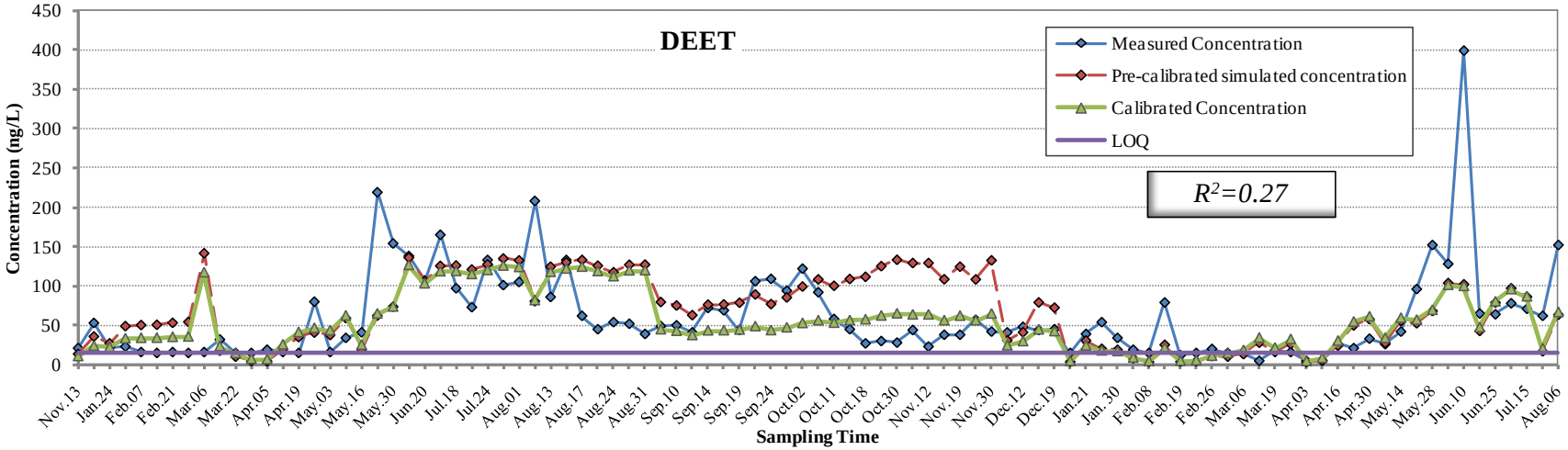


Figure 6-9: Simulated concentrations of DEET before and after calibration compared to its measured concentrations

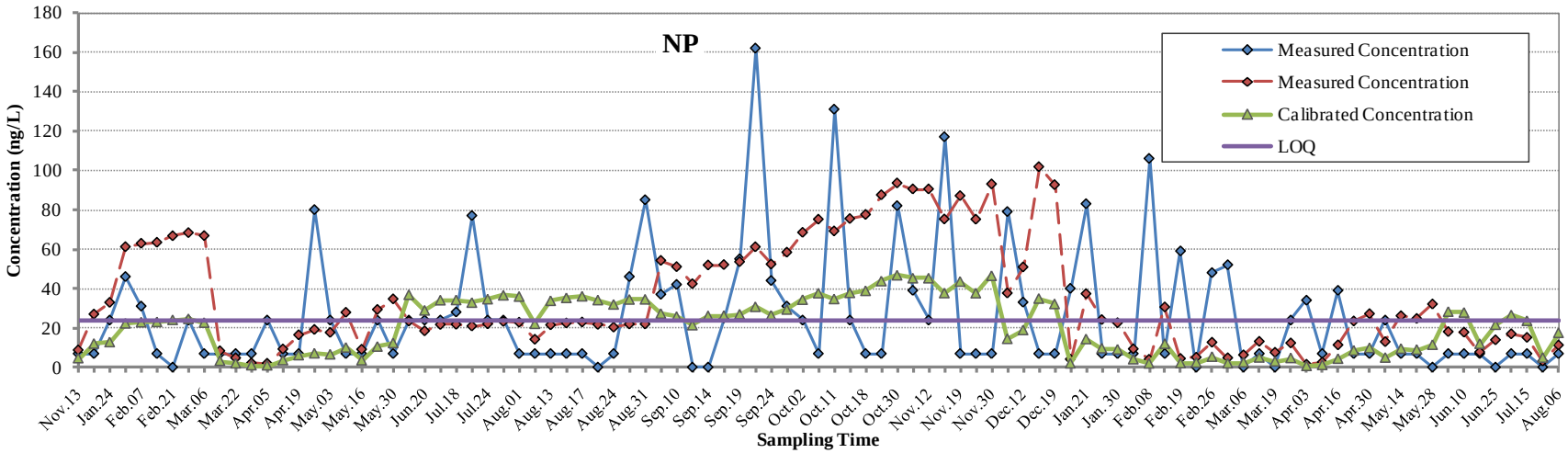


Figure 6-10: Simulated concentrations of NP before and after calibration compared to its measured concentrations

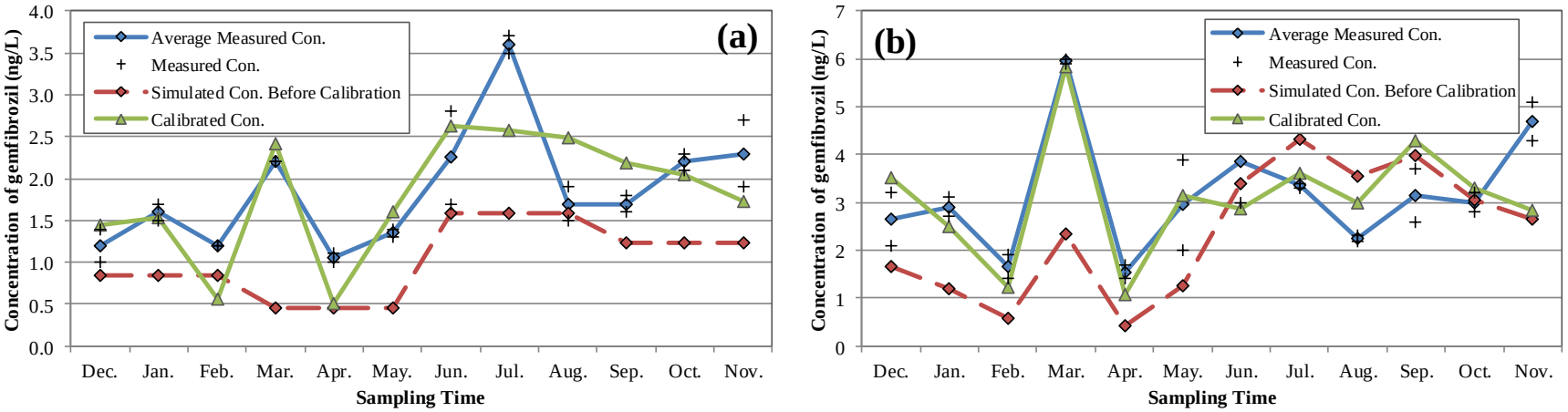


Figure 6-11: Simulated concentrations of gemfibrozil before and after calibration compared to its measured concentrations at (a) Mannheim and (b) Holmedale

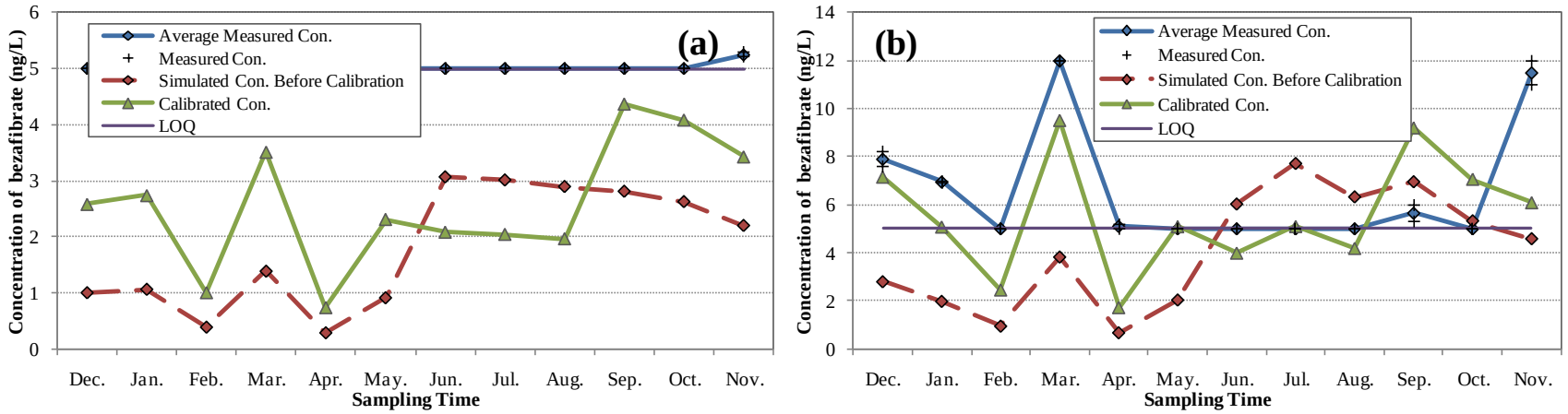


Figure 6-12: Simulated concentrations of bezafibrate before and after calibration compared to its measured concentrations at (a) Mannheim and (b) Holmedale

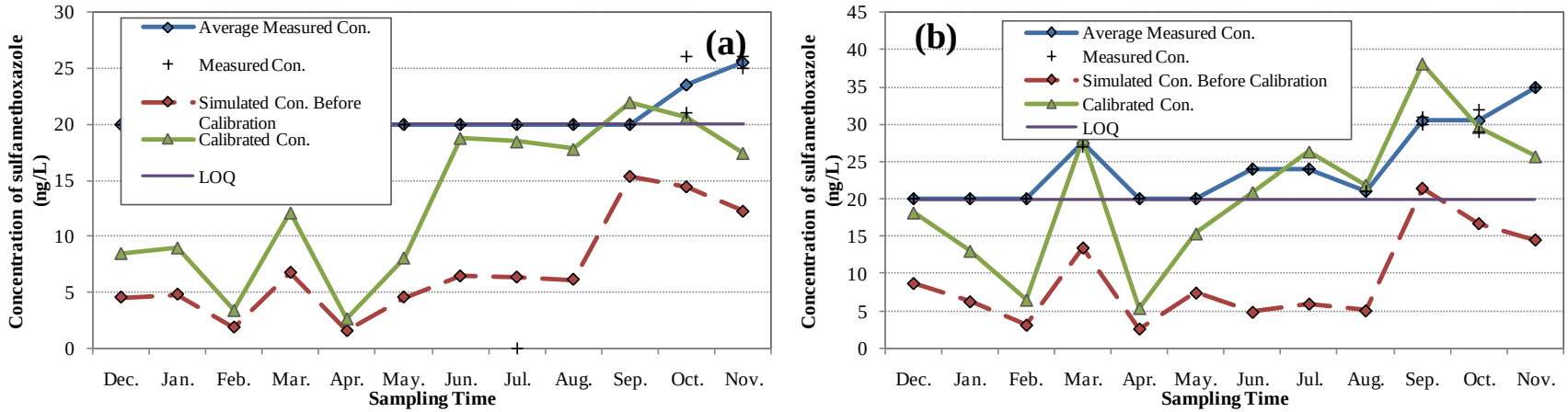


Figure 6-13: Simulated concentrations of sulfamethoxazole before and after calibration compared to its measured concentrations at (a) Mannheim and (b) Holmedale

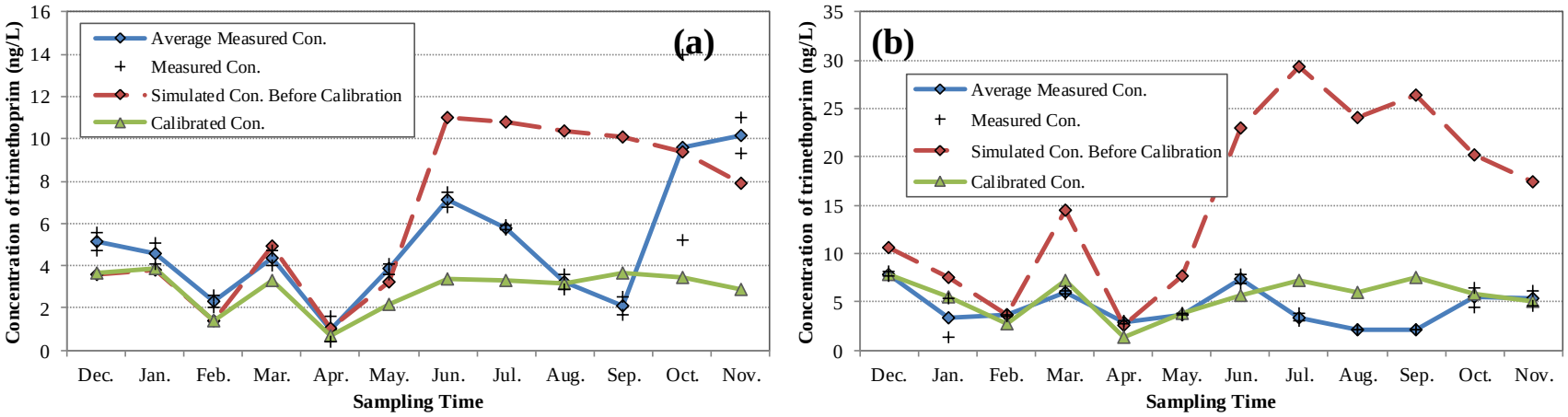


Figure 6-14: Simulated concentrations of trimethoprime before and after calibration compared to its measured concentrations at (a) Mannheim and (b) Holmedale

For some cases, the calibrated parameter values reported in Table 6-1 seemed to be unreasonable- for instance, high variability in in-stream decay value (e.g., two or three orders of magnitude), a large difference between removal efficiency of treatment plant in one season in compare to other seasons, and a lower removal rate in summer than in winter. These pattern can be expressed by some of the following facts: (1) the calibration was performed only at one sample location which is mostly effected by secondary treatment plant removal; therefore, in-stream decay, lagoon, and tertiary treatment plant removal were not sufficiently contributed in the calibration; (2) a high percent of observed concentrations for some of the compounds were reported below detection limit (e.g., bezafibrate, NP); (3) in the literature, a wide range of values was reported for each parameter value, which resulted a high correlation between parameters in the calibration exercise.

6.4 Improvement in Modelling through Seasoning

The prediction of the selected chemicals was improved by considering the seasonality of Canadian environments. In order to assess the significance of applying seasonality to the model parameters in this study, different annual and seasonal scenarios were considered (see Table 6-2). The average seasonal simulated concentrations of ibuprofen, naproxen, carbamazepine, DEET, and NP in all five scenarios were plotted in Figure 6-15 along with the measured concentrations. The comparison was based on the difference between seasonal average simulated concentrations and seasonal average measured concentrations.

Seasoning parameters showed different results in simulation of the chemicals. In most cases, applying seasonal flow (i.e. scenario 2) improved the estimation of the average concentrations compared to the average concentrations estimated using average annual flow (i.e. scenario 1); however, it yielded overestimation of the average concentrations of ibuprofen and naproxen in summer. Scenario 3 slightly improved the modelling; it only led to some degradation for NP and naproxen in summer. Seasonality of both loss and loading parameters (scenario 4 and scenario 5) significantly improved the simulation of ibuprofen, naproxen, and DEET, but it resulted in poor estimation of carbamazepine; this trend can be explained by

seasonality in loading of ibuprofen, naproxen, and DEET but relatively constant usage of carbamazepine throughout the year.

As mentioned in the previous section, there were good fits between measured and calibrated concentrations when the actual flow rates were used, though the average simulated concentrations after calibration (i.e. in scenario 5) were less than the average measured concentrations for all of the seasons and compounds. This result suggests that the average flow might not be the best strategy in estimating the average concentrations, and other types of central tendency measures like median is worth being investigated. Figure 6-16 compares the actual average and actual median flow rate values at the time of sampling with the average estimated flows. There was a good match between the average actual flow and estimated flow, while the actual median flow rates were considerably lower than the average flow. As the estimated concentrations in all cases were less than the average measured concentrations, accounting for the median flow instead of mean flow is expected to increase the simulated concentration values and probably improve the average seasonal simulation.

As another form of comparison, the percentage of the field measured concentrations lying between simulated mean flow concentrations and simulated low flow concentrations were calculated for each season and reported in Table 6-3. Simulation of ibuprofen improved considerably after calibration, especially in the fall when the number of measured concentrations between the two simulated concentrations increased from 0 in scenarios 1, 2, and 3 to 38 in scenario 5. For naproxen, seasoning all parameters improved simulation in the winter and summer but decreased the number of measured concentrations within the two predicted concentrations in the spring and fall. The highest number of measured concentrations of carbamazepine fell between the simulated concentrations when scenario 1 was applied. Scenario 4 and scenario 5 resulted in better simulation of DEET in the winter and spring but not in the summer and fall. Seasoning parameters only improved NP simulation in the winter. Overall it can be stated that, for winter and spring, applying seasonal loss parameters and loading (i.e. scenario 4 and scenario 5) slightly increased the number of measured concentrations within the two predicted concentrations over scenario 1 that employed annual hydrologic and chemical parameters. Seasoning loss parameters for fall and summer did not improve the simulation, but

seasoning loading for ibuprofen and naproxen in summer increased the percentage of measured concentrations lying between the simulated concentrations.

Table 6-2: Different chemical and hydrological scenarios employed for simulations

Scenarios/Parameters	Loss[1]	Loading	Flow	Comments
Scenario 1	avg. annual	avg. annual	annual mean and low flow	See section 3.2.1 and section 4.3.2
Scenario 2	avg. annual	avg. annual	seasonal mean and low flow	
Scenario 3	measured avg. seasonal	avg. annual	seasonal mean and low flow	average of data measured in each season presented in section 5.1
Scenario 4	measured avg. seasonal	manually-calibrated avg. seasonal	seasonal mean and low flow	See section 5.1 and section 5.2
Scenario 5	auto-calibrated avg. seasonal		seasonal mean and low flow	See section 6.3

[1]The loss parameters were in-stream decay, removal efficiency of lagoons, removal efficiency of secondary treatment plants, and removal efficiency of tertiary treatment plants.

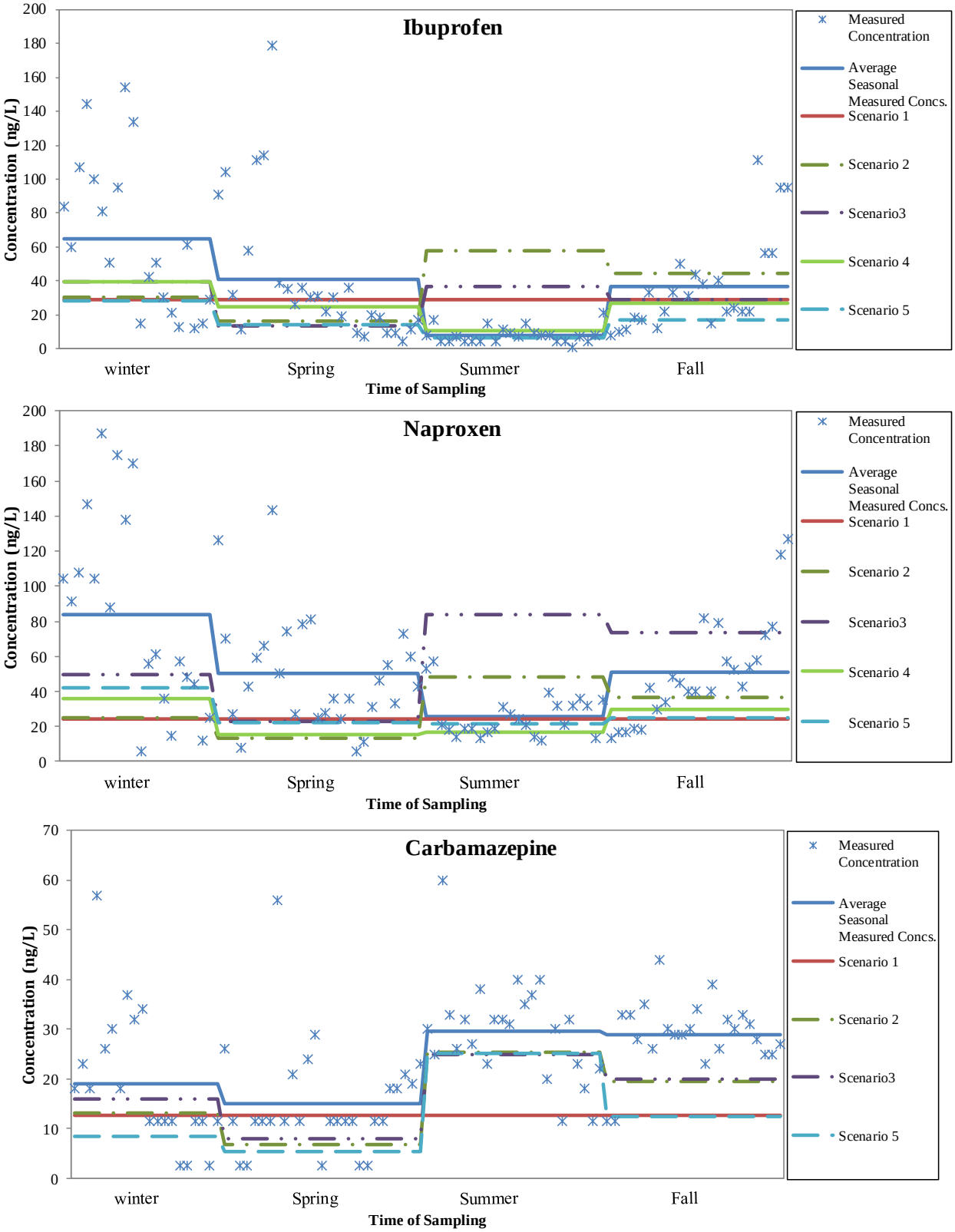


Figure 6-15: Simulated concentrations of the compounds using different scenarios compared to the measured concentrations (to be continued)

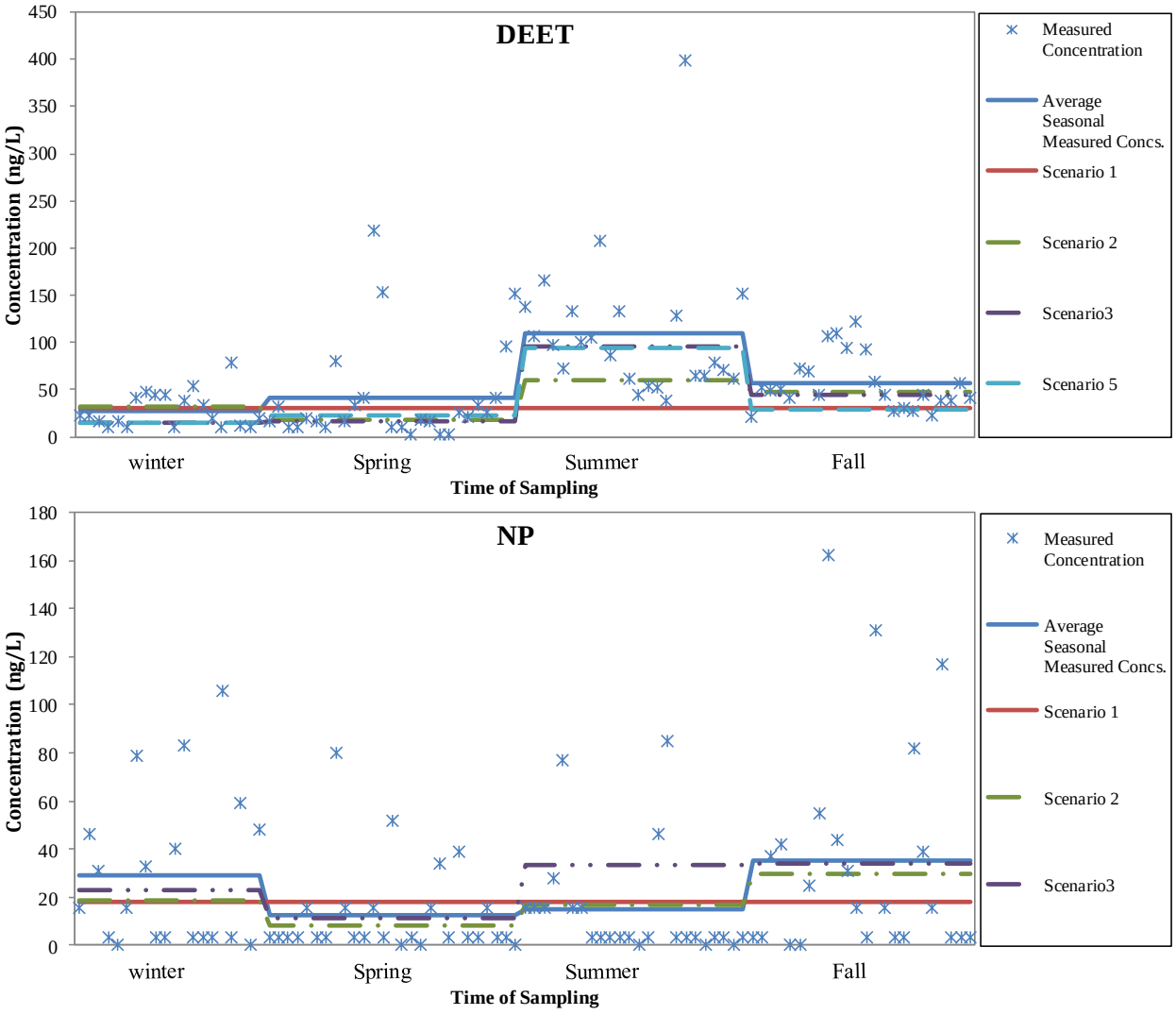


Figure 6-15: Simulated concentrations of the compounds using different scenarios compared to the measured concentrations (continued)

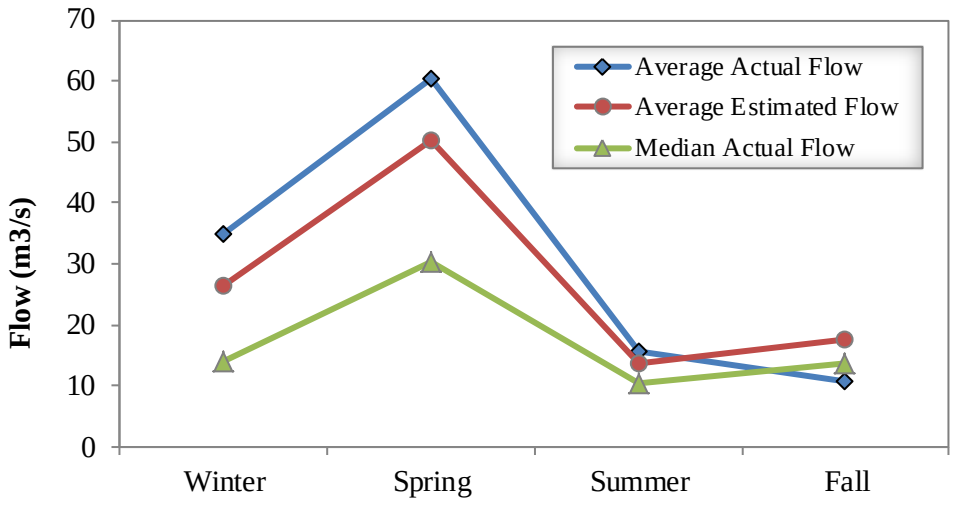


Figure 6-16: Comparison of average and median flows versus season

Table 6-3: Percentage of measured concentration data lying between the simulated low flow-based and mean flow-based concentrations

Compounds	Season	Scenario 1	Scenario2	Scenario 3	Scenario 4	Scenario 5
Ibuprofen	Winter	55	55	65	40	60
	Spring	41	56	56	56	52
	Summer	0	0	0	17	38
	Fall	46	21	38	33	50
Naproxen	Winter	45	45	65	60	50
	Spring	78	59	81	70	81
	Summer	42	8	0	46	33
	Fall	71	63	21	58	50
Carbamazepine	Winter	80	80	85	-	70
	Spring	78	78	78	-	70
	Summer	96	63	67	-	63
	Fall	100	92	92	-	50
DEET	Winter	40	40	-	65	60
	Spring	26	37	-	37	26
	Summer	67	46	-	42	33
	Fall	75	42	-	38	46
NP	Winter	40	40	50	-	-
	Spring	30	19	26	-	-
	Summer	29	25	4	-	-
	Fall	42	25	25	-	-

6.5 PhATE Model Validation

As mentioned previously, the PhATE parameters for each compound of interest were calibrated using a split-sample subset of available observation data for the Grand River watershed. Following calibration, the parameters were validated with data that was not used for calibration. Ibuprofen, naproxen and carbamazepine were the only compounds that validation phase was conducted for.

In the validation phase, ibuprofen, naproxen, and carbamazepine were simulated using the calibrated parameters and actual flows at the time of sampling. As the actual flow data at the time of sampling were not reported, to obtain the actual flow values, the flow data at the Doon and Brantford stations, the closest GRCA and WSC monitoring sites to the sample sites, were used. Figure 6-17 shows the simulated concentrations of ibuprofen, naproxen, and carbamazepine along with the corresponding measured concentration values.

For carbamazepine, as shown in Figure 6-17, there was a good fit between the simulated concentrations and the measured data at both sampled locations with the exception of the August sample event at Holmedale , when the measured concentration was extremely high (outlier), about 1µg/L. For ibuprofen, the simulated concentrations and the measured concentrations had a good fit Mannheim, while the simulated data at Holmedale did not match the measured data sufficiently well. The better model performance for Mannheim was probably due to the fact that the calibration was also performed on this segment and Holmedale was not considered in calibration. Note that this behaviour (different accuracies in segment 36 and segment 65) was not observed for carbamazepine possibly because this compound is relatively persistent in the environment. Therefore, the variation in carbamazepine concentration is generally governed by the variation in the flow rate. The validation results for naproxen were not as good as the validation results for ibuprofen and carbamazepine.

Although the accuracy in validation might not seem very high, the predicted and measured concentrations of this class of chemicals are suggested to have a favorable match as the predicted data is within a factor of 10 of the measured data [17]. According to this reference, the validation results in this study indicated relatively good fits between observed data and corresponding model output.

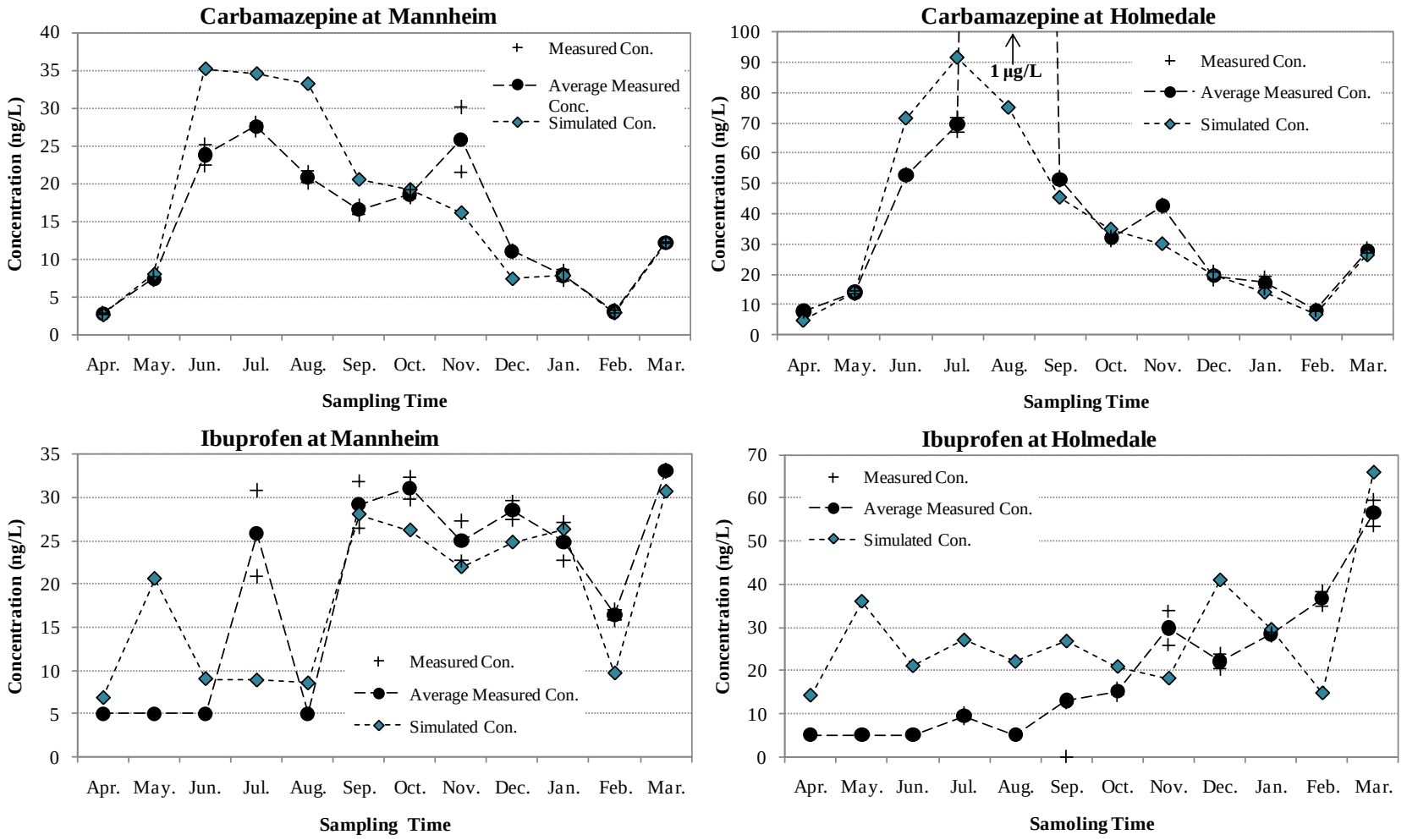


Figure 6-17: Simulated Concentrations vs. the Average of Duplicate Measured Concentrations at segment 36 and segment 65 (to be continued)

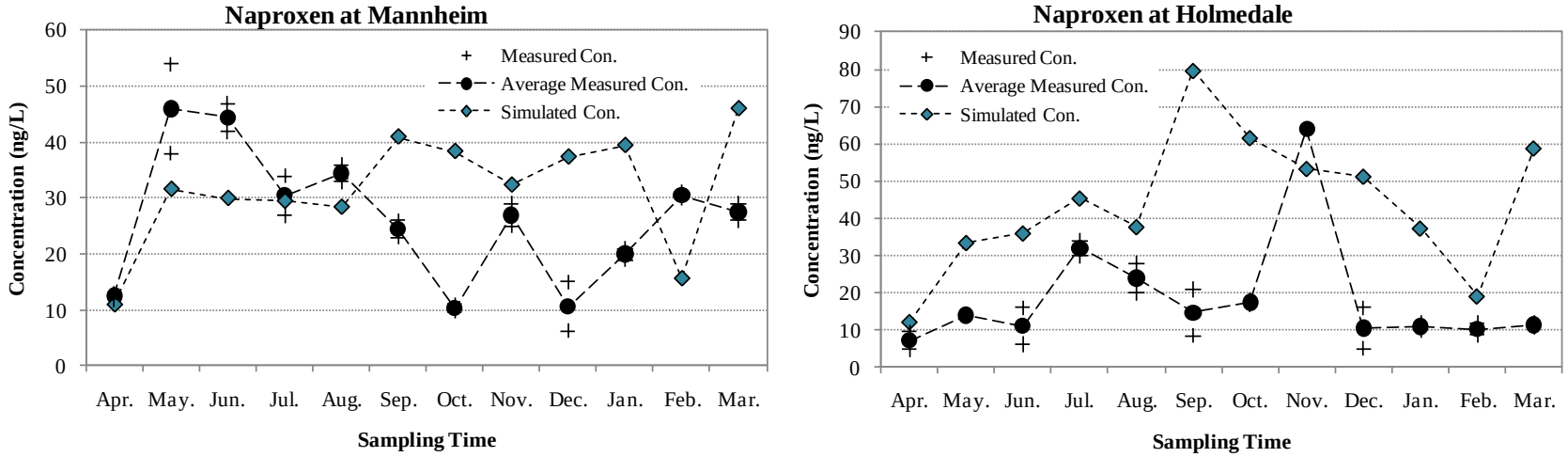


Figure 6-17: Simulated Concentrations vs. the Average of Duplicate Measured Concentrations at segment 36 and segment 65 (continued)

6.6 Identifying Segments with High Potential Risk

The concentrations of PPCPs and EDCs were predicted both spatially and temporally for the entire Grand River watershed. The PhATE model was used to predict the highest risk areas in terms of negatively impacting aquatic ecosystems in the different seasons. Determining high risk location is a valuable procedure for designing cost-effective field sampling plans [47] and in controlling and managing the treatment plants in the watershed.

In this regard, concentrations of the selected PPCPs and EDCs (i.e. ibuprofen, naproxen, carbamazepine, DEET, bezafibrate, gemfibrozil, trimethoprim) were predicted seasonally in mean and low flow conditions for the entire watershed, using the calibrated parameters (presented in section 6.3). Stream segments with high potential risk were identified using the "dirty dozen" approach, which is a popular approach used for a variety of purposes. For example, it has been used for the following purposes: (1) identifying septic tank installations which violated water quality protection rules [140]; (2) investigating highly halogenated organics that may arise environmental or human health problems [141]; defining high priority toxic chemicals that have been prohibited from use [142]; (4) detecting property owners with the highest violation of building code [143], etc. In this study, the "dirty dozen" was defined as the twelve segments in the watershed with the highest concentrations of the chemicals.

For each compound of interest and in each season, and for low flow and mean flow conditions, the dirty dozen segments were identified, separately. The outcome of this analysis consisted of two sets of stream segments with high potential risk associated with low flow and mean flow conditions. Each stream segment set was the union of all dirty dozen segment sets for the different compounds and different seasons and are shown in Figure 6-18 and Figure 6-19, respectively. The number of segments with high potential risk in the low flow condition (27 stream segments) was greater than that in the mean flow condition (20 stream segments); thus, there was a larger variability of concentrations of the compounds in the low flow condition.

As can be seen in the figures, a majority of high risk areas in the Grand River are in the stream segment portion between the point where wastewater from the Waterloo and Kitchener treatment plants discharge into the stream and Brantford. Also, the Speed River, after receiving effluent from the Guelph wastewater treatment plant is expected to be at high risk of exposure to

the chemicals. The streams exposed to the effluent of the treatment plants at Dundalk, Elmira, Baden, and Brant are at risk for short distances, but after a few kilometers (flowing downstream), the estimated concentrations are reduced. This is due to dilution and, to a lesser extent, degradation of the compounds and their sorption to solids.

The ranges of the simulated concentrations for the dirty dozen segments associated with different compounds are presented in Table 6-4. According to this table, for ibuprofen, naproxen, and bezafibrate, the highest concentrations associated with mean flow are more likely to happen in winter and fall; while for carbamazepine, DEET, gemfibrozil, and trimethoprim, the highest concentrations in mean flow will occur in summer. In the low flow condition, a clear seasonal variability pattern in the concentrations was not observed, and stream segments may be exposed to high concentrations any time of the year.

Table 6-4: Ranges of predicted concentrations in dirty dozen segments

Compound	Flow regime	Winter	Spring	Summer	Fall
Ibuprofen	mean flow	67-87	28-65	16-54	47-90
	low flow	265-458	98-447	46-207	133-568
Naproxen	mean flow	47-150	28-76	28-75	46-79
	low flow	136-724	86-479	50-138	143-304
Carbamazepine	mean flow	20-29	10-16	63-91	26-37
	low flow	74-164	46-76	151-387	90-271
DEET	mean flow	11-66	22-88	81-405	24-129
	low flow	23-247	58-392	138-767	46-418
Bezafibrate	mean flow	8-10	4-5	4-7	6-9
	low flow	31-53	18-37	10-42	20-62
Gemfibrozil	mean flow	4-6	2-4	3-7	2-5
	low flow	13-24	9-20	6-14	9-39
Trimethoprim	mean flow	8-16	3-12	5-21	5-24
	low flow	31-53	13-21	12-256	15-239

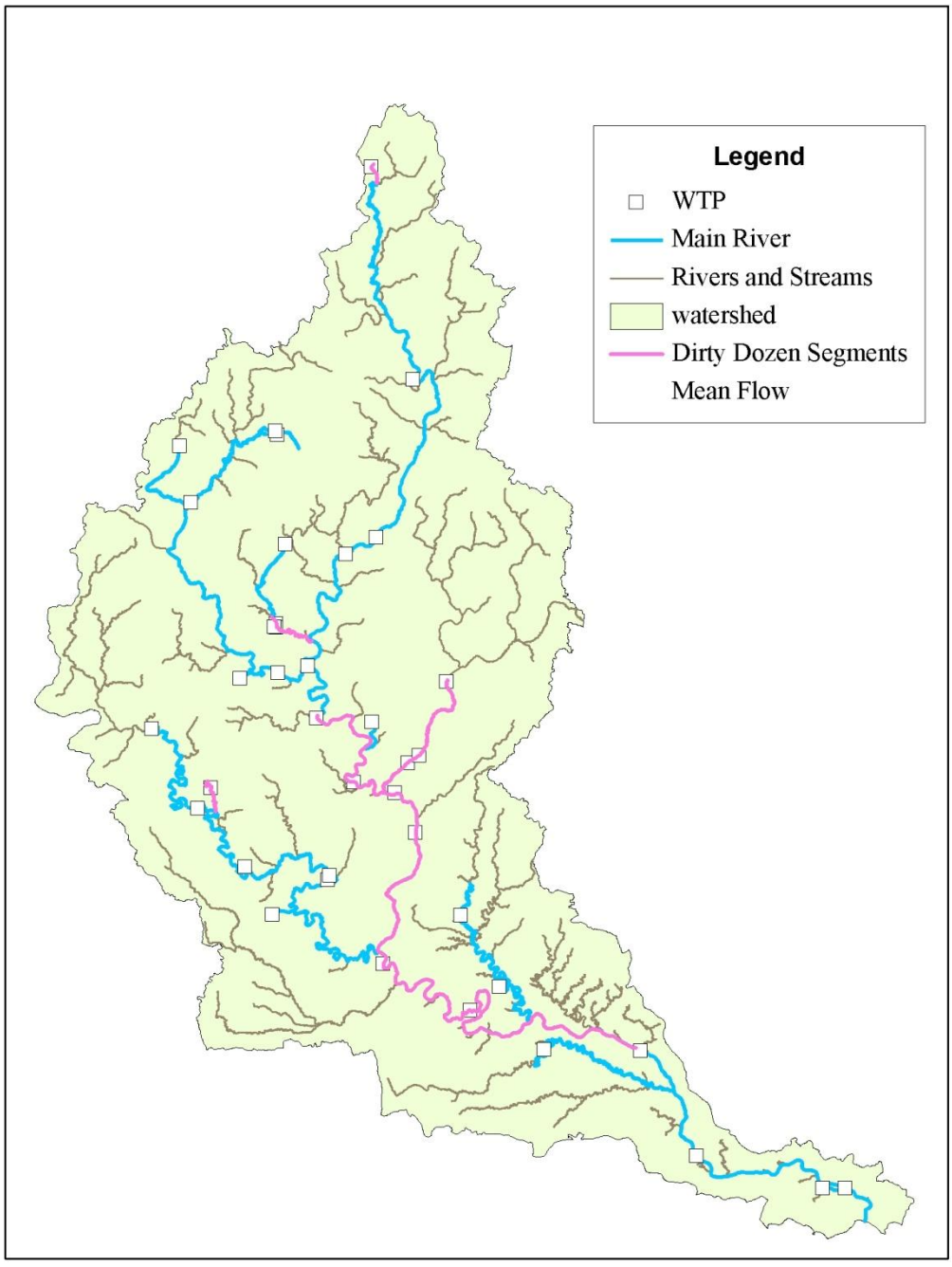


Figure 6-18: Segments with high risk at the mean flow condition.

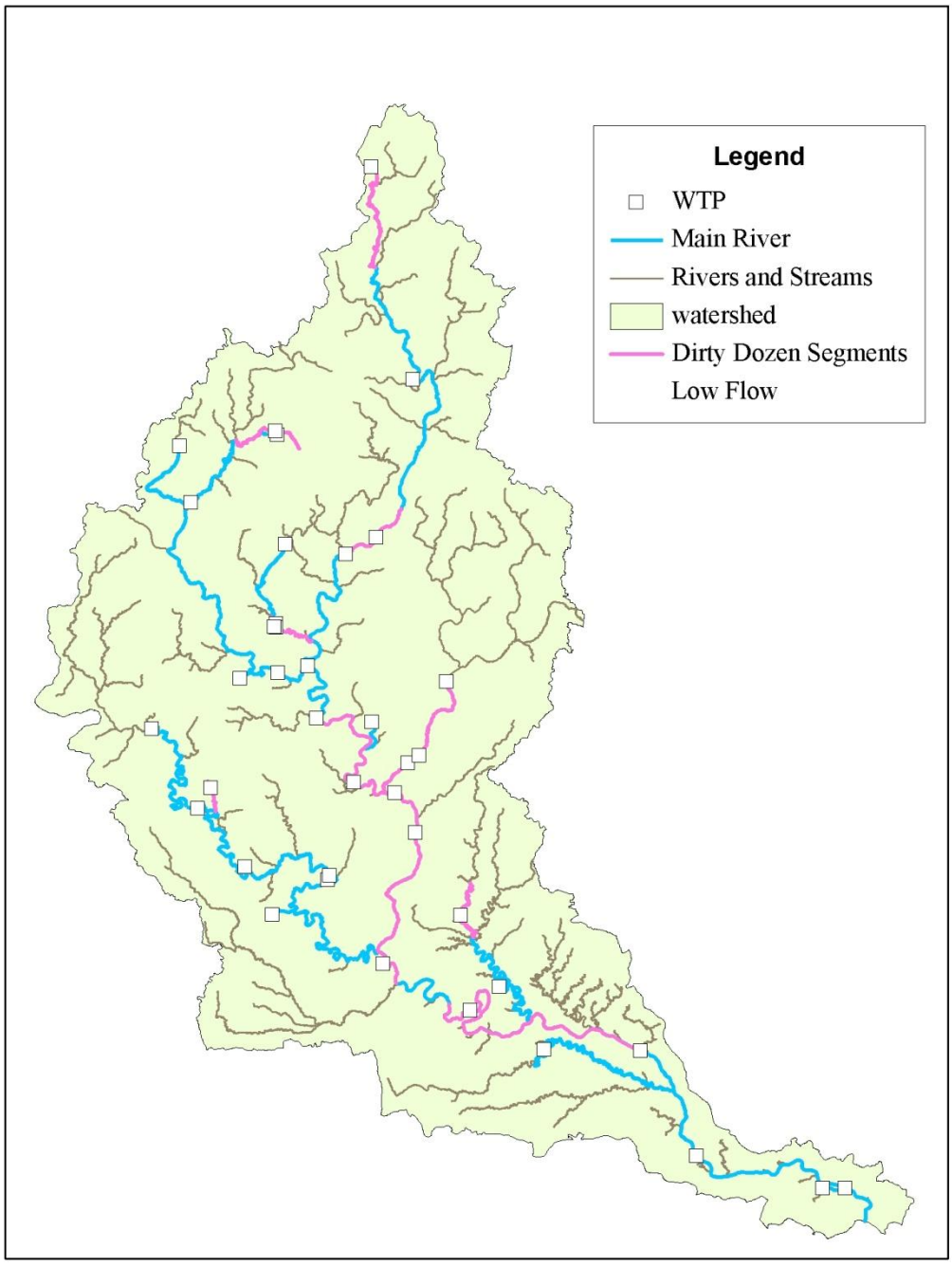


Figure 6-19: Segments with high risk at the low flow condition.

6.7 Potential Risk of PPCP toxicity to Grand River Aquatic Species

The potential for the selected compounds to exert toxicity was assessed by comparing the maximum predicted concentrations of PPCPs throughout the watershed (given in Section 6.3) to corresponding minimum effect concentrations reported in the literature (presented in Section 2.5). The European Commission (European Union) and U.S. Food and Drug Administration (FAD) proposed regulatory guidelines in order to assess the toxicological risk of pharmaceuticals in the environment. In this study, the toxicity of these compounds was assessed following these guidelines.

The cut-off values for PPCPs to undergo a risk assessment are 1μg/L and 0.001 μg/L in the US and EU [37, 144], respectively. If measured or predicted environmental concentrations exceed these cut of values, it is recommended that the toxicity potential of these compounds should be evaluated. As shown in Table 6-5, the maximum predicted concentrations of all the compounds were less than the US cut-off value but exceeded the EU cut-off value. Therefore, according to the US guideline, no further assessment is required; however, according to EU, the assessment should be continued to the next step. As suggested in the EU regularity guideline, in the next tier of risk assessment, the hazard quotient (HQ) assessment was performed in this study. The HQ was calculated as the ratio of the maximum predicted concentration to the lowest effect concentration multiplied by an assessment factor. The assessment factor was used because of the lack of enough acute and chronic toxicity effects in the literature and uncertainty in the predicted concentration; in the EU, an assessment factor of up to 1000 is suggested to account for uncertainty [144]. For the compounds with an HQ of less than one, no further assessment is required. Conversely, the compounds with an HQ greater than one may require regulations or restrictions. Importantly, for all the selected compounds except gemfibrozil, the calculated HQ values were greater than one, suggesting that further investigation may be necessary to address possible issues regarding toxicity.

Table 6-5: Toxicity risk assessment of the selected PPCPs in the Grand River watershed

Compound	Effect Concentration	Max. Predicted Concentration (µg/L)	HQ	Reference
ibuprofen	1-100 µg/L	0.568	568	[56]
ibuprofen	10 ng/L		56800	[60]
ibuprofen	1 mg/L		0.57	[54]
naproxen	2.6 mg/L	0.724	0.28	[54]
naproxen	0.33 mg/L		2.19	[61]
carbamazepine	3.76 mg/L	0.387	0.10	[54]
carbamazepine	10 ng/L		38700	[60]
carbamazepine	1 µg/L		387	[59]
gemfibrozil	1 mg/L	0.039	0.04	[54]
gemfibrozil	1.76 mg/L		0.02	[54]
gemfibrozil	0.53 mg/L		0.07	[61]
bezafibrate	1 mg/L	0.062	0.06	[54]
bezafibrate	0.047 mg/L		1.32	[61]
sulfamethoxazole	0.21 mg/L	0.254	1.21	[61]
sulfamethoxazole	0.52 mg/L		0.49	[61]
sulfamethoxazole	1-10 µg/L		254	[51]
trimethoprim	1-10 µg/L	0.256	256	[51]

Chapter 7
Summary and Conclusions

7.1 Summary

This study employed the PhATE model to seasonally predict transport of frequently detected pharmaceuticals, personal care products, and endocrine disruptors in the Grand River watershed. The simulations were performed under two flow regimes, mean flow and low flow. In the uncalibrated phase (i.e., using the default of previously published parameter values), the range defined by the simulated concentrations at the two flow conditions for each compound covered more that 50% of the measured concentrations.

Moreover, this project was undertaken to calibrate and validate the model parameters to obtain the most probable seasonal parameters for the case study.

As mentioned previously, calibration was conducted so that a good fit between *average* simulated concentrations and *average* measured concentrations would be obtained. In this study, equal weights were assumed in calibration for all observations. However if worst case conditions are of interest and prediction of the highest concentrations happening is required, in calibration, a higher weight should be assigned for these high concentrations. Also, results of calibration indicated that simulation of drugs with continuous use by humans (e.g., ibuprofen, naproxen, carbamazepine, gemfibrozil) was more accurate than the simulation of the compounds that are consumed for industrial and agricultural use (e.g., NP and DEET).

In the validation phase, the performance of the calibrated PhATE model was tested with a set of data that was not used in calibration at two sampling sites. Comparing the measured and simulated concentrations of carbamazepine showed overall, the simulated concentrations matched the measured data at both sampled locations. The simulated and measured concentrations of ibuprofen had a good fit at the sample site at which calibration was conducted, but were less well fit at the other sample site. The validation results for naproxen were not as good as the validation results for ibuprofen and carbamazepine.

Moreover, the present study was designed to identify stream segments with high potential risk of being exposed to the selected PPCPs and EDCs in the watershed in different seasons. The

results of this investigation suggested that the highest concentrations of the compounds are likely to occur in a portion of the Grand River extending from the effluents of the Waterloo and Kitchener wastewater treatment plants downstream to the municipality of Brantford and also a portion of the Speed River after receiving the effluent from the Guelph wastewater treatment plant. The streams exposed to the effluent of the treatment plants at Dundalk, Elmira, Baden, and Brant are also expected to have a higher risk for short distances, but the concentrations reduced after a few kilometers due to dilution and degradation.

Finally, to assess the toxicity potential of the selected compounds, the maximum predicted concentrations of PPCPs throughout the watershed were compared to the minimum effect concentrations reported in the literature. Simulation results showed that the concentrations of the selected compounds were less than the US cut-off value for risk assessment, and no further assessment is required for these compounds using this metric. However, according to EU regulatory guidelines, most of the PPCPs (i.e., ibuprofen, naproxen, carbamazepine, bezafibrate, sulfamethoxazole) were predicted to be at concentrations which require further assessment and/or more stringent regulations and restrictions.

7.2 Conclusions

The modified PhATE model was found to be capable of accurately simulating pharmaceutical concentrations in the Grand River watershed. The model tended to over predict concentrations, and where model predictions were poorly matched to the measured data, the misfits tended to be due to the model over-predicting rather than under-predicting. Indeed, accounting for seasonal variability in parameters improved the accuracy of the PhATE model.

The PhATE model, when actual flow and the calibrated parameters were used, accurately predicted pharmaceutical concentrations in the Grand River. From these findings it can be pointed out that the hydrologic parameters, flow and velocity, are the most important parameters for estimation of PPCPs and EDCs in the surface water. Interestingly, if the fluctuation in concentrations is described by flow variability, the model could simulate concentrations well, while when the variation in concentrations is due to other factors such as loss parameters, the model could not predict the concentrations well enough. For example, carbamazepine, a persistent compound in the environment, has relatively low and constant removal rate values;

therefore, the variation in carbamazepine concentration is generally governed by the variation in the flow rate. As such, the results showed a good fit between the simulated and measured concentrations of carbamazepine. Accordingly, the results confirmed that a better estimation of the hydrological parameters would improve the simulation accuracy of any compound in the surface water but to different extents.

The validation results showed relatively good fit between the measured data and corresponding model output, and the deviations of the simulated concentrations from the measured data were less than a factor of 10 with only one exception.

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Appendix A

Daily measured concentrations reported by [43] and [42]

Table A-1: Measured Concentration of PPCPs and EDCs from [43]
(to be continued)

Date	DEET	ibuprofen	nonylphenol	naproxen	Carbamazepine
Nov.13	21	8	nd	13	d
Nov.27	53	10	nd	17	d
Jan.24	22	84	d	104	18
Jan.31	23	60	46	91	23
Feb.7	16	107	31	108	18
Feb.14	d	144	nd	147	57
Feb.21	16	100	na	104	26
Feb.28	d	81	d	187	30
Mar.6	16	91	nd	126	26
Mar.14	32	104	nd	70	d
Mar.22	d	32	nd	27	nd
Mar.28	d	11	nd	8	nd
Apr.5	19	58	d	43	d
Apr.12	16	111	nd	59	d
Apr.19	d	114	nd	66	d
Apr.26	80	179	80	143	56
May.3	16	39	d	50	d
May.9	34	35	nd	74	21
May.16	41	26	nd	27	d
May.23	219	36	d	78	24
May.30	154	30	nd	81	29
Jun.13	138	8	d	53	30
Jun.20	107	17	d	57	25
Jul.5	165	D	d	21	60
Jul.18	97	D	28	18	33
Jul.20	73	7	77	14	26
Jul.24	133	D	d	19	32
Jul.26	101	d	d	19	27
Aug.1	105	d	nd	13	38
Aug.8	208	15	nd	17	23
Aug.13	86	d	nd	19	32
Aug.15	133	11	nd	31	32
Aug.17	62	9	nd	27	31
Aug.22	45	7	na	24	40
Aug.24	54	15	nd	21	35
Aug.29	52	9	46	14	37
Aug.31	39	8	85	12	40
Sep.6	49	11	37	17	33
Sep.10	50	18	42	19	33
Sep.12	41	17	na	18	28
Sep.14	72	33	na	42	35
Sep.17	69	12	25	30	26
Sep.19	44	22	55	34	44
Sep.21	106	33	162	48	30
Sep.24	109	50	44	45	29
Sep.27	94	31	31	40	29
Oct.2	122	44	d	40	30

Table A-2: Measured Concentration of PPCPs and EDCs reported by [43] (continued)

Date	DEET	ibuprofen	nonylphenol	naproxen	Carbamazepine
Oct.4	92	38	nd	82	34
Oct.11	58	15	131	40	23
Oct.15	45	40	d	79	39
Oct.18	27	22	nd	57	26
Oct.25	30	24	nd	52	32
Oct.30	28	22	82	43	30
Nov.1	44	22	39	54	33
Nov.12	23	111	d	58	31
Nov.14	38	56	117	72	28
Nov.19	38	56	nd	77	25
Nov.28	57	95	nd	118	25
Nov.30	42	95	nd	127	27
Dec.5	41	51	79	88	18
Dec.12	48	95	33	175	37
Dec.15	44	154	nd	138	32
Dec.19	45	134	nd	170	34
Jan.16	d	d	40	6	d
Jan.21	39	42	83	56	d
Jan.23	54	51	nd	61	d
Jan.30	34	30	nd	36	d
Feb.6	19	21	nd	15	nd
Feb.8	d	13	106	57	nd
Feb.13	79	61	nd	48	d
Feb.19	12	12	59	44	d
Feb.21	d	15	na	12	nd
Feb.26	20	29	48	25	d
Mar.4	d	31	52	25	nd
Mar.6	d	22	na	28	d
Mar.12	nd	30	nd	36	d
Mar.19	18	19	na	24	d
Mar.27	16	36	d	36	d
Apr.3	nd	9	34	6	nd
Apr.11	nd	7	nd	11	nd
Apr.16	26	20	39	31	d
Apr.24	21	18	nd	46	d
Apr.30	33	9	nd	55	18
May.7	26	9	d	33	d
May.14	42	d	nd	73	21
May.21	96	11	nd	60	19
May.28	152	17	na	43	23
Jun.4	128	8	nd	39	20
Jun.10	399	d	nd	32	30
Jun.19	65	d	nd	21	d
Jun.25	64	nd	na	32	32
Jul.10	78	7	nd	36	23
Jul.15	71	d	nd	32	18
Jul.23	62	8	na	13	d
Aug.6	152	21	nd	35	22
d is detected; nd is not detected; na is not available					

Table A-3: Measured concentration of PPCPs from Grand River near Mannheim reported by [42]

Compound \ Month		Apr-05	May-05	Jun-05	Jul-05	Aug-05	Sep-05	Oct-05	Nov-05	Dec-05	Jan-06	Feb-06	Mar-06
Ibuprofen	replicate 1	<LOQ	<LOQ	<LOQ	30.8	<LOQ	31.9	29.8	22.7	29.6	27.1	15.8	32.9
	replicate 2	<LOQ	<LOQ	<LOQ	20.9	<LOQ	26.5	32.4	27.3	27.4	22.7	17.1	33.2
naproxen	replicate 1	6.3*	21	30	26	12	38	47	27	33	26	11	25
	replicate 2	15	19	31	29	13	54	42	34	36	23	9.7*	29
carbamazepine	replicate 1	2.8	7.6	25.1	27	21.6	15.9	19.1	30.1	10.8	7.1	3.2	12.2
	replicate 2	2.7	7.1	22.4	28.1	20.1	17.1	18.1	21.5	11.2	8.5	2.8	12.1
gemfibrozil	replicate 1	1	1.4	2.8	3.5	1.9	1.8	2.1	2.7	1.4	1.5	1.2	2.2
	replicate 2	1.1	1.3	1.7	3.7	1.5	1.6	2.3	1.9	<LOQ	1.7	1.2	2.2
bezafibrate	replicate 1	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	5.3	<LOQ	<LOQ	<LOQ	<LOQ
	replicate 2	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	5.2	<LOQ	<LOQ	<LOQ	<LOQ
sulfamethoxazole	replicate 1	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	21	25	<LOQ	<LOQ	<LOQ	<LOQ
	replicate 2	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	26	26	<LOQ	<LOQ	<LOQ	<LOQ
trimethoprim	replicate 1	0.4*	4.1*	7.5*	5.7*	3.6*	1.7*	14	11	4.7*	4.1*	2.6*	4.0*
	replicate 2	1.6*	3.6*	6.8*	5.9*	2.9*	2.5*	5.2*	9.3*	5.6*	5.1*	2.0*	4.7*

Table A-4: Measured concentration of PPCPs from Grand River near Holmedale reported by [42]

Month / Compound		Apr-05	May-05	Jun-05	Jul-05	Aug-05	Sep-05	Oct-05	Nov-05	Dec-05	Jan-06	Feb-06	Mar-06
Ibuprofen	replicate 1	<LOQ	<LOQ	<LOQ	8.7	<LOQ	12.5	15.8	33.8	20.3	28.7	35	53.5
	replicate 2	<LOQ	<LOQ	<LOQ	10.1	<LOQ	<LOQ	14.4	25.9	23.8	28.2	38.3	59.6
naproxen	replicate 1	16	10	8.7*	11	4.8*	14	16	34	20	8.6*	18	64
	replicate 2	5.1*	12	12	12	9.6*	14	6.3*	30	28	21	17	64
carbamazepine	replicate 1	7.9	14.4	52.1	71.9	1015.6	50.9	32.7	42.3	18.4	19.1	8.2	26.8
	replicate 2	7.6	13.6	53.1	67.1	961	51.7	31.3	42.9	20.7	15.5	7.9	28.6
gemfibrozil	replicate 1	1.4	3.9	3	3.3	2.3	2.6	2.8	5.1	2.1	2.7	1.9	5.9
	replicate 2	1.7	2	4.7	3.4	2.2	3.7	3.2	4.3	3.2	3.1	1.4	6
bezafibrate	replicate 1	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	5.3	<LOQ	11	8.2	6.9	<LOQ	12
	replicate 2	5.2	<LOQ	<LOQ	<LOQ	<LOQ	6	<LOQ	12	7.6	7	<LOQ	12
sulfamethoxazole	replicate 1	<LOQ	<LOQ	24	24	21	31	29	35	<LOQ	<LOQ	<LOQ	27
	replicate 2	<LOQ	<LOQ	24	24	21	30	32	35	<LOQ	<LOQ	<LOQ	28
trimethoprim	replicate 1	2.8*	3.6*	6.9*	3.8*	2.2*	2.2*	6.5*	6.2*	8.1*	1.4*	3.7*	5.8*
	replicate 2	3.0*	3.9*	7.8*	3.0*	2.1*	2.2*	4.5*	4.6*	7.7*	5.4*	3.5*	6.1*

Appendix B

Water Flow Stations

Table B-1: Name, geographical coordination and record lengths of WSC stations

station identifier	*Station location*	*Record length*	*UTM Easting*	*UTM Northing*	*Decimal longitude (Degree)*	*Decimal latitude (Degree)*
2GA038	NITH RIVER ABOVE NITHBURG	30	513285	4814373	0.00	43.48
2GA018	NITH RIVER AT NEW HAMBURG	55	523406	4802541	-80.71	43.38
2GA028	CONESTOGO RIVER AT GLEN ALLAN	47	523995	4833359	-80.70	43.65
2GA042	MOOREFIELD CREEK NEAR ROTHSAY	17	522848	4851382	-80.72	43.82
2GA039	CONESTOGO RIVER ABOVE DRAYTON	31	529166	4847658	-80.64	43.78
2GA043	HUNSBERGER CREEK NEAR WILMOT CENTRE	16	530340	4801075	-80.63	43.36
2GA030	ALDER CREEK NEAR NEW DUNDEE	45	536354	4802015	-80.55	43.37
2GA024	LAUREL CREEK AT WATERLOO	41	539254	4813121	-80.51	43.47
2GA023	CANAGAGIGUE CREEK NEAR ELMIRA	50	539618	4825134	-80.51	43.58
2GA010	NITH RIVER NEAR CANNING	56	544259	4781806	-80.46	43.19
2GA034	GRAND RIVER AT WEST MONTROSE	39	541850	4825716	-80.48	43.59
2GB008	WHITEMANS CREEK NEAR MOUNT VERNON	45	550126	4774800	-80.38	43.13
2GA016	GRAND RIVER BELOW SHAND DAM	57	552951	4841983	-80.34	43.73
2GA041	GRAND RIVER NEAR DUNDALK	17	550939	4887399	-80.36	44.14
2GB001	GRAND RIVER AT BRANTFORD	56	559611	4775538	-80.27	43.13
2GA003	GRAND RIVER AT GALT	57	555433	4800047	-80.32	43.35
2GA015	SPEED RIVER BELOW GUELPH	57	559729	4819320	-80.26	43.53
2GA040	SPEED RIVER NEAR ARMSTRONG MILLS	31	558871	4831890	-80.27	43.64
2GA014	GRAND RIVER NEAR MARSVILLE	47	558473	4856536	-80.27	43.86
2GB007	FAIRCHILD CREEK NEAR BRANTFORD	43	568707	4777304	-80.16	43.15
2GA029	ERAMOSA RIVER ABOVE GUELPH	44	566017	4821769	-80.18	43.55
2GA031	BLUE SPRINGS CREEK NEAR EDEN MILLS	41	571923	4824963	-80.11	43.58
2GB010	MCKENZIE CREEK NEAR CALEDONIA	46	585525	4764893	-79.95	43.03
2GA037	SCHNEIDER CREEK AT KITCHENER	22	542393	4809528	-80.48	43.44
2GA027	GRAND RIVER AT UPPER BELWOOD	4	556363	4852918	-80.30	43.83

Appendix C

Average seasonal flow

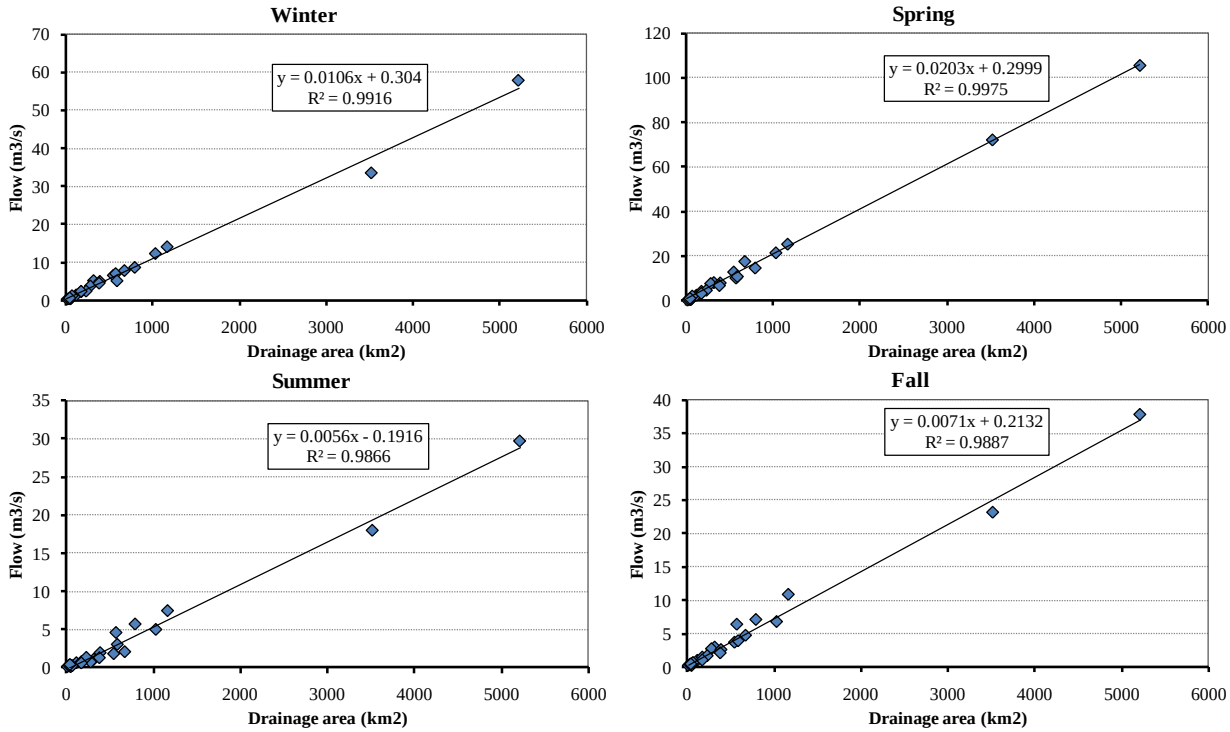


Figure C-1: Avg. seasonal flow versus drainage area for segments with drainage area > 1200km^2

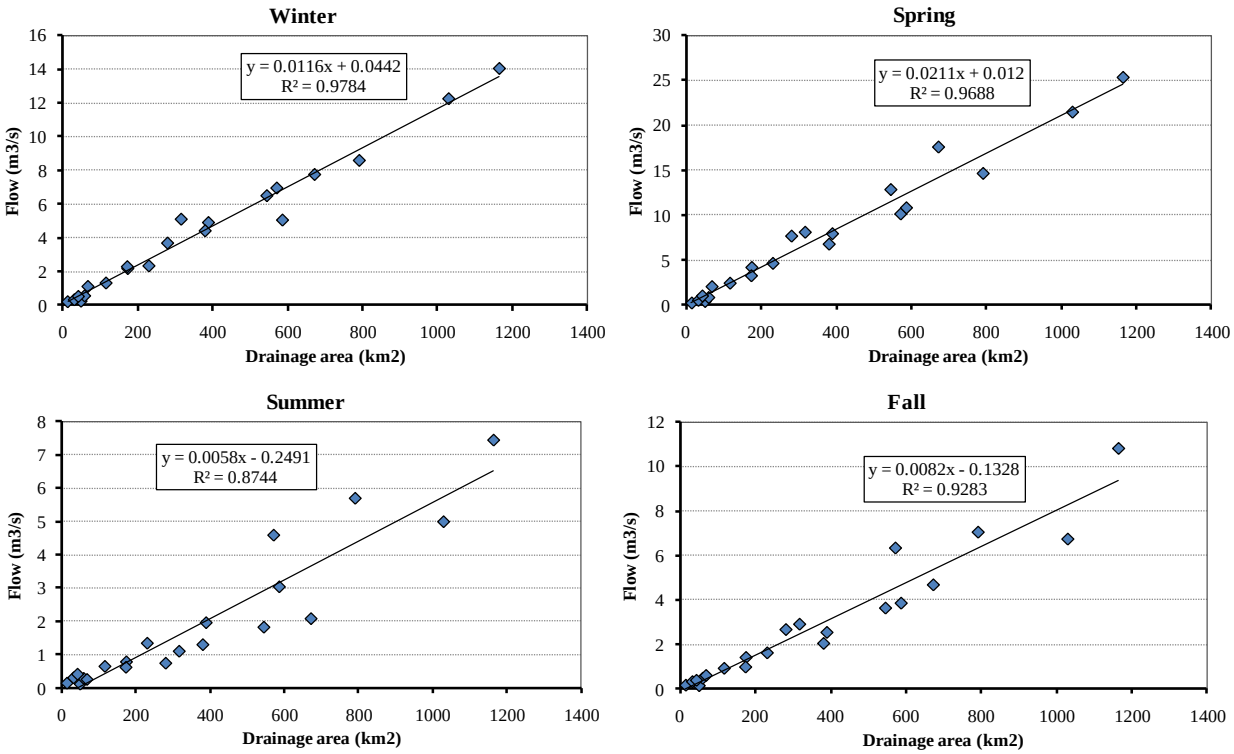


Figure C-2: Avg. seasonal flow versus drainage area for segments with drainage area < 1200 km^2

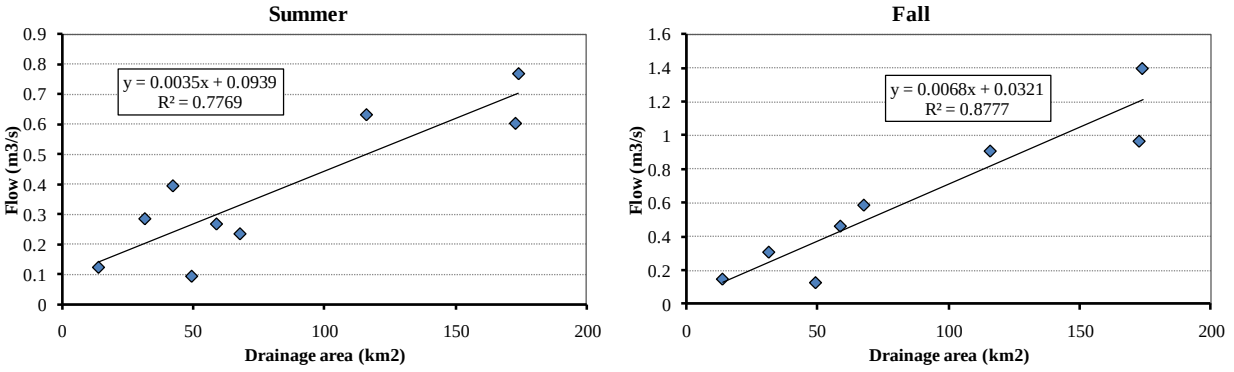


Figure C-3: Avg. seasonal flow versus drainage area for segments with drainage area < 200 km^2

Low seasonal flow

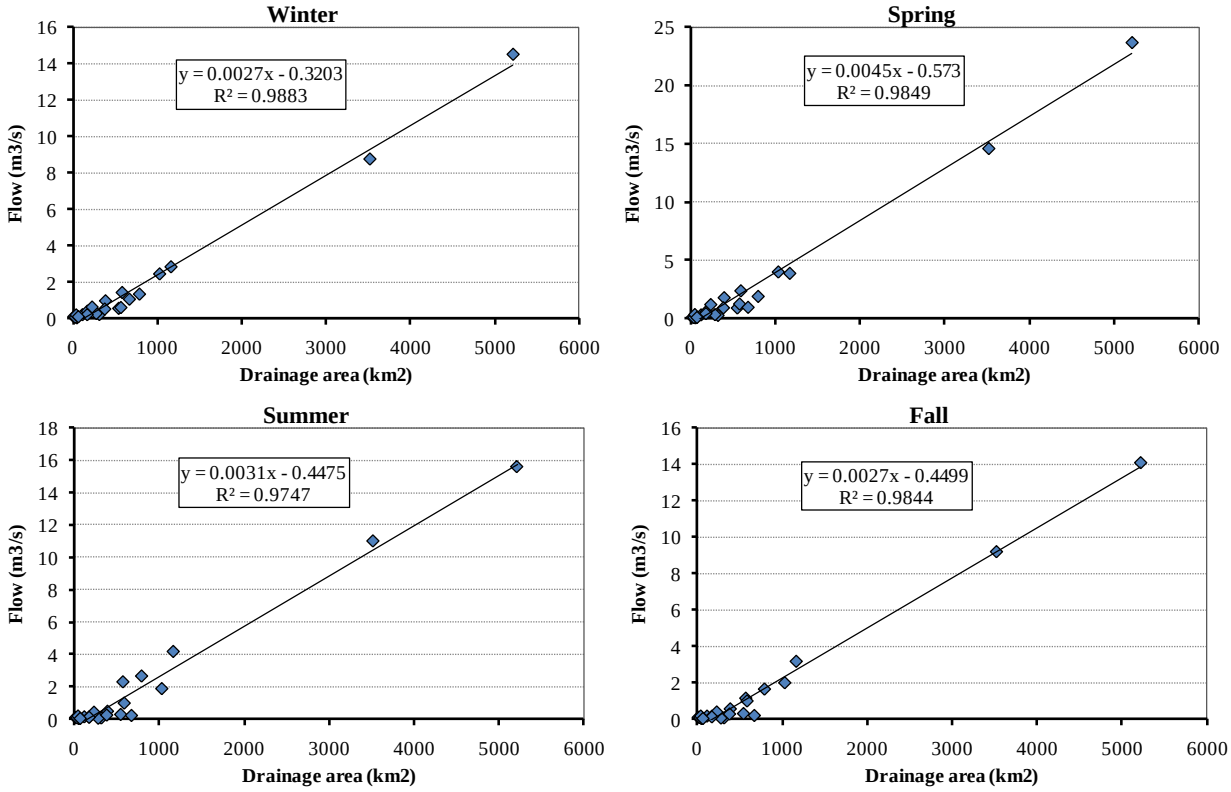


Figure C-4: Low seasonal flow versus drainage area for segments with drainage area > 1200km^2

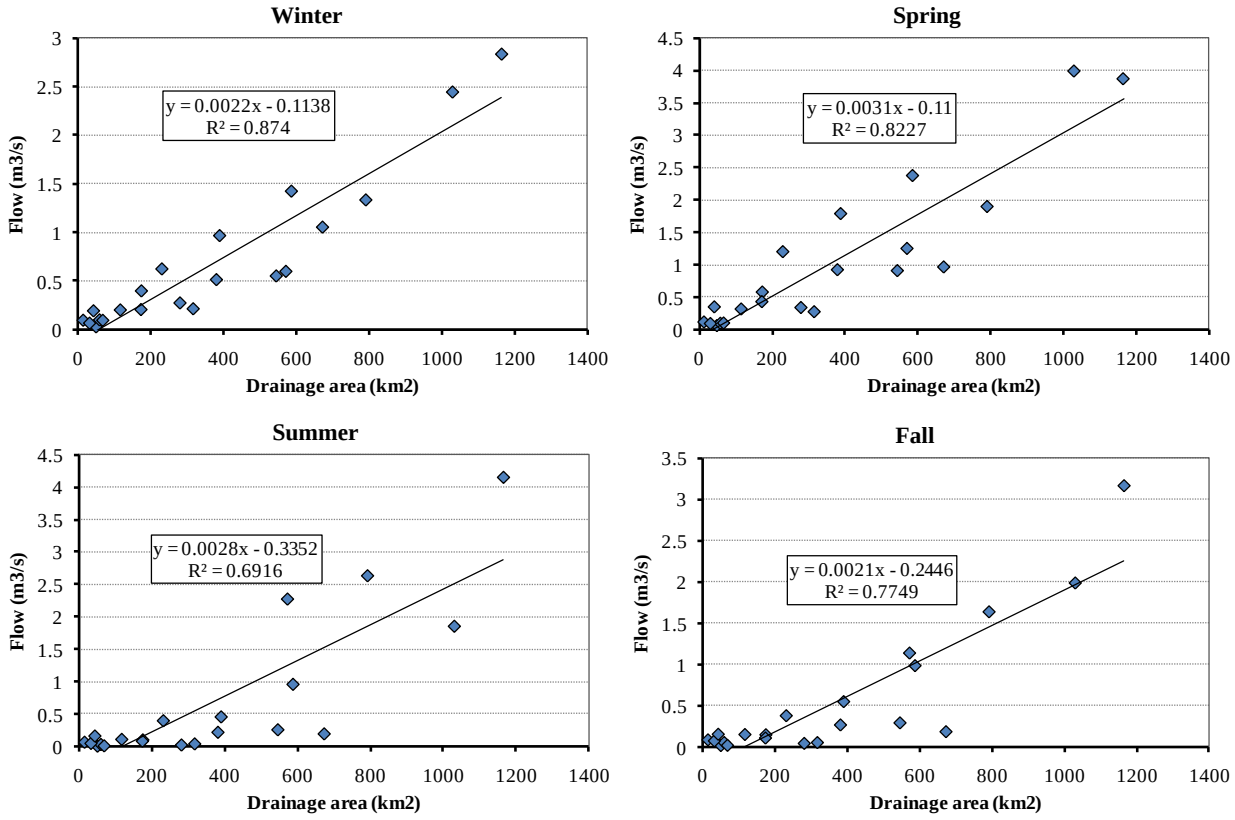


Figure C-5: Low seasonal flow versus drainage area for segments with drainage area < 1200km^2

Appendix D

Simulated Concentration versus cumulative measured concentration

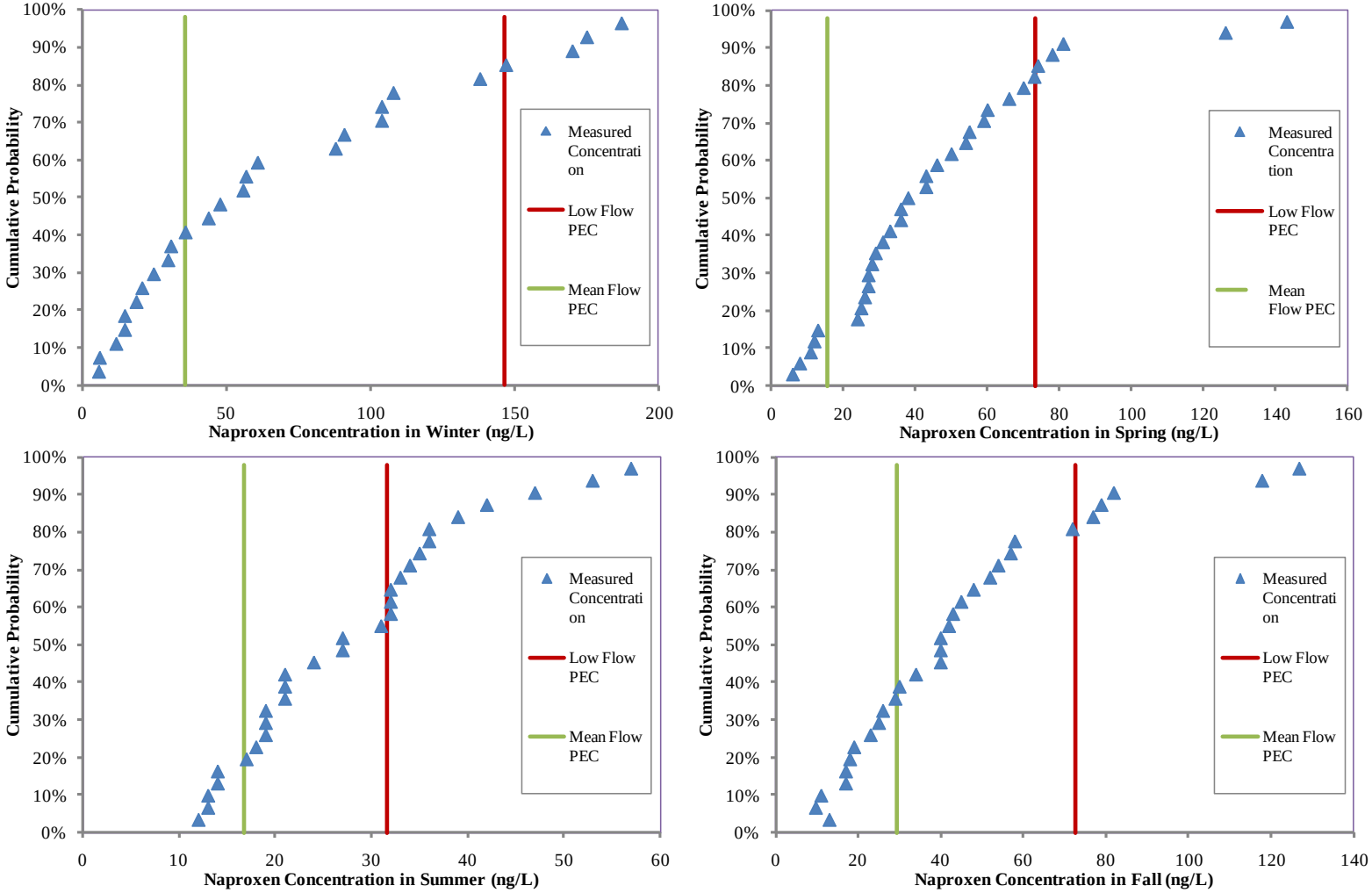


Figure D-1: Seasonal simulated concentration of naproxen versus the seasonal measured data

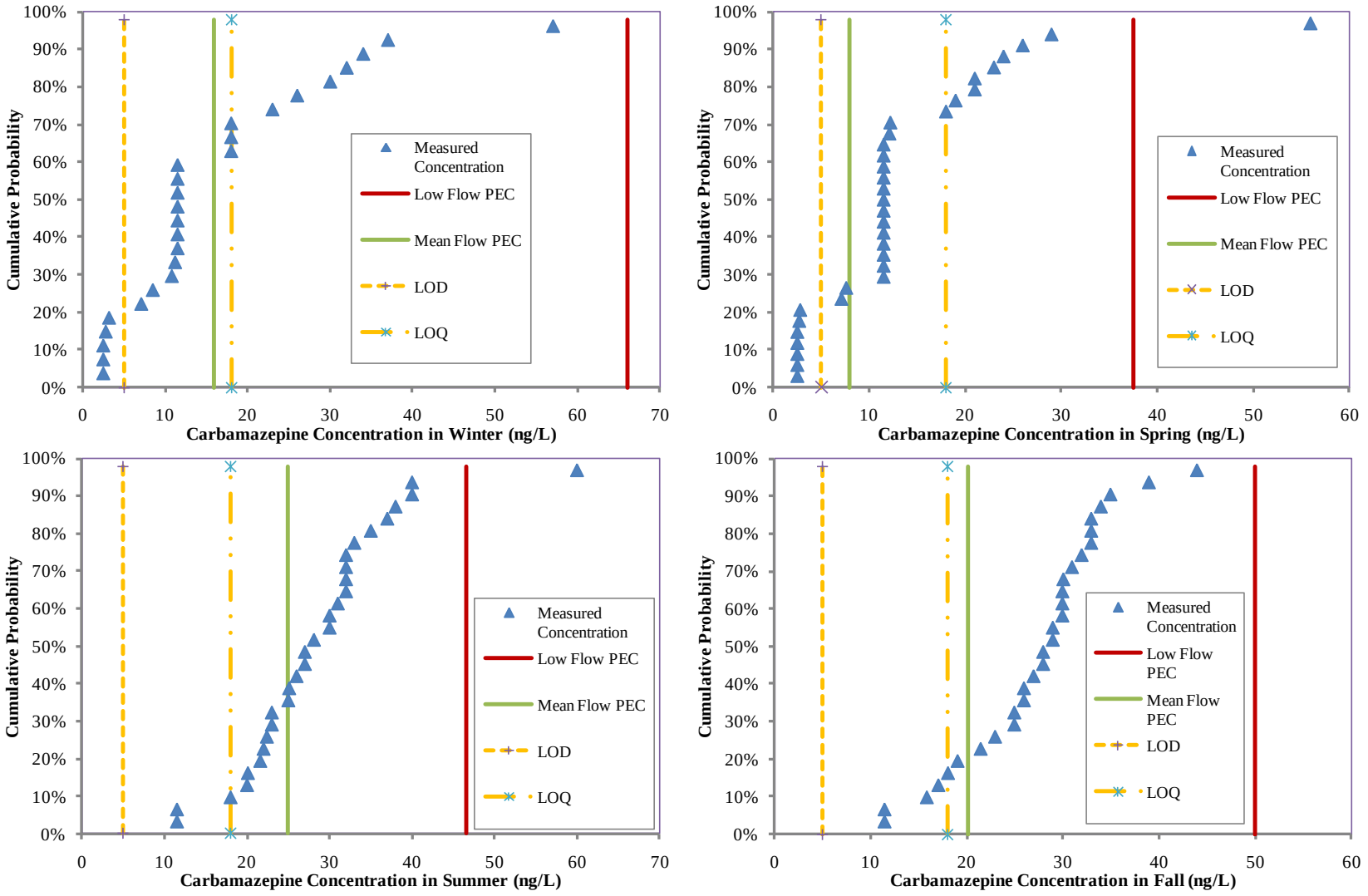


Figure D-2: Seasonal simulated concentration of carbamazepine versus the seasonal measured data

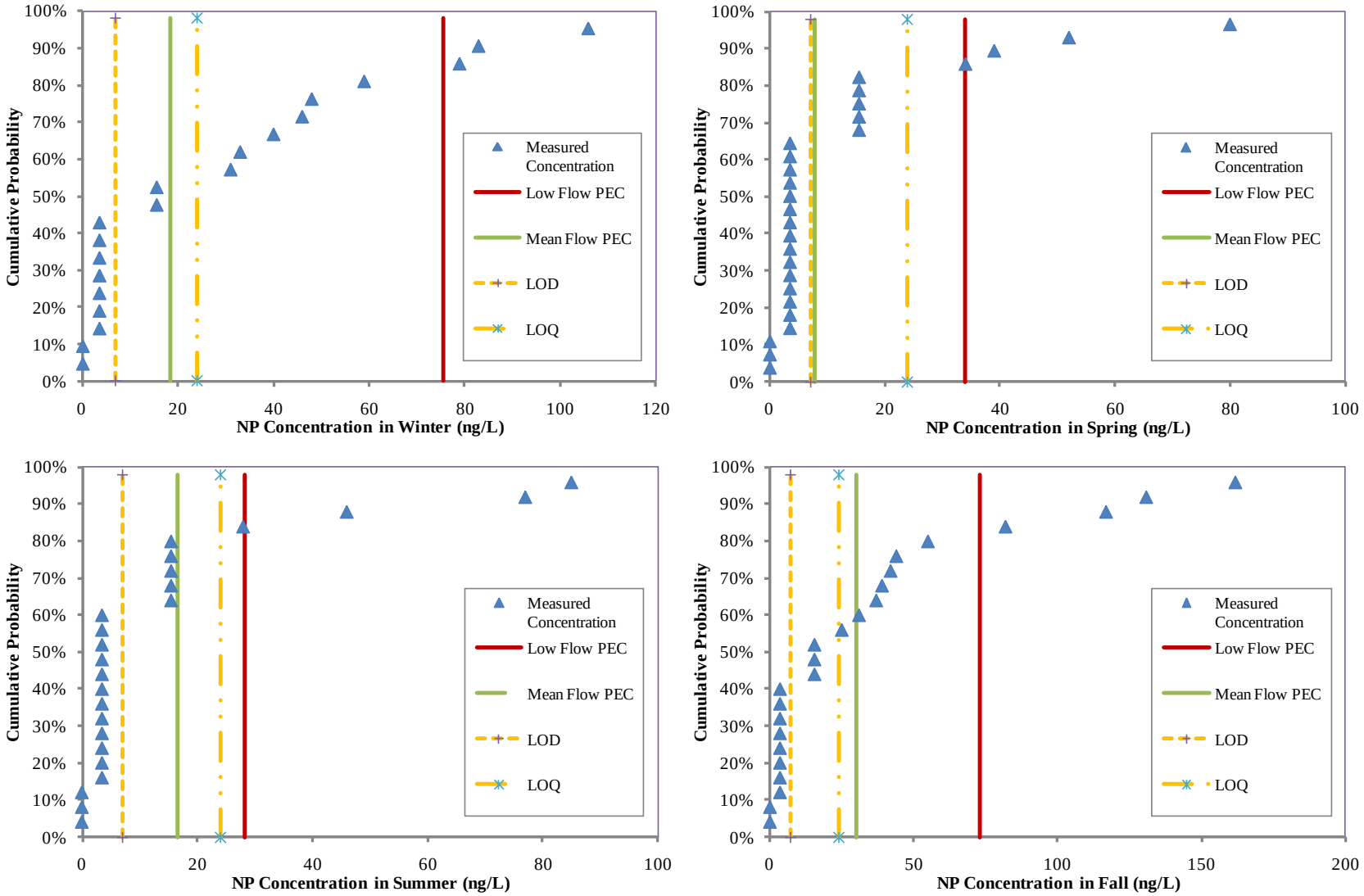


Figure D-3: Seasonal simulated concentration of NP versus the seasonal measured data

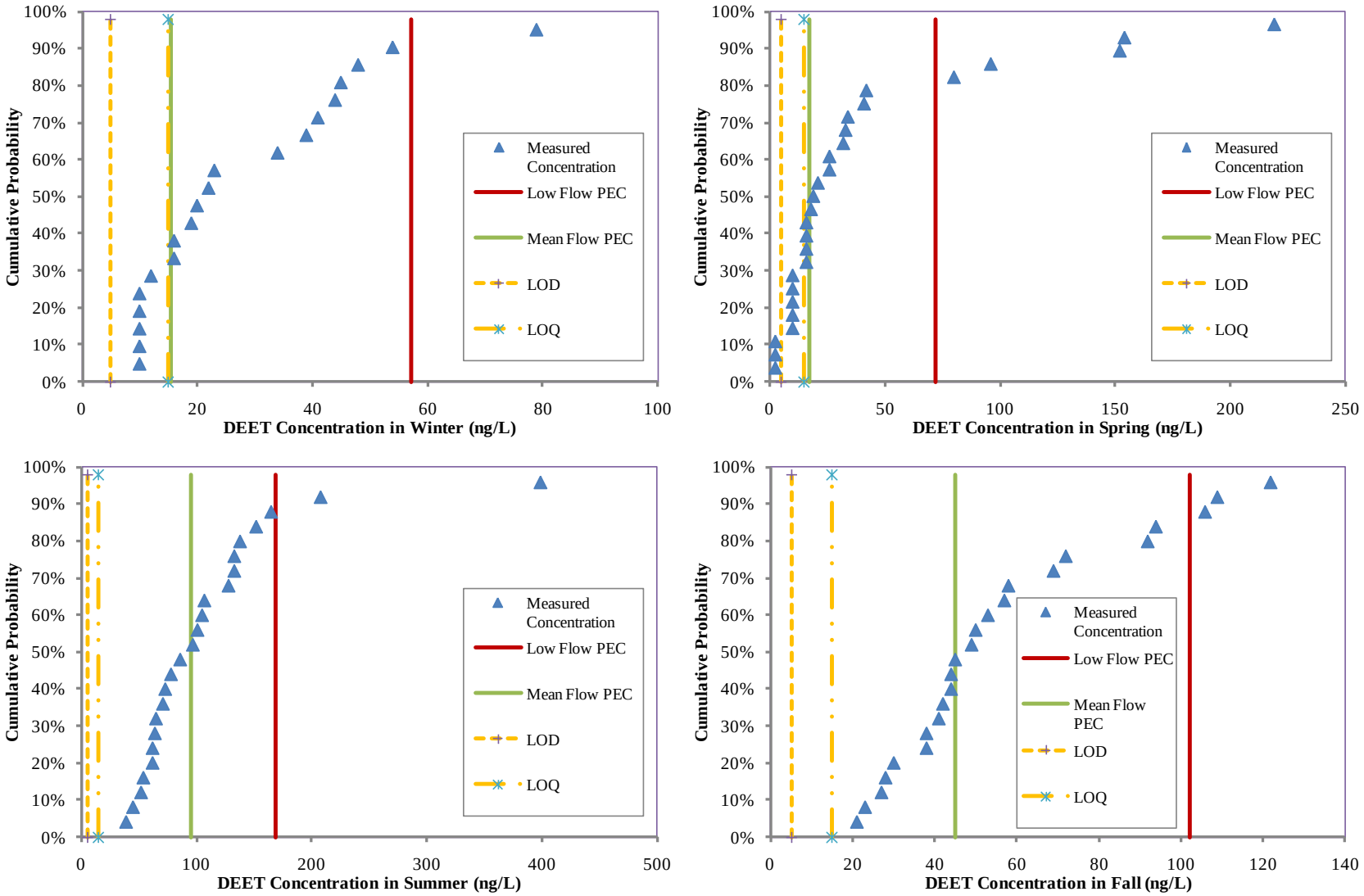


Figure D-4: Seasonal simulated concentration of DEET versus the seasonal measured data

Appendix E

Histograms for sensitivity analysis.

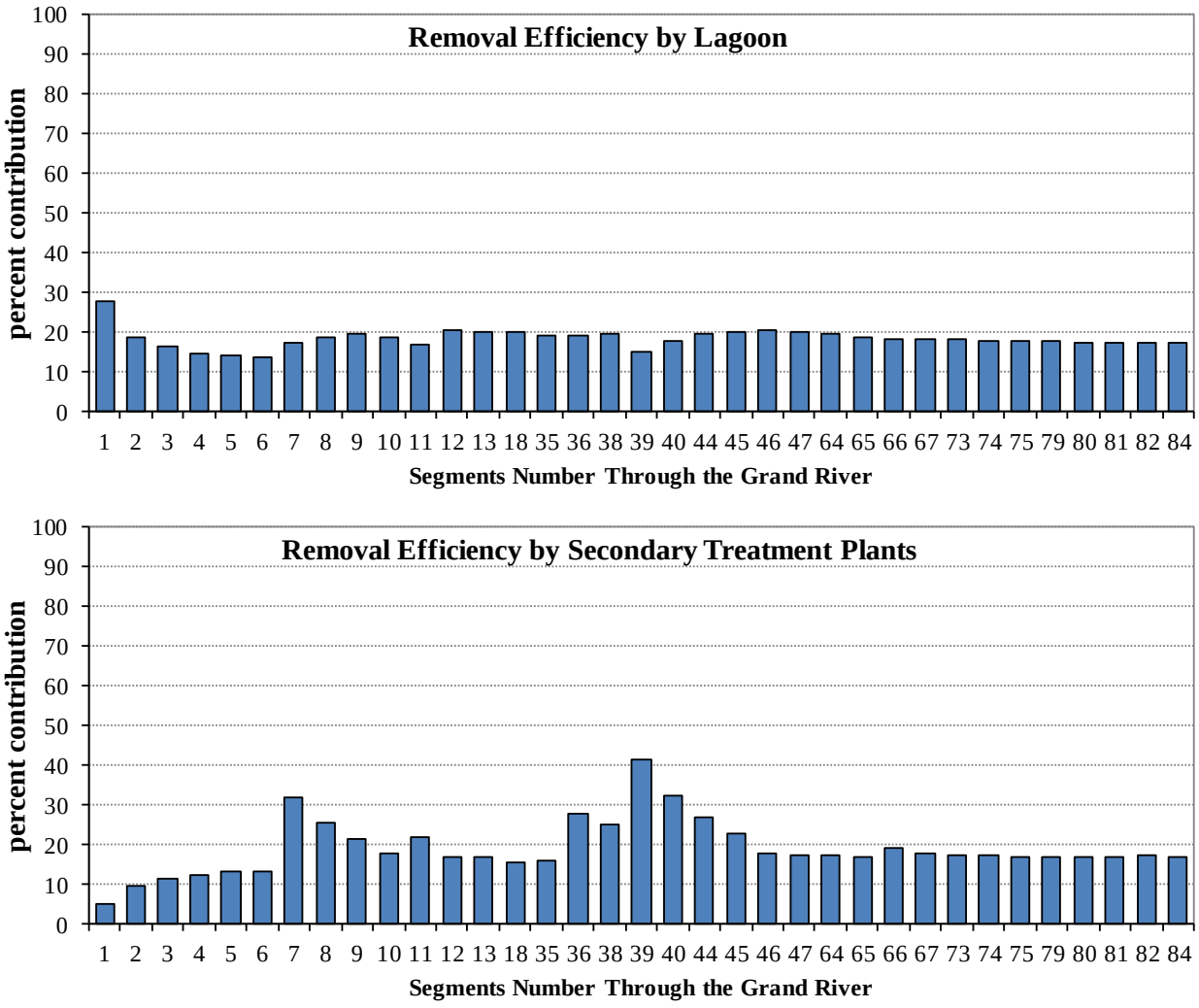
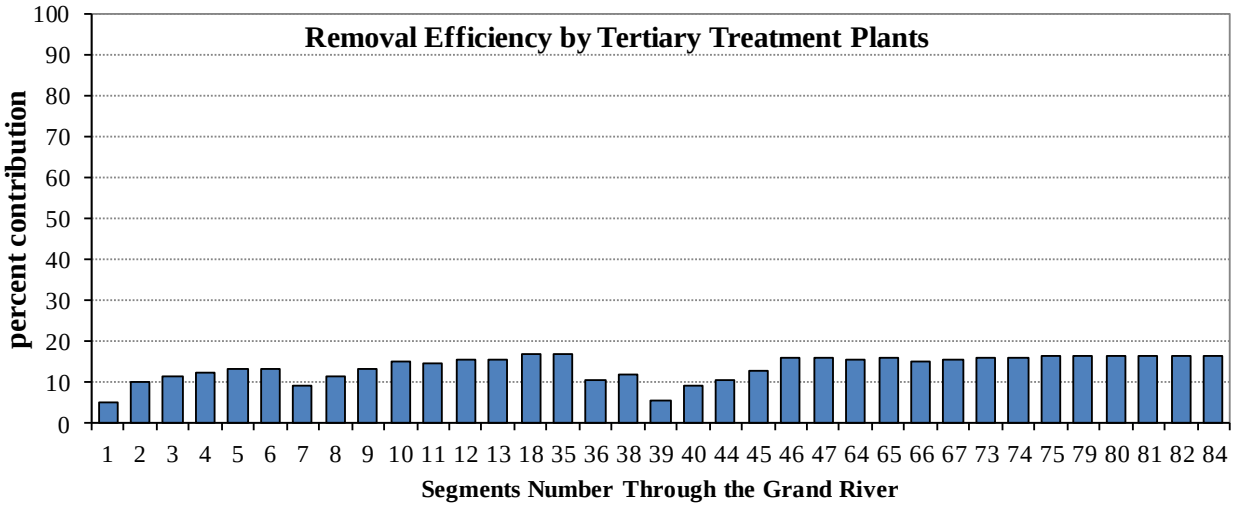
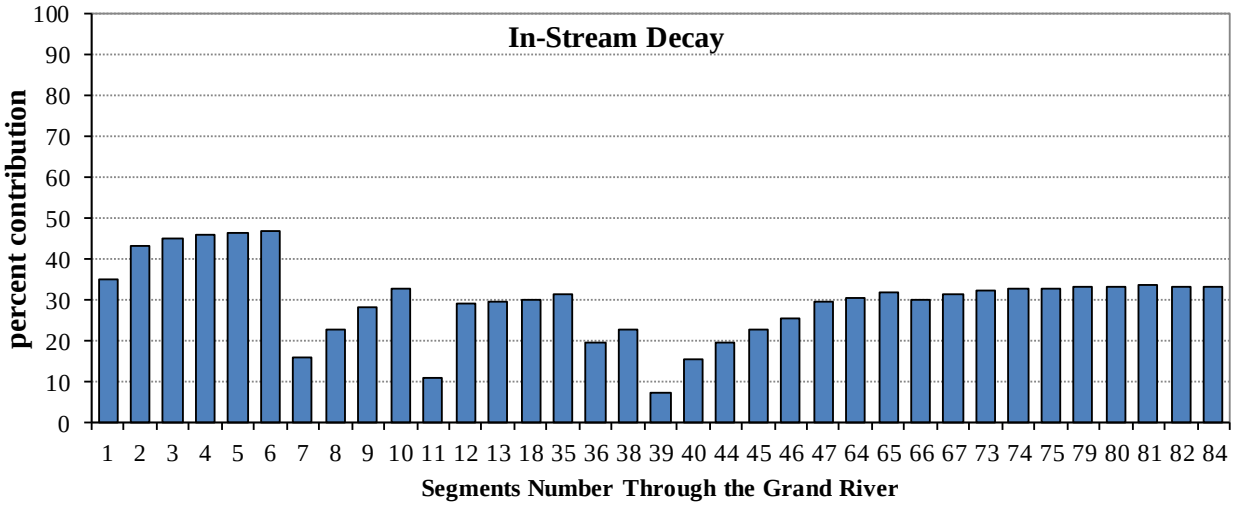


Figure E-1: The percent contribution of parameters on the concentrations of naproxen (to be continued)





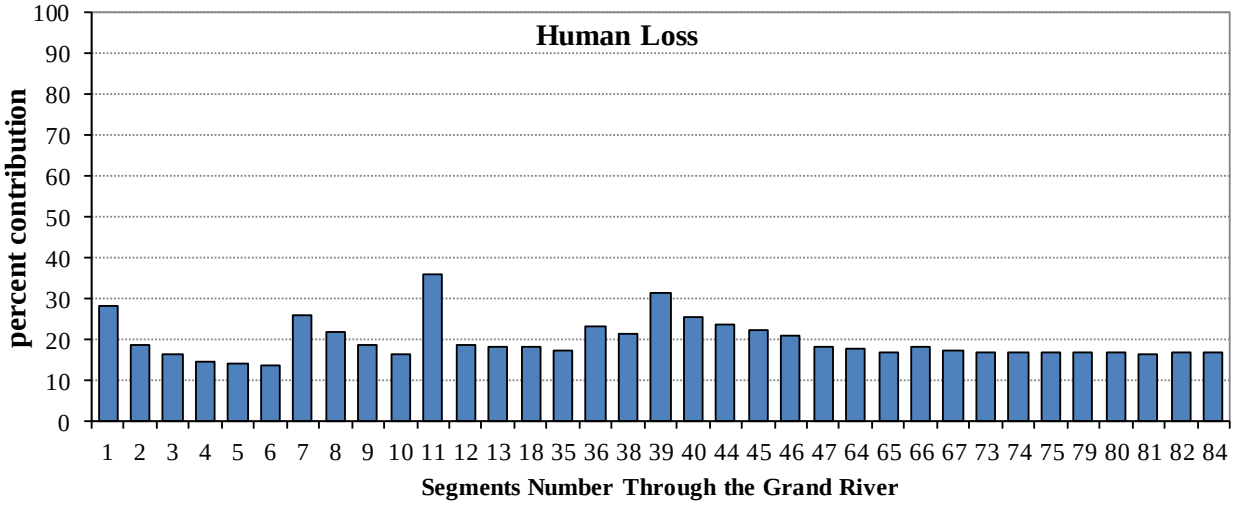


Figure E-1: The percent contribution of parameters on the concentrations of naproxen (continued)

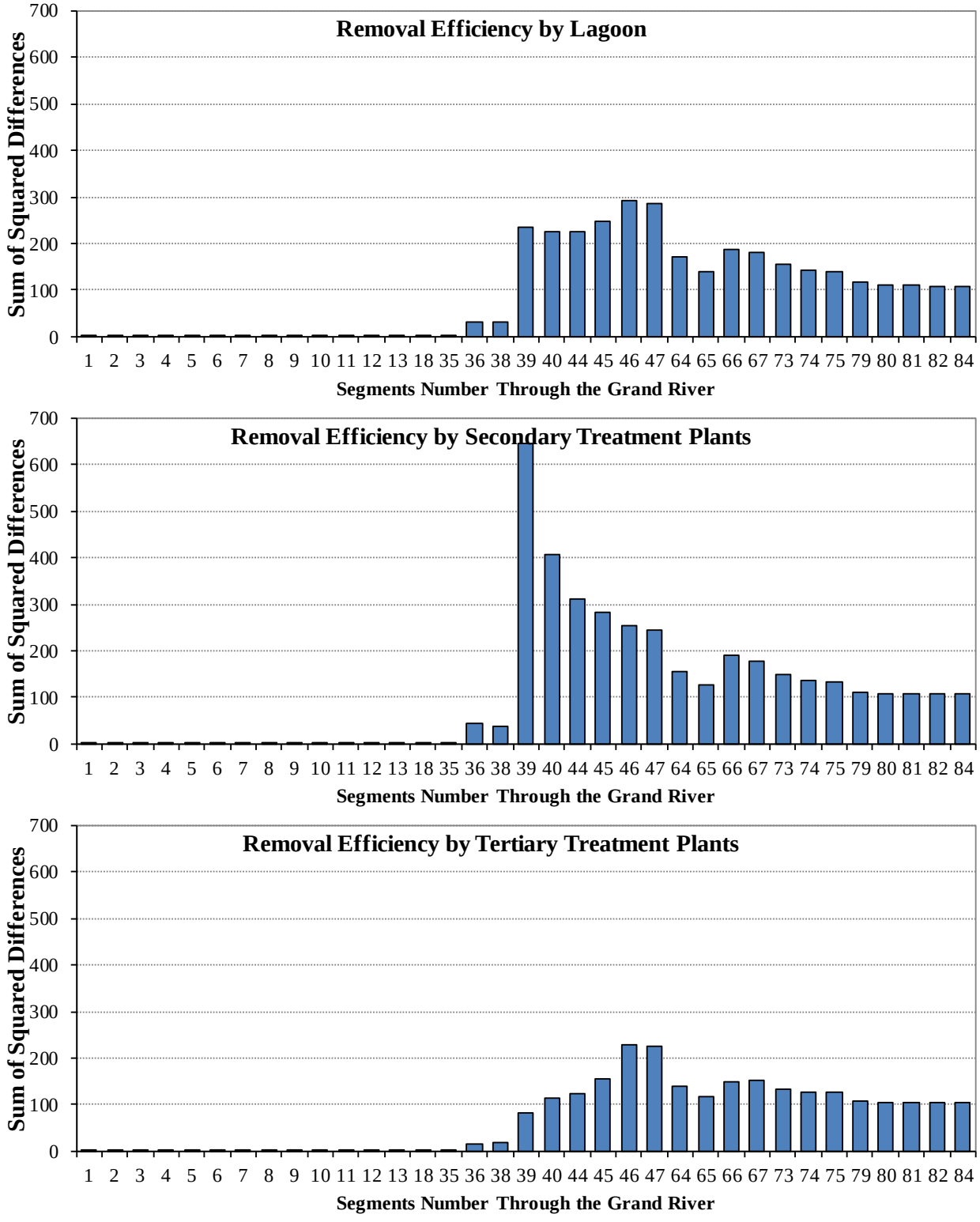


Figure E-2: The sum of squared differences of naproxen concentrations at different levels (to be continued)

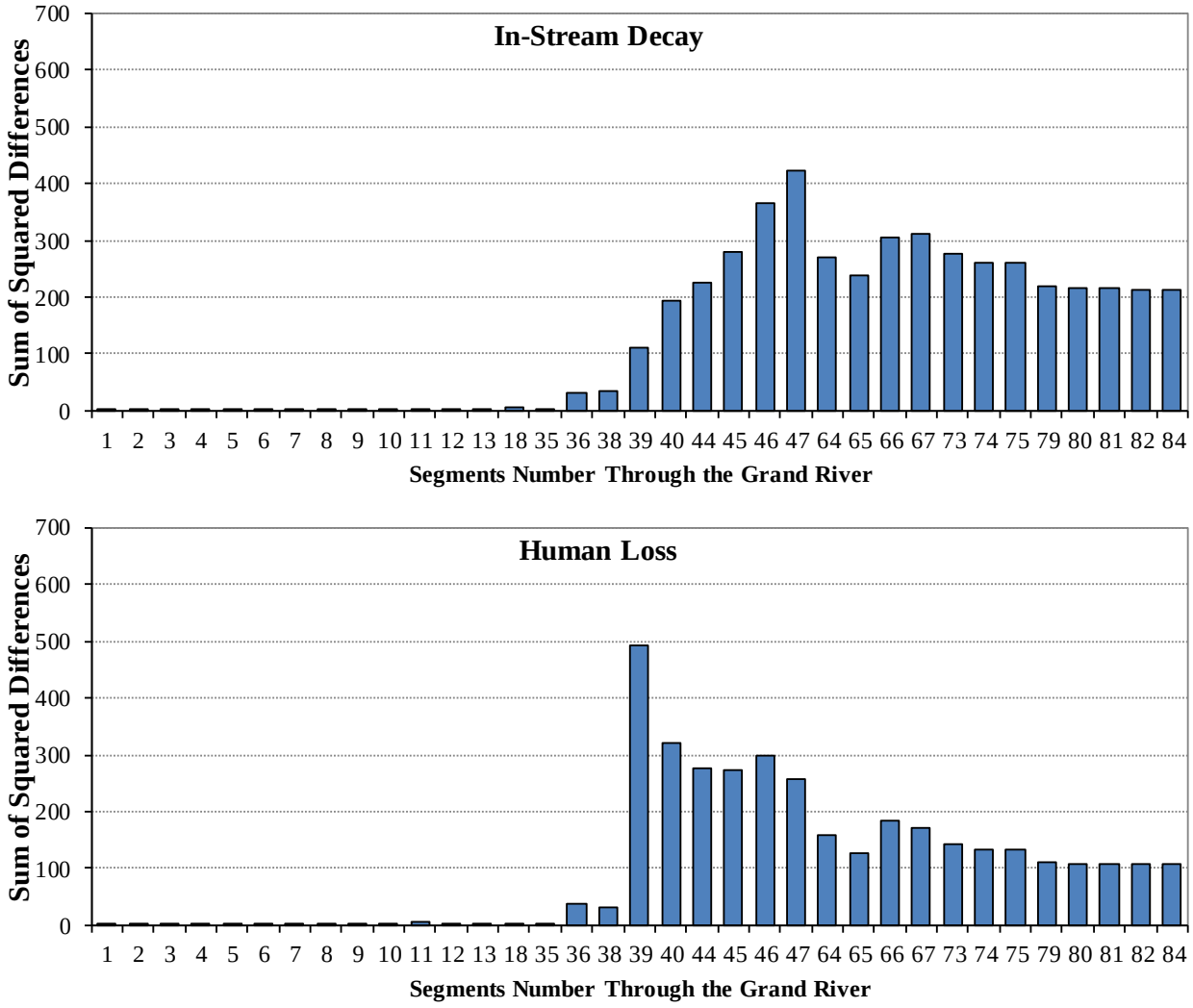
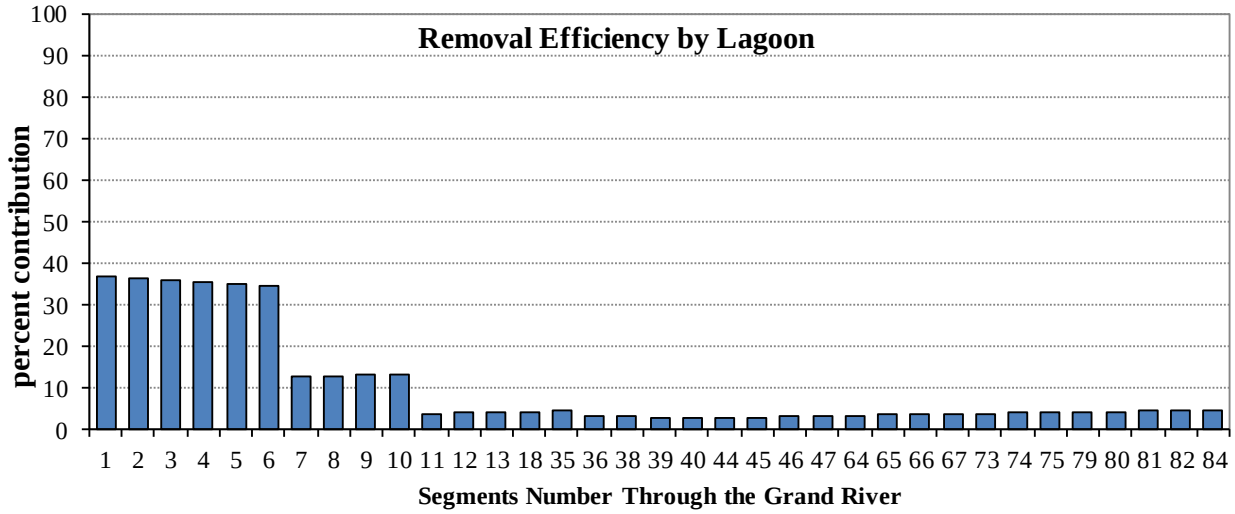
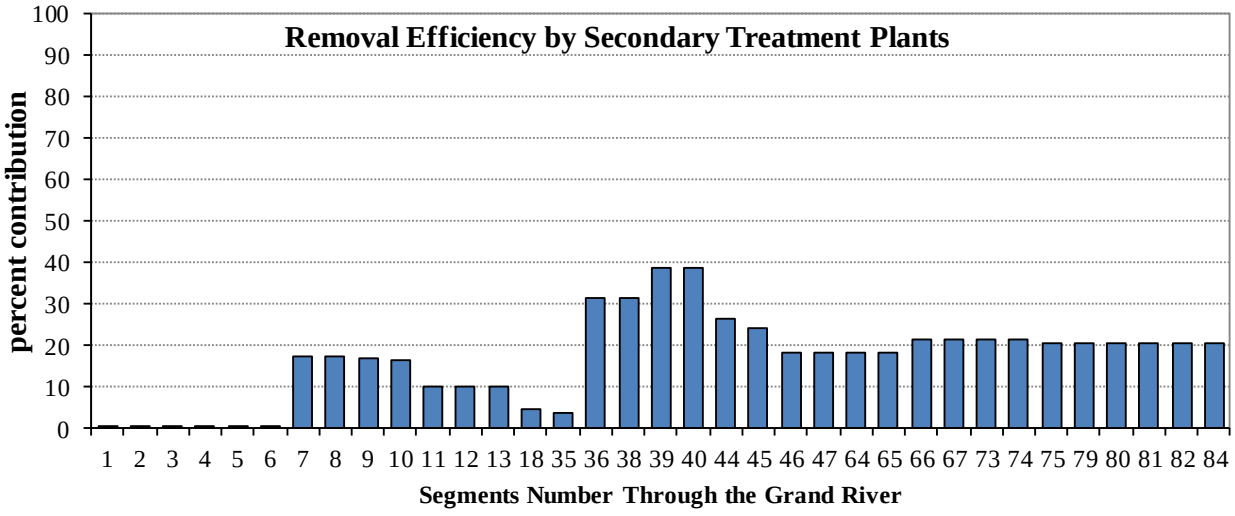


Figure E-2: The sum of squared differences of naproxen concentrations at different levels (continued)





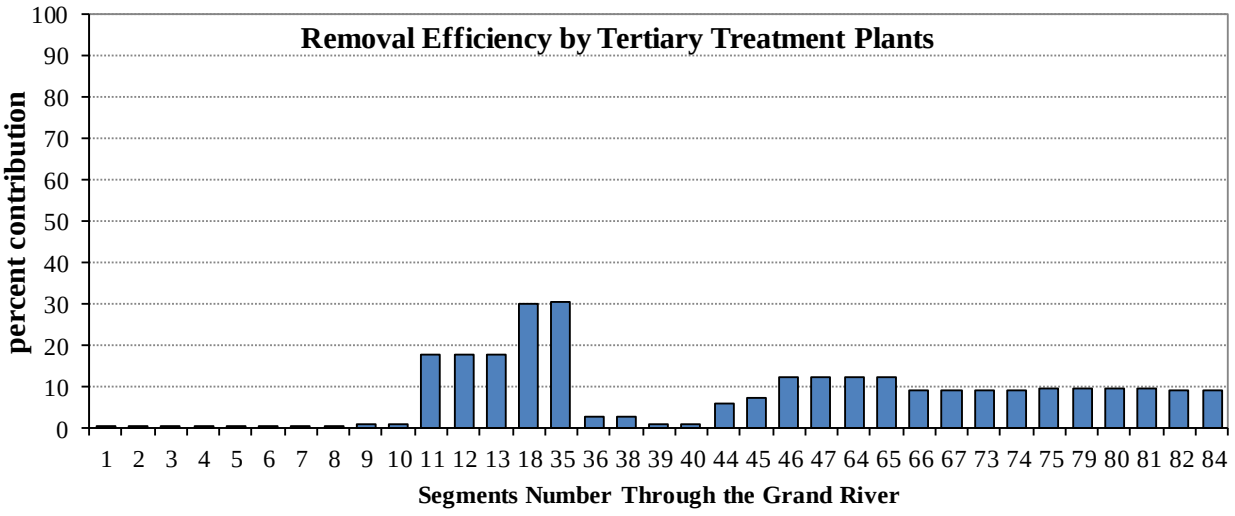


Figure E-3: The percent contribution of parameters on the concentrations of carbamazepine (to be continued)

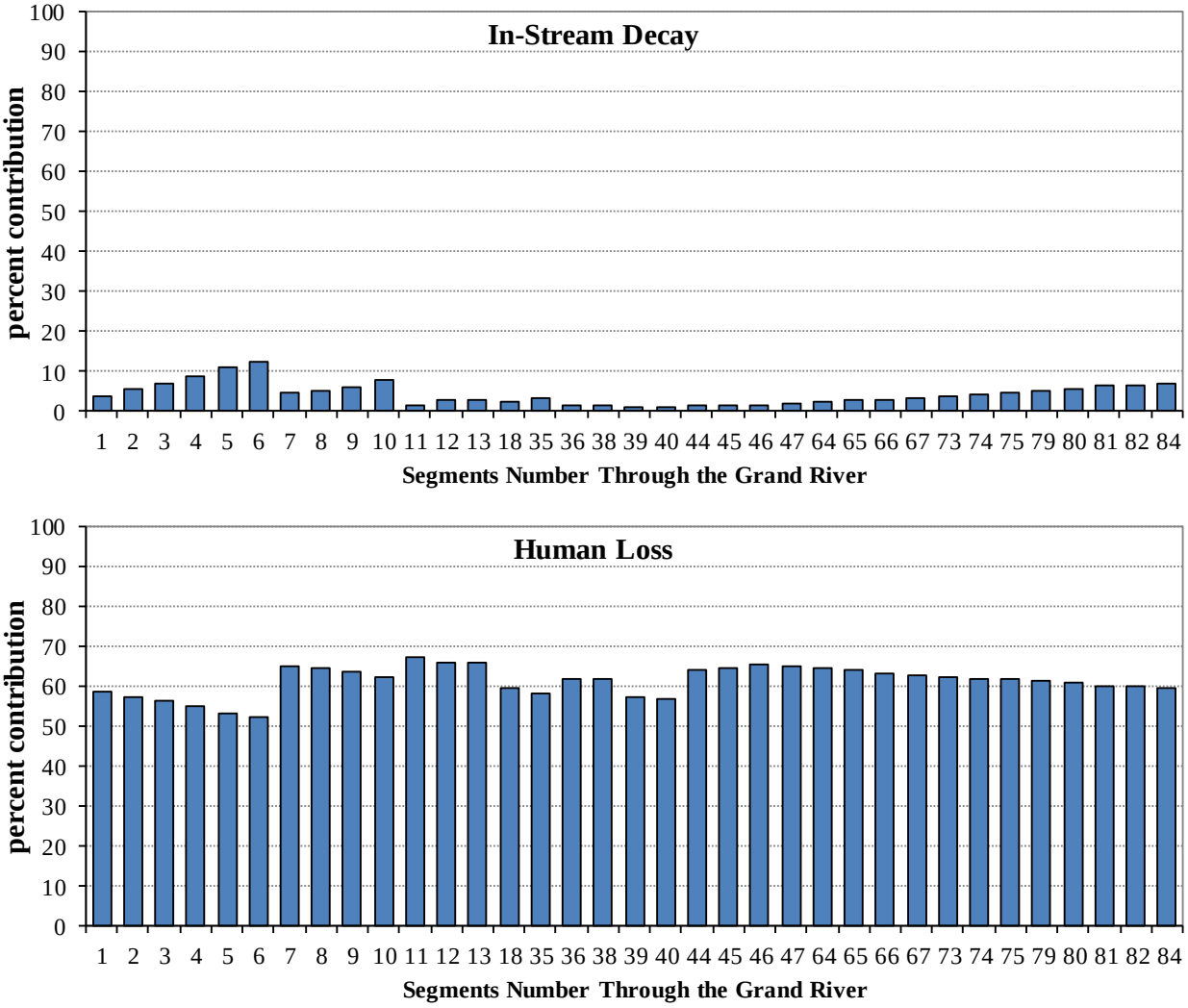


Figure E-3: The percent contribution of parameters on the concentrations of carbamazepine (continued)

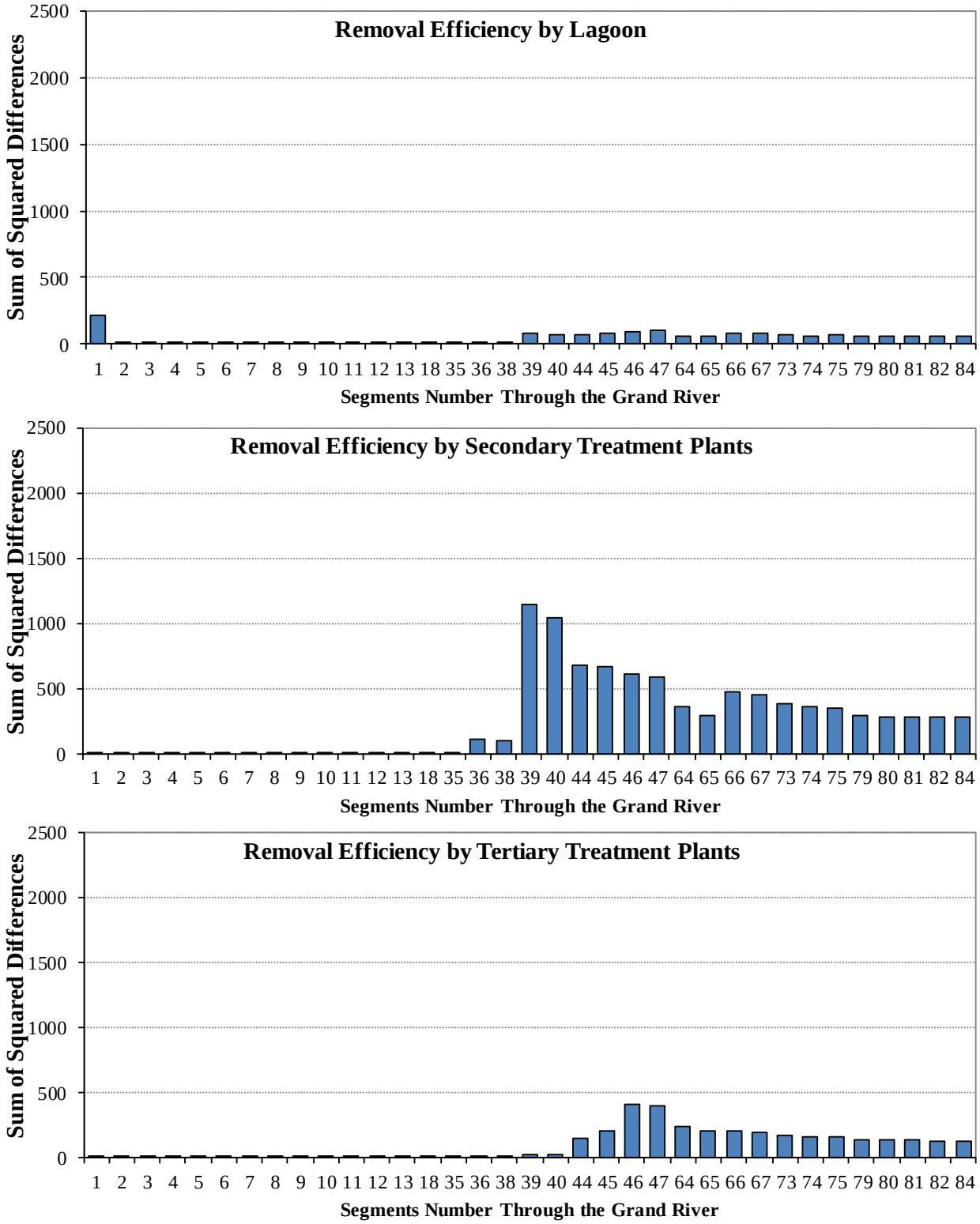


Figure E-4: The sum of squared differences of carbamazepine concentrations at different levels (to be continued)

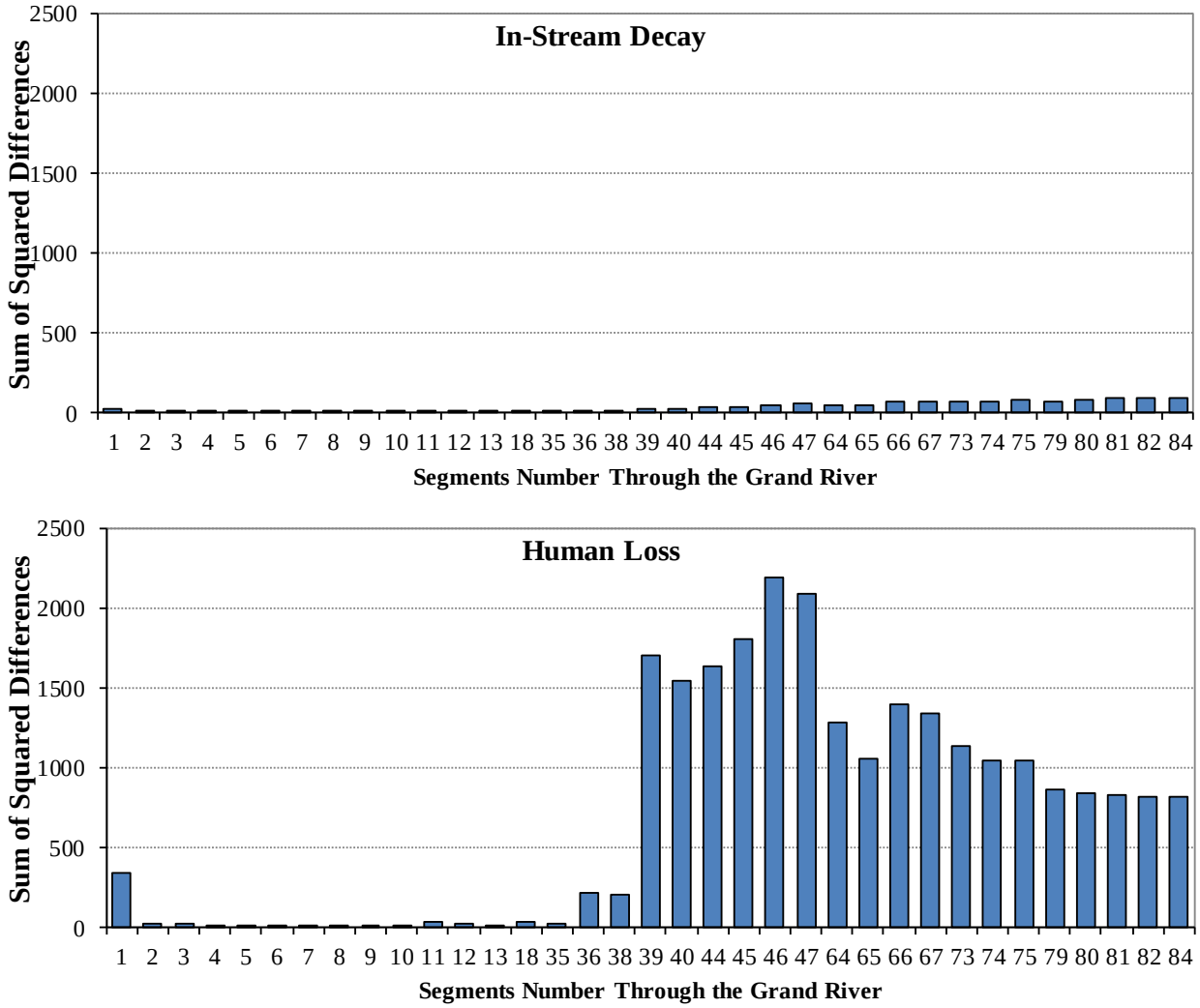
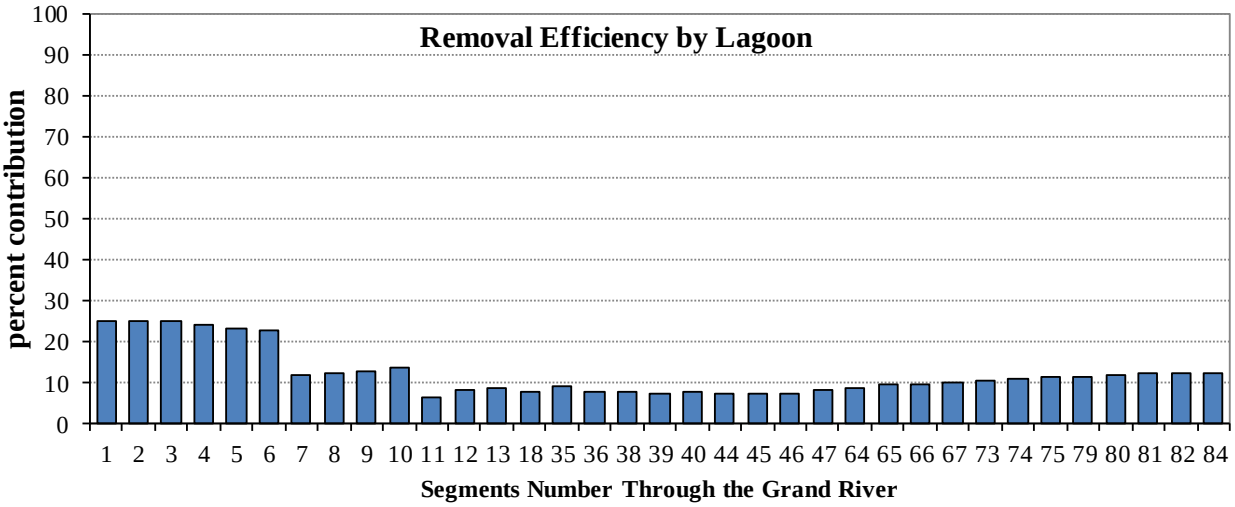
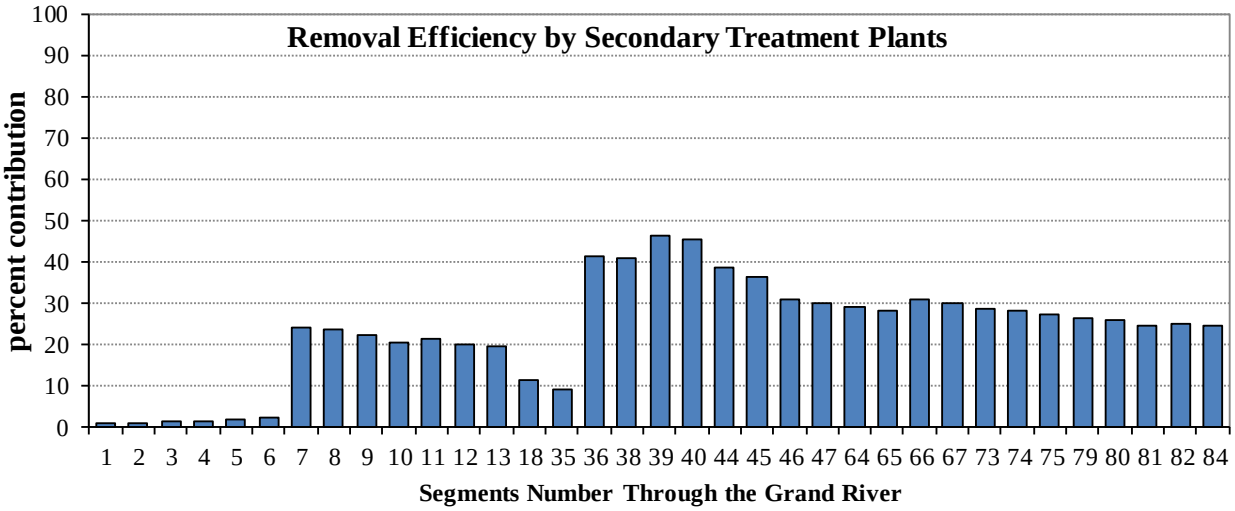


Figure E-4: The sum of squared differences of carbamazepine concentrations at different levels (continued)





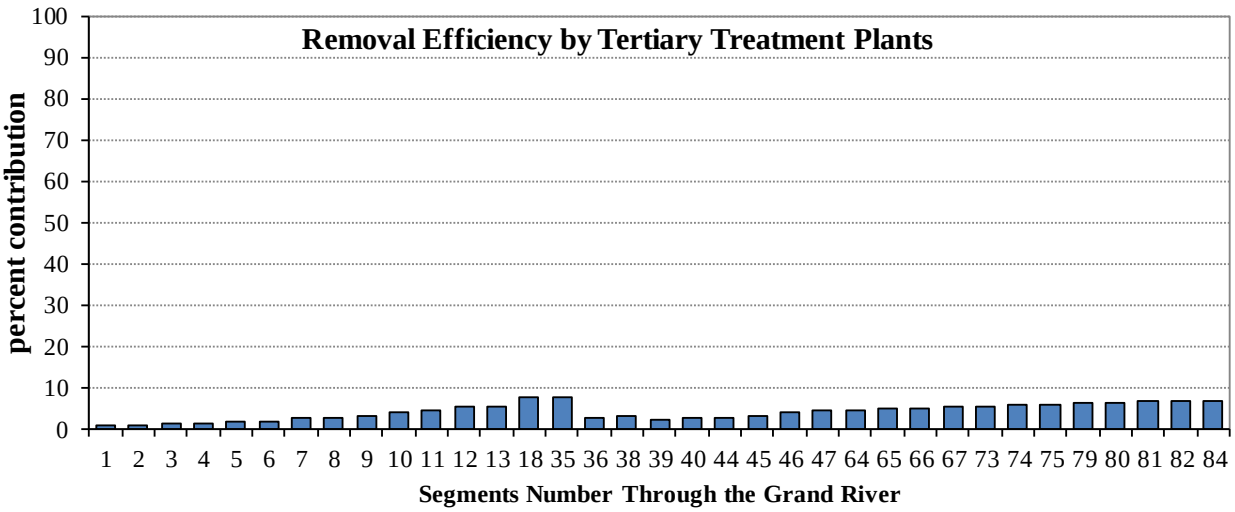


Figure E-5: The percent contribution of parameters on the concentrations of gemfibrozil (to be continued)

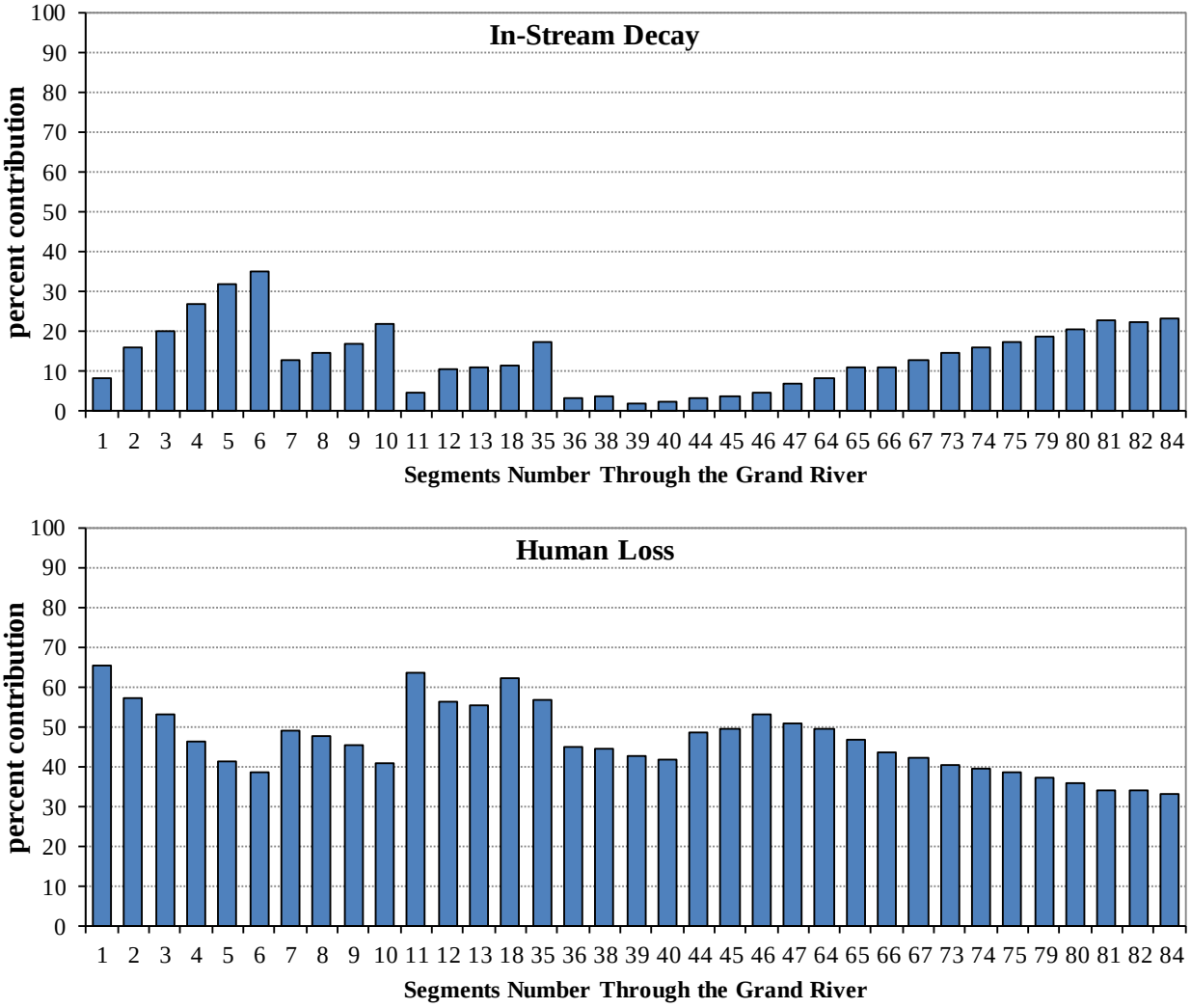


Figure E-5: The percent contribution of parameters on the concentrations of gemfibrozil (continued)

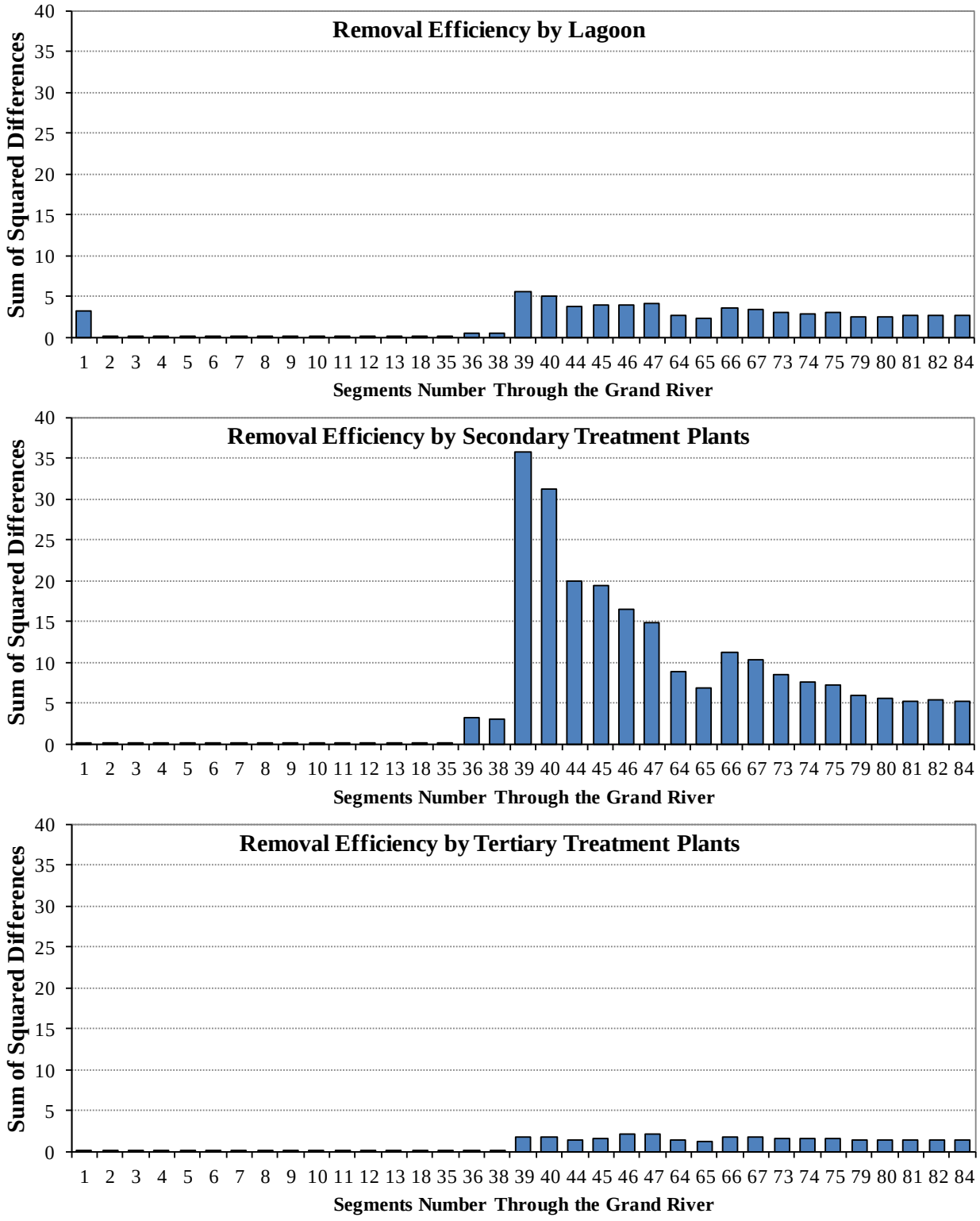


Figure E-6: The sum of squared differences of gemfibrozil concentrations at different levels (to be continued)

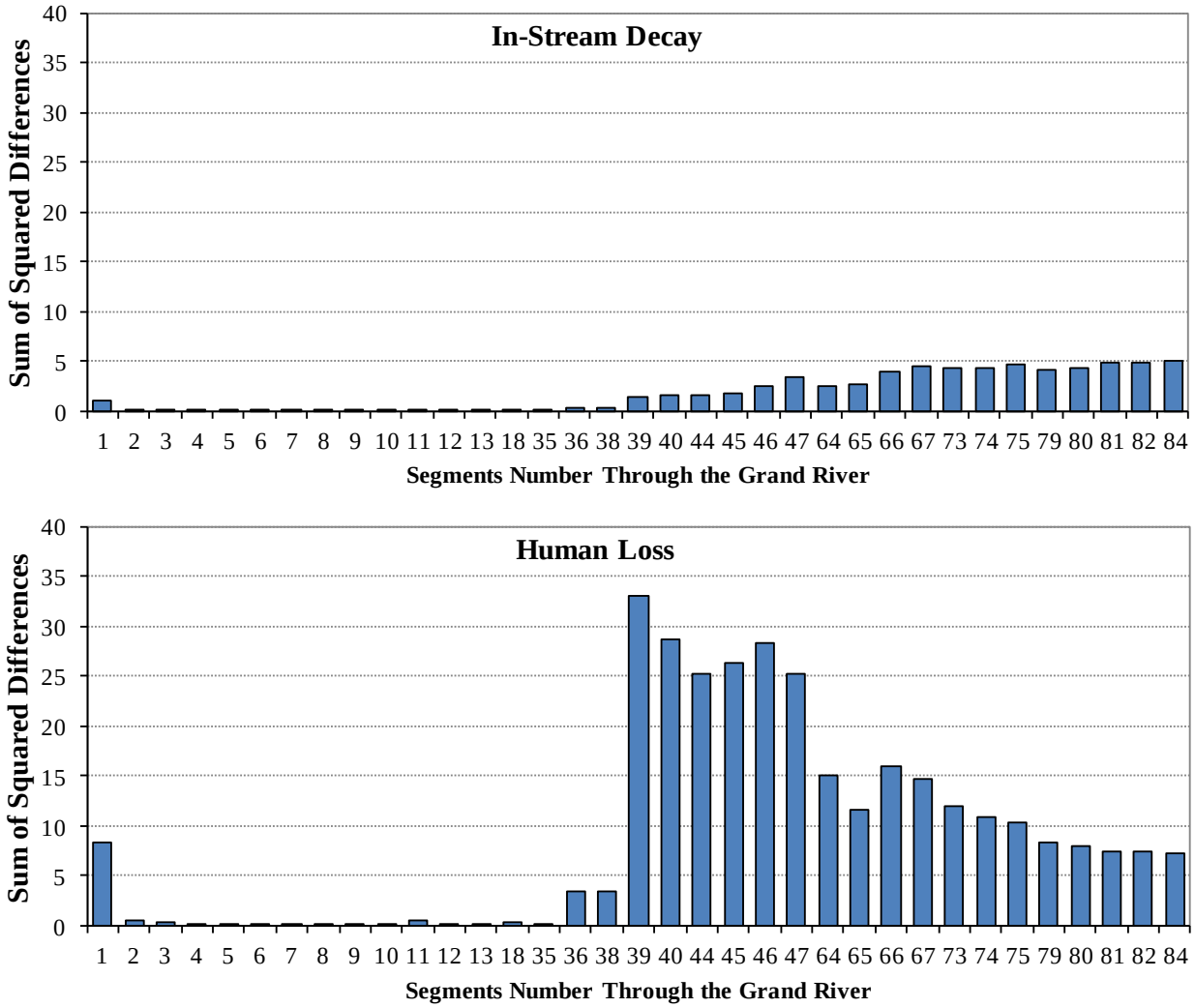
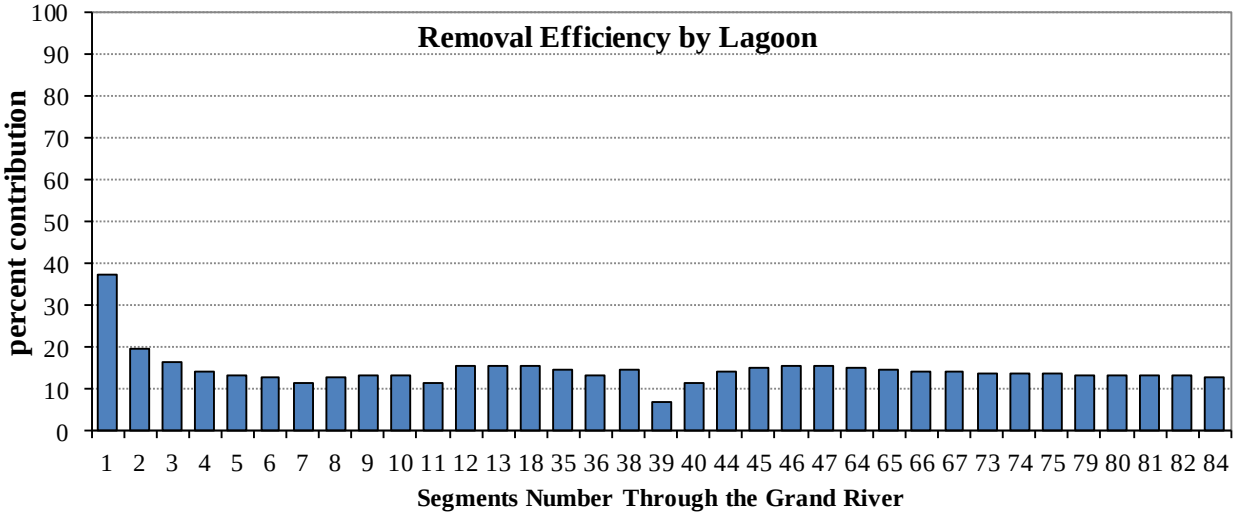
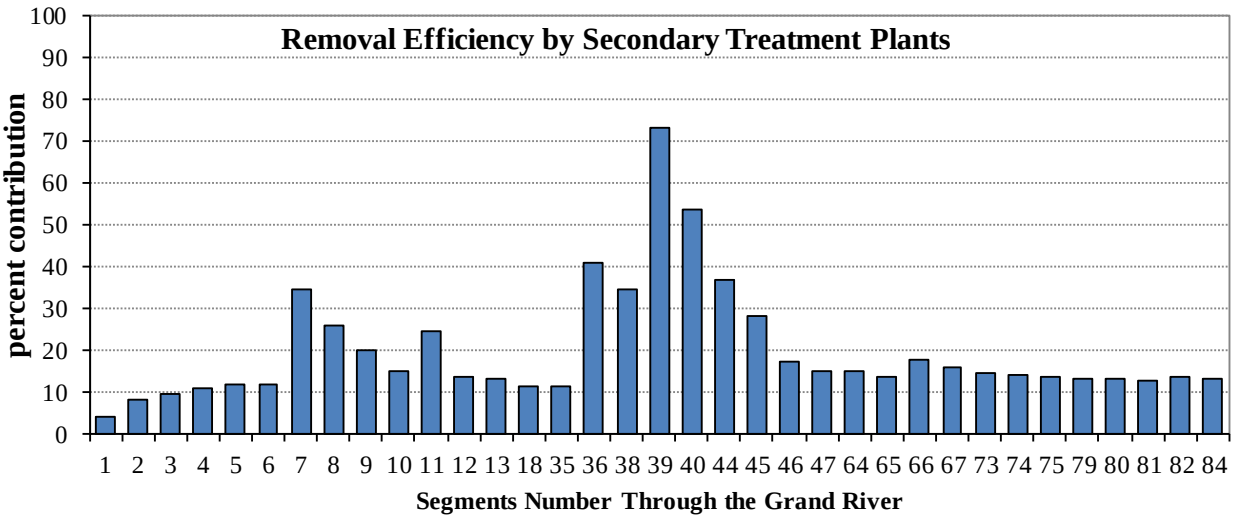


Figure E-6: The sum of squared differences of gemfibrozil concentrations at different levels (continued)





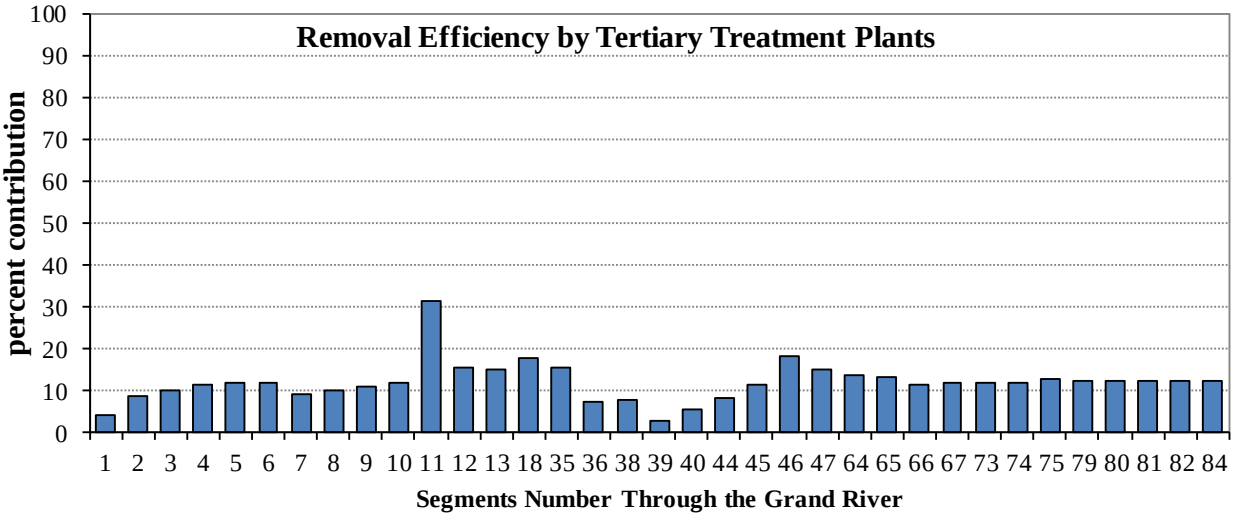


Figure E-7: The percent contribution of parameters on the concentrations of sulfamethoxazole (to be continued)

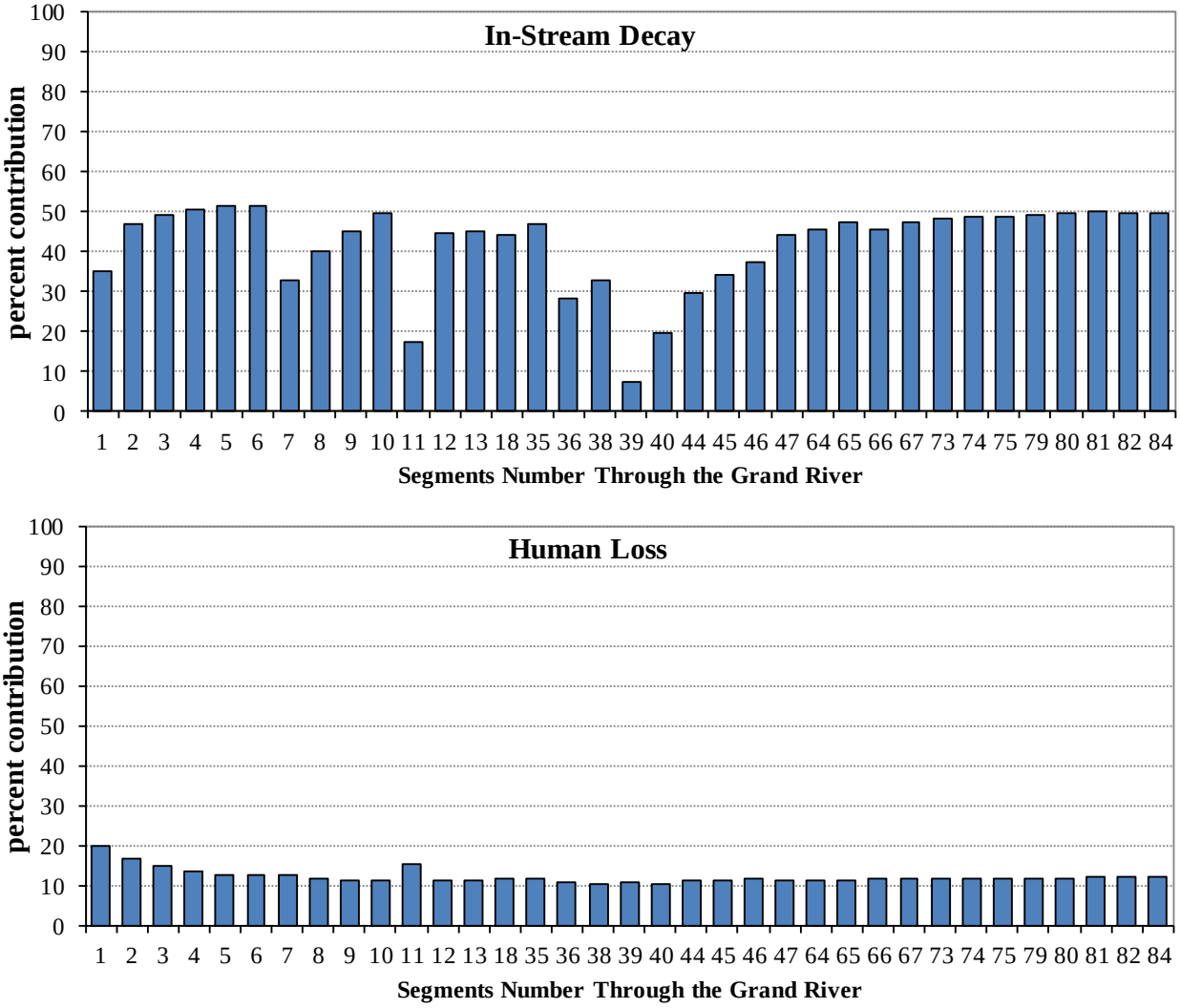
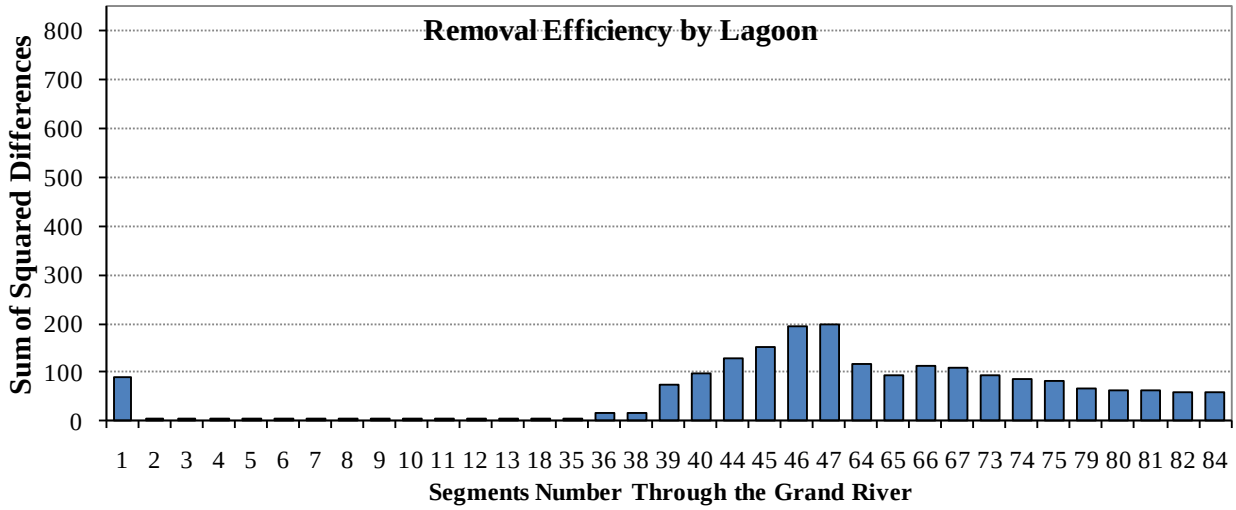
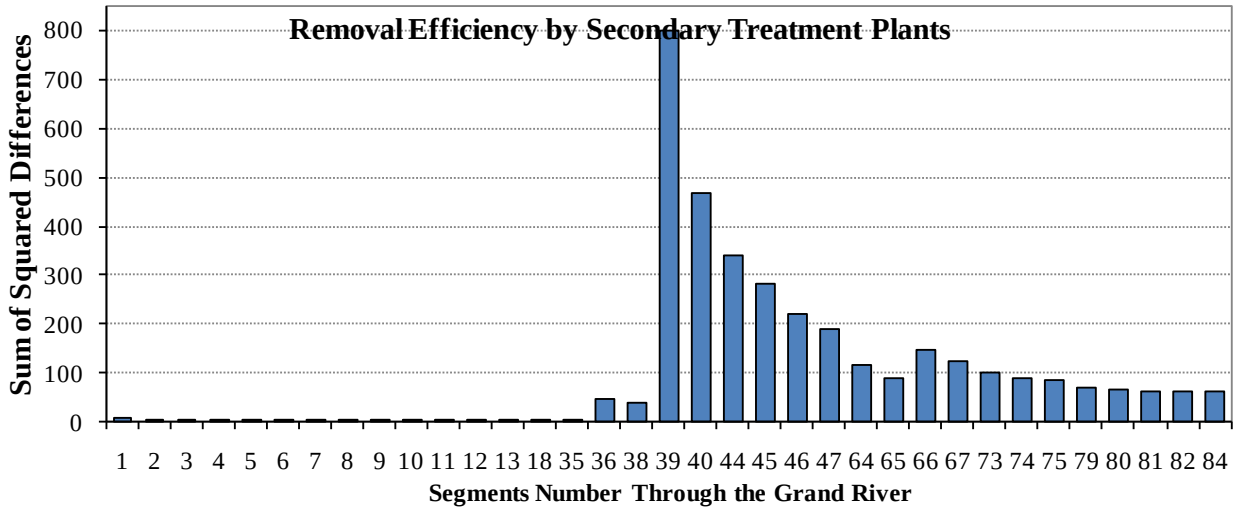


Figure E-7: The percent contribution of parameters on the concentrations of sulfamethoxazole (continued)





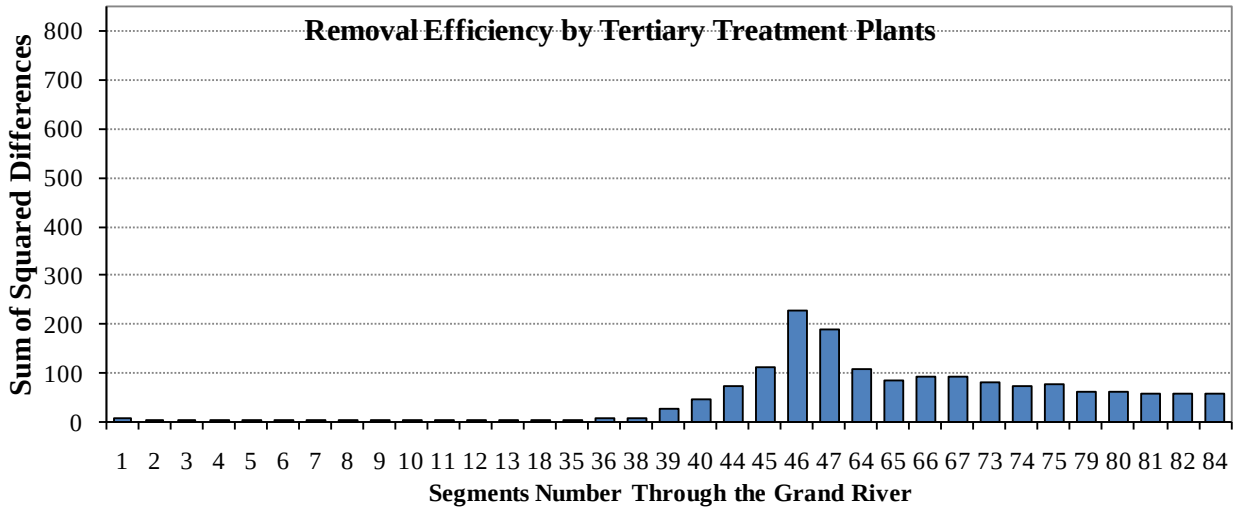
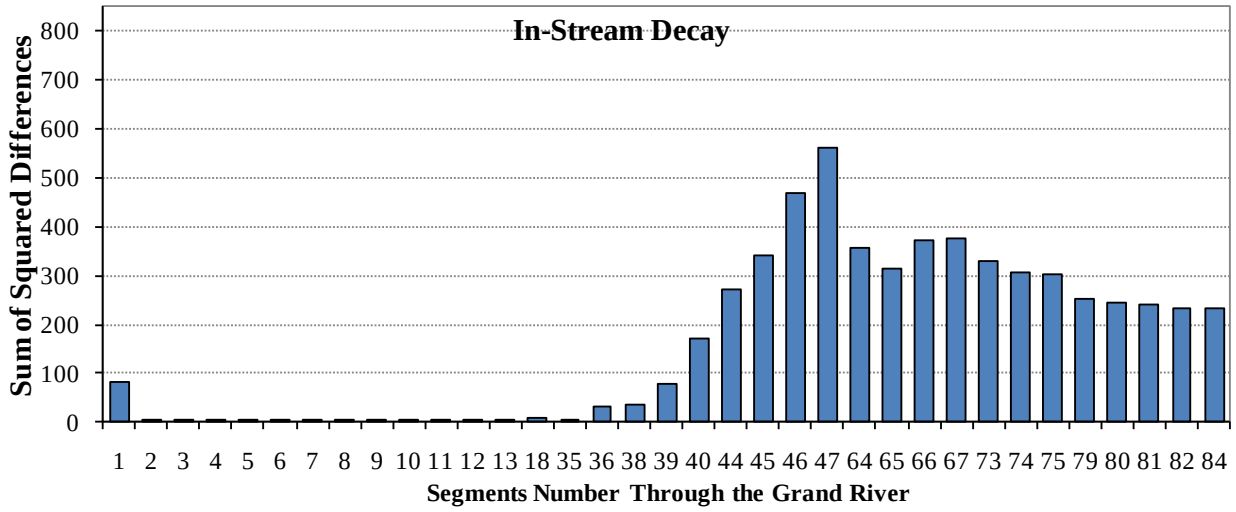


Figure E-8: The sum of squared differences of sulfamethoxazole concentrations at different levels (to be continued)



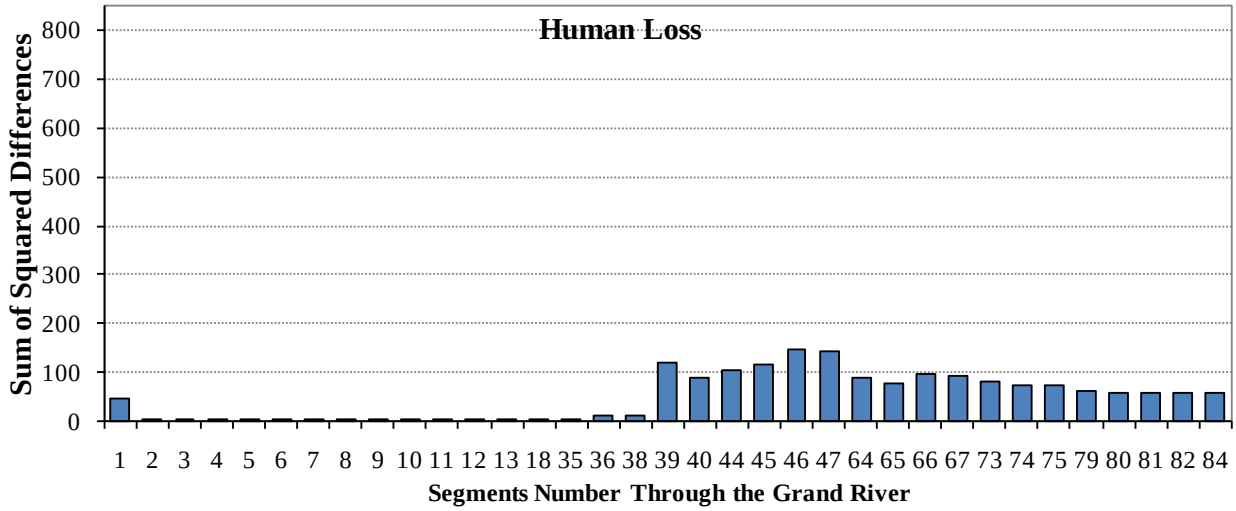


Figure E-8: The sum of squared differences of sulfamethoxazole concentrations at different levels (continued)

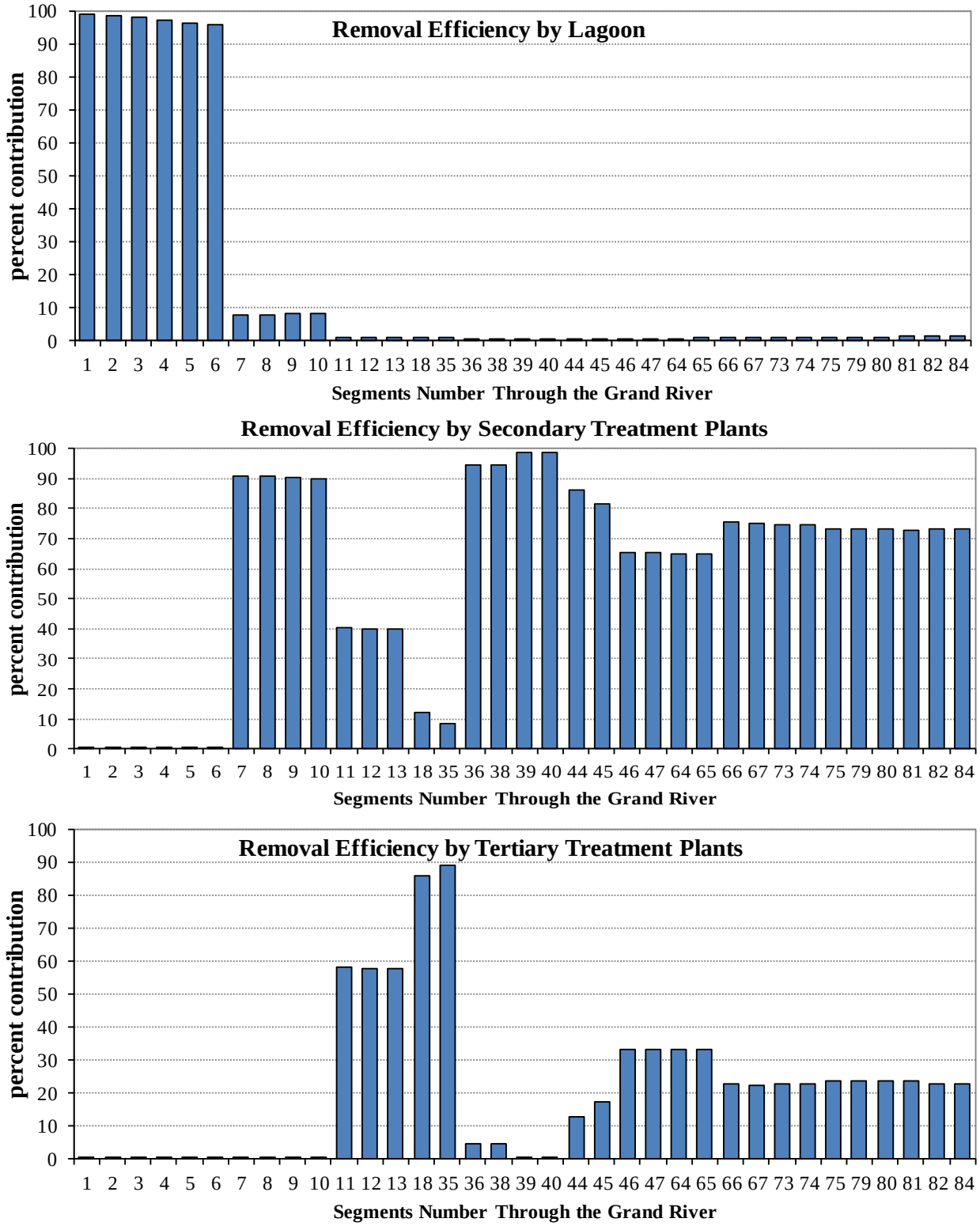


Figure E-9: The percent contribution of parameters on the concentrations of trimetoprime (No significant percent contribution was estimated for in-stream decay and human loss for this compound)

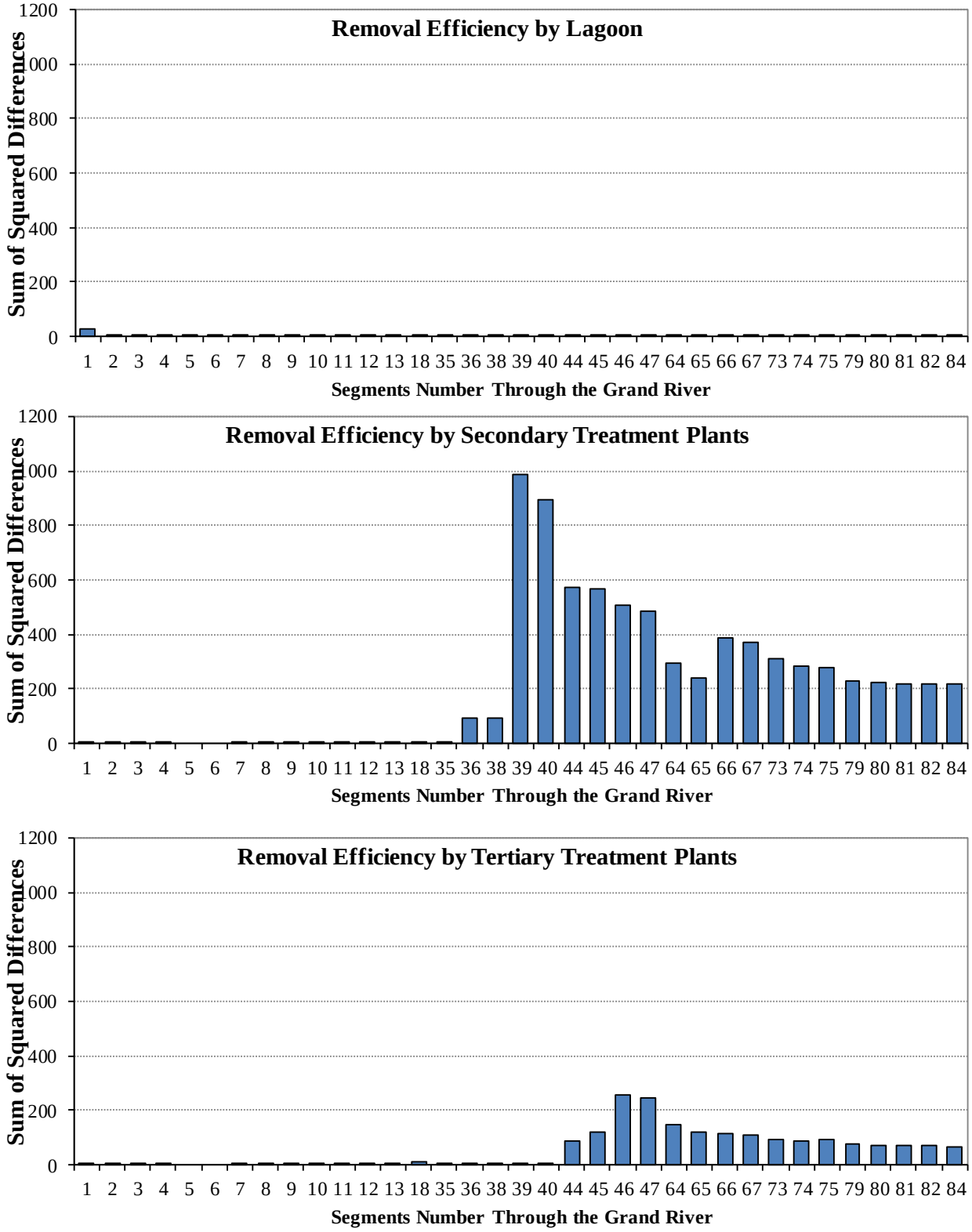


Figure E-10: The sum of squared differences of trimpethoprime concentrations at different levels