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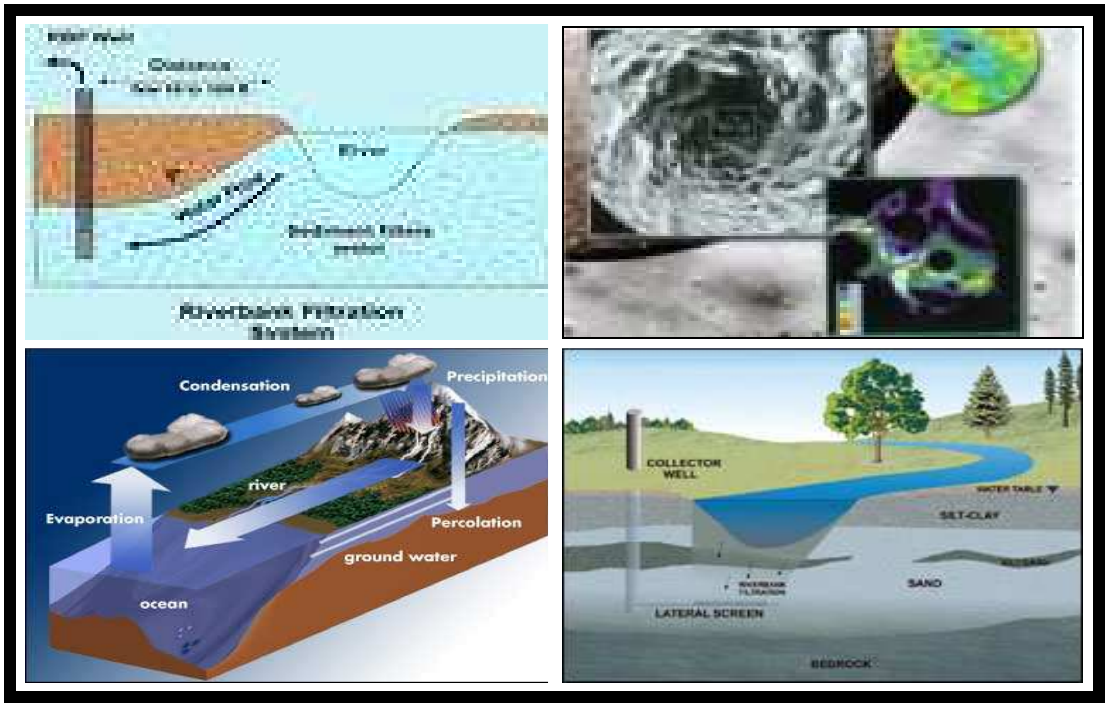

QSAR-Based Model for Assessment and Prediction of Organic Micropollutants Removal during Bank Filtration

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MSc Thesis MWI 2010/03
April 2010

UNESCO-IHE
Institute for Water Education

SWITCH

QSAR-Based Model for Assessment and Prediction of Organic Micropollutants Removal during Bank Filtration

Master of Science Thesis
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The findings, interpretations and conclusions expressed in this study do neither necessarily reflect the views of the UNESCO-IHE Institute for Water Education, nor of the individual members of the MSc committee, nor of their respective employers.

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Dedication

To

my inspiring parents, Mr. & Mrs. E.Saragih

for your encouragement and prayers through this period of my studies.

"So do not fear, for I am with you; do not be dismayed, for I am your God. I will strengthen you and help you; I will uphold you with my righteous right hand."
(Isaiah 41:10)

Abstract

Recently organic micropollutants have become a concern in scientific world related to their fate and transport in the aquatic life. Pharmaceuticals are a group of organic micropollutants that have been detected as a major contaminant in environment mainly due to uncompleted process of pharmaceuticals removal of wastewater treatment plants. A significant rise at consumption and application of pharmaceuticals recently has increased concentration of pharmaceuticals in aquatic life and may contaminate groundwater even further. Due to the persistence and mobility of pharmaceuticals in environment, it is believed that pharmaceuticals may cause toxic effect in human life although not much information is available to answer this issue.

Bank filtration is a robust technology used for water treatment that has high potentials for removal of different contaminants, including some pharmaceuticals and other emerging pollutants, from surface water at low cost. However, previous studies on fate of pharmaceuticals during riverbank filtration do not provide sufficient information or basis for a sustainable design and implementation of riverbank filtration systems for removing these contaminants. Furthermore, experimental data on organic micropollutants removal during soil passage is limited and doing experiment is time consuming and relatively expensive especially for increasing number of pharmaceuticals being produced recently.

To address this problem, this study focussed on analysis of the available data and development of QSAR-based model using the physicochemical properties of pharmaceuticals in order to describe the fate of pharmaceuticals during riverbank filtration. Extensive literature review was conducted and removal data for different classes of pharmaceuticals were complied, along with the process and site conditions, in the form of a database. Several descriptors that represent physicochemical properties of pharmaceuticals were calculated by using different commercially available software packages. The best descriptors subsets for the models were selected using the genetic-algorithm and then the developed model was analysed further by multi-linear regression.

Based on the data analysis, preliminary guidelines for the estimation of removal of six different classes of pharmaceuticals based on travel time and travel distance were developed. These guidelines can be used as a screening tool to assess removal of pharmaceuticals during bank filtration under given conditions.

Using the removal database and molecular descriptors compiled, 8 QSAR models were developed and compared with the observed values from the database. This study showed that residence time is the most important variable that contributes significantly in almost all of QSAR models developed. Another prominent descriptor for pharmaceutical removal was nCp, which is number of terminal primary carbon present. Five QSAR models developed (analgesics, antidepressant, beta blocker, blood lipid regulator and steroid hormone) have a good correlation between predicted and observed values. On the other hand, models for antibiotics, anticonvulsant, and x-ray contrast agents showed poor performance.

Keyword: micropollutants, pharmaceuticals, bank filtration, QSAR model, guidelines

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List of Acronyms and Abbreviations

ADME	Absorption, Distribution, Metabolism, And Excretion
ACS	Acetyl Sulfamethoxazole
ARR	Artificial Recharge and Recovery
BEJ	Bezafibrate
CAR	Carbamazepine
CLA	Clarithromycin
CLI	Clindamycin
CLO	Clofibric Acid
DIC	Diclofenac
DTP	Diethylenetriaminepentaacetic acid/DTPA
DOC	Dissolved Organic Carbon
EDCs	Endocrine Disrupting Compounds
E1	Estrone
E2	Estradiol
EE2	Ethynlestradiol
FEN	Fenofibric acid
GEM	Gemfibrozil
IBU	Ibuprofen
K_{ow}	Octanol-Water Partition Coefficient
LBF	Lake Bank Filtration
NAP	Natural Organic Matter
NOM	Naproxen
PEN	Pentoxifyline
PhACs	Pharmaceutically Active Compounds
PRI	Primidone
PRO	Propyphenazone
QSARs	Quantitative Structure Activity Relationships
QSBRs	Quantitative Structure Biodegradation Relationships
ROX	Roxithromycin
RBF	Riverbank Filtration
SUL	Sulfamethoxazole
TRI	Trimethoprim

1 INTRODUCTION

1.1 Background

Significant growth of population and industrial sector has brought some negative impacts to our environment particularly for water resources. Most water resources especially surface water in industrialized and urban areas are quickly deteriorating as a result of waste discharges into receiving water, which may also serve as drinking water sources (Ameda, 2008). The presence of the contaminant has potentially risked not only aquatic life but also decrease the quality of surface water (i.e. drinking water source. Furthermore, the increasing worldwide contamination of fresh water systems with thousand of micro pollutants is one of the key environmental problems humanity facing, even though compounds tend to be present at low concentration (Schwarzenbach et al., 2006).

Pharmaceutically Active Compounds (PhACs) is a class of organic micropollutant that is taking great concern in many study of drinking water quality. There are relatively recent awareness of PhACs products since 1990s through the exponentially increasing number of studies concerning this emerging class of organic micro pollutants (Massmann et al., 2008). Highest interest of study is developed in related to the occurrence and fate of PhACs in wastewater and waste water treatment plant including the process efficiency with respects to their removal. However, only few studies are done which discuss about the effect and behaviour of large number of PhACs residue in aquatic environment and in the groundwater in particular (Schwarzenbach et al., 2006).

PhACs that widely used both in human and veterinary medicine presents in many different classes, which several are known to be environmentally persistent (Zuccato et al., 2005). PhACs from various prescription classes have been detected in the aquatic environment whereas some of them have found at concentrations up to the µg/l-level in sewage influent and effluent samples and also in several surface waters located downstream from municipal sewage treatment plants (Heberer, 2002) .

Since several residue PhACs can not removed completely by conventional wastewater treatment plant, there are huge possibility for them to be remained in surface water or infiltrate to groundwater. While these sources are treated for drinking water, the removal of PhACs is relatively costly in both conventional and advance treatment technology. The removal of both compounds needs more chemicals whereas it means the treatment of water itself cost more money.

There are many studies related to improve the quality of water sources. Bank filtration is considered as a robust and multiple contaminant removal technology. Bank filtration has been applied in some parts of Central Europe, especially Germany, is a relatively low cost natural based treatment technology that has been proven to be an excellent option for the attenuation of trace organic compounds often found in surface waters (Amy, 2007; Schmidt et al., 2007). Some studies also show that bank filtration is a promising technology for pre-treatment of raw water prior to conventional water treatment by removing bulk organic matter and organic micropollutants (OMPs) including PhACs. Moreover, with combination of bank filtration and conventional

treatment plant, the cost to treat water will be reduced in accordance with low chemical consumption.

However, the potential implications of bank filtration systems under severe water quality conditions with respect to the fate of PhACs are not well known. The performance of bank filtration to remove those contaminants based on several factors including physical-chemical properties. Furthermore, to create good quality of design bank filtration, it is important to estimate the performance of bank filtration before its construction. There is a critical need for a model or decision support tool for design and operation of a bank filtration system to help users to predict its performance based on the model result. Nevertheless, there are rarely models relevant to developing a decision tool in designing a bank filtration system.

1.2 Problem Identification

Recently, high production volume of PhACs is increased significantly with varies function of consumption for curing and treating disease, improving health and increasing life span. According to a recent IMS (Intercontinental Marketing Services) report, it was said that global PhACs sales grew 5.2% in North America and comparing with Europe, it was higher, 7.1% (Robinson et al., 2007).

The interruption of PhACs to water resources most likely to occur from a sewage treatment plant point sources discharge (Focazio et al., 2008). PhACs may therefore be at continuous and low concentration. Despite this, most published aquatic toxicity data and risk assessments for PhACs are based on short-term acute studies (Halling-Sørensen et al., 1998).

Theoretically, the existing PhACs in raw water can be removed by bank filtration. If bank filtration facilities are designed and constructed properly, the groundwater used for drinking water supply can be protected efficiently from contamination with microbial organisms and inorganic or organic pollutants (Heberer et al., 2003b). As a robust technology, the performance of bank filtration in water treatment plant is observed to remove physical contaminant such turbidity and microscopic particles, chemical contaminant (Dissolved Organic Carbon/DOC, pesticides, synthetic organics, PhACs compounds, nitrate, dissolved ions, and metals), and biological contaminant (protozoa, bacteria and virus) from surface water (Ray, 2002). It is common found that the concentrations of the trace organic contaminants in the bank filtrate are much lower than in the surface water. Some mechanism are occurs instead of dilution only to decline the concentration of contaminant. Therefore long term bank filtration has capability to significantly reduce trace organic pollutions.

However, because of their location, shallowness and their close relationship with the water course, these aquifer are particularly sensitive to pollutants (Schwarzenbach et al., 1983). There is a risk of inefficient bank filtration to remove PhACs under extreme concentration considering the increasingly production of PhACs from various industry. Thus, to treat a certain surface water quality with an extreme concentration of pollutant, the application of bank filtration still required further study to asset the performance removing PhACs.

Some models such as QSAR have been developed in order to estimate the potential of degradability of organic micropollutants as a part of assessment of the fate and transport of contaminant in environment. Nevertheless, the development of QSAR is quite slow due to the biodegradation as a complex chemical and biological process consist of many steps that depends not only the amount and structure of the chemical, but also on the environmental conditions into which organic micropollutants is released (Pavan and Worth, 2008). It is necessities to develop further study of QSAR modelling to address big concern of publics with the effect of organic micropollutants including PhACs in a worldwide and to assess the potential of removal of organic micropollutants during bank filtration.

A decision has been made to balance the socio-economic and environmental impacts versus advantages of the bank filtration implementation to remove organic micropollutants and the usage of PhACs in various industries as well. A formalised decision support system such as multi-criteria criteria analysis can accommodate the process of decision making which assist the decision makers, e.g. different government agencies and stakeholder, in resolving preferences relating to the construction of bank filtration. Develop decision support system using multi criteria analysis base on QSAR modelling could be use to evaluate the potential of bank filtration to remove organic micropollutant.

1.3 Goal and Objectives

The main goal of this research is:

- To develop QSAR based models to assess and to predict removal of PhACs from a bank filtration system.

The following are specific objectives to achieve the main goal mentioned above:

- To conduct a comprehensive literature review and a compile a database on the fate of different types of PhACs during bank filtration
- To determine physical-chemical properties of PhACs that control their removal efficiencies during bank filtration, using different software
- To develop QSAR based models that establish the correlation among molecular descriptors of compounds (based on physicochemical characteristics) with the removal of pharmaceuticals during riverbank filtration

2 LITERATURE REVIEW

2.1 General Concept of Bank Filtration

Riverbank filtration (bank filtration) is not a new technology for drinking water treatment. Some countries in Europe such as German, Netherlands, France, Switzerland, and Hungary have applied bank filtration technology for production of drinking water for more than 50 years (Kim et al., 2003). Table 2-1 summarizes the percentage of drinking water production for bank filtration in some European countries. In Germany Berlin treats 75 % of drinking water demand by bank filtration while Düsseldorf, has been using riverbank filtration since 1870 as an important source for public water in the densely populated and industrialised region (Schubert, 2002). Currently many water utilities in United States also apply bank filtration as a treatment technology due to its removal efficiency and cost-effectiveness in drinking water treatment (Ray et al., 2002a)

Table 2-1: Percentage of drinking water production from bank filtration in some European countries

No	Country	Percentage
1	Slovak Republic	50
2	Hungary	45
3	Germany	16 (Berlin 60%)
4	Netherlands	5
5	Finland	48
6	Switzerland	80
7	France	50

Source:(Amy, 2008)

In the past, when the pollution of the rivers was quite low, there was possibility to apply bank filtration for drinking water without further treatment. However, increasing chemical pollution due to significant human activities, which may produce high concentrations of ammonia, organic compounds, and micropollutants in the river water, required additional pre and post-treatment step to build up the multiple-barrier water treatment system (Schmidt, 2003).

Bank filtration is a natural process by which the permeable riverbed and underlying aquifer media are used to attenuate dissolved and suspended contaminants in surface water as the water enter the aquifer and moves towards the collecting well (Ray et al., 2002b). The position of collecting well, which is possible to be constructed in vertical or horizontal well, is located in alluvial valleys adjacent to river/lakes to river or lakes from which a portion of seepage water is pumped. By this pumping mechanism, the water will flow from surface water through induced infiltration. A schematics diagram of riverbank filtration is presented in Figure 2-1. There is such a dynamic river-aquifer interaction occur where the pumping action in a pressure head gradient between the river and the production wells that induce infiltration from the river to flow downward into the wells through the alluvial deposits (Ray et al., 2002a).

While the passage of water flow through the riverbed and aquifer, the attenuation of dissolved and suspended contaminants as well as pathogen are achieved through a combination of physical chemical and biological process, such as filtration, dilution,

sorption, chemical precipitation, redox reactions, and biodegradation (Amy, 2006). Bank filtration highly efficient method for significant removal of turbidity, micro-organisms, natural organic matter (NOM), pesticides, herbicides, hydro-chemicals, and pharmaceuticals taste and odour-causing compounds, which may not removed from the surface by conventional treatment method (Sahoo et al., 2005).

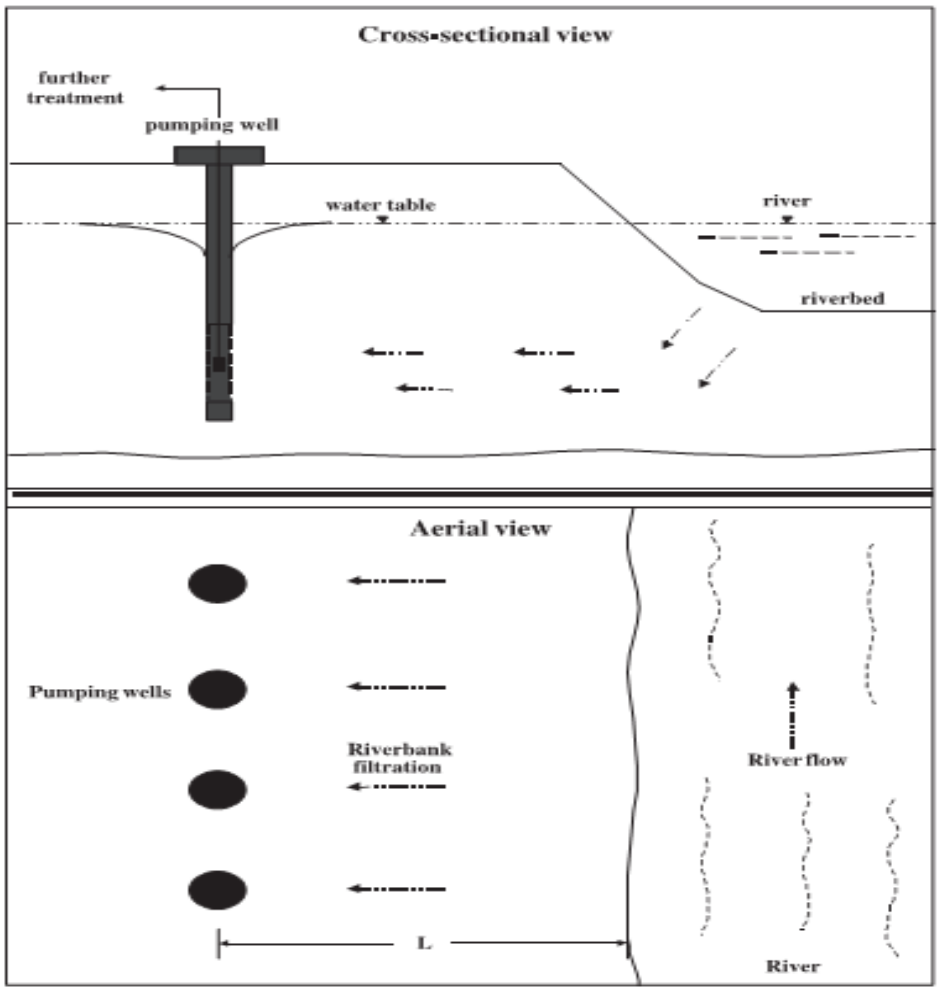

Figure 2-1: Schematic diagram of bank filtration *Source: (Kim et al., 2003)*

2.2 Mechanism of the Removal during Bank Filtration

The mechanisms of bank filtration to remove contamination is dependent on microbial activity and chemical transformation thorough physical filtering, sorption and degradation (Ray et al., 2002b). In addition, the possibility of dilution could influence the removal of contaminant during bank filtration if the concentrations of the contaminant in the groundwater are lower than in the surface water. Similarly, another study reported that the fate and transport of organic contaminants during bank filtration, are mainly affected by microbial degradation, sorption to solid matrix and attachment to colloidal particles (Kim et al., 2003). While the removal takes place during the transport of seepage water from river to collecting well, bank filtration can be efficient to remove solid particles from the infiltrating water, to decrease the concentration of biodegradable organic material and to retain adsorbable or precipitable pollutant. However, not all these mechanisms contribute extensively for the removal of the

contaminants. Adsorption and biodegradation are the primary mechanism in bank filtration that lead to attenuation of contaminant during bank filtration (Kuhlmann et al., 1995). The schematic diagram in Figure 2-2 summarizes the mechanisms of removal during bank filtration.

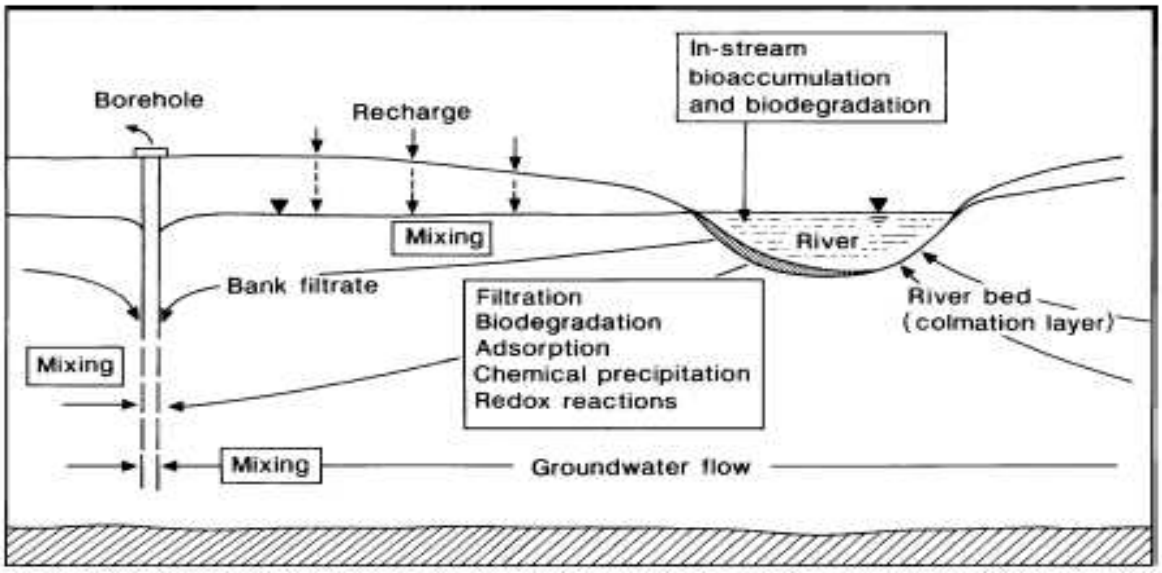

Figure 2-2: Filtration process affecting water quality during bank filtration. *Source: (Hiscock and Grischek, 2002)*

2.2.1 Physical filtration

Physical filtration process is also called mechanical filtration can eliminate large particles (Ray, 2002). There is a surface interaction between particles colloid and the pore wall of the aquifer material. The surface interaction can significantly retard solid transport, with improving pathogen 'deactivation' and degradative oxidation of non-living organics. The filtration allows exclusion effects of flow and diffusion by expressing the attachment rate of micro organisms to soil grains in terms of single collector efficiency and collision efficiency. Suspended particle may get attached with a particle of the solid medium, collector, either by interception, sedimentation or diffusion. The fraction of particles colliding with the solid grain which remain attached represents the collision efficiency which reflects the net effect of repulsive and attractive forces between the surface particles and the collector and depends on the surface characteristics of the micro organism and soil/ aquifer particles.

The filtration process during bank filtration reduced turbidity significantly. One study done in Ohio River show that there was a significant reduction of turbidity due to filtration process (Wang, 2002). The result showed 95 % of the samples collected from the collector well had a turbidity of less than 0.2 NTU. Turbidity in the collector well was relatively stable although river-water turbidity fluctuated significantly during the monitoring period (Figure 2-3).

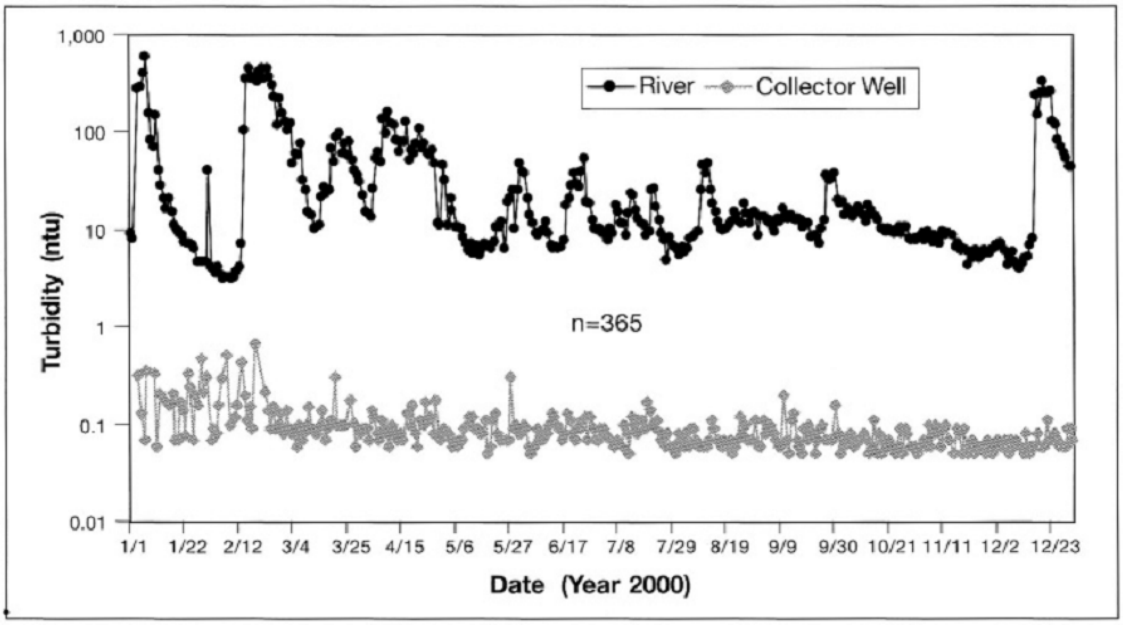

Figure 2-3: Turbidity data for the Ohio River and the collector well for the year 2000. *Source: (Wang, 2002).*

2.2.2 Sorption

In bank filtration, the physical filtration process will not remove many of the substances of concern. As a primary removal mechanism during bank filtration, most of the removal of the substances is achieved by adsorption process. A large number of micro-pollutants tend to be adsorbed on the solid surface of the porous filtration medium. Trace elements such as iron, manganese, and various heavy metals are eliminated during bank filtration, mainly by sorption processes (Schmidt, 2003). A study to support this statement confirm the removal of heavy metals in the lower River Rhine exceeded 90 % for chromium and arsenic, and was greater than 50% for cadmium, zinc, lead, copper, and nickel. The main process removal of contaminant during bank filtration was adsorption, however, this treatment has a finite lifetime before breakthrough or desorption occur without an ongoing fixing process within the sediments and aquifer materials , and aquifer materials (Sontheimer et al., 1985).

Sorption process is defined as a process for attachment of contaminants into mineral and the coating of quart grain because they result in more time for degradation process (Grischek et al., 2001). Removal contaminants such as PhACs and EDCs with hydrophobic properties tend to preferentially adsorb into suspended solids and sediment during infiltration as the first step in biological degradation of these compounds.

Adsorption capacity varies from aquifer to aquifer and from substance to substance. The empirical Freundlich Adsorption Isotherm forms a reasonable model to describing the adsorption process:

$$q_e = K\ C_e^{1/n}$$

Where:
qe = mass of absorbate/mass of absorbent
Ce = equilibrium concentration of the contaminant
1/n = dimensionless constant
K depends on q and C

Octanol-water partition coefficient (K_{ow}) values are commonly considered in determining the degree of association between the organic compounds and the solid phase. It is defined by the concentration ratio at equilibrium of organic compounds partitioned between octanol and water. Log Kow not only shows the classification of substances in hydrophobic (compounds are repelled by water) or hydrophilic (compounds have an affinity to water), but it also shows good correlation with biological activities and gives a better indication of the degree of adsorption by microorganisms with biological activity. Compounds with log Kow ≥ 2 are referred to as hydrophobic, while those with log Kow < 2 are hydrophilic. Thus, compounds with a high value of K_{ow} will be disposed to adsorb on organic content such as biomass, whereas a compound with low value remains in liquid phase. Table 2.2 summarizes log K_{ow} for some compounds..

Table 2-2: Octanol-water partition coefficient Log K_{ow} for some compounds

Compound	Log K_{ow}
Ibuprofen	3.97
Propanolol	3.48
Naproxen	3.18
Ketoprofen	3.12
Atrazine	2.61
Carbamazepine	2.45
Metoprolol	1.88
Terbutaline	0.9
Sotalol	0.24
Asenolol	0.16

(Source: Quintanilla et al., 2006)

2.2.3 Biodegradation

Like sorption, biodegradation is also a primary mechanism of removal of contaminants from water by bank filtration. Biodegradation also known as microbial degradation is referred to the biologically catalysed reduction in complexity of chemical compounds. The biodegradation processes responsible for the elimination of substances occur predominantly at the biologically active layer inside the river bed within the first few meters of filtration where intensive degradation and adsorption occur in a short resident time. In contrast to the active zone, the biological processes not intensively take place along the main flow-path between the river and the collecting well. Degradation rate and adsorption capacity are lower and mixing processes are greater (Hiscock and Grischek, 2002).

Biodegradation by aquatic life plays a major role in removal for trace organics such as PhACs and EDCs, especially for those compounds that are not only having highly-soluble but also low log K_{ow} (< 2). If PhACs have low log K_{ow} values, those substances will be highly movable and potentially contaminated groundwater. The adsorption capacity is low in this case, thus, the biodegradation process is major part of removal (Holm et al., 1995)..

The degradation kinetics of PhACs is related significantly with structure characteristics and environmental factors such as redox condition. In terms of characteristic structure, the more the branch of the hydrocarbon structure the harder degraded is the compound. This means, molecule with many branched hydrocarbon, chain are less favourable to biodegradation than un-branched chains. In term of environmental factors, redox condition is one of the key parameters as shown in Figure 2-4. A number of organic pollutants have been shown to be redox sensitive, these include PhACs active substances (Holm et al., 1995; Massmann et al., 2006), and halogenated organic compound (Grünheid et al., 2005). The redox conditions appear to affect the behaviour of number of removal of PhACs, The removal of these compounds is not complete in the absence of oxygen. Microbial degradation by aerobic bacteria is suggested to be removal process of PhACs rather than adsorption (Massmann et al., 2006).

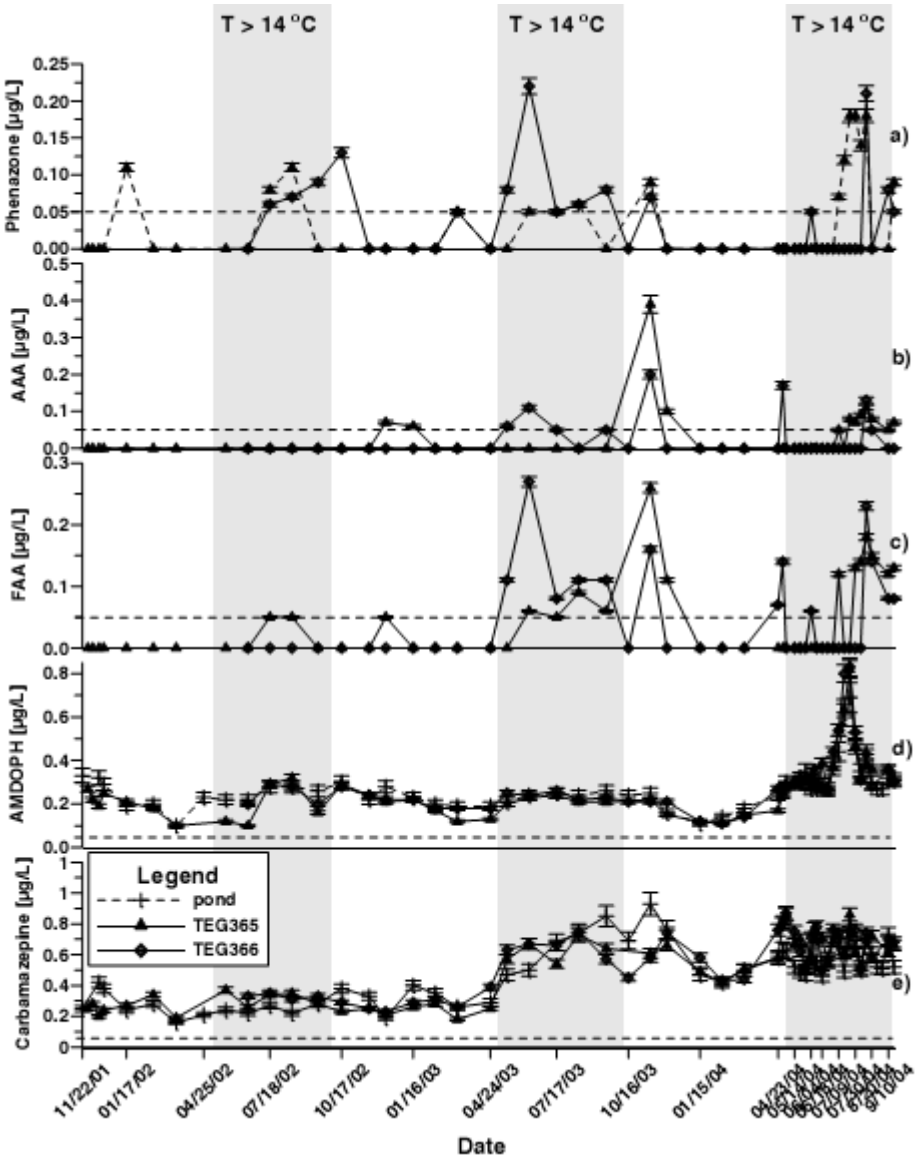

Figure 2-4: Removal of PhACs in redox-sensitive parameter. *Source: (Massmann et al., 2006)*

2.3 Factors Affecting Removal Efficiency of Bank Filtration

The pollutant efficiency of bank filtration depends on the composition of the infiltrating river of lake water, the properties of the porous filtration medium, and the biogeochemical process during filtration (Ray, 2002). Moreover, hydrologic condition, including well type and well location with respect to the river, river water temperature, characteristics of riverbank material and streamed, riverbed scouring and raw water source characteristics should be put into consideration in order to maintain quality of filtrated water from bank filtration (Sahoo et al., 2005).

2.3.1 Quality of river water (raw water source)

The quality of river water has big influence to get a good removal efficiency of bank filtration. Filtrated water from bank filtration can be used directly as a drinking water after disinfection if river pollution is not extreme. Otherwise additional treatment are required to achieve drinking water quality standards due to severe water quality of river (Kim et al., 2003).

The change of river water quality that is characterized by the number of particles, concentration of dissolved organic matter from natural and artificial sources, oxygen, ammonia, nutrients, microorganisms, and other pollutants affect characteristics of the bank filtrate (Schmidt, 2003). Figure 2.5 shows direct dependency of the bank filtrate quality condition with quality of the surface water as by investigated of adsorbable organic halogens AO (mean the amount of organic halogens present in water).

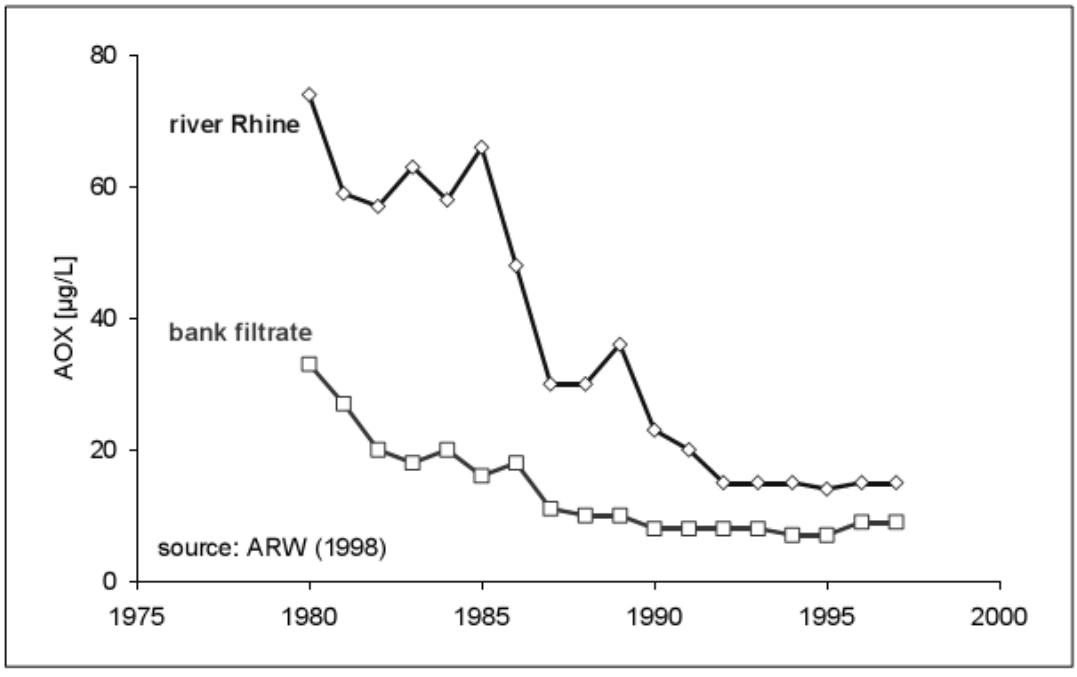

Figure 2-5: The removal of AO concentration in river water and riverbank filtrate. *Source: (Schmidt, 2003).*

As river water quality continues to improve, as seen especially in Central European countries, the organic matter load will decrease. On the other hand, increased damming of the rivers and the subsequent increase in the organic matter load due to sedimentation will decrease the oxygenation of the infiltrating water and therefore be harmful to the quality of the water withdrawn (Sahoo et al., 2005).

2.3.2 Well type and distance from the river

Contaminant removal occurs between zone of the river and production well. The type well either it is horizontal or vertical shows different depletion of contaminant. Residence time in horizontal well as compared to vertical well is less because the well is constructed directly towards the river thus more contaminant breakthrough is likely even though yielding more water (Amy, 2006). It can be said that on the one hand vertical well is better used for qualitative production, but on the other hand horizontal well is suitable used for quantitative production. A schematic configuration of bank filtration well types is shown in Figure 2-6.

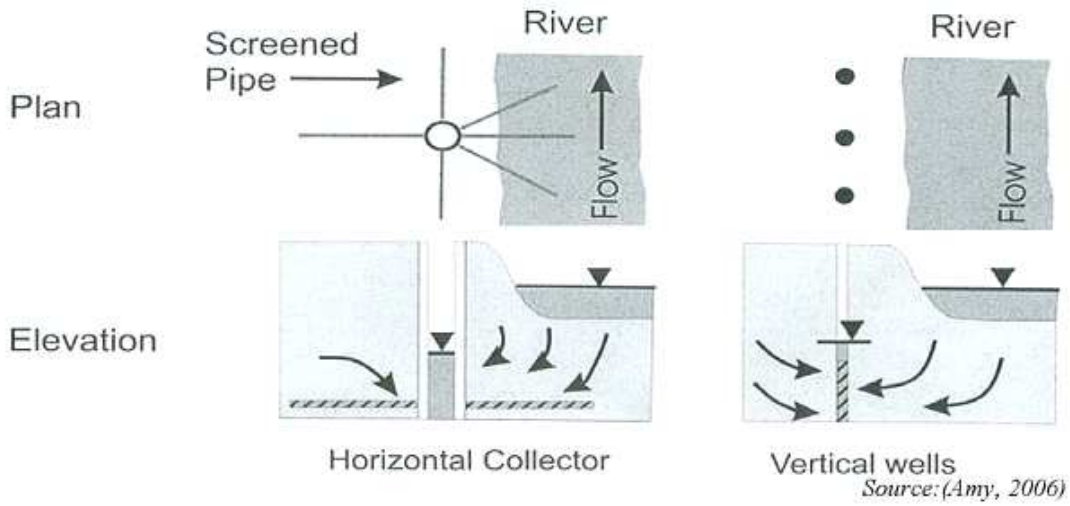

Figure 2-6: Schematic representation of horizontal and vertical well. *Source: (Amy, 2006)*

Similarly, one study on distance effect of bank filtration efficiency showed that the distance of the well from the source or the spacing between the wells affects the pumping rate and the extent of contaminant removal (Dillon et al., 2002). Adequate removal of contaminant, i.e. cyanobacterial, needed a sufficient distance from well to the river to allow adequate travel time for biodegradation. To achieve a total treatment as that applied by bank filtration in Europe, it needs a long travel distances with ranging 5-500m (Sharma et al., 2007).

2.3.3 River water temperature

Seasonal variation in water temperature should be considered to evaluate the efficiency of bank filtration. According study done by Wang et al. (2002), it was reported that the river water infiltration into the well is 10% more during summer than during winter due to the decreased water viscosity with increasing water temperature.

2.3.4 Characteristics of riverbank material

Relatively higher efficiency of contaminant removal occurs when water flow slowly and when the alluvial aquifer consists of granular material with an open pore space for water flow around the grain improving the contact of organisms with the grain surface (Schmidt, 2003). In contrast to that, the efficiency will be diminished by short path length, high heterogeneity, coarse matrices, high gradient, and high velocity.

The presence of mobile bacteria in the bank may also affect the efficiency of removal. The concentration of organic contaminants may be reduced by bacterial utilization, and the contaminants sorption onto bacteria may alter their transport behaviour. As mobile colloids, the mobility of bacteria can carry hydrophobic organic such as PhACs attached onto them in porous media (Jenkins and Lion, 1993). However, contaminant is possible to be transported further than expected by highly mobility of bacteria and there is a risk to groundwater contamination.

Effectiveness of bank filtration is also affected by clogging. Clogging may increase the efficiency of natural filtration due to its comparable characteristic to the "Schmutzdecke", as in slow sand filter, with rich in organic matter and high concentration of microbes (Goldschneider et al., 2007). The pattern of clogging in bank filtration is presented in Figure 2-7.

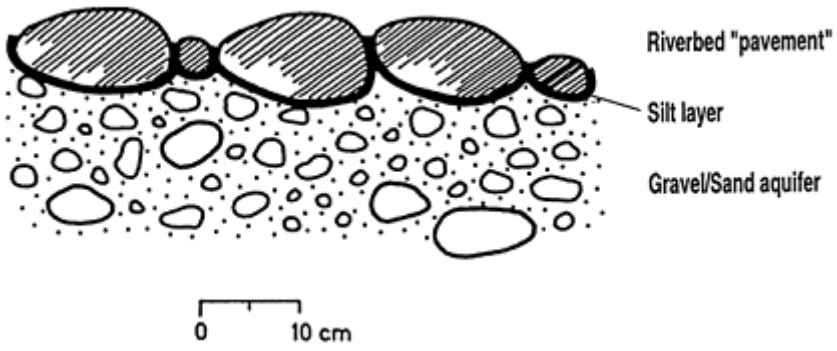

Figure 2-7: Pattern of clogged areas in the riverbed. *Source: (Schubert, 2002)*

Scouring due to bed load transport in the river limited clogging rate because it removed the deposit in region (Schubert, 2002). The characteristics of source water quality is controlled by land use and climatic conditions and during floods in rivers passing through agricultural watersheds often contain high concentration of farm chemical (Ray et al., 2002b).

2.3.5 Hydro-geochemical of bank filtration

Some information of hydro-geochemical of bank filtration was added as additional descriptor that gives information about characteristic of bank filtration. To study the fate and transport of pharmaceutical in bank filtration is not merely about the physicochemical properties of its compound but also it is important to understand the characteristic of bank filtration.

Combination of molecular descriptor and hydro-geochemical of bank filtration increases the performance of developed QSAR model. QSAR model created base on integral approach that consider characteristic of bank filtration and physicochemical compounds properties.

2.3.5.1 Travel time

Commonly, travel time affected the removal of pharmaceutical in bank filtration. Longer residence time tend to increase the efficiency of removal contaminant (Ameda, 2008). Furthermore it was reported that travel time is considered as an important design

parameter in bank filtration (Grunheid et al., 2005). The removal of organic matter in subsurface is generally considered as a function of time.

Travel time times range of each group of pharmaceutical is varied. Ranges of residence time recorded from literature-base data are in the range of 1-200 days. However, compare with others group, hormone steroid has a very wide range of residence time from 90 - 3000 days. High concentration of pharmaceutical from waste water treatment plant, tertiary effluent, caused the removal of pollutant by artificial recharge need longer time.

2.3.5.2 Infiltration distance

Removal of pharmaceutical during bank filtration is usually influenced by infiltration distance. Longer infiltration distance may give more efficient removal of pharmaceutical (Maeda, 2008). Most of the removal predominantly takes place in the first few metres of the infiltration pathway. It was also said that the feasibility of anoxic conditions for bank filtration depend on flow path length of bank filtration (Grischek et al., 2001). Therefore, the distance of the production wells from river or lake must be optimally selected to achieve quality improvements in the subsurface treatment.

The range of removal distance of pharmaceutical from literature-base data is 2 - 270 m. Its approach was to achieve total treatment plant in term of provide drinking water quality. Literally, the treatment process during bank filtration was expected to remove all contaminant from the water as the bank filtration systems in mostly European country (Sharma et al., 2007).

2.3.5.3 Redox conditions

Redox condition of aquifer is the master chemical variable in the degradation of trace organic compounds during bank filtration and had a more pronounced effect compare to residence time of the infiltrated water in the aquifer. Especially for polar organic compound, redox condition has important role because their removal efficiency is extremely dependent on the underlying redox processes. (Schmidt et al., 2007).

From the literature-based data, each compound of one group has preference for different redox condition. Group of blood lipid regulator, analgesic, beta blocker, X-ray contrast media, and steroid hormone, showed almost similar removal efficiency in both conditions oxic and anoxic (Heberer and Adam, 2004; Heberer et al., 2003b; Pekdeger, 2006; Scheytt et al., 2004; Schmidt et al., 2007; Verstraeten et al., 2002b).

Group of anticonvulsant and antibiotics have tendency for a better removal at anoxic condition instead of oxic condition. However, the efficiency of anticonvulsant removal was still lower compare to antibiotics. It means that this group relatively degraded hardly during bank filtration (Heberer and Adam, 2004; Heberer et al., 2003a; Heberer et al., 2003b; Massmann et al., 2006; Mechlinski and Heberer, 2005; Pekdeger, 2006; Schmidt et al., 2007).

Group of antidepressant has no data about the redox condition of the site so that the behaviour of this group under certain redox condition can not be assumed.

2.4 Investigation of Organic Micropollutants Behaviour during Bank Filtration

Organic micropollutants are identifiable water constituents having a concentration in the µg/l range. All those organics which can be found in the µg/l range or still lower concentration are considered as micropollutants, while the overall organics concentration in most of our drinking water will be in the mg/l range. This means that micro-pollutant are define on the one side through their low concentration. But on the other side, the words itself means, they must be pollutants (Sontheimer et al., 1985).

Trace organic micropollutants in bank filtration have been studied in various research projects since improved analytical methods allow their detection in ranges below 1 µg/l (Grünheid et al., 2005). Several studies were conducted to address the occurrence of micro-pollutant such as PhACs and EDC during bank filtration.

The behaviour of the micropollutants during bank filtration is varied depending upon their biodegradability, sorption affinity, etc. Some pesticides and petroleum hydrocarbons were removed substantially. On the other hand persistent organic micropollutants had low, less than 30%, removal efficiency (Ray, 2002). Figure 2-8 showed removal efficiency of some micropollutants fate during bank filtration at the lower Rhine.

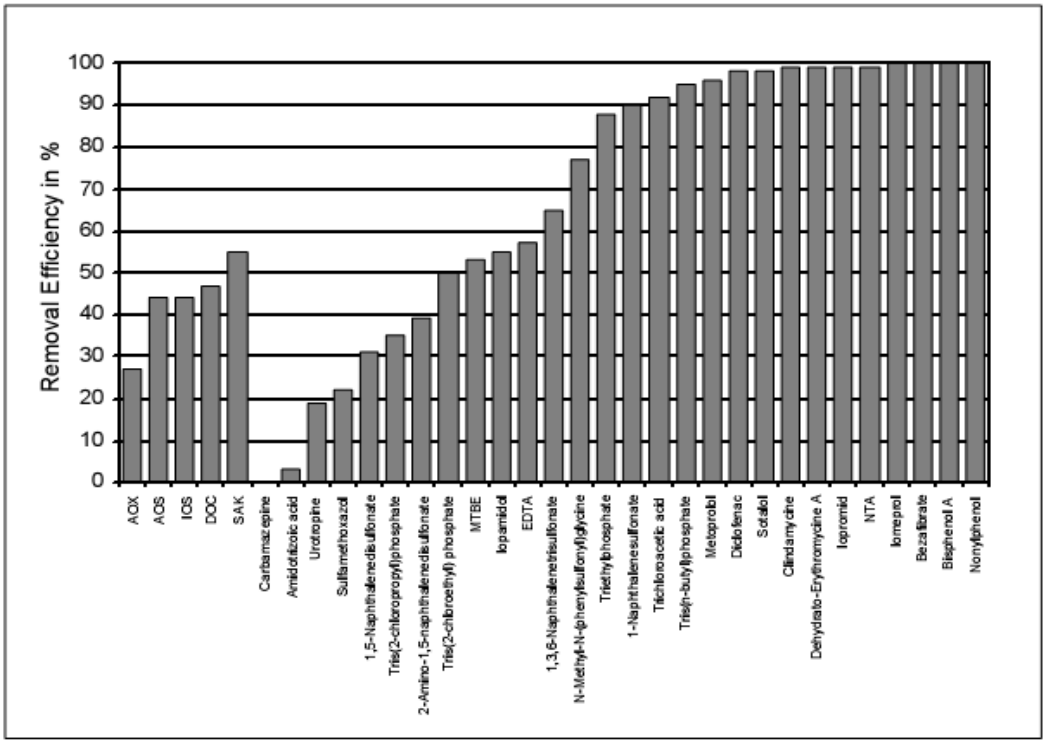

Figure 2-8: Removal efficiency of organic micropollutants during bank filtration at the lower. *Source: (Schmidt, 2003)*

2.4.1 Pharmaceutically Active Compounds (PhACs)

PhACs are defined as unused, residue or metabolites of pharmaceuticals drugs that are administered to human or animal for various benefits including treatment and prevention of diseases (Khan and Rorije, 2002). They are various in range from compounds used for cancer treatment and birth control to antibiotic used to combat

infection and to compounds used to relieve pain (e.g. aspirin and ibuprofen). They are found in personal care products as fragrances, disinfectants, and antiseptic, sunscreen agent, and preservatives. They are emerging environmental contaminants, extensively, and increasingly being used in human and veterinary medicine (Nikolaou et al., 2007). The main categories of human PhACs and the most commonly used products are shown in Figure 2-9.

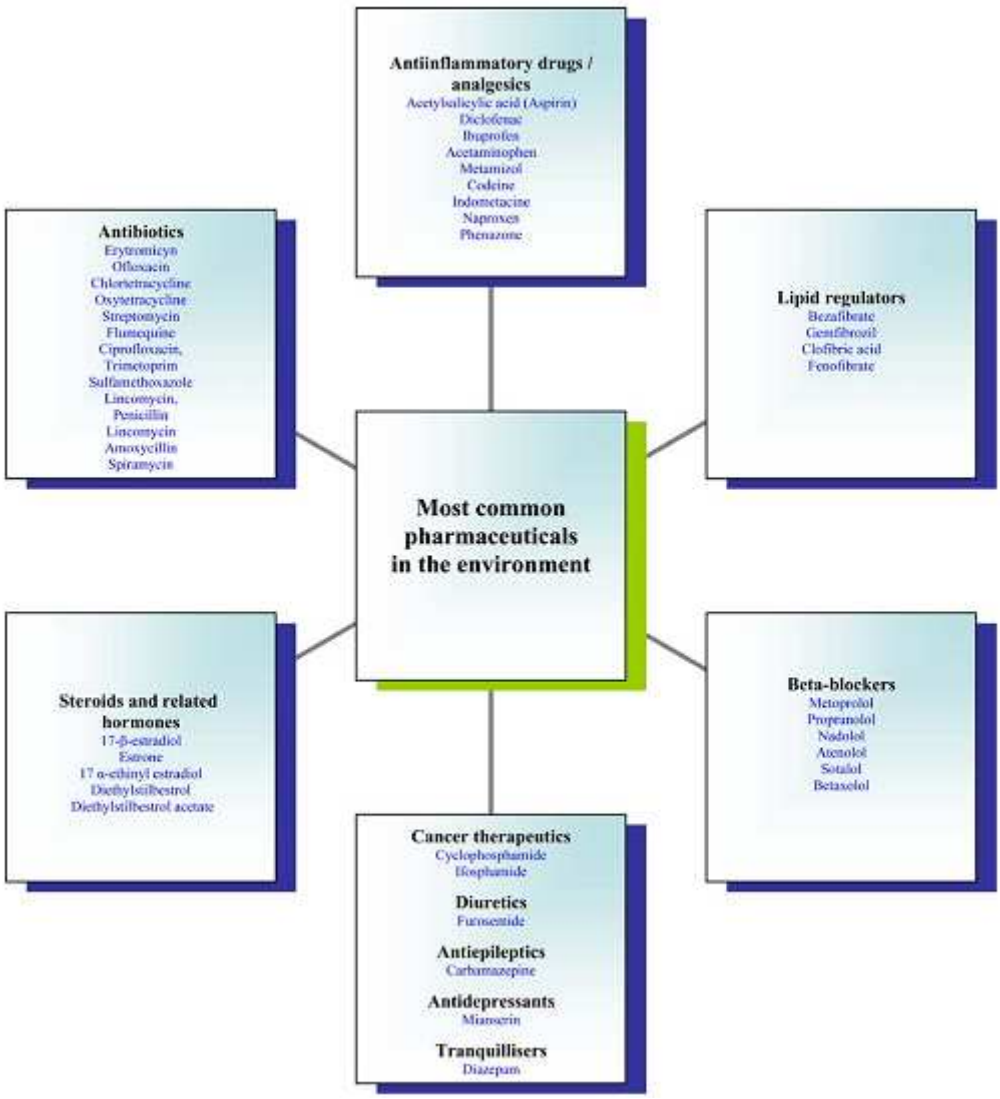

Figure 2-9: The most common PhACs compounds in the environment. *Source: (Nikolaou et al., 2007).*

Some of PhACs in Europe are used as painkiller, antibiotic, antidiabetics, beta blockers, contraceptives, lipid regulators, antidepressant, impotence drugs and cytostatic agents (Ternes and Joss, 2006).

Polar organic molecules such as PhACs are increasingly problematic class of contaminants in bank filtration system that the discharge of PhACs almost unchanged from municipal sewage treatment plants (Heberer, 2002). PhACs such as clofibric acid (a blood lipid regulator used in human medical care), diclofenac and ibuprofen were detected at individual concentrations of up to several mg/L in groundwater samples from aquifers near to contaminated water course.

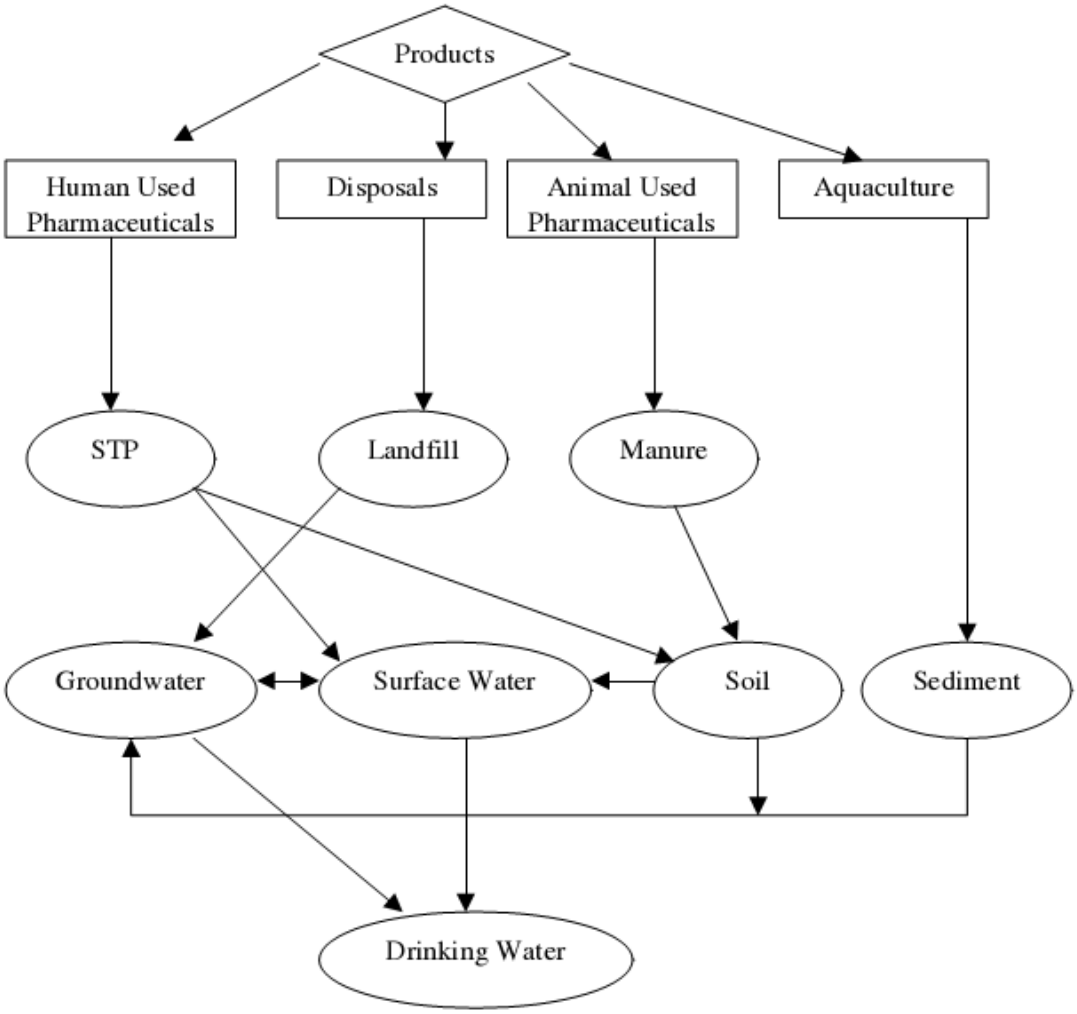

Figure 2-10: Source and pathways of the occurrence of PhACs residues in aquatic environment. *Source: (Kim and Carlson, 2005)*

Since PhACs are designed to have a specific mode of action and in many cases for some persistence in the body, these feature among others entail these compounds towards evaluation for potential effects on aquatic flora and fauna (Fent et al., 2006). However discharge of effluent into surface water results in chronic low-concentration exposure of aquatic organism to these compounds, without unknown impacts (Cooper et al., 2008). There is a risk that humans might be exposed to PhACs through potable water drawn from contaminated supplies (Jones et al., 2005). Even though this risk is likely to be relatively minor, the increasing demands on the fresh water supplies of the world will probably lead to greater incidences of indirect and direct water-reuse situations as the spatial and temporal distances between waste water and drinking water become further reduced. A schematic of source and pathways of occurrence of PhACs residues in aquatic environment is presented in Figure 2-10.

Table 2-3: Concentration of PhACs compounds found in treated drinking water worldwide.

Compound	Therapeutic group	Maximum concentration detected ($ng\,l^{-1}$)	Country
Bezafibrate	Lipid regulator	27	Germany
Bleomycin	Anti-neoplastic	13	UK
Clofibric acid	Lipid regulator	Positive identification	UK
		70	Germany
		165	Germany
		270	Germany
		170	Germany
		5.3	Italy
Carbamazepine	Anti-epileptic	24	Canada
		258	USA
Diazepam	Psychiatric drug	10	UK
		23.5	Italy
Diclofenac	Analgesic and anti-pyretic	6	Germany
Gemfibrozil	Lipid regulator	70	Canada
Ibuprofen	Analgesic and anti-pyretic	3	Germany
Phenazone	Analgesic and anti-pyretic	250	Germany
		400	Germany
Propylphenazone	Analgesic and anti-pyretic	80	Germany
		120	Germany
Tylosin	Macrolide antibiotic, used as a growth promoter for livestock	1.7	Italy

Source: (Jones et al., 2005)

The presence of antibiotics is likely to be of the most because it could lead to the development of resistant pathogen. The use of antibiotic may have resulted in the emergence of multi-resistant bacteria or the resistance of known pathogenic bacteria transmitted in the aquatic environment at unknown concentrations (Verstraeten et al., 2002b).

PhACs compounds showed different levels of concentration in aquatic life depending on their own characteristics as it shown in Table 2-3. (Jones et al., 2002) in his study said that many compounds of PhACs are predicted to degrade to any great extent and to adsorb to sludge. Ibuprofen, sulphasalaxine and mebeverine hydrochloride were all predicted to adsorb to sludge and quenine sulphate and mefenamic acid were all predicted to almost exclusively adsorb to sludge. (Holm et al., 1995) described the occurrence of PhACs in leachate plume. The result showed indication of strong attenuation of PhACs compounds under strongly anaerobic conditions. Compounds such as carbamazepine and clofibric acid were reported to be partly recalcitrant during underground passage (Ternes et al., 2004)

2.4.2 Endocrine Disrupting Compounds (EDCs)

Endocrine disrupting compounds (EDCs) is defined as an exogenous substance or mixture that affects the function of the endocrine system and consequently causes adverse health effects or an exogenous agent that interferes with synthesis, production, transport, binding action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development and

behaviour (Birkett and Lister, 2003). There are many implication of human-made compound in disrupting endocrine function in animals and human life worldwide, including agriculture and industrial chemical (Birkett and Lister, 2003).

The occurrence of EDCs in aquatic life presents a major concern because of the harmful effect observed on the reproduction, growth and development in certain species of wildlife. They increase in some human reproductive disorders and some cancer which could be related to disturbance of the endocrine system. However, there is no substantial evidence yet to proof this opinion.

Generally there are three major classes of EDCs that are put into consideration namely estrogenic (compounds that mimic or block natural estrogens), androgenic (compounds that that mimic or block natural testosterone and thyroidal (compounds with direct or indirect impacts to the tyroid) (Snyder et al., 2007). EDCs have been identified as responsible for estrogenic effects observed in fish present in surface waters. The most causative EDCs have been determined as the steroid estrogens, estrone (E1), 17ß-estradiol (E2), and ethynlestradiol (EE2). E1 and E2 are naturally occurring; however, EE2 is synthetic compounds from contraceptive sources. These compounds have been investigated and found by researchers that they occur in wastewater effluent as it shown in Table 2-4. The presence of these compounds in the aquatic environment has been primarily attributed to their incomplete removal during the sewage treatment process. The fate of EDCs present within the effluent is partly dependent on the type of receiving water as well as the compounds own physicochemical properties. Estrogenic effects are reduced after discharge into receiving waters because of dilution, degradation and sorption processes.

Fate and transport of EDCs depend on hydrology conditions and on physical, chemical, and biological processes in the aquifer (Verstraeten et al., 2002b). Many types of transport and transformation such as biotic and abiotic degradation, filtration, sorption/desorption, can lead to attenuation or complete removal of them. And through these processes, bank filtration can affectively remove EDCs together with others contaminants presented in drinking water.

Table 2-4: Mean concentrations ng/l of biologically active estrogens found in effluent samples of sewage treatment plants throughout the world

Country	Year of study	17β-Estradiol (E2)	17α-Ethinylestradiol (EE2)	Estrone (E1)
Netherlands	1997	<0.6–12 (0.9)	<0.2–7.5 (<Limit of detection[a])	<0.4–47 (4.5)
Germany	1997	<Limit of detection[b]	1	9
Brazil	1997	<Limit of detection[c]	1	7
Canada	1997	6	9	3
England	1995–1996	5	<Limit of detection[d]	3
Italy	1999–2000	1	0.45	9.3
Spain	2000	<5.65	<5	<5.125
United States	1997	1.7856	0.4015	Not analyzed
Mean		<2.69	<2.17	5.85

Note: Sources: Netherlands (Belfroid et al. 1999); Germany, Brazil, Canada (Ternes et al. 1999b); England (Desbrow et al. 1998); Italy (Baronti et al. 2000); Spain (Petrovic et al. 2002); and United States (Snyder et al. 1999).

[a]0.3–1.8 ng/L.

[b]1 ng/L.

[c]0.2 ng/L.

[d]<0.2 ng/L.

Source: (Huang et al., 2003)

2.5 Physical-Chemical Properties of PhACs

To assess the attenuation of PhACs through bank filtration, it is necessary to understand mechanism of thoroughly the role of physical and chemical properties on fate and behaviour of PhACs in water. Some physicochemical properties of selected PhACs are presented in Table 2-5.

Table 2-5: Physical and chemical properties of some selected PhACs

No.	Name	CAS No.	MW (g/mol)	pKa	log Kow	Classification
1	Gemfibrozil	25812-30-0	250.34	4.70	4.77	HP - ionic
2	Diclofenac	15307-86-5	296.16	4.15	4.51	HP - ionic
3	Bezafibrate	41859-67-0	361.82	3.61	4.25	HP - ionic
4	Ibuprofen	15687-27-1	206.29	4.91	3.97	HP - ionic
5	Fenoprofen	53-16-7	242.28	4.5	3.9	HP - ionic
6	Naproxen	22204-53-1	230.27	4.15	3.18	HP - ionic
7	Ketoprofen	22071-15-4	254.29	4.45	3.12	HP - ionic
8	Clofibric acid	882-09-7	214.645	3.20	2.88	HP - ionic
9	Carbamazepine	298-46-4	236.28	14	2.45	HP-neutral
10	Phenacetine	62-44-2	179.2182	2.2	1.94	HL - ionic
11	Paracetamol	103-90-2	151.17	9.38	0.46	HL - neutral
12	Pentoxifylline	6493-05-6	278.31	6.00	0.29	HL - ionic
13	Caffeine	58-08-2	194.19	10.40	0.07	HL - neutral

Source: (Quintanilla, 2006)

2.5.1 Solubility

Solubility is the property of a solid, liquid, or gaseous chemical substance called solute to dissolve in a liquid solvent to form a homogenous solution (Wikipedia, 2009). The solubility of a given compound in water reflects its affinity for water. Thus, the more soluble in water, the more efficiently the component remains in the aqueous solution, and the less adsorption on the bank filtration.

2.5.2 Polarity (dipole moment)

Polarity connected to solubility. This physical properties influences intermolecular forces and therefore leads to some compounds or molecules being labelled as polar or non-polar. While polar molecules dissolve in water due its polar nature, non-polar substances are water insoluble.

2.5.3 Hydrophobicity (octanol-water partition coeficient)

The octanol-water partition coefficient (K_{ow}) is often used to describe hydrophobicity. Among partition effects of non-ionic organic compounds in various solvent-water mixtures, the partition coefficients in octanol-water mixtures have received attention

because of the observed correlations between the octanol-water partition coefficients and the partition effects with the natural organic substances (Chiou et al., 1981).

Hydrophobicity is the affinity of some compounds to aqueous phase which influences the fate and transport of some compounds and limits their degradations during treatment process. Many of trace organic compounds with hydrophobicity are extremely polar compounds and in turn posses limited sorption properties and high chemical and biological persistency in the environment (Ternes and Joss, 2006). They have high mobility and able to transport further and to risk groundwater quality. On the other hand, hydrophobicity favours the removal of PhACs with low affinity to water during treatment processes. Sorption is one of the significant removal mechanisms of PhACs. Some of PhACs adsorb to surface of biota or solids because of their nature (non-polar and hydrophobic).

2.6 Modelling Organic Micropollutants Removal during Bank Filtration

2.6.1 Introduction about models

Regulatory bodies around the world have concern to organic micropollutants since these substances are found extremely persistent in environmental media, able to undergo long range transport via water and the atmosphere far away from their source, accumulate in the tissue of living organisms, and in some cases cause adverse biological effects after long-term exposure. They use the persistence as the basis regulatory of the risk management measures of organic micropollutants for human health and environmental (Pavan and P.Worth, 2006). The persistence of the organic micropollutants is generally base on the degradability of the substances. It is determined by experiment so that a substance degraded in an experimental test system is considered not persistent in the environment. (Pavan and Worth, 2008). Criteria of persistency in different regulatory program are presented in Table 2-6.

Table 2-6: Criteria of persistency in different regulatory programmes.

Regulatory programme	Criteria
OSPAR	Non-readily biodegradable or half-life in water >50 days
EU (REACH) criteria used in the identification of PBTs	Half-life >60 days in marine water, or >40 days in fresh or estuarine water, or >180 days in marine sediment, or >120 days in fresh or estuarine water sediment, or >120 days in soil
EU (REACH) criteria used in the identification of vPvBs	Half-life >60 days in marine, fresh or estuarine water, or >180 days in marine, fresh or estuarine water sediment, or >180 days in soil
USA (EPA control action[a])	Transformation half-life >2 months
USA (EPA ban pending[b])	Transformation half-life >6 months
Canada (Toxic Substance Management Program)	Half life in air >2 days, water >2 months, sediment >6 months, soil >1 year
Canada (Canadian Domestic Substances List)	Half life in air >2 days, water >6 months, sediment >1 year, soil >6 months

[a] Testing and release control required.
[b] Commercialisation denied except if testing justifies removing chemical from "high risk concern".

Source :(Pavan and Worth, 2008)

Different models have been used to predict the behaviour of organic micropollutants in water and their subsequent removal during water treatment. Some studies have been performed on biodegradation models, including qualitative well as quantitative such as QSARs (Quantitative Structure-Activity Relationships) and QSBRs (Quantitative Structure-Biodegradation Relationships). However, the development of QSBRs has been relatively slow compared with proliferation of QSARs, especially for toxicity of the biodegradability endpoint (Pavan and Worth, 2008).

2.6.2 QSAR modelling

A quantitative structure activity relationship (QSAR) is a method that relates a physical, chemical, biological, environmental activity of a set of compounds quantitatively to their physicochemical descriptors (Liu and Yu, 2005; Roy et al., 2008). QSAR model investigate relationships by building mathematical models in a statistical way.

To understand the distribution of organic pollutant is not always dependent on experimental data (Liu et al., 2006). In case no experimental data, the calculation of descriptors contain molecular structure can estimate compounds' behaviour that fit with experimental data. Develop QSAR modelling based on molecular structure is not only able to predict the behaviour of known pharmaceuticals but also new compounds that have not known yet. Prediction of unknown compounds will be referred to relevant molecular properties of its compound.

The quality of a QSAR model is most widely measured with R^2 value which shows the goodness of fit of the model itself to reproduce the internal data in the training (Yangali-Quantanilla et al., 2010)The model with the largest R^2 is stated as the best linear model. However it cannot explain the prediction power of the model. It needs another technique to evaluate the prediction power such as leave-out-one-cross-validation technique, in which one case at a time is iteratively held-out from the training set and the rest is used for model development and the excluded case is predicted by the developed model (Gramatica, 2007). The prediction power of the model usually estimated by the goodness of prediction parameter Q2, which is in general, a $Q2 > 0.5$ is regarded as good and $Q2 > 0.9$ as excellent (Eriksson et al., 2003).

2.6.3 Application of QSAR model in removal of pharmaceuticals

Many previous study of QSAR model are being applied in many discipline like assessment, toxicity prediction, biodegradability of chemicals, and prediction of chemical pollutant fate in the environment (Gramatica et al., 2000; Hayashi et al., 1999; Liu and Yu, 2005; Okey and Stensel, 1996; Yangali-Quantanilla et al., 2010).

One example of QSAR model was done by Liu and Yu (2005) to estimate the soil sorption coefficient (log Koc) of substituted anilines and phenol based on descriptors of octanol-water partition coefficient (log Kow), molecular connectivity indices, and quantum chemical parameters.

The result of the model gave equation as following:

$$\textbf{Log Koc} = 1.002 + 0.582 \log \text{Kow}$$

R^2 of the model is 0.765. This model was regarded as a satisfactory model with R^2 larger than 0.7. This means that log Kow was the largest correlated descriptors with log Koc than any other descriptors.

2.6.4 Advantages and limitations of QSAR

2.6.4.1 Advantages of QSAR

The advantage of this approach is that once an acceptable model is developed, it able to predict removal pharmaceuticals basis of the compound structure without laboratory

testing other than the calibration data set. Unlike experimental determination, QSAR model needs less time-consuming and less cost.

2.6.4.2 Limitations of QSAR

Limitations of QSAR are:

- Model of QSAR selected variable based on the good combination among interaction of all independent variable through statistical way without consider the meaning of the selected variable in the environmental so that if the developed model may be contained unimportant variable which is not contribute to the process of removal in the real situation.
- Dependent on the quality of input descriptors. It needs more observation to select the group of descriptors that describe the most critical structural and physicochemical features associated with activity.

3 RESEARCH METHODOLOGY

The research methodology adopted in this MSc study included

i. desk study and data collection
ii. development of preliminary guideline
iii. calculation and selection of descriptors
iv. multiple regression analysis of selected descriptor and field data
v. validation and prediction using the QSAR model developed.

A schematic of research methodology used in this research is presented in Figure 3-1.

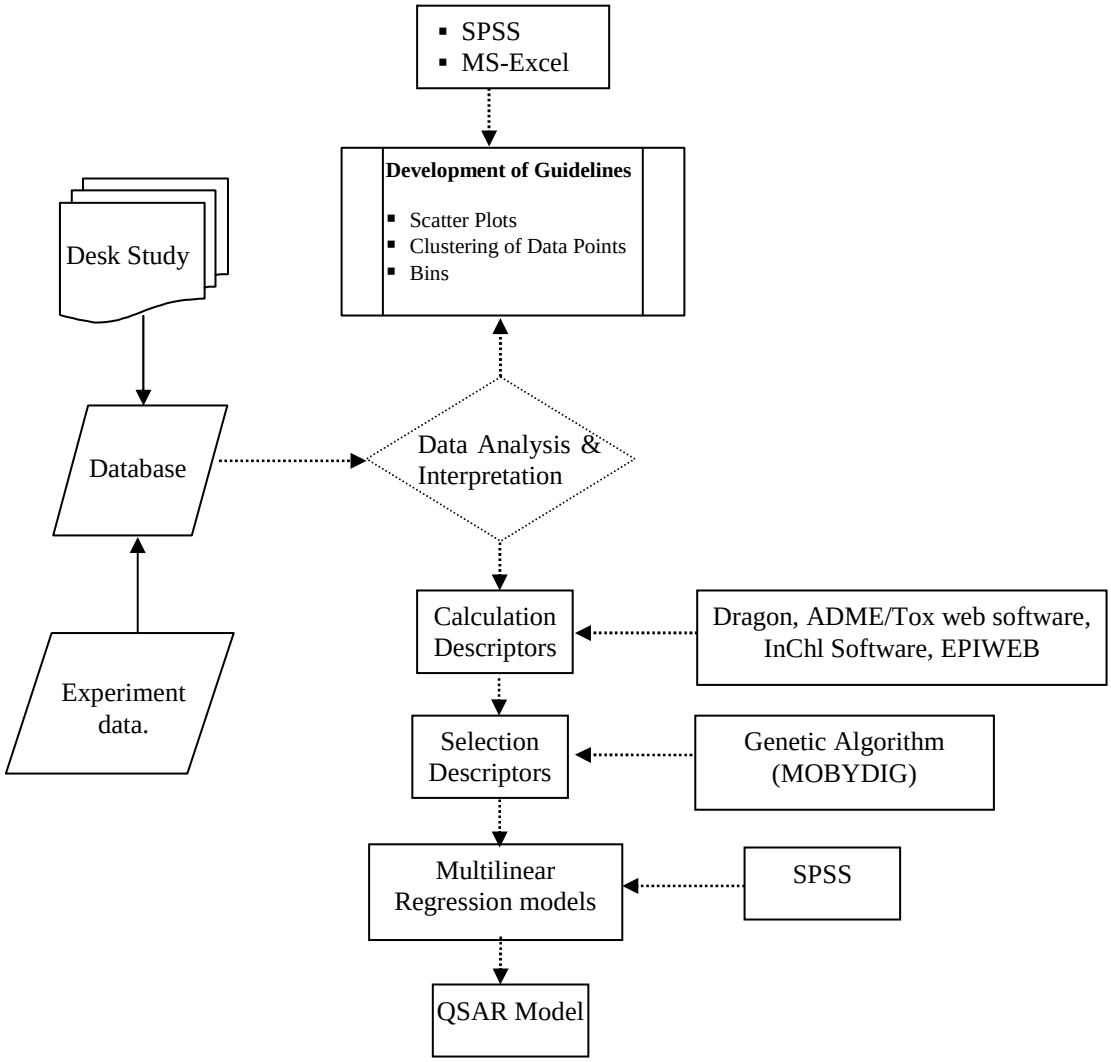

Figure 3-1: Scheme of research methodology

Each of those steps is elaborated below:

3.1 Desk Study & Data Collection

A desk study was carried out through a comprehensive literature review on RBF systems and their capacities to attenuate PhACs. Understanding of the underlying active mechanisms and processes was sought in this review. The major groups/categories of PhACs were identified and information on the removals of PhACs from RBF and literature based studies was compiled. Hence, the literature survey database is used as the sources of data for this analytical study of pharmaceutical removal in RBF systems. This comprehensive data was then analysed using a combination of software packages which included; Dragon, ADME/Tox web software, InChl Software, SPSS 16.0, MS-Excel,. These tools were used to ultimately develop preliminary guideline and QSAR modelling to predict removal efficiency of PhACs.

3.1.1 Literature Survey

A literature survey of previous studies was carried out on the fate and transport of PhACs in bank filtration systems bank filtration systems and column studies. The total number of literature sources and the corresponding type of studies are summarised in Table 3-1. The trace organic compounds were compiled into groups which are indicated in Figure 3-2.

Table 3-1: Literature sources and study types used to compile database

Type of study		Number of cases	No of Literature
Laboratory-scale batch and column studies		45	18
Field Study	RBF	73	2
	LBF	178	
	ARR	31	
TOTAL		327	20

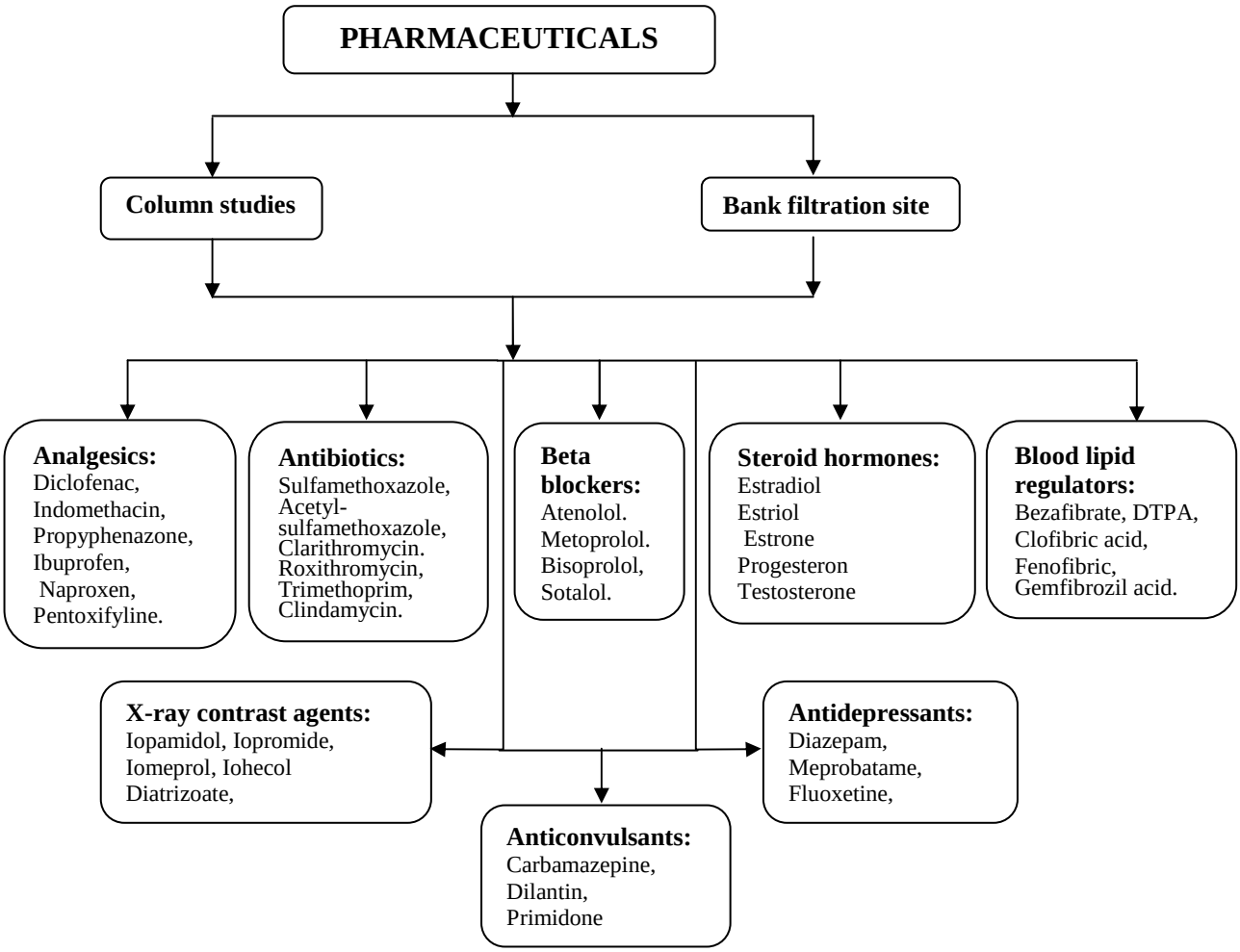

Figure 3-2: Trace organic compound groups used in compilation of database

3.1.2 Selected PhACS

Based on how PhACs can be removed during bank filtration by mechanisms like filtration, biodegradation, adsorption, among others; a list of selected pharmaceuticals compounds and their main physicochemical properties. (See Appendix C).

From each of these studies the following information related to the PhACs, was compiled in an MS-Excel spreadsheet:

- The study site
- Type of study (bank filtration)
- PhACs & group
- Achieved removal efficiency
- Travel/residence time of the compound in the system
- Travel distance/well distance from the surface water source
- Redox conditions (Aerobic or anaerobic conditions)

Reliable data of pharmaceuticals are needed to develop a prediction model of pharmaceuticals removal efficiency during bank filtration. Collected data from some literatures through study desk is called as a literature-based data. The pharmaceuticals compounds in the literature based data were separated into their therapeutic function group. There are 8 groups of pharmaceuticals in this study namely analgesics, antibiotics, beta blockers, steroid hormones, anticonvulsants, x-ray contrast agents, antidepressants, and lipid regulators.

Data were collected from 20 studies whereas 18 of them were done in the field study and the rest of them were done in the column study. Data shows the removal efficiencies of pharmaceuticals for 37 pharmaceuticals. The summary is shown Table 3-2:

Table 3-2: Data summary of pharmaceuticals based on therapeutic function

Sub-Group	Total
Blood lipid regulators	5
Analgesics	6
Anticonvulsants	3
Antibiotics	6
Steroid hormones	5
Beta blockers	4
X-ray contrast agents	5
Antidepressants	3
Total	**37**

Most of the field studies were carried out in German such as at Lake Tegel, Lake Wannsee, River Rhine, River Ruhr and River Elbe. Only few of them were done in USA (such as in California Tucson and Colorado) and Yugoslavia (Sava River). Data collected varied due to the geochemical of each location and the weather when the study conducted.

Based on literature-based data, 327 cases of removal efficiency of pharmaceuticals were prepared in the attached file which shows that 73 data for RBF (riverbank filtration), 178 data for LBF (lake bank filtration), and 31 for ARR (artificial recharge and recovery) site. The removal efficiency of Pharmaceuticals data were detected from filtrated water that collected in monitoring well and production well. Database shows 174 samples were taken from monitoring well, 153 samples were taken from production well and the remaining data were taken from batch column.

3.2 Data Analysis and Interpretation

3.2.1 Developed guidelines

The obtained information from the literature sources (literature-based database), was used to predict the removal of pharmaceuticals during bank filtration systems that could be used as a preliminary screening. This was done by means of scatter plots and clustering techniques.

Data on pharmaceuticals compounds from various bank filtration and laboratory studies under varying site conditions was compiled with special emphasis on the information on their removal ratios, the retention time and distances of the wells to the surface water, T

For each category, this information was compiled in Microsoft Excel and scatter plots of the removal ratios against the retention time and distance of the wells from the surface water sources, were created using Microsoft Excel software too. For each scatter plot scenario, the plots were grouped into bins, basing on the spread/clustering of the points and the distinct distance between the groups.

The means and the standard deviations for each bin were computed and the standard deviation used to give a measure of spread of the points, in the creation of the bin predictive removal efficiency range. These computations were used in the development of predictive removal efficiency ranges for each bin, which yielded a range of anticipated removal efficiencies corresponding to the given range of either the residence times or well-surface water distances. For each trace organics category, the ranges of the influent and effluents were noted.

These predictive removal performance can be useful as a guideline in giving a preliminary prediction of the removal efficiency expected from a given bank filtration site. It may also be useful in guiding operation of such a system, through managing the residence times by way of the pumping regimes, to achieve certain removal efficiencies of the target trace organic compounds.

3.2.2 Clustering techniques

This approach was used in the analysis of the literature-based data and was applied to separate the data into groups or clusters. Excel was used to generate scatter plots of the removal efficiencies against the travel time and distances respectively. These plotted data points were then grouped into bins basing on the clustering of the data points. Effort was made to have the clusters/groups as similar as possible, while the difference between the groups was expected to be as large as possible.

3.3 Analyses molecular descriptors

3.3.1 Data set

Developed QSAR models are constructed for diverse and heterogeneous group of pharmaceuticals in bank filtration considering lot of type of pharmaceuticals with different characteristic. It was expected that group classification based on therapeutic function would increase the accuracy of developed model to prediction removal of pharmaceutical during bank filtration.

3.3.2 Calculation of descriptors

To obtain of QSAR model, characteristics of pharmaceuticals are represented by molecular descriptors. Calculations of descriptors were carried out by ADME/Tox web software, Chem3D Ultra, EPIWEB, Dragon. Brief explanations of different software are:

i. DRAGON (TALETE, Italy): is an application for the calculation of molecular descriptors. These descriptors can be used to evaluate molecular structure-activity or structure-property relationships.
ii. ADME/Tox platform is an online software that calculate important ADME (absorption, distribution, metabolism, and excretion) properties of chemicals

such as octanol-water partition coefficient (logP), pKa, octanol-water distribution coefficient (logD), aqueous solubility (logs), etc.

iii. Chem3D is molecular modeling component of a suite of tools produced by Cambridge Software, ChemOffice. Chem3D is able to display standard molecular modeling outputs, such as electron densities, electrostatic potentials, and molecular orbitals.

iv. EPIWEB, a QSAR modelling (U.S.EPA): is used to predict environmental and physical/chemical property (such as log Kow, Solubility, biodegradability, etc) of PhACs that are considered as descriptors in QSBR

The calculation of descriptors is described below:

a. Dragon calculated 235 descriptors that give information about constitutional descriptors, connectivity indices and functional group counts
b. Chem3D Ultra calculated 4 descriptors namely value of Dipole, Highest Occupied Molecular Orbital (HOMO), Lower Unoccupied Molecular Orbital (LUMO), and Heat of Formation (HOF)
c. ADME/Tox web software calculated 2 descriptors, log Ka and log D
d. EPIWEB calculated 12 descriptors namely biowin 1, biowin 2, biowin 3, biowin 4, biowin 5, biowin 6, biowin 7, half life in water, half life soil, half life in sediment, Kow.

All descriptors are checked to ensure the value of each descriptor is available for each compounds in one group and there is a variation in these values. Descriptors for which values are not available for every compound in one group are excluded as well as the descriptors that have a constant value for every compound in one group in the data set.

3.3.3 Selection of descriptors

3.3.3.1 MOBYDIG

MOBYDIG is a software package that has been developed by the Milano Chemometrics and QSAR Research Group for the calculation of regression models by using genetic algorithms for variable selection to obtain an optimal subset of predictive models. Several validation tools and graphical options are available

MOBYDIG software is used to select descriptors that have most significant influence to the removal process of pharmaceutical. But before the selection process by MOBYDIG, all values of descriptors should be checked first. This step is a pre-selection technique to help reducing number of descriptors manually. All descriptors are checked to ensure the value of each descriptor is available for each compounds in one group and there is a variation in these values. Descriptors for which values are not available for every compound in one group are excluded as well as the descriptors that have a constant value for every compound in one group in the data set.

3.3.3.2 Genetic Algorithm

Genetic algorithm will select the most relevant descriptors to the removal process of pharmaceuticals and show affecting degree of different descriptors for removal process. QSAR analysis produces a function of small number of descriptors that can accurately predict the removal of pharmaceutical.

In this work, a program from Talete, MOBYDIG was used to perform genetic algorithm, which used selection technique to choose the most relevant variables with respect to the specific problem, in this case about removal pharmaceutical during bank filtration. Selection process was done by considering populations of models generated through a reproduction process and optimized according to a defined objective function related to the model quality (Gharagheizi, 2007).

Genetic algorithm calculated not only R^2 but also Q^2, the goodness of prediction parameter of leave-one-out cross validation technique. This technique is used to evaluate prediction in which one case at a time is iteratively held-out from the training set and the rest is used for model development and the excluded case is predicted by the developed model (Gramatica, 2007)

3.4 Multilinear Regression Analysis

Multilinear regression analysis is a general statistical technique used to analyze the relationships between a single dependent variable and several independent variables (Hair *et al.*, 2006). The main objective of this statistical method was to predict the dependent variable with a set of independent variables. This technique was applied in the development of multiple regression expressions predicting the removal of pharmaceuticals during bank filtration. Further to that, most of the other compounds showed relatively low correlations with the site variables. In the estimation of these models, part of the key objective was to maximise the predictive power of the independent variables as represented in the variety.

The first step in the multiple regression analysis was the selection of the dependent and independent variables to be used in the analysis. Pharmaceuticals removal was selected as the dependent variable while the selected descriptors by MOBYDIG were regarded as independent variable. Numbers of independent variables in multilinear regression analyses referred to a numbers of descriptors chosen by MOBYDIG. It analysed the same descriptors as selected by MOBYDIG.

The specified regression model was of the simplest linear form, $y = b_1x_1 + b_2x_2 + ... + b_nx_n + c$. For each trial regression specification, the following key statistics were checked:

Pearson's R^2 (coefficient of determination)
Pearson's R^2 was given in the model summary of the results and was used to check the percent of variance in the dependent variable explained by the given independent variables. Various trial regressions were carried out to achieve the highest possible value of R^2.

Significance of the coefficient estimates (t-statistic and p-value)
Significance of the coefficient estimates (t-statistic and p-value) was used to test for the significance of the individual predicted coefficients. If any coefficient estimate had a t-statistic less than 2.5, there was a possibility that the true value of the parameter was zero and so the term was dropped from the equation (Berthouex and Brown, 2002). In addition to this test, the significance values of the coefficients were also checked to ensure that they had a value, $P<0.05$, at a 2-tailed level.

Significance of the regression model
The F-statistic and corresponding p - value as given by the ANOVA table in the results, were used to check the significance of the regression model and the F-statistic. The model was considered significant for higher values of F and $p<0.05$.

A backward selection method was the order in which the predictor (independent) variables were entered into the model. In this method all the predictor variables were entered into the model and the weakest predictor variable was then removed and the regression re-calculated. If this significantly weakened the model by reducing the coefficient of determination, then the predictor variable was re-entered -otherwise it was deleted. This procedure was then repeated until only useful predictor variables remained in the model (Brace *et al.*, 2003).

3.5 Validation of the Model/Prediction

For validation of QSAR models in this study adopted internal validation or cross validation. The outcome from cross validation procedure is cross-validated Q2 which is used as a criterion of both robustness and predictive ability of the model. A high Q2 value ($Q2 >0.5$) is considered as a proof of high predictive ability of the model. It means that the model is good performance. Furthermore, if $Q2>0.9$, the model is regarded as excellent model (Eriksson et al., 2003).

4 RESULTS AND DISCUSSION

4.1 Development of Guidelines

Based on the literature review and database of removal of different classes of pharmaceuticals, preliminary guidelines for prediction of their removal based on residence time and travel distance was developed for 6 classes of compounds. Each of them is elaborated separately in the following sections:

4.1.1 Blood lipid regulators

This category consisted of bezafibrate, diethylenetriaminepentaacetic acid (DTPA), clofibric acid, fenofibric acid, gemfibrozil, that information was gathered from two bank filtration systems, Lakes Tegel and Wannsee in Germany (Heberer and Adam, 2004; Heberer et al., 2003b; Heberer et al., 2004; Pekdeger, 2006; Scheytt et al., 2004; Schmidt et al., 2007; Verstraeten et al., 2002b). The generated scatter plots showing the removal efficiencies for blood lipid regulator with residence time and with distance is presented in Figure 4-1 and Figure 4-2. The analysis of each bins created for the removal of blood lipid regulator with residence time is summarised in Table 4-1 and Table 4-2 . It showed that most of the data points occur above 50% removal efficiency, within a residence time of 0–200 days and distance between 0 m and 150 m. The analysis scatter plot is made with ranging of residence time 0-200 days and travel distance ranging from 0 to150 m.

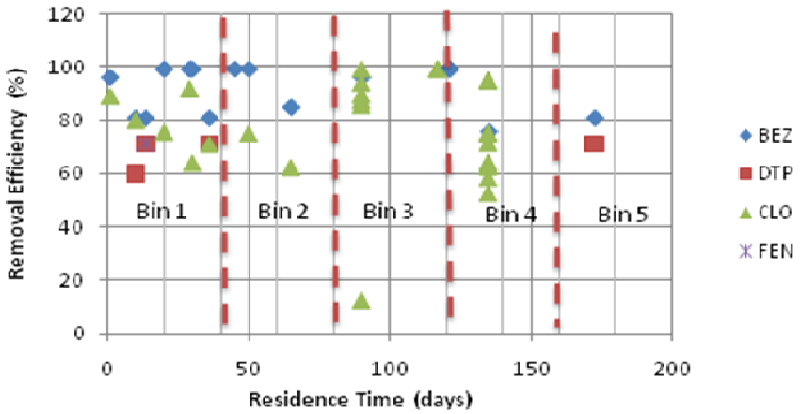

Figure 4-1: Plot of removal efficiency of blood lipid regulator with residence time

Table 4-1: Analysis of scatter plot of blood lipid regulator removal with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-60	0-5	0-40	60-99	17	81	13	57-68
		40-80	62-99	5	84	16	68-83
		80-120	13-99	9	85	28	83-92
		120-160	53-95	16	76	16	92-94
		160-200	71-81	2	76	7	>94

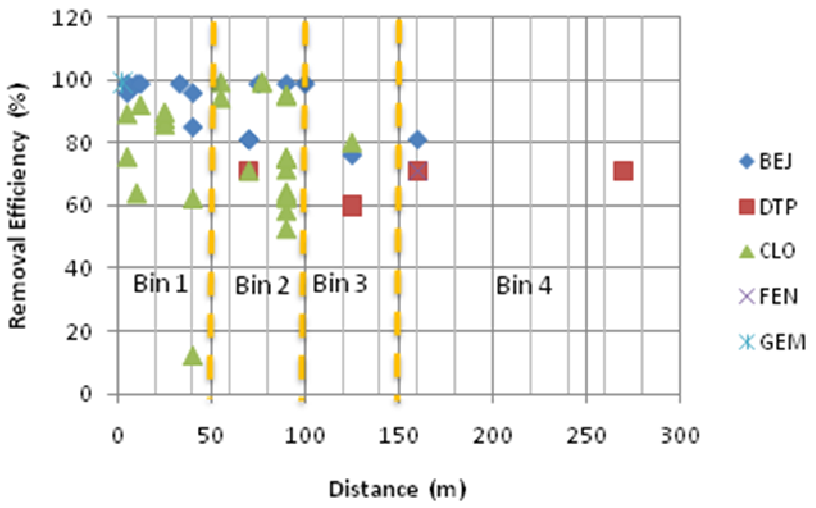

Figure 4-2: Plot of removal efficiency of blood lipid regulators

Table 4-2: Analysis of scatter plot of blood lipid regulator removal with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-60	0-5	0-50	13-99	19	86	21	65-69
		50-100	62-99	28	80	15	69-83
		100-150	60-80	3	72	11	83-95
		>150	71-81	4	74	5	95-100

4.1.2 Analgesics

Diclofenac, indomethacin, propyphenazone, naproxen, pentoxifyline, and ibuprofen, are an analgesic that used to relive pain. An analgesic is also common PhACs that often detected from bank filtration sites Lakes Tegel and Wannsee in Germany (Heberer and Adam, 2004; Heberer et al., 2003a; Heberer et al., 2003b; Heberer et al., 2004; Massmann et al., 2006; Pekdeger, 2006; Schmidt et al., 2007; Verstraeten et al., 2002b). Scatter plots of the removal efficiencies for analgesic with residence times and distances are presented below (Figure 4.3 and Fig4.4) and the analyses are presented in Table 4-4 and Table 4-5. It can be noted that bank filtration removes analgesic greater than 60%, within a residence time 40 - 173 days and distance above 100 meters. Moreover, there were some correlations observed between analgesic removal and travel distances that the removal of analgesic increased with travel distances. Travel distance may play an important role in the removal of analgesics. Some studies noted that travel time is an important parameter for designing bank filtration (Grischek et al., 2001; Schmidt et al., 2007)

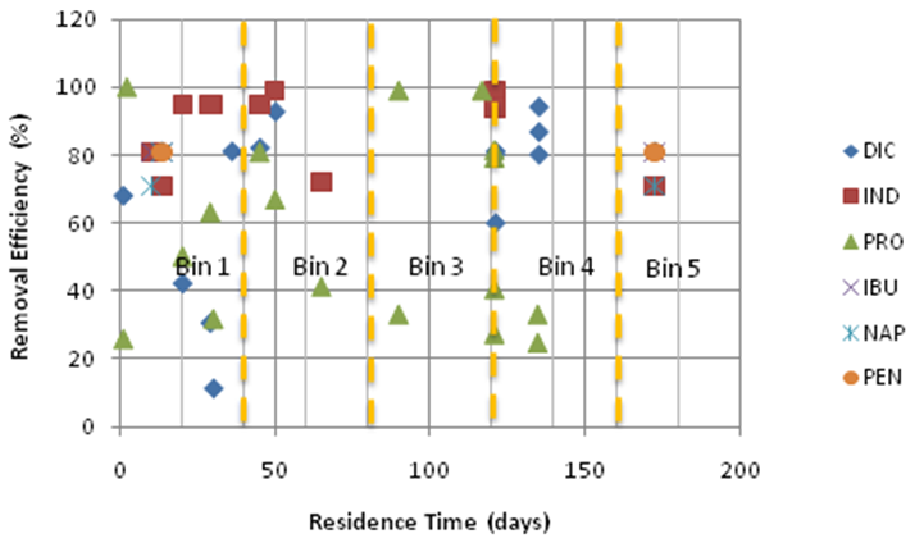

Figure 4-3: Plot of removal efficiency of analgesic with residence time

Table 4-3: Analysis of scatter plot of analgesic removal with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-485	0-301	0-40	8-99	28	71	28	43-64
		40-80	91-100	7	82	18	64-77
		80-120	93-99	20	82	14	77-96
		120-173	71-99	13	88	11	96-100

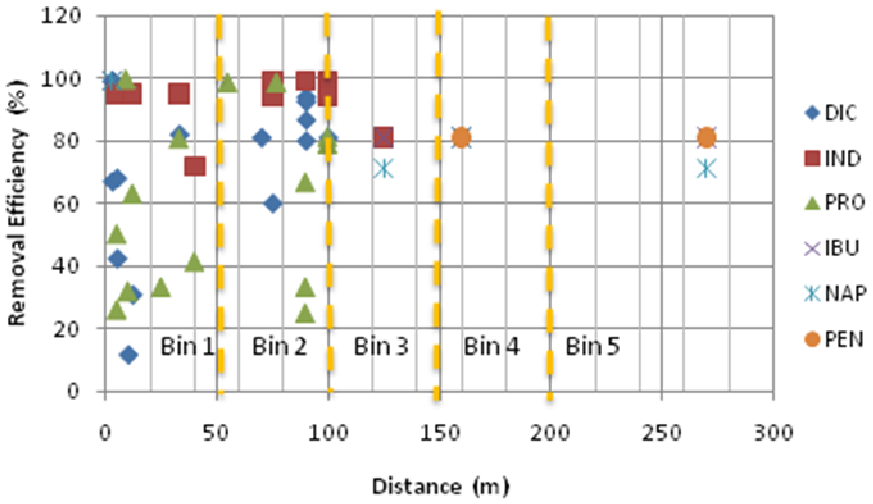

Figure 4-4: Plot of removal efficiency of analgesic with distance

Table 4-4: Analysis of scatter plot of analgesic removal with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-230	0-170	0-50	Dec-99	29	70	30	41-60
		50-100	25-81	19	81	22	60-72
		100-150	71-81	3	78	6	72-75
		150-200	81	5	79	4	75-83
		200-270	71-81	5	77	5	83-100

4.1.3 Anticonvulsants

Carbamazepine and primidone are commonly used for anticonvulsants (Heberer et al., 2003a; Heberer et al., 2003b; Heberer et al., 2004; Massmann et al., 2006; Mechlinski and Heberer, 2005; Pekdeger, 2006; Schmidt et al., 2007). Scatter plots of anticonvulsant with residence times and distances are presented Figure 4-5 and Figure 4-6 and the analyses of the scatter plot are shown in Table 4-6 and Table 4-7. It can be noted that most of the data points occur above 50% removal efficiency, within a residence time 0 - 40 days and distances more than 0 to 50 meters. Anticonvulsants concentrations seem to be reduced as travel distances and residence times increased. Table 4-5 showed that some cases of removal of anticonvulsant were removed until 90%. In fact, previous studies have shown that carbamazepine and primidone were persistent compounds during wastewater or water treatment processes. The removal of anticonvulsants are removed due to dilution by groundwater and it removed less on the way to the subsoil (Heberer et al., 2004). Therefore, more data are required to investigate if the removal of anticonvulsants is possible during bank filtration.

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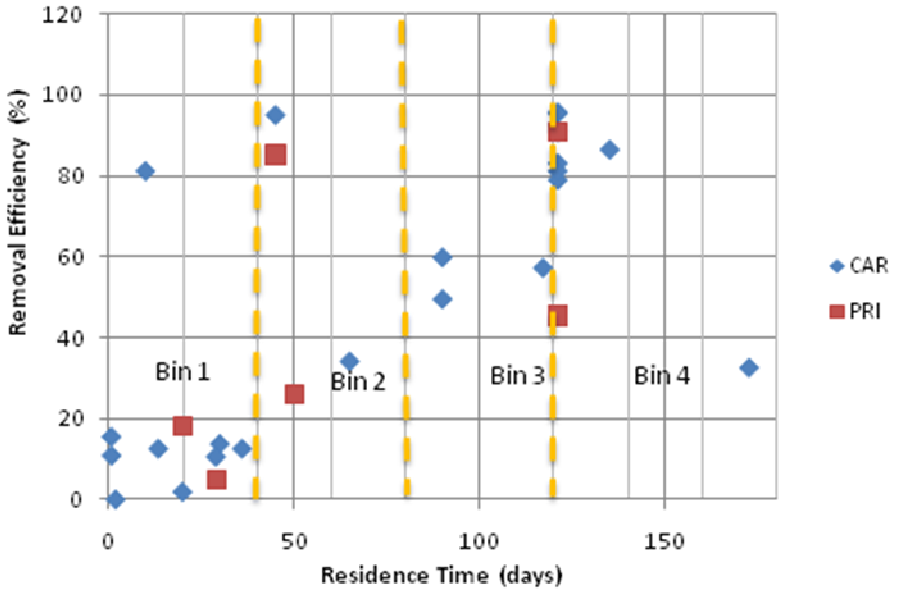

Figure 4-5: Plot of removal efficiency of anticonvulsants with residence time

Table 4-5: Analysis of scatter plot of anticonvulsant removal with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-583	5-520	0-40	0-81	11	16	22	0-30
		40-80	26-95	4	60	30	30-50
		80-120	49-60	3	55	5	50-54
		120-173	33-95	12	76	22	54-76

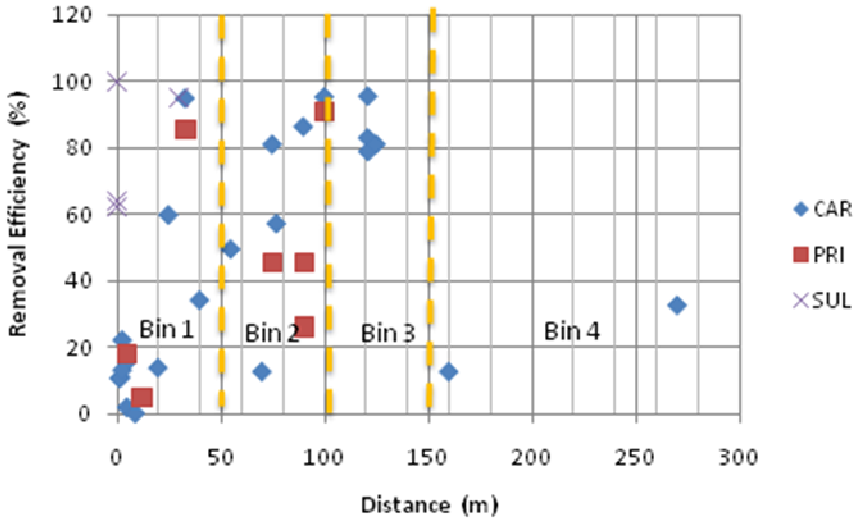

Figure 4-6: Plot of removal efficiency of anticonvulsants with distance

Table 4-6: Analysis of scatter plot of anticonvulsants removal with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-583	5-520	0-50	2-95	16	27	28	0-8
		50-100	13-91	10	59	28	8-31
		100-150	79-95	4	85	7	31-77
		>150	13-33	2	23	14	77-85

4.1.4 Antibiotics

Sulfamethoxazole, acetyl-sulfamethoxazole, clarithromycin, roxithromycin, clindamycin, trimethoprim were detected from bank filtration sites from Lake Tegel and Lake Wannsee, Berlin, Germany (Grunheid et al., 2005; Grunheid and Jekel, 2005; Heberer et al., 2008; Schmidt et al., 2007). Scatter plots of the removal efficiencies for antibiotic with residence times and distances are presented below in Figure 4-7 and Figure 4-8 and the analyses of the scatter plot are shown in Table 4-8 and Table 4-9. It can be noted that mostly the removal of antibiotics occurs above 40% within a residence time 0 - 40 days and distance 0-50 meters. Table 4-5 and Table 4-8 showed that some cases increased more by increasing time and distance. Moreover, antibiotics are removed as travel distances and residence time increased. All antibiotics were

completely removed within 2-4 months of travel times except for sulfamethoxazole due to sulfamethoxazole which is redox dependence. Sulfamethoxazole which was removed better under anoxic conditions (Heberer et al., 2008; Schmidt et al., 2007)

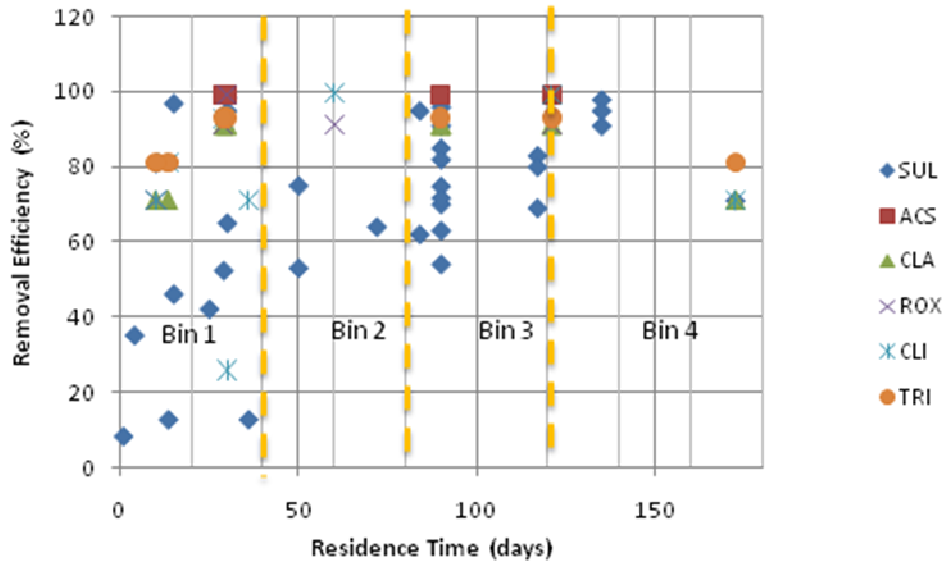

Figure 4-7: Plot of removal efficiency of antibiotics with residence time

Table 4-7: Analysis of scatter plot of antibiotics removal with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-485	0-301	0-40	8-99	28	71	28	43-64
		40-80	91-100	7	82	18	64-77
		80-120	93-99	20	82	14	77-96
		120-173	71-99	13	88	11	96-100

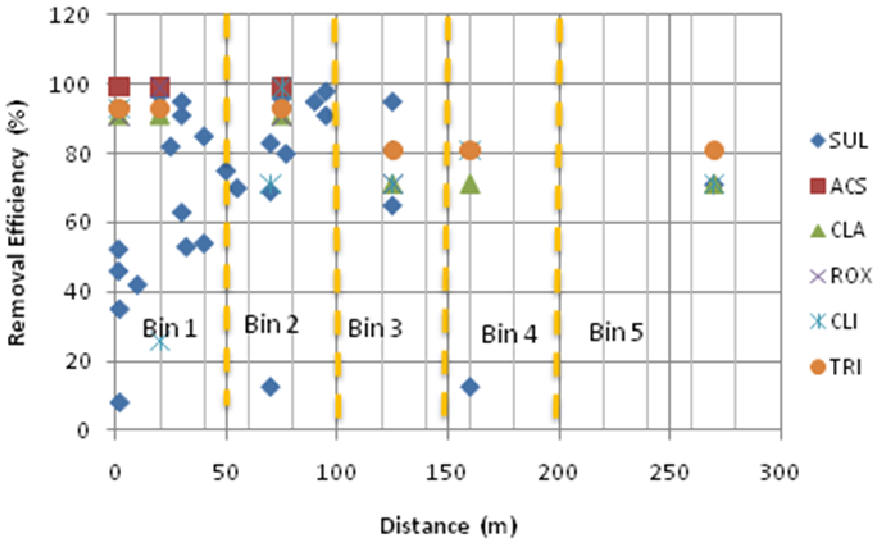

Figure 4-8: Plot of removal efficiency of antibiotics with distance

Table 4-8: Analysis of scatter plot of antibiotics removal with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-485	0-301	0-50	8-99	35	78	25	54-62
		50-100	13-99	16	84	22	62-66
		100-150	65-95	7	76	10	66-69
		150-200	13-81	4	61	33	69-79
		200-270	71-81	4	74	5	79-94

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4.1.5 Beta blockers

Atenolol, metoprolol, bisoprolol and sotalol were detected from bank filtration sites river Rhine, Elbe and Ruhr, Germany (Schmidt et al., 2007). Scatter plot of beta blockers with residence times and travel distances are presented below in Figure 4-9 and Figure 4-10 and the analyses are presented in Table 4-10 and Table 4-11. However, guidelines are not significant to predict the removal efficiency of beta blocker because the influent data range of beta blocker concentration is not known and limited data are available. Previous studies showed some beta blockers such as atenolol, metoprolol, and bisoprolol were removed greater than 70% at bank filtration sites located in the river Rhine, Elbe and Ruhr (Schmidt et al., 2007). Some beta blockers are expected removed by sorption or biodegradation during soil passage (Maeng et al., 2009).

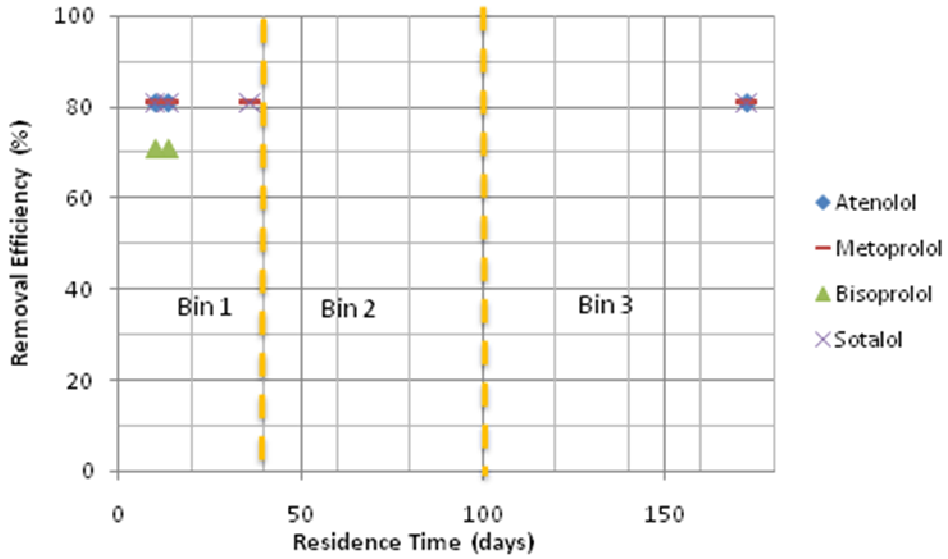

Figure 4-9: Plot of removal efficiency of beta blockers with residence time

Table 4-9: Analysis of scatter plot of beta blockers with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
-	-	0-40	71-81	6	79	5	74-79
		40-100	-	0	-	-	79-81
		100-170	81	3	81	0	81-100

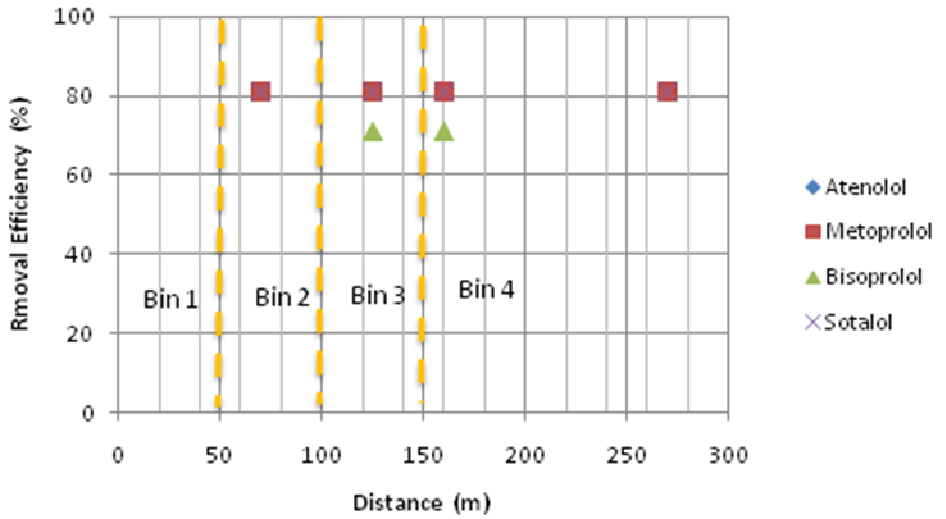

Figure 4-10: Plot of removal efficiency of beta blockers with distance

Table 4-10: Analysis of scatter plot of beta blockers with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Avarage (%)	Standard Deviation (ng/l)	Predictive Removal (%)
-	-	0-50	0	0	-	-	71-74
		50-100	81	2	81	0	74-76
		100-150	71-81	4	79	5	76-81
		>150	71-81	7	80	4	81-84

4.1.6 X-ray contrast agents

Iopamidol, iopromide, iomeprol and ioxhecol are X-ray contrast agents that are often detected in the source water of bank filtration sites in Berlin, Germany (Grunheid et al., 2005; Grunheid and Jekel, 2005; Schittko et al., 2004; Schmidt et al., 2007). Scatter plots of X-ray contrast agents detected from bank filtration sites are shown in Figure 4-11 and 4-12 and the analysis of the scatter plot are shown in Table 4-12 and Table 4-13. Most of X-ray contrast agents were removed higher than 40% within residence times between 0 and 40 days and distances between 0 and 50 meters. Figure 4-11 and 4-12 showed that Iopromide, iopamidol and iomeprol were significantly removed (>80%) and found to be easily removable compounds during bank filtration. These class of compound are suggested to be removed under anoxic condition (Grunheid et al., 2005)

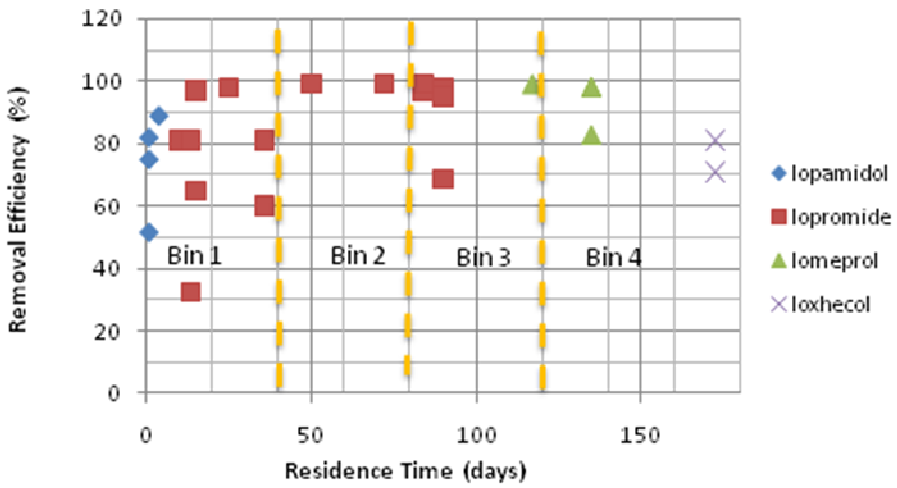

Figure 4-11: Plot of removal efficiency of x-ray contrast agents with residence time

Table 4-11: Analysis of scatter plot of x-ray contrast agents with residence time

Influent Range (ng/l)	Effluent Range (ng/l)	Residence Time (days)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-1102	0.2-464	0-40	33-98	19	77	15	43-64
		40-80	99	3	99	0	64-77
		80-120	69-99	8	94	10	77-96
		120-180	71-98	7	85	10	96-100

Figure 4-12: Plot of removal efficiency of x-ray contrast agents with residence time

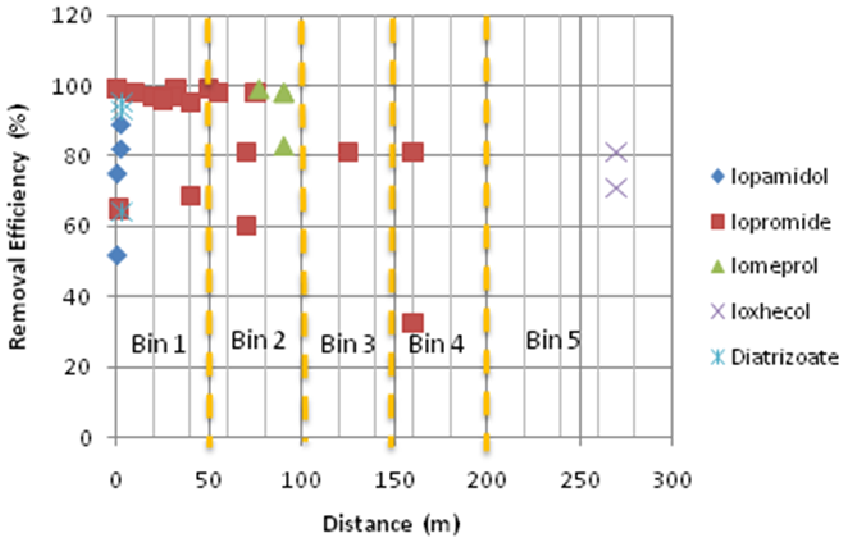

Table 4-12: Analysis of scatter plot of x-ray contrast agent with distance

Influent Range (ng/l)	Effluent Range (ng/l)	Distance (m)	Removal Ratio (%)	Number of cases	Average (%)	Standard Deviation (%)	Predictive Removal (%)
0-1102	0.2-464	0-50	52-99	18	87	15	72-75
		50-100	60-99	10	88	13	75-81
		100-150	81	4	81	0	81-84
		150-200	33-81	4	69	24	84-93
		200-270	71-81	4	79	5	93-100

4.2 Molecular Descriptors

A large number of theoretical molecular descriptors were calculated using DRAGON, Chem3D Ultra, ADME / Tox web software, and EPIWEB. DRAGON estimates constitutional descriptors (maximum 48 descriptors), connectivity indices (maximum 33 descriptors) and functional group counts (maximum 154 descriptors). SMILES (Simplified Molecular Input Line Entry System) code of each compound is given by using ADME/Tox web software, and subsequently converted into 3-D structure by using InChl Softwares. Chem3D Ultra was used to convert 3-D structure of each compound into a MDL mol-file which is an input data of DRAGON. 235 descriptors were estimated by DRAGON and are shown in Appedix C.

For the calculation of the others descriptors, EPIWEB was used to calculate descriptors that give physicochemical properties of compounds such as log Kow, solubility, biodegradability of pharmaceuticals.

Furthermore, calculation of pKa and log D are also equally important like descriptors that are mentioned above. An acid dissociation constant (pKa) was used to determine the speciation of the organic compound in ionic species at pH 7 whereas log D together with log Kow were used to determine hydrophobicity of compounds. A log D is the ratio of the equilibrium concentrations of all species (unionized and ionized) of a molecule in octanol to the same species in the water phase and log Kow is the octanol-water partition coefficient. Value pKa and log D were calculated by ADME/Tox web software.

Based on the pKa and log Kow values, the compounds were classified as hydrophilic neutral, hydrophilic ionic, hydrophobic ionic and hydrophobic neutral. Compounds with log Kow ≥ 2 were referred to as hydrophobic; on the other hand, those compounds with log Kow < 2 were referred to as hydrophilic (Yangali-Quantanilla et al., 2010). Nevertheless, this classification was not used as a descriptor because the presence of Kow and pKa already represent it.

The value of Dipole, Highest Occupied Molecular Orbital (HOMO), Lower Unoccupied Molecular Orbital (LUMO) and Heat Of Formation (HOF) were calculated by Chem3D Ultra software which is related to the positive and negative charge and polar interaction between the molecules (Liu et al., 2006).

4.3 QSAR models for different group of pharmaceuticals based on therapeutic usage

A multi linear regression model was used for QSAR model development. The selected descriptors from MOBYDIG were taken as independent variables, while the removal efficiency of pharmaceuticals is considered as dependent variables. Using multilinear regression, each variable in the model that carried out by MOBYDIG was evaluated to check the significance of its contributions.
The general linear equation took the following form :

$$y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_q x_{qi} + \varepsilon_i \qquad (1)$$

whereas,
y_i : response variable or dependent variable for i = 1, 2, … , n
$x_1, x_2, \ldots, x_i$: independent variable i.e descriptors
$\beta_1, \beta_2, \ldots, \beta_i$: regression coefficients
β_0 : intercept
ε_i : error term; mean value is zero.

4.3.1 Removal of analgesics

50 cases of analgesics from bank filtration sites were used to construct a QSAR model to predict the removal of analgesic during bank filtration (Heberer and Adam, 2004; Heberer et al., 2003a; Heberer et al., 2003b; Heberer et al., 2004; Pekdeger, 2006; Schmidt et al., 2007; Verstraeten et al., 2002b). All compounds are listed as below (detail data see appendix A1):
a. Diclofenac : 15 data
b. Indometachine : 12 data
c. Propyphenazone : 15 data
d. Ibuprofen : 3 data
e. Naproxen : 3 data
f. Pentoxifiline : 2 data

Total 100 descriptors in Appendix A.1 were calculated by a number of software that already mentioned above. Genetic algorithm was used to select descriptors that are the most important to describe the fate of analgesics. However the best developed model only had R^2 0.23. This value indicated that the model is not enough reliable to predict the removal of analgesic. Since the performance of QSAR model is dependent on the quality of input data, it is important to make some selection of input data to increase the performance of developed model.

Grouping input data based on location of sample collection improved the prediction power of the model in is shown in Table 4-13.

Table 4-13: Trial of different selection of training data

Classification of input data	Number of data						Total Data	% R^2 Model
	Dic	Indo	Propy	Ibu	Nap	Pento		
1. All analgesic data	15	12	15	3	3	2	50	22.7
2. Data from Lake Wannsee	9	9	7	3	-	-	25	60.95
3. Data Lake Tegel	2	1	8	3	-	-	11	-*
4. RBF (riverbank filtration)	**4**	**2**	-	**3**	**3**	**2**	**14**	**76.3**
5. LBF (lakebank filtration)	10	9	13	-	-	-	32	44.7
6. ARR (artificial recharge recovery)	1	1	2	-	-	-	4	-*

* Genetic algorithm process was blocked so that no model was generated

The best model has R^2 76.3 % with the linear equation model can be written as:

REMOVAL = 572.421 X4Av -3.6 nCp - 1.4 nCbH + 59, 8

The Q^2 for this model is 69.06%. Since $Q^2 > 0.5$, it is regarded as a good model (Eriksson et al., 2003). The involved molecular descriptors in above model and their corresponding meanings were given in Table 4-15.

Table 4-14: Descriptors of the best linear model for analgesics by MOBYDIG and their meanings

Descriptors	Meaning
X4Av	Average valence connectivity index Chi-4; connectivity indices
nCp	Number of terminal primary Carbon (sp3), functional group count
nCbH	Number unsubstituted benzene C (sp2); functional group count

The next step was to perform multi-linear regression in order to ensure the model contained a set of appropriate predictor variables. All variables were assessed with statistic approaches through Pearson's R, significance of coefficient estimates, and significance of the regression as presented in the Table 4-16, Table 4-17, Table 4-18, and Table 4-19.

Table 4-17 showed the correlation of each variable with others to identify any high correlations among independent variables in terms of prevention of collinearity in the developed regression model because it makes the estimation of the regression model can not be uniquely computed (Ameda, 2008). Another study also noted that models with variables correlated with each other are no significance (Liu and Yu, 2005). It was found that there was no collinearity in the developed model. The closest correlation among independent variables was detected between X4Av and nCp at 0.578.

Furthermore, it showed that dependent variable, removal efficiency of analgesics has closer correlation with X4Av rather than with others independent variables. Coefficient of variable in Table 4-19 specify that X4Av has the highest positive effect on the removal of analgesics during bank filtration while on the contrary nCp and nCbH indicated almost the same scale of negative effect on the removal of analgesics during bank filtration. Higher average valence of connectivity index of Chi-4, X4Av, increases removal of efficiency because X4Av increased of hydrophobic effects and compound tendency to bind with the soil organic matter (Gramatica et al., 2000; Kier and Hall, 2000). In contrast, the present of nCp and nCbH will reduce removal efficiency due to as an electronegative atom (i.e., electrostatic interaction), the greater the number of

them in the molecule lead to a higher the probability of H-bonding with the water and the lower the sorption will happen (Gramatica et al., 2000).

Table 4-15: Model summary for analgesics

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.873[a]	.763	.691	2.604

a. Predictors: (Constant), nCbH, X4Av, nCp

b. Dependent Variable: Removal efficiency of analgesics

Table 4-16: Correlations of all variables for analgesics

		REM	X4Av	nCp	nCbH
Pearson Correlation	REM	1.000	.541	.085	-.360
	X4Av	.541	1.000	.578	.047
	nCp	.085	.578	1.000	-.404
	nCbH	-.360	.047	-.404	1.000
Sig. (1-tailed)	REM	.	.023	.386	.103
	X4Av	.023	.	.015	.437
	nCp	.386	.015	.	.076
	nCbH	.103	.437	.076	.
N	REM	14	14	14	14
	X4Av	14	14	14	14
	nCp	14	14	14	14
	nCbH	14	14	14	14

Table 4-17: ANOVA result showing significance of the regression model for analgesics

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	217.900	3	72.633	10.711	.002[a]
	Residual	67.815	10	6.781		
	Total	285.714	13			

a. Predictors: (Constant), nCbH, X4Av, nCp

b. Dependent Variable: Removal efficiency of analgesics

Table 4-18: Estimated coefficients of the independent variables for analgesics

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	59.802	4.898		12.210	.000
	X4Av	572.421	111.198	1.048	5.148	.000
	nCp	-3.489	.948	-.818	-3.682	.004
	nCbH	-1.399	.344	-.739	-4.068	.002

The model was checked for the amount of error in the prediction of removal of analgesics. The error computation was presented in the Appendix B.1 and the graph was shown on the Figure 4-13. It showed that the accuracy of prediction of removal efficiency of developed model with average error computation value around 0.08 % is good. Small error computation due to the observed data was not varied and number of data input is few. Before developed model is applied to predict the removal efficiency of analgesic during bank filtration, it needs validation using others data.

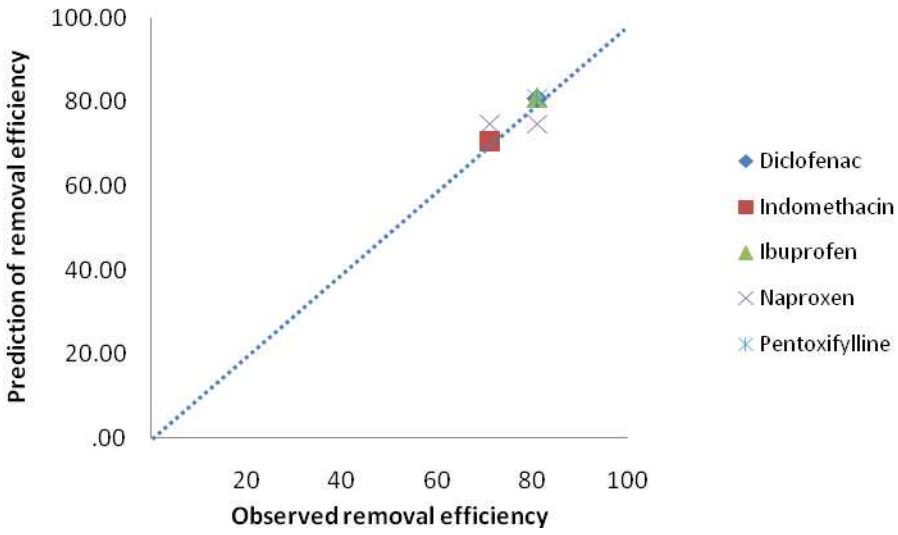

Figure 4-13: Observed versus predicted of removal efficiency of analgesics

4.3.2 Removal of antibiotics

56 cases of antibiotics from bank filtration sites were used to construct a QSAR model to predict the removal of antibiotics during bank filtration (Grunheid et al., 2005; Grunheid and Jekel, 2005; Heberer et al., 2008; Schmidt et al., 2007). All compounds are listed as below (detail data see Appendix A2) :

a. Sulfamethoxazole: 30 cases
b. Acetyl Sulfamethoxazole: 3 cases
c. Clarithromycin: 6 cases
d. Roxithromycin : 4 cases
e. Clindamycin : 7 cases
f. Trimetroprim : 2 cases

Total 103 descriptors in Appendix C were calculated by a number of software that already mentioned above. Genetic algorithm was used to select descriptors that are the most important to explain the fate of analgesics. The best developed model only had R^2 34.4. This value indicated that the model is not reliable to predict the removal of analgesic. Several trials of selection input data was carried out but R^2 model could not be improved. The best equation model that was generated by MOBYDIG was generated as follow:

$$\mathbf{REMOVAL = 0.194\ TIME + 11.805\ KOWEX + 29.978\ B2 + 42.238}$$

The Q^2 for the model is 0.26. Because Q^2 was lower than 0.5 hence it is not considered as a good model(Eriksson et al., 2003). However some trials of selection of input data

did not improve the Q2 of this model. The involved molecular descriptors in above model and their corresponding meaning were given in Table 4-19.

Table 4-19: Descriptors of the best linear model for antibiotics by MOBYDIG and their meanings

Descriptors	Meaning
TIME	Residence time
KOWEX	Log Kow (n-octanol/water partition coefficients)
B2	Biowin2 (a general indication of biodegradability under aerobic conditions)

All variables of developed model were analyzed further with multi-linear regression. The result of statistical analyzes were seen on Table 4-20, Table 4-21, Table 4-22, Table 4-23. According to Table 4-20, it was concluded that the correlation among independent variables did not create collinearity in the developed linear model so that the model was considered significance. Moreover, the significance of each variable was analyzed with the value of p in Table 4-23, that showed all variables have $p<0.05$ therefore they did not exclude from the model.

From the coefficient of variable in Table 4-23, all variables gave positive contributions in the removal of antibiotics during bank filtration. More numbers of variables will increase removal efficiency of antibiotics during bank filtration. Time gave the smallest contribution into removal of antibiotics compared to KOWEX and B2 that almost gave the same effect into removal of analgesic during bank filtration. The intensive removal through degradation and adsorption occurred within a very short residence time (Hiscock and Grischek, 2002) as also stated in one of study that most of compounds were removed a lot in the first few meters during bank filtration (Ameda, 2008).

The contribution of KOWEX as well as B2 is considered important in removal of antibiotics during bank filtration. KOWEX i.e. log Kow associates to the hydrophobic properties of organic chemicals. The larger log Kow of compounds, the more easily antibiotics adsorbed by organic phase of soil than by water phase. Large value of log Kow will increase the value of Koc that was commonly used as an indicator of good soil sorption (Liu and Yu, 2005).

In term of B2, removal of antibiotics appears to be redox-dependent. Thus, antibiotics were removed more efficiently under oxic infiltration condition. A previous study of fate of macrolide antibiotics during bank filtration got higher removal efficiency (93%) of its compounds under seasonally oxic conditions instead of only 26% of removal efficiency during anoxic infiltration(Heberer et al., 2008).

Table 4-20: Correlations of all variable (dependent and independent variable) for antibiotics

		REM	TIME	KOWEX	B2
Pearson Correlation	REM	1.000	.383	.224	.221
	TIME	.383	1.000	-.090	-.007
	KOWEX	.224	-.090	1.000	-.391
	B2	.221	-.007	-.391	1.000
Sig. (1-tailed)	REM	.	.002	.048	.051
	TIME	.002	.	.255	.480
	KOWEX	.048	.255	.	.001
	B2	.051	.480	.001	.
N	REM	56	56	56	56
	TIME	56	56	56	56
	KOWEX	56	56	56	56
	B2	56	56	56	56

Table 4-21: Model summary for antibiotics

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.583[a]	.339	.301	20.175

a. Predictors: (Constant), B2, TIME, KOWEX

b. Dependent Variable: REM

Table 4-22: ANOVA result showing significance of the regression model for antibiotics

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	10871.665	3	3623.888	8.903	.000[a]
	Residual	21165.715	52	407.033		
	Total	32037.380	55			

a. Predictors: (Constant), B2, TIME, KOWEX

b. Dependent Variable: REM

Table 4-23: Estimated coefficients of the independent variables for antibiotics

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	42.138	7.814		5.393	.000
	TIME	.194	.052	.423	3.730	.000
	KOWEX	11.805	3.521	.413	3.353	.001
	B2	29.978	9.537	.385	3.143	.003

a. Dependent Variable: REM

The model was checked for the amount of error in the prediction of removal of analgesic. The error computation was presented in the Appendix B.2 and the graph of predictions versus observed was shown on the Figure 4-14. Unlike analgesic, observed data of removal efficiency of antibiotics were various. Nonetheless, the model can not predict removal efficiency of antibiotics as well as the model of removal analgesic. Error computation 26.77 % created big different between prediction and observed removal efficiency.

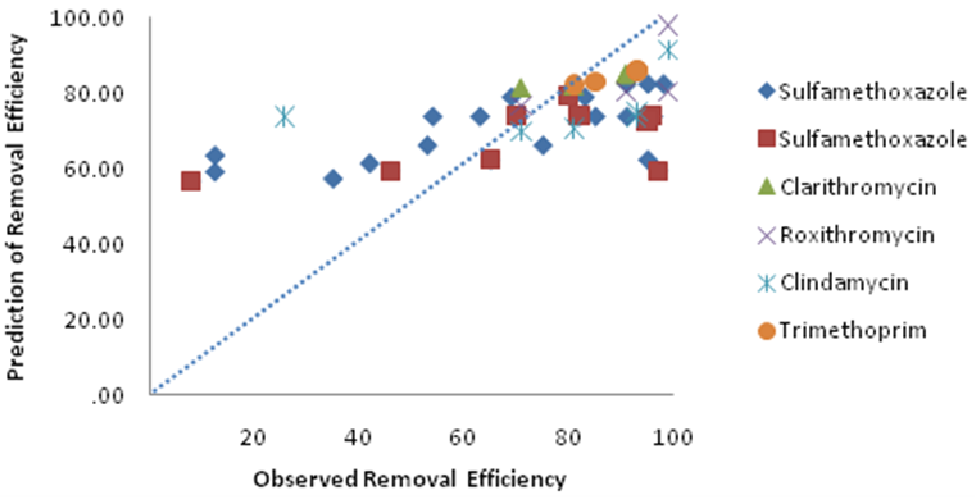

Figure 4-14: Observed versus predicted of removal efficiency of antibiotics

4.3.3 Removal of beta blockers

13 cases of beta blockers from bank filtration sites were used to construct a QSAR model to predict the removal of antibiotics during bank filtration (Schmidt et al., 2007). All compounds are listed as below (detail data see Appendix A.3):

a. Atenolol: 3 data
b. Metoprolol : 4 data
c. Bisoprolol : 2 data
d. Sotalol : 4 data

Total 85 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with 2 selected variables as following equation:

$$\mathbf{REMOVAL = 0.039\ TIME - 4.646\ nCp + 91.124}$$

This model has R^2 91.2 % and predictive power, Q^2 81.06 %. This model is considered as a good model since the Q>0.5 and it is almost closer to category excellent whereas Q>0.9 (Eriksson et al., 2003). In addition, there is no collinearity in this model since the correlation between independent variables of developed model is only 0.263 (Table 4-25). The involved molecule descriptors in above models and their meaning are given in the Table 4-24.

Table 4-24: Descriptors of the best linear model for beta blockers by MOBYDIG and their meanings

Descriptors	Meaning
TIME	Residence time
nCp	Number of functional group count

The developed model was analysed with multi-linear regression as shown in Table 4-26, Table 4-27, Table 4-28, and Table 4-29. All variables and models have significance value less than 0.05 which is mean that all variables were still remain in the model, otherwise a process of elimination reduce the performance of the model.

Table 4-25: Correlations of all variable (dependent and independent variable) for beta blockers

		REM	TIME	nCp
Pearson Correlation	REM	1.000	.699	-.812
	TIME	.699	1.000	-.263
	nCp	-.812	-.263	1.000
Sig. (1-tailed)	REM	.	.004	.000
	TIME	.004	.	.193
	nCp	.000	.193	.
N	REM	13	13	13
	TIME	13	13	13
	nCp	13	13	13

Table 4-26: Model summary for beta blockers

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.955[a]	.912	.895	1.679

a. Predictors: (Constant), nCp, TIME

b. Dependent Variable: REM

The coefficient of variables in Table 4-28 can be interpreted that removal efficiency will be increased by increase time which is explained by previous study that residence time is one of factor to assess the performance of bank filtration improves water quality (Wang, 2002). Higher removal of beta blockers regulators are achieved during bank filtration but most of beta blockers removal occurs within the first meter of infiltration. Subsequently time will not anymore affect the removal of beta blockers.
On the other hand, nCp has greater influence than time in a negative side. Enhance the value of nCp reduced removal of efficiency of beta blockers. nCp increased the reaction of compound with water therefore the adsorption of beta blockers with the soil was decreased(Gramatica et al., 2000).

Table 4-27: ANOVA result showing significance of the regression model for beta blockers

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	293.050	2	146.525	51.995	.000[a]
	Residual	28.181	10	2.818		
	Total	321.231	12			

a. Predictors: (Constant), nCp, TIME

b. Dependent Variable: REM

Table 4-28: Estimated coefficients of the independent variables for beta blockers

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	91.124	1.748		52.130	.000
	TIME	.039	.007	.522	5.376	.000
	nCp	-4.646	.669	-.674	-6.948	.000

a. Dependent Variable: REM

The model was checked for the amount of error in the prediction of removal efficiency of beta blockers. The error computation is presented in Appendix B-3 and the graph was shown in Figure 4-15 belows:

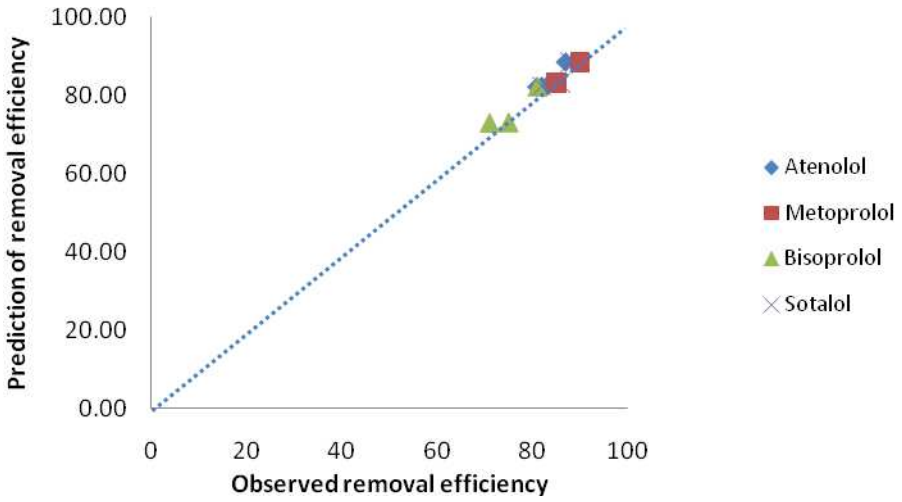

Figure 4-15: Observed versus predicted of removal efficiency of beta blockers

With error computation of prediction removal of beta blockers only 0.03 %, the model performance gave good accuracy to predict removal of beta blockers during bank filtration.

4.3.4 Removal of steroid hormones

17 out of 29 cases of steroid hormones compounds were used to construct QSAR model of removal steroid hormones during bank filtration (Mansell and Drewes, 2004; Snyder et al., 2007; Zühlke, 2004). All compounds are listed as below (details data are presented in Appendix B-4):

a. Estradiol: 3 data
b. Estriol: 3 data
c. Estrone : 5 data
d. Progesterone : 3 data
e. Testosterone : 3 data

Total 91 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with only one selected variables as follows:

REMOVAL = 0.003 DIST + 99.09

This equation was analyzed with multilinear regression and the statistical results are shown in Table 3-29, Table 4-30, Table 4-31, and Table 4-32. The model consists of only one variable, DIST, which means infiltration distance. The result of significance test in Table 4.32 shows that the DIST with value significance < 0.05 has an important contribution to the performance of the model. Moreover, in accordance to R^2 99.6% and Q^2 99.3%, the model is consider as an excellent model whereas the Q^2 > 90 % (Eriksson et al., 2003).

The developed model indicates infiltration distance has a positive effect in the removal process of steroid hormones. Enhance infiltration distance generated higher removal efficiency of steroid hormones. Long infiltration distances allows for more effective of attenuation process of compound in bank filtration. An investigation of the previous study emphasizes the dependence of bank filtration on flow path length (Grischek et al., 2001; Sharma et al., 2007). Bank filtration system required relatively longer travel distance to achieve total treatment plant compare to such treatment that only simply removed particular item such as cryptosporidium.

Table 4-29: Correlations of all variable (dependent and independent variable) for steroid hormones

		REM	DIST
Pearson Correlation	REM	1.000	.996
	DIST	.996	1.000
Sig. (1-tailed)	REM	.	.000
	DIST	.000	.
N	REM	17	17

Table 4-30: Model summary for steroid hormones

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.996[a]	.993	.992	.0066

a. Predictors: (Constant), DIST

Table 4-31: ANOVA result showing significance of the regression model for steroid hormones

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.090	1	.090	2074.348	.000[a]
	Residual	.001	15	.000		
	Total	.091	16			

a. Predictors: (Constant), DIST

b. Dependent Variable: REM

Table 4-32: Estimated coefficients of the independent variables for steroid hormones

Model		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
1	(Constant)	99.090	.002		56280.110	.000
	DIST	.003	.000	.996	45.545	.000

a. Dependent Variable: REM

The model was checked for the amount of error in the prediction of removal efficiency of steroid hormones. The error computation is presented in Appendix B-3 and the graph was shown in Figure 4-16 below:

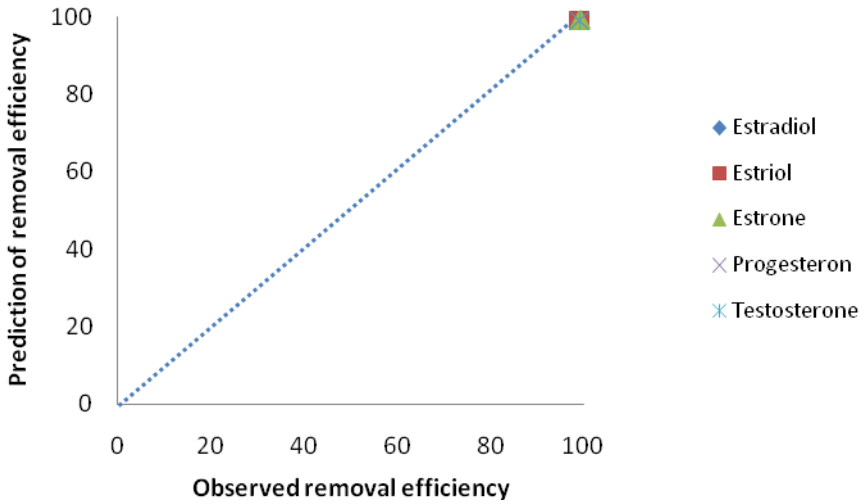

Figure 4-16: Observed versus predicted of removal efficiency of steroid hormones

Due to the observed removal of efficiency contained almost the same value, so that the graph showed one point on the line. Base on this data, this model has good accuracy to predict removal efficiency of steroid hormones.

4.3.5 Removal of anticonvulsants

27 data of anticonvulsants compounds were selected to construct QSAR model of removal analgesic during bank filtration (Heberer et al., 2003a; Heberer et al., 2003b; Massmann et al., 2006; Mechlinski and Heberer, 2005; Pekdeger, 2006; Schmidt et al., 2007). Data were selected base on the similarity of site source of data sampling due to increase high performance of model. All compounds are listed as below (detail see in Appendix A-5):

a. Carbamemazepine : 21 data
b. Primidone : 6 data

Total 96 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with only one selected variables as follows:

REMOVAL = 0.426 TIME + 18.09

This model was analysed with multilinear regression with the analytical result was shown in Table 4-33, Table 4-34, Table 4-35, and Table 4-36. Collinearity is not found

in the model hence the variable of model is only one, TIME. From Table 4-36, variable TIME has good significance (<0.05) therefore TIME is remained in the model.

Positive coefficient of TIME in the developed model is interpreted by the removal of anticonvulsant is TIME dependence. Removal efficiency will be increased by increasing residence time. As it was shown in one of study about carbamazepine (member of anticonvulsant) that residence time has the positive effect on the elimination process during bank filtration (Ameda, 2008).

Table 4-33: Correlations of all variable (dependent and independent variable) for anticonvulsants

		REM	TIME
Pearson Correlation	REM	1.000	.633
	TIME	.633	1.000
Sig. (1-tailed)	REM	.	.000
	TIME	.000	.
N	REM	27	27
	TIME	27	27

Table 4-34: Model summary for anticonvulsants

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.633[a]	.401	.377	2.751499112589736E1

a. Predictors: (Constant), TIME

b. Dependent Variable: REM

Table 4-35:ANOVA result showing significance of the regression model for anticonvulsants

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	12652.805	1	12652.805	16.713	.000[a]
	Residual	18926.868	25	757.075		
	Total	31579.673	26			

a. Predictors: (Constant), TIME

b. Dependent Variable: REM

Table 4-36: Estimated coefficients of the independent variables for anticonvulsants

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	18.089	8.886		2.036	.053
	TIME	.426	.104	.633	4.088	.000

a. Dependent Variable: REM

The model was checked for the amount of error in the prediction of removal efficiency of anticonvulsants. The error computation is presented in Appendix B-4 and the graph was shown in Figure 4-17below:

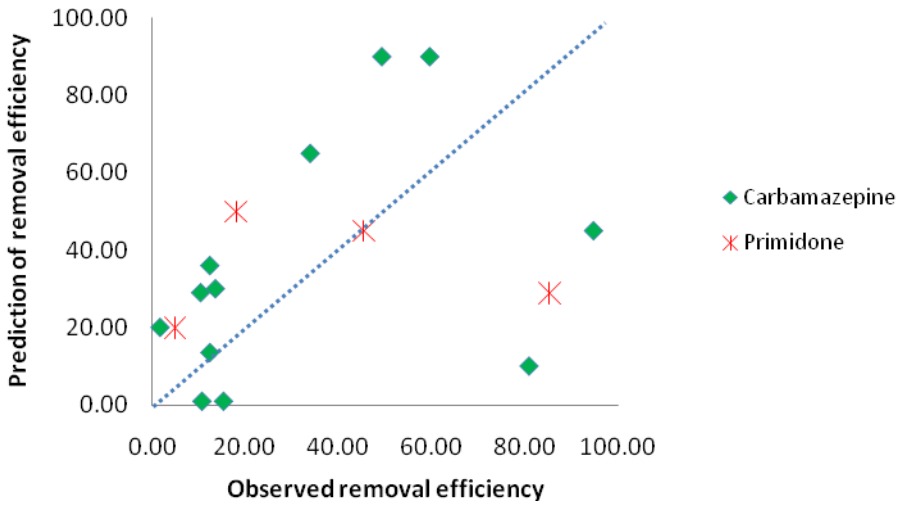

Figure 4-17: Observed versus predicted of removal efficiency of anticonvulsants

From Figure 4-17 we can conclude that the equation model is not good enough to predict removal efficiency of anticonvulsant. Only few observed data are fitted with the prediction removal of developed model. It is also shown by R^2 value 40.11% and Q^2 23.7 % that can not put as a good model. According to one study about regulatory acceptance of QSARs (Eriksson et al., 2003), a model is categorized a good model if Q^2 > 50% .

4.3.6 Removal of x-ray contrast agents

35 cases of x-ray contrast agents compounds were used to construct QSAR model of removal analgesic during bank filtration(Grunheid et al., 2005; Grunheid and Jekel, 2005; Schittko et al., 2004; Schmidt et al., 2007) . All compounds are listed as below:

a. Iopamidol : 4 data
b. Iopromide : 20 data
c. Iomeprol : 4 data
d. Ioxecol : 4 data
e. Diatrizoate : 3 data

Total 88 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with only one selected variables as follows:

REMOVAL = 0.094 TIME - 12.444 nCp + 8.376 nROH + 76.637

This model has R^2 64.2 % and predictive power, Q^2 42.19 %. This model can not be considered as a good model since the Q^2 < 0.5 (Eriksson et al., 2003). The involved molecule descriptors in above models and their meaning are given in the Table 4-38.

Table 4-37: Descriptors of the best linear model for x-ray contrast agents by MOBYDIG and their meanings

Descriptors	Meaning
TIME	Residence time
nCp	Number of terminal primary Carbon (sp3), functional group count
nROH	Number of hydroxyl groups, functional group counts

Statistical analysis by multilinear regression for above model is shown in Table 4-38, Table 4-39, Table 4-40, and Table 4-41. Each independent variable has significance less than 0.05 so that the all variable are still remain in the final model.

Refer to the equation of developed model, removal efficiency of X-ray contrast agent is influenced by residence time. Larger removal efficiency will be obtained by increase residence time. As an important parameter design of bank filtration, long terms bank filtration appears to have capability to significantly remove organic pollutant concentration (Grunheid et al., 2005).

In contrast with time, nCp gives a negative effect in removal process of X-ray contrast agent. nCp participate to reduce the attenuation of X-ray contrast agent during bank filtration. Greater nCp increase the probability of H-bonding with water and therefore a decreasing of soil sorption in bank filtration (Gramatica et al., 2000).

The presence of nROH gives positive contribution in removal process of x-ray contrast agents. nROH affected the removal process by biodegradability (Pavan and Worth, 2008). This structure is susceptible to common oxidation process so that the compound is readily biodegradable (Hongwei et al., 2004).

The model was checked for the amount of error in the prediction of removal efficiency of beta blockers. The error computation is presented in Appendix B-4 and the graph was shown in Figure 4-18.

Table 4-38: Correlations of all variable (dependent and independent variable) for x-ray contrast agents

		REM	TIME	nCp	nROH
Pearson Correlation	REM	1.000	.349	-.497	.098
	TIME	.349	1.000	-.037	-.075
	nCp	-.497	-.037	1.000	.614
	nROH	.098	-.075	.614	1.000
Sig. (1-tailed)	REM	.	.020	.001	.287
	TIME	.020	.	.416	.335
	nCp	.001	.416	.	.000
	nROH	.287	.335	.000	.
N	REM	35	35	35	35
	TIME	35	35	35	35
	nCp	35	35	35	35
	nROH	35	35	35	35

Table 4-39: Model summary for x-ray contrast agents

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.801[a]	.642	.607	9.3514

a. Predictors: (Constant), nROH, TIME, nCp

b. Dependent Variable: REM

Table 4-40:ANOVA result showing significance of the regression model for x-ray contrast agents

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	4853.218	3	1617.739	18.499	.000[a]
	Residual	2710.906	31	87.449		
	Total	7564.123	34			

a. Predictors: (Constant), nROH, TIME, nCp

b. Dependent Variable: REM

Table 4-41:Estimated coefficients of the independent variables for x-ray contrast agents

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	76.637	6.207		12.347	.000
	TIME	.094	.028	.366	3.398	.002
	nCp	-12.444	1.885	-.900	-6.604	.000
	nROH	8.376	1.686	.678	4.967	.000

a. Dependent Variable: REM

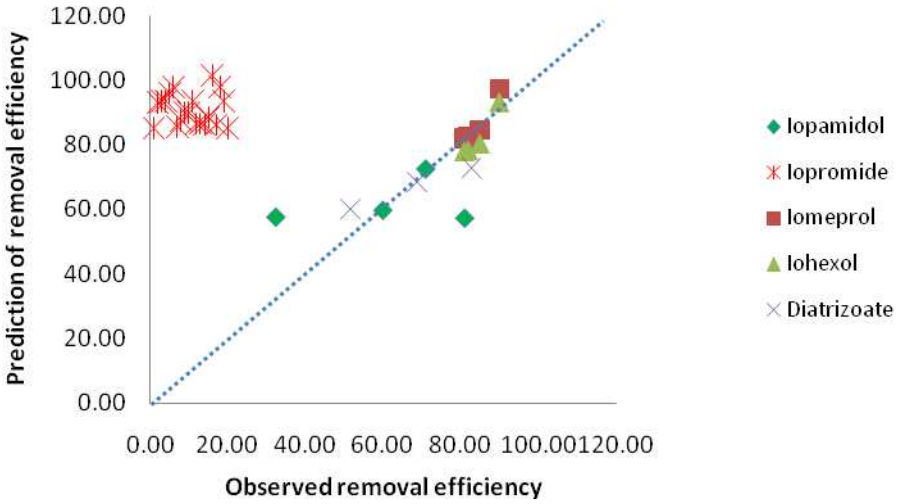

Figure 4-18: Observed versus predicted of removal efficiency of x-ray contrast agents

According to the Figure 4-18, the model prediction is not much different from observed data except for Iopromide. As a hydrophilic compound, Iopromide is a very stable chemical so that increasing time will not efficiently remove it during bank filtration. It need more specific model that accommodate the activity of Iopromide during bank filtration.

4.3.7 Removal of antidepressants

8 cases of antidepressants compounds were used to construct QSAR model of removal analgesic during bank filtration (Snyder et al., 2007). All compounds are listed as below:

a. Diclofenac : 2 data
b. Indometachine : 3 data
c. Propyphenazone : 3 data

Total 103 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with only one selected variables as follows:

REMOVAL = 1127.377 X4Av + 9.054

This model was analysed with multilinear regression with the analytical result was shown in Table 4-42, Table 4-43, Table 4-44, and Table 4-45. Collinearity is not found in the model hence the variable of model is only one, X4Av, which means average connectivity index chi-0 (connectivity indices). From Table 4-45, variable X4AV has good significance (<0.05) therefore X4Av is remained in the model.

The removal efficiency of antidepressants is effected by X4AV which is indicated the size of compounds. Increase X4AV means increase the size that leads to increased hydrophobic effects and compound tendency to bind with the soil organic matter (Gramatica et al., 2000). Adsorption process removes antidepressants during bank filtration.

Developed model has R^2 84.7% and Q^2 73.83%. This model is regarded as a good model due to $Q^2 > 0.5$ ((Eriksson et al., 2003). As a good model the prediction should not quite different with observed removal efficiency of antidepressants. The error computation for prediction of removal efficiency is shown in Figure 4-19 and the error computation calculation is presented in Appendix B-7.

Table 4-42: Correlations of all variable (dependent and independent variable) for antidepressants

		REM	X4Av
Pearson Correlation	REM	1.000	.920
	X4Av	.920	1.000
Sig. (1-tailed)	REM	.	.001
	X4Av	.001	.
N	REM	8	8
	X4Av	8	8

Table 4-43: Model summary for antidepressants

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.920[a]	.847	.822	9.349

a. Predictors: (Constant), X4Av

b. Dependent Variable: REM

Table 4-44: ANOVA result showing significance of the regression model for antidepressants

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	2907.364	1	2907.364	33.265	.001[a]
	Residual	524.404	6	87.401		
	Total	3431.769	7			

a. Predictors: (Constant), X4Av

b. Dependent Variable: REM

Table 4-45: Estimated coefficients of the independent variables for antidepressants

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	9.054	11.950		.758	.477
	X4Av	1127.377	195.469	.920	5.768	.001

a. Dependent Variable: REM

Figure 4-19 shows that the model can prediction is almost the same as observed removal efficiency of antidepressants so that this model is significant enough to predict the removal efficiency of antidepressants.

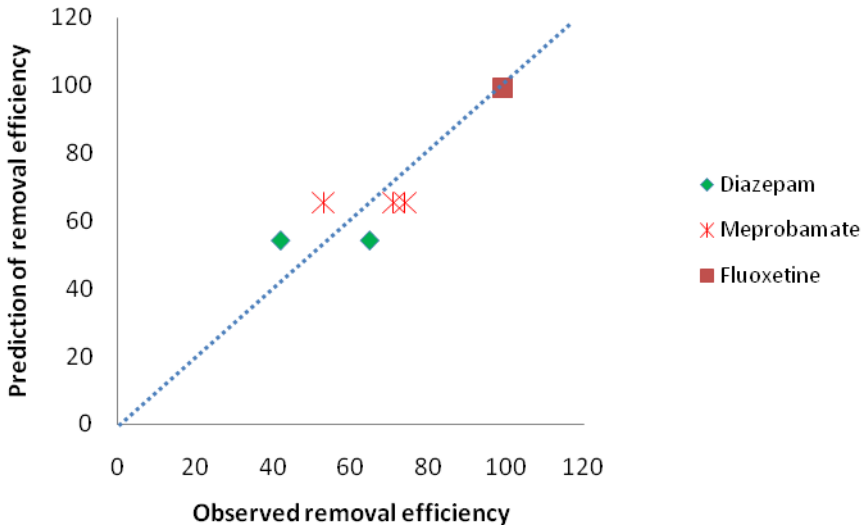

Figure 4-19: Observed versus predicted of removal efficiency of antidepressants

4.3.8 Removal of blood lipid regulators

10 out of 46 cases of blood lipid regulators compounds were selected to construct QSAR model of removal analgesic during bank filtration (Heberer and Adam, 2004; Heberer et al., 2003a; Heberer et al., 2003b; Heberer et al., 2004; Pekdeger, 2006; Scheytt et al., 2004; Schmidt et al., 2007; Verstraeten et al., 2002b). All compounds are listed as below (detail data in Appendix A-8):

a. Bezafibrate : 4 data
b. DTPA: 4 data
c. Clorofibric acid : 2 data

Total 104 numbers of descriptors in Appendix C3 were calculated. Through genetic algorithm, the best model was obtained with only one selected variables as follows:

$$\mathbf{REM = 0.062\ TIME + 35.096\ B1 + 57.078}$$

This model has R^2 76.03 % and predictive power, Q^2 55.05 %. This model can not be considered as a good model since the $Q^2 < 0.5$ (Eriksson et al., 2003). The involved molecule descriptors in above models and their meaning are given in the Table 4-46.

Table 4-46: Descriptors of the best linear model for blood lipid regulators by MOBYDIG and their meanings

Descriptors	Meaning
TIME	Residence time
B1	Linier model (Biowin 1) , biodegradation probability

The coefficient of variables of the developed model can be interpreted that removal efficiency will be increased by increase time which is explained by previous study that detention time is one of determination factor to assess the effectiveness of bank filtration improves water quality (Wang, 2002). Extension retention time removed more blood lipid regulators during bank filtration but only in a limited time hence most of removal occurring within the first meter of filtration. A short distance of a few meters between the bank and observation well can lead to dramatics decreases (Heberer et al., 2004)

In term of B1, removal of blood lipid regulators appears to be redox-dependent. Thus, lipid regulators were removed more efficiently under oxic infiltration condition. However it was only shown by particular compound such as EDTA. Bezafibrate and clorofibric did not show significant difference under anoxic and oxic conditions (Schmidt et al., 2007).

Table 4-47: Correlations of all variable (dependent and independent variable) for blood lipid regulators

		REM	TIME	B1
Pearson Correlation	REM	1.000	.479	.721
	TIME	.479	1.000	.005
	B1	.721	.005	1.000
Sig. (1-tailed)	REM	.	.081	.009
	TIME	.081	.	.494
	B1	.009	.494	.
N	REM	10	10	10
	TIME	10	10	10
	B1	10	10	10

Table 4-48: Model summary for blood lipid regulators

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.864[a]	.746	.674	4.871

a. Predictors: (Constant), B1, TIME

b. Dependent Variable: REM

Table 4-49: ANOVA result showing significance of the regression model for blood lipid regulators

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	488.441	2	244.221	10.295	.008[a]
	Residual	166.059	7	23.723		
	Total	654.500	9			

a. Predictors: (Constant), B1, TIME

b. Dependent Variable: REM

Table 4-50: Estimated coefficients of the independent variables for blood lipid regulators

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	57.078	4.979		11.464	.000
	TIME	.062	.025	.475	2.497	.041
	B1	35.096	9.296	.719	3.775	.007

a. Dependent Variable: REM

The model was checked for the amount of error in the prediction of removal efficiency of blood lipid regulators. The error computation is presented in Appendix B-8 and the graph was shown in Figure 4-20. The model prediction is not quite different from observed removal efficiency. It means that the model has a good accuracy to predict removal efficiency of blood lipid regulators.

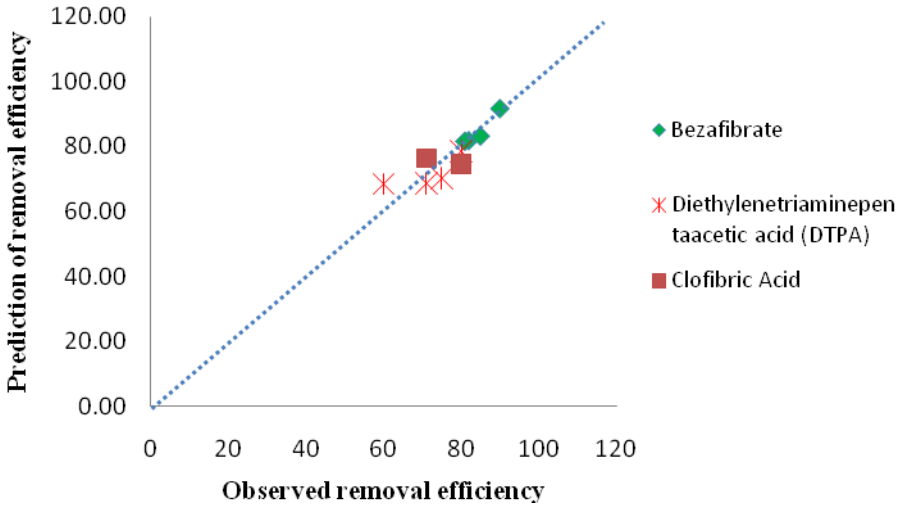

Figure 4-20: Observed versus predicted of removal efficiency of blood lipid regulators

4.4 Summary of QSAR Models for Pharmaceuticals

Summary for all QSAR model of removal of pharmaceutical based on therapeutic usage is shown on Table 4-51. It can be seen from Table 4-51 that residence time variable, TIME, almost appears in all QSAR model. As it mention in some of previous study that time is an important parameter design of river bank filtration in order to have a significant attenuation of pharmaceuticals during bank filtration (Ameda, 2008; Grischek et al., 2001; Schmidt et al., 2007). Another prominent variable is nCp, which is appearing in 3 out of models that contribute negatively to the removal efficiency of pharmaceuticals.

It is found that QSAR model of steroid hormones and anti depressants only consisted of one variable. Variable in the model of steroid hormones is travel distance, DIST, which is directly related to residence time (Ameda, 2008). Furthermore, it was observed that removal of analgesics and antidepressants are not directly related to time and distance but on X4Av which is average valence connectivity index Chi-4.

Table 4-51: Summary of QSAR model to predict removal of pharmaceuticals base on therapeutic usage

Group	Model Equation	% R2
1. Analgesics	REM = 572.421 X4Av -3.489 nCp - 1.399 nCbH + 59.802	76.3
2. Antibiotics	REM = 0.194 TIME + 11.805 KOWEX+ 29.978B2 + 42.238	33.9
3. Beta Blockers	REM = 0.039 TIME - 4.646 nCp + 91.124	91.2
4. Anticonvulsants	REM = 0.426 TIME +18.09	40.11
5. X Rays	REM = 0.094 TIME - 12.444 nCp + 8.376 nROH+ 76.637	64.2
6. Steroid Hormones	REM = 0.003 DIST + 99.09	99.3
7. Anti depressants	REM = 3431.769 X4Av + 9.064	84.67
8. Blood Lipid Regulators	REM = 0.062 TIME + 35.096 B1 + 57.078	74.6

Table 4-52 shows the prediction of removal efficiency of different classes of PhACs for different residence time based on QSAR-models developed.

Table 4-52: Removal efficiencies predicted from QSAR models

Group	Residence Time		
	10 days	**100 days**	**200 days**
1.Analgesics	81	81	81
2.Antibiotics	59	76	95
3.Beta blockers	82	86	90
4.Anticonvulsants	22	60	103
5.X Rays	57	66	75
6.Steroid hormones	0	0	0
7.Antidepressants	54	54	54
8.Blood lipid regulators	82	87	93

From in Table 4-52, the prediction from QSAR models shows that the removal efficiency of pharmaceuticals is increased by increase time. However the model can not apply to predict removal efficiency of pharmaceuticals if time is higher than 200 days due to the range time in the database between 0-200 days. Its effect is shown in anticonvulsants group. The removal of anticonvulsants is not relevant anymore by increase time higher than 200 day hence in 200 days the removal efficiency already 100%.

On the other hand, increase time did not affect the removal efficiency f analgesics, steroid hormones, and antidepressants groups because their developed model is not contain time as an important variable. Therefore increase time is not change their concentration during bank filtration.

4.5 Limitations of the Study

The selection of descriptors in the modelling is not always interpretable. The descriptors selected by genetic algorithm as the best combinations correlated to a response are prudently the best for understanding mechanism.

QSAR model is very dependable on the quality of descriptors. It needs thorough research to calculate descriptors that could present the best model with the best understanding mechanism in practice.

Furthermore, these models can be used to predict the removal of different classes of PhACs for the residence time range of 0.9 to 200 days only. Results ma not be reliable when the time is more than 200 days.

5 CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Based on the data analysis, guidelines and QSAR models developed during this study the following conclusions can be made:

- Six preliminary guidelines developed can be used as a screening tool to assess removal of pharmaceuticals during bank filtration under given conditions.
- Based on the guidelines, antibiotic, analgesic, beta blockers and steroid hormones are generally removed efficiently during bank filtration (from 50 to 90%).
- Most of the pharmaceuticals are removed more than 50% in 50 days within 100 meter distance during bank filtration.
- Unlike others antibiotic compounds, sulfamethoxale is a redox dependent. It is removed more efficiently under anoxic condition.
- As a persistent compound, the attenuation of anticonvulsant observed during bank filtration (< 50%) was mainly due to dilution from native groundwater.
- 8 QSAR model were developed for prediction of removal of different classes of pharmaceuticals. Out of these, 5 of them (analgesics, antidepressant, beta blocker, blood lipid regulator and steroid hormone) showed a good performance while 3 of them (antibiotics, anticonvulsant, and x-ray contrast agents) showed poor performance.
- Residence time was found to be the most important variable that contributes significantly in almost all of QSAR models developed. Removal efficiency of pharmaceuticals during bank filtration can be increased by enhancing the residence time.
- A number of terminal primary carbon present (nCp) was another prominent descriptor that influences on the removal of several classes of pharmaceuticals during bank filtration. Higher the value of nCp, the removal of pharmaceuticals will be low.
- It was observed that the development of QSAR model is highly dependent on quality of data. Each bank filtration site has different characteristics including hydrogeochemical conditions, travel distances, residence times etc. Moreover, the proper selection of the molecular descriptors that define or correlate with different mechanisms taking place during bank filtration is very important to get a representative QSAR model.

5.2 Recommendations

The following is recommended based on the findings of this study:

- QSAR model is very dependable on the input molecular descriptors. Therefore, it would be more helpful in QSAR model development if there is a guideline to choose descriptors that more relevant to represent the behaviour of pharmaceuticals during bank filtration.
- To increase the accuracy of the QSAR model, the quality of removal database should be improved. Preferably, removal data should be collected from the experiments under similar conditions and from similar field sites. This is because QSAR models developed do not incorporate local environmental conditions.
- The prediction power of the QSAR model is dependent on the numbers of each compound in the input data set. While preparing QSAR model for a class of pharmaceuticals (e.g. therapeutic usage), there should be equal representation of all the major compounds belonging to that class. Otherwise the developed model is not representative for the whole class.
- There is a need for further study to develop general QSAR-based models to assess or predict the removal of pharmaceuticals during bank filtration, by incorporating both field based parameters as well as molecular descriptors, so that it could be applied in different situations.

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7 APPENDIX

Appendix A-Literature-data base of pharmaceuticals

Appendix A-1: Analgesics group

Compound	Removal Ratio (%)		Units	Influent	Effluent	Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data				Well	Ref	Input data	Ref	Input data	
Diclofenac	67	67				Column 1			2.8	2.8	Snyder et.al (2007)
Diclofenac	>99	99.1				Column 2			2.8	2.8	Snyder et.al (2007)
Diclofenac	>99	99.1				Column 3			2.8	2.8	Snyder et.al (2007)
Diclofenac	60	60	ng/l	25	10	+	>120	121	75	75	Heberer, et.al (2004)
Diclofenac	>80	81	ng/l	25	<5	+	>120	121	100	100	Heberer, et.al (2004)
Diclofenac	80	80	ng/l	25	5	+	>120	121			Heberer, et.al (2004)
Diclofenac	>67	68	ng/l	15	<5	++	<1	0.9	0	0	Heberer, et.al (2004)
Diclofenac	-33	-33	ng/l	15	20	++	90	90	40	40	Heberer, et.al (2004)
Diclofenac	-133	-133	ng/l	15	35	+	135	135	125	125	Heberer, et.al (2004)
Diclofenac	-8	-8	ng/l	26	28	++	65	65	40	40	Heberer et al.,(2003b) & Pekdeger (2006)
Diclofenac	12	12	ng/l	26	23	++	30	30	10	10	Heberer et al.,(2003b) & Pekdeger (2006)
Diclofenac	42	42	ng/l	26	15	++	20	20	5	5	Heberer et al.,(2003b) & Pekdeger (2006)
Diclofenac	31	31	ng/l	26	18	++	<30	29	12	12	Heberer et al.,(2003b) & Pekdeger (2006)
Diclofenac	>81	82	ng/l	26	<5	+	45	45	33	33	Heberer et al.,(2003b) & Pekdeger (2006)
Diclofenac	80	80	µg/l	75	15	+	135	135	90	90	Heberer et al.(2003a)
Diclofenac	>93	94	µg/l	75	<5	+	135	135	90	90	Heberer et al.(2003a)
Diclofenac	87	87	µg/l	75	10	+	135	135	90	90	Heberer et al.(2003a)
Diclofenac	93	93	ng/l	135	10	+	50	50	90	90	(Heberer and Adam 2004)
Diclofenac	>80%	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Diclofenac	>80%	81				+	12-60	36	70	70	Schmidt et al.,2007
Diclofenac	>80%	81				+	45-300	172.5	270	270	Schmidt et al.,2007
Indomethacin	>80%	81				+	5-15	10	125	125	Schmidt et al.,2007
Indomethacin	>99	99.1	ng/l	20	<0.2	+	50	50	90	90	(Heberer and Adam 2004)
Indomethacin	>71	72	ng/l	17	5	++	65	65	40	40	Heberer et al.,(2003b) & Pekdeger (2006)
Indomethacin	>94	95	ng/l	17	Nd	++	30	30	10	10	Heberer et al.,(2003b) & Pekdeger (2006)
Indomethacin	>94	95	ng/l	17	Nd	++	20	20	5	5	Heberer et al.,(2003b) & Pekdeger (2006)
Indomethacin	>94	95	ng/l	17	Nd	++	<30	29	12	12	Heberer et al.,(2003b) & Pekdeger (2006)

Indomethacin	>94	95	ng/l	17	Nd	+	45	45	33	33	Heberer et al.,(2003b) & Pekdeger (2006)
Indomethacin	>99	99.1	ng/l	15	<0.15	+	>120	121	75	75	Heberer, et.al (2004)
Indomethacin	>99	99.1	ng/l	15	<0.15	+	>120	121	100	100	Heberer, et.al (2004)
Indomethacin	>99	99.1	ng/l	15	<0.15	+	>120	121			Heberer, et.al (2004)
Indomethacin	>93	94	ng/l	15	nd	+	>120	121	75	75	Heberer, et.al (2003a)
Indomethacin	>93	94	ng/l	15	nd	+	>120	121	100	100	Heberer, et.al (2003a)
Indomethacin	>93	94	ng/l	15	nd	+	>120	121			Heberer, et.al (2003a)
Indomethacin	>70%	71				+	7-20	14	160	160	Schmidt et al.,2007
Indomethacin	>70%	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Propyphenazone	67	67	ng/l	120	39.6	+	50	50	90	90	(Heberer and Adam 2004)
Propyphenazone	33	33	ng/l	60	40	++	90	90	25	25	Verstraeten et al.(2002b)
Propyphenazone	>98	99	ng/l	60	nd	++	90	90	55	55	Verstraeten et al.(2002b)
Propyphenazone	>98	99	ng/l	60	nd	++	117	117	77	77	Verstraeten et al.(2002b)
Propyphenazone	25	25	ng/l	60	45	+	135	135	90	90	Verstraeten et al.(2002b)
Propyphenazone	33	33	ng/l	60	40	+	135	135	90	90	Verstraeten et al.(2002b)
Propyphenazone	-75	-75	ng/l	60	105	+	135	135	90	90	Verstraeten et al.(2002b)
Propyphenazone	41	41	ng/l	147	86	++	65	65	40	40	Heberer et al., (2003b) & Pekdeger (2006)
Propyphenazone	32	32	ng/l	147	100	++	30	30	10	10	Heberer et al., (2003b) & Pekdeger (2006)
Propyphenazone	50	50	ng/l	147	73	++	20	20	5	5	Heberer et al., (2003b) & Pekdeger (2006)
Propyphenazone	63	63	ng/l	147	54	++	<30	29	12	12	Heberer et al., (2003b) & Pekdeger (2006)
Propyphenazone	81	81	ng/l	147	28	+	45	45	33	33	Heberer et al., (2003b) & Pekdeger (2006)
Propyphenazone	-10	-10	ng/l	145	160	+	>120	121	75	75	Heberer, et.al (2004)
Propyphenazone	79	79	ng/l	145	30	+	>120	121	100	100	Heberer, et.al (2004)
Propyphenazone	28	28	ng/l	145	105	+	>120	121		0	Heberer, et.al (2004)
Propyphenazone	26	26	ng/l	230	170	++	<1	0.9	0	0	Heberer, et.al (2004)
Propyphenazone	-313	-313	ng/l	230	950	++	90	90	40	40	Heberer, et.al (2004)
Propyphenazone	-4	-4	ng/l	230	240	+	135	135	125	125	Heberer, et.al (2004)
Propyphenazone	-26	-26	ng/l	135	170	+	>120	121	75	75	Heberer, et.al (2003a)
Propyphenazone	81	81	ng/l	135	25	+	>120	121	100	100	Heberer, et.al (2003a)
Propyphenazone	41	41	ng/l	135	80	+	>120	121		0	Heberer, et.al (2003a)

Propyphenazone	100	100				++	<3	2	<10	9	Massmann, et.al (2006)
Ibuprofen	>99	99.1				Column 1			2.8	2.8	Snyder et.al (2007)
Ibuprofen	>99	99.1				Column 2			2.8	2.8	Snyder et.al (2007)
Ibuprofen	>99	99.1				Column 3			2.8	2.8	Snyder et.al (2007)
Ibuprofen	>80	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Ibuprofen	>80	81				+	45-300	172.5	270	270	Schmidt et al.,2007
Ibuprofen	>80	81				+	5-15	10	125	125	Schmidt et al.,2007
Naproxen	>98	99				Column 1			2.8	2.8	Snyder et.al (2007)
Naproxen	>98	99				Column 2			2.8	2.8	Snyder et.al (2007)
Naproxen	>98	99				Column 3			2.8	2.8	Snyder et.al (2007)
Naproxen	>80	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Naproxen	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Naproxen	>70	71				+	5-15	10	125	125	Schmidt et al.,2007
Pentoxifyline	>80	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Pentoxifyline	>80	81				+	45-300	172.5	270	270	Schmidt et al.,2007

Appendix A-2: Antibiotics group

Compound	Removal Ratio (%)		Units	Influent	Effluent	Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data				Well	Ref	Input data	Ref	Input data	
Sulfamethoxazole	63	63				++	90	90	30	30	Jekel and Grünheid (2005)
Sulfamethoxazole	91	91				++	90	90	30	30	Jekel and Grünheid (2005)
Sulfamethoxazole	54	54				++	90	90	40	40	Jekel and Grünheid (2005)
Sulfamethoxazole	85	85				++	90	90	40	40	Jekel and Grünheid (2005)
Sulfamethoxazole	69	69				++	117	117	70	70	Jekel and Grünheid (2005)
Sulfamethoxazole	83	83				++	117	117	70	70	Jekel and Grünheid (2005)
Sulfamethoxazole	91	91				+	135	135	95	95	Jekel and Grünheid (2005)
Sulfamethoxazole	98	98				+	135	135	95	95	Jekel and Grünheid (2005)
Sulfamethoxazole	95	95				Column[4]	30	30	125	125	Jekel & Grünheid (2005)
Sulfamethoxazole	97	97	ng/l	224	6.72	++	15	15	20	20	Grünheid and Jekel (2005)
Sulfamethoxazole	46	46	ng/l	224	120.96	++	15	15	1.5	1.5	Grünheid and Jekel (2005)
Sulfamethoxazole	64	64	ng/l	224	80.64	++	72	72		0	Grünheid and Jekel (2005)
Sulfamethoxazole	62	62	ng/l	224	85.12	++	84	84		0	Grünheid and Jekel (2005)
Sulfamethoxazole	96	96	ng/l	224	8.96	+	90	90	75	75	Grünheid and Jekel (2005)
Sulfamethoxazole	8	8	ng/l	485	446.2	++	<1	0.9	2	2	(Grunheid et al., 2005)
Sulfamethoxazole	95	95	ng/l	485	24.25	++	84	84	30	30	(Grunheid et al., 2005)
Sulfamethoxazole	82	82	ng/l	485	87.3	++	90	90	25	25	(Grunheid et al., 2005)
Sulfamethoxazole	70	70	ng/l	485	145.5	++	90	90	55	55	(Grunheid et al., 2005)
Sulfamethoxazole	80	80	ng/l	485	97	++	117	117	77	77	(Grunheid et al., 2005)
Sulfamethoxazole	95	95	ng/l	485	24.25	+	135	135	90	90	(Grunheid et al., 2005)
Sulfamethoxazole	35	35	ng/l	463	300.95	++	4	4	2	2	(Grunheid et al., 2005)
Sulfamethoxazole	42	42	ng/l	463	268.54	++	25	25	10	10	(Grunheid et al., 2005)
Sulfamethoxazole	53	53	ng/l	463	217.61	++	50	50	32	32	(Grunheid et al., 2005)
Sulfamethoxazole	75	75	ng/l	463	115.75	+	50	50	50	50	(Grunheid et al., 2005)
Sulfamethoxazole	0-25	12.5				+	7-20	13.5	160	160	Schmidt et al.,2007
Sulfamethoxazole	0-25	12.5				+	12-60	36	70	70	Schmidt et al.,2007
Sulfamethoxazole	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Sulfamethoxazole	>80	81				+	5-15	10	125	125	Schmidt et al.,2007
Sulfamethoxazole	99	99	ng/l	151	2	+	>120	121	75	75	Heberer et.al 2008
Sulfamethoxazole	99	99	ng/l	152	2	++	~30	30	20	20	Heberer et.al 2008
Sulfamethoxazole	52	52	ng/l	151	72	++	<30	29	1.5	1.5	Heberer et.al 2008
Sulfamethoxazole	75	75	ng/l	151	38	++	60-120	90			Heberer et.al 2008
Sulfamethoxazole	72	72	ng/l	152	43	++	60-120	90			Heberer et.al 2008
Acetyl Sulfamethoxazole	>90	99.1	ng/l	7	nd	+	>120	121	75	75	Heberer et.al 2008
Acetyl Sulfamethoxazole	>99	99.1	ng/l	7	nd	++	~30	30	20	20	Heberer et.al 2008
Acetyl Sulfamethoxazole	>99	99.1	ng/l	7	nd	++	<30	29	1.5	1.5	Heberer et.al 2008

Acetyl Sulfamethoxazole	>99	99.1	ng/l	7	nd	++	60-120	90		0	Heberer et.al 2008
Acetyl Sulfamethoxazole	>99	99.1	ng/l	7	nd	++	60-120	90		0	Heberer et.al 2008
Clarithromycin	>70	71				+	7-20	13.5	160	160	Schmidt et al.,2007
Clarithromycin	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Clarithromycin	>70	71				+	5-15	10	125	125	Schmidt et al.,2007
Clarithromycin	>90	91	ng/l	8.9	nd	+	>120	121	75	75	Heberer et.al 2008
Clarithromycin	>90	91	ng/l	8.9	nd	++	~30	30	20	20	Heberer et.al 2008
Clarithromycin	>90	91	ng/l	8.9	nd	++	<30	29	1.5	1.5	Heberer et.al 2008
Clarithromycin	>90	91	ng/l	8.9	nd	++	60-120	90		0	Heberer et.al 2008
Clarithromycin	>90	91	ng/l	8.9	nd	++	60-120	90		0	Heberer et.al 2008
Roxithromycin	>70	71				+	5-15	10	125	125	Schmidt et al.,2007
Roxithromycin	>90	91	ng/l	11	nd	+	>120	121	75	75	Heberer et.al 2008
Roxithromycin	>98	99	ng/l	11	<LOQ (0.2)	++	~30	30	20	20	Heberer et.al 2008
Roxithromycin	>90	91	ng/l	11	nd	++	<30	29	1.5	1.5	Heberer et.al 2008
Roxithromycin	>90	91	ng/l	11	nd	++	60-120	60		0	Heberer et.al 2008
Roxithromycin	>90	91	ng/l	11	nd	++	60-120	60		0	Heberer et.al 2008
Clindamycin	>80	81				+	7-20	13-Jan	160	160	Schmidt et al.,2007
Clindamycin	>70	71				+	12-60	36	70	70	Schmidt et al.,2007
Clindamycin	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Clindamycin	>70	71				+	5-15	10	125	125	Schmidt et al.,2007
Clindamycin	>98	99	ng/l	31	nd	+	>120	121	75	75	Heberer et.al 2008
Clindamycin	26	26	ng/l	31	23	++	~30	30	20	20	Heberer et.al 2008
Clindamycin	93	93	ng/l	31	2.2	++	<30	29	1.5	1.5	Heberer et.al 2008
Clindamycin	>99.68	99.70	ng/l	31	nd (<0.1)	++	60-120	60		0	Heberer et.al 2008
Clindamycin	>99.68	99.70	ng/l	31	nd (<0.1)	++	60-120	60		0	Heberer et.al 2008
Trimethoprim	>80	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Trimethoprim	>81	81				+	45-300	172.5	270	270	Schmidt et al.,2007
Trimethoprim	>82	81				+	5-15	10	125	125	Schmidt et al.,2007
Trimethoprim	>90	93	ng/l	12	nd	+	>120	121	75	75	Heberer et.al 2008
Trimethoprim	>92	93	ng/l	12	nd	++	~30	30	20	20	Heberer et.al 2008
Trimethoprim	>92	93	ng/l	12	nd	++	<30	29	1.5	1.5	Heberer et.al 2008
Trimethoprim	>92	93	ng/l	12	nd	++	60-120	90			Heberer et.al 2008
Trimethoprim	>92	93	ng/l	12	nd	++	60-120	90			Heberer et.al 2008

+ Production well

++ Monitoring well

Appendix A-3: Beta blockers group

Compound	Removal Ratio (%)		Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data	Well	Ref	Input data	Ref	Input data	
Atenolol	>80	81	+	7-20	13.5	160	160	Schmidt et al.,2007
Atenolol	>80	81	+	45-300	172.5	270	270	Schmidt et al.,2007
Atenolol	>80	81	+	5-15	10	125	125	Schmidt et al.,2007
Metoprolol	>80	81	+	7-20	13.5	160	160	Schmidt et al.,2007
Metoprolol	>80	81	+	12-60	36	70	70	Schmidt et al.,2007
Metoprolol	>80	81	+	45-300	172.5	270	270	Schmidt et al.,2007
Metoprolol	>80	81	+	5-15	10	125	125	Schmidt et al.,2007
Bisoprolol	>70	71	+	7-20	13.5	160	160	Schmidt et al.,2007
Bisoprolol	>70	71	+	5-15	10	125	125	Schmidt et al.,2007
Sotalol	>80	81	+	7-20	13.5	160	160	Schmidt et al.,2007
Sotalol	>80	81	+	12-60	36	70	70	Schmidt et al.,2007
Sotalol	>80	81	+	45-300	172.5	270	270	Schmidt et al.,2007
Sotalol	>80	81	+	5-15	10	125	125	Schmidt et al.,2007

+ Production well

++ Monitoring well

Appendix A-4 : Steroid hormones group

Compound	ID	Removal Ratio (%)		Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
		Reference	Input Data	Well	Ref	Input data	Ref	Input data	
Estradiol	ETD	>99	99.1	Column 1			2.8	2.8	Snyder et.al (2007)
Estradiol	ETD	>99	99.1	Column 2			2.8	2.8	Snyder et.al (2007)
Estradiol	ETD	>99	99.1	Column 3			2.8	2.8	Snyder et.al (2007)
Estradiol	ETD	>99	99.1	++	360	360		0	Mansell and Drewes (2004)
Estradiol	ETD	>99	99.1	++	540	540		0	Mansell and Drewes (2004)
Estradiol	ETD	>99	99.1	++	724	724		0	Mansell and Drewes (2004)
Estradiol	ETD	>99	99.1	++	2920	2920		0	Mansell and Drewes (2004)
Estriol	ETS	>99	99.1	Column 1			2.8	2.8	Snyder et.al (2007)
Estriol	ETS	>99	99.1	Column 2			2.8	2.8	Snyder et.al (2007)
Estriol	ETS	>99	99.1	Column 3			2.8	2.8	Snyder et.al (2007)
Estriol	ETS	>99	99.1	++	360	360		0	Mansell and Drewes (2004)
Estriol	ETS	>99	99.1	++	540	540		0	Mansell and Drewes (2004)
Estriol	ETS	>99	99.1	++	724	724		0	Mansell and Drewes (2004)
Estriol	ETS	>99	99.1	++	2920	2920		0	Mansell and Drewes (2004)
Estrone	ETN	>99	99.1	Column 1			2.8	2.8	Snyder et.al (2007)
Estrone	ETN	>99	99.1	Column 2			2.8	2.8	Snyder et.al (2007)
Estrone	ETN	>99	99.1	Column 3			2.8	2.8	Snyder et.al (2007)
Estrone	ETN	>99	99.1	++	90	90	40	40	Zuehlke et.al (2004)
Estrone	ETN	>99	99.1	+	50	50	90	90	Zuehlke et.al (2004)
Progesteron	PRO	>99	99.1	Column 1			2.8	2.8	Snyder et.al (2007)
Progesteron	PRO	>99	99.1	Column 2			2.8	2.8	Snyder et.al (2007)
Progesteron	PRO	>99	99.1	Column 3			2.8	2.8	Snyder et.al (2007)
Testosterone	TES	>99	99.1	Column 1			2.8	2.8	Snyder et.al (2007)
Testosterone	TES	>99	99.1	Column 2			2.8	2.8	Snyder et.al (2007)
Testosterone	TES	>99	99.1	Column 3			2.8	2.8	Snyder et.al (2007)
Testosterone	TES	>99	99.1	++	360	360		0	Mansell and Drewes (2004)
Testosterone	TES	>99	99.1	++	540	540		0	Mansell and Drewes (2004)
Testosterone	TES	>99	99.1	++	724	724		0	Mansell and Drewes (2004)
Testosterone	TES	>99	99.1	++	2920	2920		0	Mansell and Drewes (2004)

+ Production well

++ Monitoring well

Appendix A-5: Anticonvulsant group

Compound	Removal Ratio (%)		Units	Influent	Effluent	Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data				Well	Ref	Input data	Ref	Input data	
Carbamazepine	15	15	ng/l	583	493	++	<1	0.9	5	5	Mechlinski and Heberer (2005)
Carbamazepine	11	11	ng/l	583	520	++	<1	0.9	2	2	Mechlinski and Heberer (2005)
Carbamazepine	60	60	ng/l	583	235	++	90	90	25	25	Mechlinski and Heberer (2005)
Carbamazepine	49	49	ng/l	583	295	++	90	90	55	55	Mechlinski and Heberer (2005)
Carbamazepine	57	57	ng/l	583	250	++	117	117	77	77	Mechlinski and Heberer (2005)
Carbamazepine	86	86	µg/l	583	80	+	135	135	90	90	Mechlinski and Heberer (2005)
Carbamazepine	34	34	ng/l	329	217	++	65	65	40	40	Heberer et al., (2003b) & Pekdeger (2006)
Carbamazepine	2	2	ng/l	329	323	++	20	20	5	5	Heberer et al., (2003b) & Pekdeger (2006)
Carbamazepine	95	95	ng/l	329	17	*	45	45	33	33	Heberer et al., (2003b) & Pekdeger (2006)
Carbamazepine	0	0				++	<3	2	<10	9	Massmann, et.al (2006)
Carbamazepine	14	14	ng/l	380	328	++	~30	30	20	20	Mechlinski and Heberer (2005)
Carbamazepine	11	11	ng/l	380	340	++	<30	29	1.5	1.5	Mechlinski and Heberer (2005)
Carbamazepine	83	83	ng/l	380	65	+	>120	121	75	121	Mechlinski and Heberer (2005)
Carbamazepine	79	79	ng/l	330	70	+	>120	121	75	121	Heberer, et.al (2004)
Carbamazepine	95	95	ng/l	330	15	+	>120	121	100	121	Heberer, et.al (2004)
Carbamazepine	81	81	ng/l	315	60	+	>120	121	75	75	Heberer, et.al (2003a)
Carbamazepine	95	95	ng/l	315	15	+	>120	121	100	100	Heberer, et.al (2003a)
Carbamazepine	0-25	12.5				+	7-20	13.5	160	160	Schmidt et al.,2007
Carbamazepine	0-25	12.5				+	12-60	36	70	70	Schmidt et al.,2007
Carbamazepine	26-50	32.5				+	45-300	172.5	270	270	Schmidt et al.,2007
Carbamazepine	>80	81				+	5-15	10	125	125	Schmidt et al.,2007
Primidone	26	26	ng/l	135	99.9	+	50	50	90	90	(Heberer and Adam 2004)
Primidone	18	18	ng/l	61	50	++	20	20	5	5	Heberer et al., (2003b) & Pekdeger (2006)
Primidone	5	5	ng/l	61	58	++	<30	29	12	12	Heberer et al., (2003b) & Pekdeger (2006)
Primidone	85	85	ng/l	61	9	+	45	45	33	33	Heberer et al., (2003b) & Pekdeger (2006)
Primidone	45	45	ng/l	55	30	+	>120	121	75	75	Heberer et al. (2003a)
Primidone	91	91	ng/l	55	5	+	>120	121	100	100	Heberer et al. (2003a)

+ Production well

++ Monitoring well

Appendix A-6: X-ray contrast agents group

Compound	Removal Ratio (%)		Units	Influent	Effluent	Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data				Well	Ref	Input data	Ref	Input data	
Iopamidol	26-50	32.5				+	7-20	13.5	160	160	Schmidt et al.,2007
Iopamidol	51-70	60				+	12-60	36	70	70	Schmidt et al.,2007
Iopamidol	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Iopamidol	>80	81				+	5-15	10	125	125	Schmidt et al.,2007
Iopromide	82	82	ng/l	841	151	++	<1	0.9	2	2	Grünheid et al. (2005)
Iopromide	97	97	ng/l	841	25.23	++	84	84	30	30	Grünheid et al. (2005)
Iopromide	96	96	ng/l	841	33.64	++	90	90	25	25	Grünheid et al. (2005)
Iopromide	98	98	ng/l	841	16.82	++	90	90	55	55	Grünheid et al. (2005)
Iopromide	99	99	ng/l	841	8.41	++	117	117	77	77	Grünheid et al. (2005)
Iopromide	98	98	ng/l	841	16.82	+	135	135	90	90	Grünheid et al. (2005)
Iopromide	89	89	ng/l	737	81.07	++	4	4	2	2	Grünheid et al. (2005)
Iopromide	98	98	ng/l	737	14.74	++	25	25	10	10	Grünheid et al. (2005)
Iopromide	99	99	ng/l	737	7.37	++	50	50	32	32	Grünheid et al. (2005)
Iopromide	99	99	ng/l	737	7.37	+	50	50	50	50	Grünheid et al. (2005)
Iopromide	98	98	µg/l	10	0.2	+	90	90	75	75	Grünheid and Jekel (2005)
Iopromide	65	65	ng/l	1102	385.7	++	15	15	1.5	1.5	Grünheid and Jekel (2005)
Iopromide	97	97	ng/l	1102	33.06	++	15	15	20	20	Grünheid and Jekel (2005)
Iopromide	99	99	ng/l	1102	11.02	++	72	72		0	Grünheid and Jekel (2005)
Iopromide	99	99	ng/l	1102	11.02	++	84	84		0	Grünheid and Jekel (2005)

+ Production well

++ Monitoring well

Appendix A-7: Antidepressants group

Compound	Removal Ratio (%)		Source	Distance (well - S/water) (m)		BF Site
	Reference	Input Data	Well	Ref	Input data	
Diazepam	-8	-8	Column 1	2.8	2.8	Snyder et.al (2007)
Diazepam	42	42	Column 2	2.8	2.8	Snyder et.al (2007)
Diazepam	65	65	Column 3	2.8	2.8	Snyder et.al (2007)
Meprobatame	53	53	Column 1	2.8	2.8	Snyder et.al (2007)
Meprobatame	71	71	Column 2	2.8	2.8	Snyder et.al (2007)
Meprobatame	74	74	Column 3	2.8	2.8	Snyder et.al (2007)
Fluoxetine	>99	99.1	Column 1	2.8	2.8	Snyder et.al (2007)
Fluoxetine	>99	99.1	Column 2	2.8	2.8	Snyder et.al (2007)
Fluoxetine	>99	99.1	Column 3	2.8	2.8	Snyder et.al (2007)

+ Production well

++ Monitoring well

Appendix A-8: Lipid regulators group

Compound	Removal Ratio (%)		Units	Influent	Effluent	Source	Travel/ Time (days)		Distance (well - S/water) (m)		BF Site
	Reference	Input Data				Well	Ref	Input data	Ref	Input data	
Bezafibrate	>97	99	ng/l	30	nd	++	50	50	90	90	Heberer and Adam (2004)
Bezafibrate	85	85	ng/l	60	9	++	65	65	40	40	Heberer et al.,(2003b) & Pekdeger (2006)
Bezafibrate	>98	99	ng/l	60	ND	++	30	30	10	10	Heberer et al.,(2003b) & Pekdeger (2006)
Bezafibrate	>98	99	ng/l	60	ND	++	20	20	5	5	Heberer et al.,(2003b) & Pekdeger (2006)
Bezafibrate	>98	99	ng/l	60	ND	++	<30	29	12	12	Heberer et al.,(2003b) & Pekdeger (2006)
Bezafibrate	>98	99	ng/l	60	ND	+	45	45	33	33	Heberer et al.,(2003b) & Pekdeger (2006)
Bezafibrate	>80	81				+	7-20	13.5	160	160	Schmidt et al.,2007
Bezafibrate	>80	81				+	12-60	36	70	70	Schmidt et al.,2007
Bezafibrate	>80	81				+	45-300	172.5	270	70	Schmidt et al.,2007
Bezafibrate	>80	81				+	5-15	10	125	70	Schmidt et al.,2007
Bezafibrate	>98	99	ng/l	60	nd	+	>120	121	75	75	Heberer, et.al (2004)
Bezafibrate	>98	99	ng/l	60	nd	+	>120	121	100	100	Heberer, et.al (2004)
Bezafibrate	>95	96	ng/l	20	nd	++	<1	0.9	0	0	Heberer, et.al (2004)
Bezafibrate	>95	96	ng/l	20	nd	++	90	90	40	40	Heberer, et.al (2004)
Bezafibrate	>75	76	ng/l	20	<5	+	135	135	125	125	Heberer, et.al (2004)
Diethylenetriaminepentaacetic acid (DTPA)	>70	71				+	7-20	13.5	160	160	Schmidt et al.,2007
Diethylenetriaminepentaacetic acid (DTPA)	>70	71				+	12-60	36	70	70	Schmidt et al.,2007
Diethylenetriaminepentaacetic acid (DTPA)	>70	71				+	45-300	172.5	270	270	Schmidt et al.,2007
Diethylenetriaminepentaacetic acid (DTPA)	51-70	60				+	5-15	10	125	125	Schmidt et al.,2007
Clofibric Acid	75	75	ng/l	20	-1480	+	50	50	90	90	(Heberer and Adam 2004)
Clofibric Acid	88	88	ng/l	120	15	++	90	90	25	25	Verstraeten et al.(2002b)
Clofibric Acid	>99	99.1	ng/l	120	nd	++	90	90	55	55	Verstraeten et al.(2002b)
Clofibric Acid	>99	99.1	ng/l	120	nd	++	117	117	77	77	Verstraeten et al.(2002b)
Clofibric Acid	63	63	ng/l	120	45	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	75	75	ng/l	120	30	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	58	58	ng/l	120	50	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	86	86	ng/l	140	20	++	90	90	25	25	Verstraeten et al.(2002b)
Clofibric Acid	>93	94	ng/l	140	<10	++	90	90	55	55	Verstraeten et al.(2002b)
Clofibric Acid	>99	99.1	ng/l	140	nd	++	117	117	77	77	Verstraeten et al.(2002b)
Clofibric Acid	64	64	ng/l	140	50	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	75	75	ng/l	140	35	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	71	71	ng/l	140	40	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	89	89	ng/l	190	20	++	90	90	25	25	Verstraeten et al.(2002b)
Clofibric Acid	63	63	ng/l	190	70	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	53	53	ng/l	190	90	+	135	135	90	90	Verstraeten et al.(2002b)
Clofibric Acid	95	95	ng/l	190	10	+	135	135	90	90	Verstraeten et al.(2002b)

Clofibric Acid	62	62	ng/l	61	23	++	65	65	40	40	Heberer et al.,(2003b) & Pekdeger (2006)
Clofibric Acid	64	64	ng/l	61	22	++	30	30	10	10	Heberer et al.,(2003b) & Pekdeger (2006)
Clofibric Acid	75	75	ng/l	61	15	++	20	20	5	5	Heberer et al.,(2003b) & Pekdeger (2006)
Clofibric Acid	92	92	ng/l	61	5	++	<30	29	12	12	Heberer et al.,(2003b) & Pekdeger (2006)
Clofibric Acid	13	13	ng/l	40	35	++	90	90	40	40	Heberer, et.al (2004)
Clofibric Acid	>70	71				+	12-60	36	70	70	Schmidt et al.,2007
Clofibric Acid	>80	80				+	5-15	10	125	125	Schmidt et al.,2007
Clofibric Acid	63	63	ng/l	120	45	+	135	135	90	90	Scheytt et al. (2004)
Clofibric Acid	75	75	ng/l	140	35	+	135	135	90	90	Scheytt et al. (2004)
Clofibric Acid	95	95	ng/l	190	10	+	135	135	90	90	Scheytt et al. (2004)

+ Production well

++ Monitoring well

Appendix B - Error computation of the model prediction of each QSAR model

Appendix B-1: Error computation of the model prediction of analgesics

Name compound	REM	Predicted Rem	Residual	% Error
Diclofenac	81	80.92	.08	.095
Diclofenac	81	80.92	.08	.095
Diclofenac	81	80.92	.08	.095
Diclofenac	81	80.92	.08	.095
Indomethacin	71	70.57	.43	.613
Indomethacin	71	70.57	.43	.613
Ibuprofen	81	80.95	.05	.063
Ibuprofen	81	80.95	.05	.063
Ibuprofen	81	80.95	.05	.063
Naproxen	81	74.83	6.17	7.623
Naproxen	71	74.83	-3.83	-5.388
Naproxen	71	74.83	-3.83	-5.388
Pentoxifylline	81	80.93	.07	.090
Pentoxifylline	81	80.93	.07	.090
Mean prediction error				-.084 %

Appendix B-2: Error computation of the model prediction of antibiotics

Name Compound	REM	Predicted REM	Residual	% Error
Sulfamethoxazole	63	73.92	-10.92	-17.33
Sulfamethoxazole	91	73.92	17.08	18.77
Sulfamethoxazole	54	73.92	-19.92	-36.88
Sulfamethoxazole	85	73.92	11.08	13.04
Sulfamethoxazole	69	79.15	-10.15	-14.71
Sulfamethoxazole	83	79.15	3.85	4.64
Sulfamethoxazole	91	82.63	8.37	9.19
Sulfamethoxazole	98	82.63	15.37	15.68
Sulfamethoxazole	95	62.30	32.70	34.43
Sulfamethoxazole	65	62.30	2.70	4.16
Sulfamethoxazole	97	59.39	37.61	38.77
Sulfamethoxazole	46	59.39	-13.39	-29.11
Sulfamethoxazole	96	73.92	22.08	23.00
Sulfamethoxazole	8	56.66	-48.66	-608.24
Sulfamethoxazole	95	72.75	22.25	23.42
Sulfamethoxazole	82	73.92	8.08	9.86
Sulfamethoxazole	70	73.92	-3.92	-5.60
Sulfamethoxazole	80	79.15	0.85	1.07
Sulfamethoxazole	95	82.63	12.37	13.02
Sulfamethoxazole	35	57.26	-22.26	-63.60
Sulfamethoxazole	42	61.33	-19.33	-46.02
Sulfamethoxazole	53	66.17	-13.17	-24.85
Sulfamethoxazole	75	66.17	8.83	11.77
Sulfamethoxazole	13	59.10	-46.60	-372.80
Sulfamethoxazole	13	63.46	-50.96	-407.66
Sulfamethoxazole	71	89.90	-18.90	-26.62
Sulfamethoxazole	81	58.42	22.58	27.87
Sulfamethoxazole	99	79.92	19.08	19.27
Sulfamethoxazole	99	62.30	36.70	37.08
Sulfamethoxazole	52	62.10	-10.10	-19.43
Acetyl Sulfamethoxazole	99.1	106.52	-7.42	-7.49
Acetyl Sulfamethoxazole	99.1	88.89	10.21	10.30
Acetyl Sulfamethoxazole	99.1	88.70	10.40	10.50
Clarithromycin	81	82.06	-1.06	-1.31
Clarithromycin	95	112.86	-17.86	-18.79
Clarithromycin	71	81.38	-10.38	-14.62
Clarithromycin	95	102.88	-7.88	-8.29
Clarithromycin	91	85.25	5.75	6.31
Clarithromycin	91	85.06	5.94	6.53
Roxithromycin	71	76.54	-5.54	-7.80

Roxithromycin	99	98.04	0.96	0.97
Roxithromycin	99	80.41	18.59	18.77
Roxithromycin	91	80.22	10.78	11.85
Clindamycin	81	70.59	10.41	12.86
Clindamycin	93	74.94	18.06	19.42
Clindamycin	99	101.38	-2.38	-2.41
Clindamycin	71	69.91	1.09	1.54
Clindamycin	99	91.41	7.59	7.67
Clindamycin	25.81	73.78	-47.97	-185.90
Clindamycin	92.90	73.59	19.32	20.79
Trimethoprim	85	82.97	2.03	2.39
Trimethoprim	96	113.76	-17.76	-18.50
Trimethoprim	81	82.29	-1.29	-1.59
Trimethoprim	95	103.79	-8.79	-9.25
Trimethoprim	93	86.16	6.84	7.35
Trimethoprim	93	85.97	7.03	7.56
Mean prediction error				-26.77

Appendix B-3: Error computation of the model prediction of beta blockers

Name compound	REM	Predicted Rem	Residual	% Error
Atenolol	83	82.36	0.64	.770
Atenolol	87	88.59	-1.59	-1.825
Atenolol	81	82.22	-1.22	-1.511
Metoprolol	82	82.36	-0.36	-.440
Metoprolol	85	83.24	1.76	2.068
Metoprolol	90	88.59	1.41	1.569
Metoprolol	81	82.22	-1.22	-1.511
Bisoprolol	75	73.07	1.93	2.575
Bisoprolol	71	72.93	-1.93	-2.720
Sotalol	82	82.36	-0.36	-.440
Sotalol	86	83.24	2.76	3.207
Sotalol	88	88.59	-0.59	-.668
Sotalol	81	82.22	-1.22	-1.511
Mean prediction error				-.033

Appendix B-4: Error computation of the model prediction of steroid hormones

Name compound	REM	Predicted Rem	Residual	% Error
Estradiol	99.1	99.09911	0.000888	.001
Estradiol	99.1	99.09911	0.000888	.001
Estradiol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.2	99.22324	-0.02324	-.023
Estrone	99.4	99.39008	0.009915	.010
Progesteron	99.1	99.09911	0.000888	.001
Progesteron	99.1	99.09911	0.000888	.001
Progesteron	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Mean error computation				.000

Appendix B-5: Error computation of the model prediction of anticonvulsants

Name compound	REM	Predicted Rem	Residual	% Error
Estradiol	99.1	99.09911	0.000888	.001
Estradiol	99.1	99.09911	0.000888	.001
Estradiol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estriol	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.1	99.09911	0.000888	.001
Estrone	99.2	99.22324	-0.02324	-.023
Estrone	99.4	99.39008	0.009915	.010
Progesteron	99.1	99.09911	0.000888	.001
Progesteron	99.1	99.09911	0.000888	.001
Progesteron	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Testosterone	99.1	99.09911	0.000888	.001
Mean error computation				.000

Appendix B-6: Error computation of the model prediction of x-ray contrasts

Name compound	REM	Predicted Rem	Residual	% Error
Iopamidol	32.50	57.56	-25.06	-77.10
Iopamidol	60.00	59.66	0.34	0.56
Iopamidol	71.00	72.45	-1.45	-2.04
Iopamidol	81.00	57.23	23.77	29.35
Iopromide	82.05	85.33	-3.29	-4.01
Iopromide	97.00	93.12	3.88	4.00
Iopromide	96.00	93.68	2.32	2.42
Iopromide	98.00	93.68	4.32	4.41
Iopromide	99.00	96.21	2.79	2.82
Iopromide	98.00	97.89	0.11	0.11
Iopromide	89.00	85.62	3.38	3.79
Iopromide	98.00	87.59	10.41	10.62
Iopromide	99.00	89.93	9.07	9.16
Iopromide	99.00	89.93	9.07	9.16
Iopromide	98.00	93.68	4.32	4.41
Iopromide	65.00	86.65	-21.65	-33.32
Iopromide	97.00	86.65	10.35	10.66
Iopromide	82.00	86.51	-4.51	-5.51
Iopromide	85.00	88.62	-3.62	-4.26
Iopromide	90.00	101.41	-11.41	-12.67
Iopromide	81.00	86.19	-5.19	-6.40
Iopromide	98.00	97.89	0.11	0.11
Iopromide	95.00	93.68	1.32	1.39
Iopromide	75.00	85.33	-10.33	-13.78
Iomeprol	82.00	82.45	-0.45	-0.54
Iomeprol	85.00	84.55	0.45	0.53
Iomeprol	90.00	97.34	-7.34	-8.15
Iomeprol	81.00	82.12	-1.12	-1.38
Iohexol	82.00	78.38	3.62	4.42
Iohexol	85.00	80.48	4.52	5.31
Iohexol	90.00	93.27	-3.27	-3.63
Iohexol	81.00	78.05	2.95	3.64
Diatrizoate	82.71	72.77	9.94	12.02
Diatrizoate	68.75	68.55	0.20	0.29
Diatrizoate	51.67	60.21	-8.54	-16.53
Mean error computation				-2.00

Appendix B-7: Error computation of the model prediction of antidepressants

Name compound	REM	Predicted Rem	Residual	% Error
Diazepam	42	54.14918	-12.1492	-28.93
Diazepam	65	54.14918	10.85082	16.69
Meprobamate	53	65.42295	-12.423	-23.44
Meprobamate	71	65.42295	5.577049	7.85
Meprobamate	74	65.42295	8.577049	11.59
Fluoxetine	99.1	99.24426	-0.14426	-0.15
Fluoxetine	99.1	99.24426	-0.14426	-0.15
Fluoxetine	99.1	99.24426	-0.14426	-0.15
Mean error computation				-2.08

Appendix B-8: Error computation of the model prediction of lipid regulators

Name compound	REM	Predicted Rem	Residual	% Error
Bezafibrate	82	81.73	0.27	0.33
Bezafibrate	85	83.13	1.87	2.20
Bezafibrate	90	91.64	-1.64	-1.82
Bezafibrate	81	81.51	-0.51	-0.63
Diethylenetriaminepentaacetic acid (DTPA)	71	68.73	2.27	3.20
Diethylenetriaminepentaacetic acid (DTPA)	75	70.13	4.87	6.49
Diethylenetriaminepentaacetic acid (DTPA)	80	78.64	1.36	1.70
Diethylenetriaminepentaacetic acid (DTPA)	60	68.51	-8.51	-14.19
Clofibric Acid	71	76.30	-5.30	-7.46
Clofibric Acid	80	74.67	5.33	6.66
Mean error computation				-0.35

Appendix C: CD Containing Calculated Molecular Descriptors

Appendix D: Analysis of Literature Database

Appendix D1: Removal efficiencies of different class of pharmaceutically active compounds during soil/aquifer-based natural treatment

Therapeutic use	Compound	Removal efficiencies (%)				References
		Low (<25%)	Moderately low (26-50)	Relatively high (51-79)	High (>80)	
Antibiotics	Sulfamethoxazole	Rhine A (0-25), Rhine B (0-25), Lake Tegel-LBF[27] (8),	Lake Wannsee[13] (46), Lake Tegel-ARR[5] (35), Lake Tegel-ARR[6] (42)	Lake Tegel-ARR[1] (75), Lake Tegel-ARR[7] (53), Elbe (>70), Lake Wannsee[15] (64), Lake Wannsee[16] (62), Lake Wannsee[19] (52), Lake Wannsee[20] (75), Lake Wannsee[21] (72), Column[5](65), Lake Tegel-LBF[14] (63), Lake Tegel-LBF[16] (54), Lake Tegel-LBF[18] (69), Lake Tegel-LBF[31] (70)	Lake Wannsee[3] (99), Lake Tegel-LBF[1] (95), Ruhr (>80), Lake Wannsee[14] (97), Lake Wannsee[17] (96), Lake Wannsee[18] (99), Column[4](95), Lake Tegel-LBF[15] (91), Lake Tegel-LBF[17] (85), Lake Tegel-LBF[19] (83), Lake Tegel-LBF[20] (91), Lake Tegel-LBF[21] (98), Lake Tegel-LBF[1] (95), Lake Tegel-LBF[28] (95), Lake Tegel-LBF[29] (82), Lake Tegel-LBF[31] (80),	Grünheid et al. (2005) Schmidt et al. (2007) Heberer et al. (2008) Grünheid and Jekel (2005) Jekel and Grünheid (2005)
	Acetyl-sulfamethoxazole				Lake Wannsee[3] (>90), Lake Wannsee[18] (>99), Lake Wannsee[19] (>99), Lake Wannsee[20] (>99), Lake Wannsee[21] (>99)	Heberer et al. (2008)
	Clarithromycin			Rhine A (>70), Elbe (>70), Ruhr (>70)	Lake Wannsee[3] (>90), Lake Wannsee[18] (>90), Lake Wannsee[19] (>90), Lake Wannsee[20] (>90), Lake Wannsee[21] (>90)	Schmidt et al. (2007) Heberer et al. (2008)
	Roxithromycin			Ruhr (>70)	Lake Wannsee[3] (>90),Lake Wannsee[18] (>98), Lake Wannsee[19] (>90), Lake Wannsee[20] (>90), Lake Wannsee[21] (>90)	Schmidt et al. (2007) Heberer et al. (2008)
	Trimethoprim				Lake Wannsee[3] (>90), Lake Wannsee[18] (>92), Lake Wannsee[19] (>92), Lake Wannsee[20] (>92), Lake Wannsee[21] (>92), Rhine A (>80), Elbe (>80), Ruhr (>80)	Heberer et al. (2008) \ Schmidt et al. (2007)
	Clindamycin		Lake Wannsee[18] (26)	Rhine B (>70), Elbe (>70), Ruhr (>70)	Lake Wannsee[3] (>98), Lake Wannsee[19] (93), Lake Wannsee[20] (>99.68), Lake Wannsee[21] (>99.68), Rhine A (>80)	Heberer et al. (2008) Schmidt et al. (2007)
Non-steroidal anti-inflammatory drugs (NSAID) and analgesics	Diclofenac	Lake Wannsee[8] (-8), Lake Wannsee[9] (12), Lake Tegel-LBF[11] (-33), Lake Tegel-LBF[12](-133)	Lake Wannsee[10] (42), Lake Wannsee[11] (31)	Column 1 (67), Lake Wannsee[4] (60), Tegel-LBF[13](>67)	Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80), Lake Tegel-ARR[3] (93), Column 2(>99), Column 3 (>99), Lake Wannsee[5] (>80), Lake Wannsee[6] (80), Lake Wannsee[12] (>81), Lake Wannsee[24] (80), Lake Wannsee[25] (>93), Lake Wannsee[26] (87)	Heberer and Adam (2004) Snyder et al. (2007) Schmidt et al. (2007) Heberer et al. (2004) Heberer et al.,(2003b) & Pekdeger (2006) Heberer et al. (2004), Heberer et al.(2003a)
	Ibuprofen				Rhine A (>80), Elbe (>80), Ruhr (>80), Column 1 (>99), Column 2(>99), Column 3 (>99)	Schmidt et al. (2007) Snyder et al. (2007)

	Indomethacin			Rhine A (>70), Elbe (>70), Lake Wannsee[8] (>71)	Lake Tegel-ARR[3] (>95), Lake Wannsee-well[4] (>99), Lake Wannsee-well[5] (>99), Lake Wannsee-well[6] (>99), Lake Wannsee[9] (>94), Lake Wannsee[10] (>94), Lake Wannsee[11] (>94), Lake Wannsee[12] (>94), Lake Wannsee[24](>93), Lake Wannsee[25] (>93), Lake Wannsee[26] (>93)	Schmidt et al. (2007), Heberer and Adam (2004) Heberer et al. (2004) Heberer et al.,(2003b) & Pekdeger (2006) Heberer et al.(2003a)
	Naproxen			Elbe (>70), Ruhr (>70)	Rhine A (>80), Column 1 (>98), Column 2 (>98), Column 3 (>98)	Schmidt et al. (2007) Snyder et al. (2007)
	Phenazone	Lake Wannsee[2] (10)		Lake Wannsee[1] (66)	Lake Tegel-ARR[4] (90)	Massmann et al. (2006) Massmann et al. (2008)
	FAA (formylaminoantipyrine)		Lake Wannsee[2] (36)	Lake Wannsee[1] (72)	Lake Tegel-ARR[4] (89)	Massmann et al. (2006) Massmann et al. (2008)
	AAA (acetoaminoantipyrine)		Lake Wannsee[2] (45)		Lake Wannsee[1] (90), Lake Tegel-ARR[4] (96)	Massmann et al. (2006) Massmann et al. (2008)
	AMDOPH (1-acetyl-1-methyl-2-dimethyloxamoyl-2-phenylhydrazide)	Lake Wannsee[1] (0), Lake Wannsee[2] (0), Lake Tegel-ARR[4] (0)				Massmann et al. (2006) Massmann et al. (2008)
	Propyphenazone	Lake Wannsee[4] (-10), Lake Tegel-LBF[12] (-313), Lake Tegel-LBF[13] (-4), Lake Lake Tegel-LBF[37] (-75), Lake Wannsee[24] (-26)	Lake Wannsee[6](28) Lake Wannsee[8] (41), Lake Wannsee[9] (32), Lake Wannsee[10] (50), Lake Tegel-LBF[11] (26) Lake Tegel-LBF[32] (33), Tegel-LBF[35] (25), Lake Tegel-LBF[36] (33), Lake Wannsee[26] (41)	Lake Tegel-ARR[3] (67), Lake Wannsee[5] (79), Lake Wannsee[11] (63)	Lake Tegel-ARR[4] (100), Lake Wannsee[12] (81), Lake Tegel-LBF[33] (>98), Lake Tegel-LBF[34](>98), Lake Wannsee[25] (81)	Heberer and Adam (2004) Massmann et al. (2006) Massmann et al. (2008) Heberer et al. (2004) Heberer et al.,(2003b) & Pekdeger (2006), Verstraeten et al.(2002b)
	Pentoxifyline				Rhine A (>80), Elbe (>80),	Schmidt et al. (2007)
Anticonvulsants	Carbamazepine	Rhine A (0-25), Rhine B (0-25), Lake Tegel-ARR[4] (0), Column 1 (-3), Column 2 (22), Column 3 (13), Lake Tegel-LBF[9] (15), Lake Tegel-LBF[22](11), Lake Wannsee[7](11) Lake Wannsee[9] (-11), Lake Wannsee[22](14), Lake Wannsee[10] (2), Lake Wannsee[11] (-10)	Tegel-LBF[24](49), Lake Wannsee[8] (34)	Elbe (51-70), Lake Wannsee[4] (79), Tegel-LBF[23](60), Tegel-LBF[25](57)	Ruhr (>80), Lake Wannsee[5] (95), Lake Wannsee[6] (91), Lake Wannsee[12] (95), Lake Wannsee[23](83), Lake Wannsee[24](81), Lake Wannsee[25](95), Lake Wannsee[26](90), Lake Tegel-LBF[26](86),	Massmann et al. (2006) Schmidt et al. (2007) Snyder et al. (2007) Mechlinski &Heberer (2005) Heberer et al. (2004) Heberer et al.,(2003b) & Pekdeger (2006) Heberer et al.,(2003a)
	Dilantin	Column 1 (-11), Column 3 (22)	Column 2 (28)			Snyder et al. (2007)

Appendix D1 (continued)

Therapeutic use	Compound	Removal efficiencies (%)				References
		Low (<25%)	Moderately low (26-50)	Relatively high (51-79)	High (>80)	
	Primidone	Tucson (0), Lake Wannsee[8] (-11), Lake Wannsee[9] (-2), Lake Wannsee[10] (18), Lake Wannsee[11] (5)	Lake Wannsee[4] (33), Lake Wannsee[6] (42), Lake Tegel-ARR[3] (26), e Wannsee[24] (45), Lake Wannsee[26] (45),		Lake Wannsee[5] (83), Lake Wannsee[12] (85), Lake Wannsee[25] (91)	Heberer and Adam (2004) Heberer et al. (2004) Drewes et al. (2002) Heberer et al.,(2003b) & Pekdeger (2006), Heberer et al.(2003a)
Antidepressants	Meprobamate			Column 1 (53), Column 2 (71), Column 3 (74)		Snyder et al. (2007)
	Fluoxetine				Column 1 (>99), Column 2 (>99), Column 3 (>99)	Snyder et al. (2007)
	Diazepam	Column 1 (-8),	Column 2 (42),	Column 2 (65),		Snyder et al. (2007)
Beta blockers	Atenolol				Rhine A (>80), Elbe (>80), Ruhr (>80)	Schmidt et al. (2007)
	Metoprolol,				Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80)	Schmidt et al. (2007)
	Bisoprolol			Rhine A (>70), Ruhr (>70)		Schmidt et al. (2007)
	Sotalol				Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80)	Schmidt et al. (2007)
Lipid regulators	Bezafibrate			Lake Tegel-LBF[13](>75)	Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80), Lake Tegel-ARR[3] (>97) Lake Wannsee[8] (95%), Lake Wannsee[9] (>98), Lake Wannsee[10] (>98), Lake Wannsee[11] (>98), Lake Wannsee[12] (>98), Lake Wannsee[4] (>98), Lake Wannsee[5] (>98), Lake Wannsee[6] (>98), Lake Tegel-LBF[11](>95), Lake Tegel-LBF[12](>95)	Heberer and Adam (2004) Schmidt et al. (2007) Heberer et al.,(2003b) & Pekdeger (2006) Heberer et al. (2004)
	Fenofibric acid			Rhine A (>70), Rhine B (>70)		Schmidt et al. (2007)
	Clofibric acid	Lake Tegel-LBF[3](-20), Lake Wannsee[4] (-58), Lake Wannsee[5] (-92), Lake Wannsee[6] (-108) Lake Wannsee[12](-85), Lake Tegel-LBF[12](13), Lake Tegel-LBF[13](-25), Lake Tegel-LBF[33](-26), Lake Tegel-LBF[34](-53),		Lake Tegel-ARR[3] (75), Lake Tegel-LBF[4](63), Lake Tegel-LBF[5](75), Lake Wannsee[8] (62), Lake Wannsee[9] (64), Lake Wannsee[10] (75), Lake Tegel-LBF[35](63,64,63), Lake Tegel-LBF[36](75,75,53), Lake Tegel-LBF[37](58,71),	Ruhr (>80) Lake Tegel-LBF[11](88),Lake Tegel-LBF[6](95), Lake Wannsee[11] (92), Lake Tegel-LBF[32](88,86,89), Lake Tegel-LBF[33](>99, >93), Lake Tegel-LBF[34](>99, >99), Lake Tegel-LBF[37](95),	Heberer and Adam (2004) Heberer et al. (2004) Schmidt et al. (2007) Scheytt et al. (2004) Heberer et al.,(2003b) & Pekdeger (2006) Verstraeten et al.(2002b)

	Gemfibrozil				Column 1 (>99), Column 2 (>99), Column 3 (>99)	Snyder et al. (2007)
	DTPA (Diethylenetriaminepentaacetic acid)			Rhine A (>70), Rhine B (>70), Elbe (>70), Ruhr (>51)		Schmidt et al. (2007)
X-ray contrast media	AOI		Lake Tegel-ARR[1] (30)	Lake Tegel-LBF[1] (60), Lake Tegel-LBF[7] (63)		Grünheid et al. (2005) Schittko et al. (2004)
	Iopromide			Column 1 (64), Lake Tegel-LBF[8] (75), Wannsee[13] (65)	Lake Tegel-LBF[1] (98), Lake Tegel-LBF[7] (95), Lake Tegel-LBF[27] (82), Lake Tegel-LBF[28](97), Lake Tegel-LBF[29] (96), Lake Tegel-LBF[30] (98), Lake Tegel-LBF[31] (99), Lake Tegel-ARR[1] (99), Lake Tegel-ARR[5] (89), Lake Tegel-ARR[6] (98), Lake Tegel-ARR[7] (99), Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80), Column 2(93), Column 3 (95), Lake Wannsee[14] (97), Lake Wannsee[15] (99), Lake Wannsee[16] (99), Wannsee[17] (98)	Grünheid et al. (2005) Schmidt et al. (2007) Snyder et al. (2007) Schittko et al. (2004) Grünheid and Jekel (2005)
	Iopamidol	Rhine A (0-25)	Rhine B (26-50)	Elbe (>70)	Ruhr (>80)	Schmidt et al. (2007)
	Iomeprol				Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80)	Schmidt et al. (2007)
	Ioxhexol				Rhine A (>80), Rhine B (>80), Elbe (>80), Ruhr (>80)	Schmidt et al. (2007)
	Diatrizoate			Lake Tegel-LBF[7] (69), Lake Tegel-LBF[8] (52)	Lake Tegel-LBF[10] (83)	Schittko et al. (2004)
Psycho-stimulant	Caffeine				Column 1 (95), Column 2(97), Column 3 (98)	Snyder et al. (2007)
Steroid hormone	Estradiol (E2)				Column 1 (>99), Column 2 (>99), Column 3 (>99), NW2 (>99), NW4(>99), 2U(>99%), 6U(>99%)	Mansell and Drewes (2004), Snyder et al. (2007)
	Estriol (E3)				Column 1 (>99), Column 2 (>99), Column 3 (>99), NW2 (>99), NW4(>99), 2U(>99%), 6U(>99%)	Mansell and Drewes (2004), Snyder et al. (2007)
	Estrone (E1)				Lake Tegel-LBF[2] (>99), Lake Tegel-ARR[2] (>99), Column 1 (>99), Column 2 (>99), Column 3 (>99),	Zuehlke et al. (2004) Snyder et al. (2007)
	Progesterone,				Column 1 (>99), Column 2 (>99), Column 3 (>99)	Snyder et al. (2007)
	Testosterone				Column 1 (>99), Column 2 (>99), Column 3 (>99), NW2 (>99), NW4(>99), 2U(>99%), 6U(>99%)	Mansell and Drewes (2004), Snyder et al. (2007)
Complexing Agent	EDTA	Elbe (0-25), Ruhr (0-25)		Rhine A (51-70), Rhine B (51-70),		Schmidt et al. (2007)

Appendix D2: Well types, travel distances, residence times, redox conditions for BF and ARR sites described in Appendix D1

Name	Type	Source/well	Distance (m)	Residence time (d)	Redox conditions	References
Lake Tegel-LBF[1]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Grünheid et al. (2005)
Lake Tegel-LBF[2]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Zuehlke et al. 2004
Lake Tegel-LBF[3]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Heberer et al. (2004)
Lake Tegel-LBF[4]	LBF	Lake Tegel/12^{+}	90	135	Anoxic	Scheytt et al. (2004)
Lake Tegel-LBF[5]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Scheytt et al. (2004)
Lake Tegel-LBF[6]	LBF	Lake Tegel/14^{+}	90	135	Anoxic	Scheytt et al. (2004)
Lake Tegel-LBF[7]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Schittko et al. (2004)
Lake Tegel-LBF[8]	LBF	Lake Tegel/3311^{++}	5	<1	Oxic	Schittko et al. (2004)
Lake Tegel-LBF[9]	LBF	Lake Tegel/3311^{++}	5	<1	Oxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[10]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Schittko et al. (2004)
Lake Tegel-LBF[11]	LBF	Lake Tegel/3311^{++}	5	<1	Oxic	Heberer et al. (2004)
Lake Tegel-LBF[12]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Heberer et al. (2004)
Lake Tegel-LBF[13]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Heberer et al. (2004)
Lake Tegel-LBF[14]	LBF	Lake Tegel/3301^{++}	40	90	Oxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[15]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[16]	LBF	Lake Tegel/3302^{++}	70	90	Oxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[17]	LBF	Lake Tegel/3302^{++}	70	90	Anoxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[18]	LBF	Lake Tegel/3303^{++}	77	117	Oxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[19]	LBF	Lake Tegel/3303^{++}	77	117	Anoxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[20]	LBF	Lake Tegel/13^{+}	90	135	Oxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[21]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Jekel and Grünheid (2005)
Lake Tegel-LBF[22]	LBF	Lake Tegel/3310^{++}	2	<1	Oxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[23]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[24]	LBF	Lake Tegel/3302^{++}	55	90	Anoxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[25]	LBF	Lake Tegel/3303^{++}	77	117	Anoxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[26]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Mechlinski and Heberer (2005)
Lake Tegel-LBF[27]	LBF	Lake Tegel/3310^{++}	2	<1	Oxic	Grünheid et al. (2005)
Lake Tegel-LBF[28]	LBF	Lake Tegel/371UP^{++}	30	84	Anoxic	Grünheid et al. (2005)
Lake Tegel-LBF[29]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Grünheid et al. (2005)
Lake Tegel-LBF[30]	LBF	Lake Tegel/3302^{++}	55	90	Anoxic	Grünheid et al. (2005)
Lake Tegel-LBF[31]	LBF	Lake Tegel/3303^{++}	77	117	Anoxic	Grünheid et al. (2005)
Lake Tegel-LBF[32]	LBF	Lake Tegel/3301^{++}	40	90	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-LBF[33]	LBF	Lake Tegel/3302^{++}	55	90	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-LBF[34]	LBF	Lake Tegel/3303^{++}	77	117	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-LBF[35]	LBF	Lake Tegel/12^{+}	90	135	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-LBF[36]	LBF	Lake Tegel/13^{+}	90	135	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-LBF[37]	LBF	Lake Tegel/14^{+}	90	135	Anoxic	Verstraeten et al.(2002b)
Lake Tegel-ARR[1]	ARR	Lake Tegel/well20^{+}	50	50	Oxic	Grünheid et al. (2005)
Lake Tegel-ARR[2]	ARR	Lake Tegel/$^{+}$	90	50	Oxic	Zuehlke et al. (2004)
Lake Tegel-ARR[3]	ARR	Lake Tegel/$^{+}$	90	50	Oxic	Heberer and Adam (2004)
Lake Tegel-ARR[4]	ARR	Lake Tegel/TEG365^{++}	<10	<3	Oxic	Massmann et al. (2006)
Lake Tegel-ARR[5]	ARR	Lake Tegel/365^{++}	2	4	Oxic	Grünheid et al. (2005)
Lake Tegel-ARR[6]	ARR	Lake Tegel/368UP^{++}	10	25	Oxic	Grünheid et al. (2005)

Lake Tegel-ARR[7]	ARR	Lake Tegel/369UP^{++}	32	50	Oxic	Grünheid et al. (2005)
Lake Wannsee[1]	LBF	Lake Wannsee /BE206^{++}	1.5	<30	Oxic	Massmann et al. (2008)
Lake Wannsee[2]	LBF	Lake Wannsee /BE205^{++}	20	~30	Anoxic	Massmann et al. (2008)
Lake Wannsee[3]	LBF	Lake Wannsee /well#3^{+}	75	>120	Anoxic	Heberer et al. (2008)
Lake Wannsee[4]	LBF	Lake Wannsee /well#3^{+}	75	>120	Anoxic	Heberer et al. (2004)
Lake Wannsee[5]	LBF	Lake Wannsee /well#4^{+}	100	>120	Anoxic	Heberer et al. (2004)
Lake Wannsee[6]	LBF	Lake Wannsee /well#5^{+}		>120	Anoxic	Heberer et al. (2004)
Lake Wannsee[7]	LBF	Lake Wannsee /BE206^{++}	1.5	<30	Oxic	Mechlinski and Heberer (2005)
Lake Wannsee[8]	LBF	Lake Wannsee /3339^{++}	40	65	Oxic	Heberer et al.,(2003b) & Pekdeger (2006)
Lake Wannsee[9]	LBF	Lake Wannsee /3338^{++}	10	30	Oxic	Heberer et al.,(2003b) & Pekdeger (2006)
Lake Wannsee[10]	LBF	Lake Wannsee /3337^{++}	5	20	Oxic	Heberer et al.,(2003b) & Pekdeger (2006)
Lake Wannsee[11]	LBF	Lake Wannsee /3335^{++}	16	<30	Oxic	Heberer et al.,(2003b) & Pekdeger (2006)
Lake Wannsee[12]	LBF	Lake Wannsee /Br#4^{+}	33	45	Anoxic	Heberer et al.,(2003b) & Pekdeger (2006)
Lake Wannsee[13]	LBF	Lake Wannsee /BE206^{++}	1.5	15	Oxic	Grünheid and Jekel (2005)
Lake Wannsee[14]	LBF	Lake Wannsee /BE205^{++}	20	15	Anoxic	Grünheid and Jekel (2005)
Lake Wannsee[15]	LBF	Lake Wannsee /BE202OP^{++}		72	Oxic	Grünheid and Jekel (2005)
Lake Wannsee[16]	LBF	Lake Wannsee /BE203^{++}		84	Oxic	Grünheid and Jekel (2005)
Lake Wannsee[17]	LBF	Lake Wannsee / well#3^{+}	75	90	Anoxic	Grünheid and Jekel (2005)
Lake Wannsee[18]	LBF	Lake Wannsee / BE205^{++}	20	~30	Anoxic	Heberer et al. (2008)
Lake Wannsee[19]	LBF	Lake Wannsee /BE206^{++}	1.5	<30	Oxic	Heberer et al. (2008)
Lake Wannsee[20]	LBF	Lake Wannsee /BE202OP^{++}		60-120	Oxic	Heberer et al. (2008)
Lake Wannsee[21]	LBF	Lake Wannsee /BE203^{++}		60-120	Oxic	Heberer et al. (2008)
Lake Wannsee[22]	LBF	Lake Wannsee /BE205^{++}	20	~30	Anoxic	Mechlinski and Heberer (2005)
Lake Wannsee[23]	LBF	Lake Wannsee /well#3^{+}	75	>120	Anoxic	Mechlinski and Heberer (2005)
Lake Wannsee[24]	LBF	Lake Wannsee /well#3^{+}	75	>120	Anoxic	Heberer et al.(2003a)
Lake Wannsee[25]	LBF	Lake Wannsee /well#4^{+}	100	>120	Anoxic	Heberer et al.(2003a)
Lake Wannsee[26]	LBF	Lake Wannsee /well#5^{+}		>120	Anoxic	Heberer et al.(2003a)
Rhine A	RBF	Rhine/$^{+}$	160	7-20	Oxic	Schmidt et al. (2007)
Rhine B	RBF	Rhine/$^{+}$	70	12-60	Anoxic	Schmidt et al. (2007)
Elbe	RBF	Elbe/$^{+}$	270	45-300	Anoxic	Schmidt et al. (2007)
Ruhr	RBF	Ruhr/$^{+}$	125	5-15	Anoxic	Schmidt et al. (2007)
Tucson	ARR	WR-205		2190		Drewes et al. (2002)
NW2	ARR	Tertiary effluent/$^{++}$		360		Mansell and Drewes (2004)
NW4	ARR	Tertiary effluent/$^{++}$		540		Mansell and Drewes (2004)
2U	ARR	Tertiary effluent/$^{++}$		724		Mansell and Drewes (2004)
6U	ARR	Tertiary effluent/$^{++}$		2920		Mansell and Drewes (2004)
Column1, 2, 3	column	Colorado River water	2.8			Snyder et al. (2007)
Column 4	Column	Lake Tegel water	30	30	Oxic	Jekel and Grünheid (2005)
Column 5	Column	Lake Tegel water	30	30	Anoxic	Jekel and Grünheid (2005)

+ Production well ; ++ Monitoring welL