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Table of contents

1	Conclusion and Outlook.....	5
2	Introduction	8
3	Revision of literature on PPs and procedure of data evaluation	9
3.1	Consumption behaviour of PPs in European Countries.....	9
3.2	Exposure data	11
4	Results and Discussion of the data evaluation	13
4.1	MEC/PEC-Comparison.....	13
4.2	PPs as indicator substances	20
4.2.1	Identification of indicators for wastewater originated contamination of the environment.....	20
4.2.2	Identification of indicators for basic removal of polar contaminants in Wastewater treatment.....	22
4.2.3	Input of veterinary PPs.....	23
4.2.4	Input of PPs from hospitals	26
4.2.5	Indicators for contamination of ground- and drinking water with wastewater	27
5	Data gaps.....	30
5.1	Availability and comparability of data for environmental exposure.....	30
5.2	New PP candidates for environmental analysis	30
6	Minutes of the Knappe Workshop	32
7	List of abbreviations and acronyms	34
8	References	35
9	Annex I: Measured environmental concentrations of pharmaceuticals in the aquatic environment.....	39
10	Annex II: Consumption of PPs in 5 European countries	69
11	Annex III: Predicted environmental concentrations (PEC) in raw sewage water and surface water.....	75
12	Annex IV: Removal behaviour of PPs in sewage treatment plants (WWTP).....	82
13	Annex V: References of the data compilation	85

Tables

Table 1: Mean annual consumption of selected pharmaceuticals in metric tons for France, Germany, Poland, Spain and the UK (England, Wales). Data available for the period from 1999-2006.....	10
Table 2: Average annual consumption of selected pharmaceuticals in g per person and year for France, Germany, Poland, Spain and the UK. Data available for the period from 1999-2006	10
Table 3: Numbers of measured occurrence data in the WP1 - data compilation for aquatic matrices in different countries	11
Table 4 :Rating of PEC/A-MEC-ratios	15
Table 5: Comparison of PEC/A-MEC values: WWTP influent.....	17
Table 6: Comparison of PEC/A-MEC values: WWTP effluent.....	18
Table 7: Comparison of PEC/A-MEC values: surface water.....	19
Table 8: Pharmaceutical agents eligible as environmental indicator compounds for the share of treated wastewater (average $PNR_i \approx 1$)	22
Table 9: Pharmaceutical agents eligible as environmental indicator compounds for the presence of raw or insufficiently treated wastewater (average $PNR_i < 0.2$)	22
Table 10: Occurrence of antibiotics for veterinary use in surface and ground water.	25
Table 11: PPs with $PEC_{WWTPinf}$ higher than 1 $\mu\text{g/L}$, for which measurements in the aquatic environment in Europe have not been reported.	31
Table 12: Compounds undergoing major phase I metabolism	31
Table A-I. 1: Averaged environmental concentrations (A-MEC) and maximal concentrations of pharmaceuticals measured in surface water, wastewater treatment plant influent and effluent.	39
Table A-I. 2: Averaged environmental concentrations (A-MEC) and maximal concentrations of pharmaceuticals measured in ground water, bank filtrate, drinking water, and marine water.....	56
Table A-II. 1: Annual consumption of pharmaceuticals in g per year and person for France, Germany, Poland, Spain and the UK (Average of 1999-2006).	69
Table A-II. 2: Average annual consumption of pharmaceuticals in metric tons for France, Germany, Poland, Spain and the UK. Data available for the period from 1999-2006 were averaged.	72
Table A-III. 1: Predicted environmental concentrations (PEC) of pharmaceuticals in raw sewage water (WWTP influent) calculated for France, Germany, Poland, Spain and the UK from the consumption data given in Annex I (PECa: PEC calculated without excreted PP fraction ($E=1$), PECb: PEC calculated with excreted PP fraction).....	75
Table A-III. 2: Predicted environmental concentrations (PEC) of pharmaceuticals in surface water (SW) calculated for France, Germany, Poland, Spain and the UK from the consumption data given in Annex I. (PECa: PEC calculated without excreted PP fraction ($E=1$), PECb: PEC calculated with excreted PP fraction).	80
Table A-IV. 1: Number of measured samples and average removal of PPs in wastewater treatment plants	82

STATUS, CONFIDENTIALITY AND ACCESSIBILITY							
Status			Confidentiality			Accessibility	
S0	Approved/Released		R0	General public		Work-space	
S1	Reviewed		R1	Restricted to SWIFT6WFD members		Internet	
S2	Pending for review		R2	Restricted to European. Commission	x	Paper	x
S3	Draft for comments	X					
S4	Under preparation						

1 Conclusion and Outlook

Within WP 1 of the Knappe project an extensive data compilation on the environmental occurrence of PPs was created, containing 58400 measurements of 178 pharmaceutical products in 22 countries in WWTPinfluent, WWTPeffluent, surface water, groundwater, bank filtrate, marine water and drinking water. Average mean environmental concentration (AMECs) were calculated from the compiled data for each PP, characterizing the exposure situation in the seven compartments of the aquatic environment in each country, from which measurements were available.

Additionally, consumption data of PPs for five European countries (France, Germany, Poland, Spain and the UK) was used to predict their environmental concentrations following the approach used in the EU-Project Poseidon. A comparison revealed that predicted and averaged measured environmental concentrations matched well for WWTPinfluent. For WWTPeffluent and surface water the agreement of the data was limited to some extent, as consumption data was frequently lacking the PPs used in freely available OTC-products. Furthermore, transformation processes in surface waters were not covered by the prediction model.

The data compilation was used to establish a set of indicator substances for the determination of the wastewater share in surface waters and for determining whether a water body is influenced by poorly or raw wastewater.

Indicator substances for the determination of the wastewater share are:

- Diatrizoate (iodinated X-ray contrast medium)
- Iopamidol (iodinated X-ray contrast medium)
- Carbamazepine (antiepileptic)
- Erythromycin (Antibiotic)¹
- Metoprolol (betablocker)

¹ Usage of the sum of erythromycin and anhydro-erythromycin is recommended.

Surface waters contaminated with these compounds are expected to contain a variety of other polar persistent organic compounds, which were also not removed during wastewater treatment.

Indicator substances showing the presence of non- or poorly treated wastewater are:

- Ibuprofen (Analgesic)
- Paracetamol (Analgesic)
- Salicylic acid (Analgesic)
- Bezafibrate (Lipid regulator)

The presence of these indicator substances which are readily (bio)degradable in wastewater treatment, in surface waters indicate the input of non- or poorly treated wastewater with potential consequences for water quality and water usage, concerning pollutants and pathogens.

No PPs could be classified as indicator substances specific for the input from hospitals or veterinary medicine. Potential indicator substances for hospital input either lacked the specificity of only being used and excreted in a hospital environment or their environmental concentrations were too low for a reliable quantification.

Due to the different registration situation in the various countries, with deviating and/or overlapping use in human and veterinary medicine, no pharmaceutical compounds are in general fully attributable to veterinary purposes only.

Indicator substances expected to be present in groundwater which influenced by wastewater are the following, all being relatively polar and persistent:

- Diatrizoate (iodinated X-ray contrast medium)
- Iopamidol (iodinated X-ray contrast medium)
- Carbamazepine (antiepileptic)
- Sulfamethoxazole (Antibiotic)

Currently, the available data on the consumption and the occurrence of PPs in the aquatic environment on a European level is of very limited comparability.

Efforts should be made to achieve a common book keeping system on the usage of all pharmaceutical products within the EU, including prescribed PPs, OTC drugs, and all compounds used for diagnosis and in hospitals.

The available environmental exposure data on PPs is very limited in quantity, concerning the diversity of PPs, their metabolites and environmental transformation products, the numbers of available measurements in the different aquatic/marine compartments being measured and concerning data quality, concerning sampling, analysis and data evaluation.

Future monitoring studies should close the existing data gaps in the current knowledge and overcome the challenge of data comparability.

2 Introduction

For several years the presence of PPs has been investigated in various aqueous matrices such as raw wastewater, wastewater treatment plant (WWTP) effluents, surface water, groundwater and even drinking water (Heberer 2002; Sacher et al. 2001; Ternes 1998). Recent works have reported the presence of a large variety of PPs in the WWTP effluent and surface waters with concentrations up to several $\mu\text{g/L}$. More than 150 PPs have been detected in various environmental samples. This is partly caused by the continuous improvement of the analytical techniques and the development of specific analytical methods for environmental matrices. The majority of the pharmaceutical residues enters municipal WWTPs via domestic and hospital wastewaters or through discharges of the pharmaceutical industry. The pharmaceuticals most frequently detected in WWTPs are antibiotics, antiepileptics, antiphlogistics, X-ray contrast media, lipid regulators, betablockers and tranquillizers. These compounds vary strongly in their chemical structure and their physico-chemical properties. PPs are ubiquitously detected in treated municipal wastewater which represents the main origin for the contamination of surface water and ground waters with PPs. Therefore, the presence of human pharmaceuticals can be used to indicate to which extent matrices such as rivers, ground water and drinking water are influenced by municipal wastewater. Furthermore, specific indicator substances might be relevant for different contamination sources such as raw and treated wastewater, industrial wastewater, run off from agricultural fields after manure application, hospitals, nurse homes, landfill sites etc. In principle, the percentage of wastewater (treated and non treated) in rivers and ground water can be estimated when appropriate indicator pharmaceuticals are selected.

The aims of this work were the prediction of environmental concentrations for PPs and the verification of their agreement with measured data. Another objective was to evaluate whether the presence of PP indicators could be used to determine the proportion of different contaminating sources in rivers, lakes and drinking water. Finally all compiled data was used to identify data gaps in the current knowledge on PPs in the environment, which might then be used as a starting point in future studies.

The results of the study can then be used, together with output from WP2 and WP4, to develop a classification system to prioritize the environmental risks of PPs. The classification system is supposed to support water managers, health authorities and especially panels involved in the establishment of river basin management plans and in the development of strategies to minimize point and diffuse pollutions of surface waters. Thus, it is foreseen to

identify compounds of most concern (from WP4), which should be integrated in future monitoring programs.

3 Revision of literature on PPs and procedure of data evaluation

Compared with the list in D 1.1. the data collection was enlarged by several new references, taking into account about 40 additional pharmaceuticals. This resulted in a list of more than 170 references, which were used for the data compilation. Literature data were assembled to quantitatively assess the occurrence of pharmaceuticals in seven compartments: WWTP influents and WWTP effluents, surface water (rivers and lakes), groundwater, bank filtrate, drinking water and marine water. Based on the data evaluation, we suggest a selection of representative PPs, which could serve as indicators for wastewater originated contamination of the aquatic environment.

3.1 Consumption behaviour of PPs in European Countries

Consumption data was obtained from the countries participating in Knappe: France, Germany, Poland, Spain, and the UK (England and Wales). The data from France reflects the total amount consumed including those quantities sold without prescription - freely over the counter (OTC-drugs). In contrast, the data from Germany are mainly based on the numbers of prescribed daily doses for the different pharmaceuticals multiplied by the respective amount of a defined daily dose (DDD). The substance specific amounts of the DDDs were obtained from the WHO (World Health Organization 2006) for the most relevant application.

For England and Wales the quantities were obtained by summing up all prescribed amounts of each compound considering the various products, packages sizes and formulations, while for Spain and Poland only the number of sold packages were available. Hence the consumption was calculated by multiplying the number of packages sold by the average quantity of pharmaceutical contained. Apart the therapeutic pharmaceuticals, consumption data for diagnostics, e.g. iodinated contrast media, are hardly available.

The consumption data from Germany, Poland, Spain and the UK (England and Wales) do not include OTC-drugs. The quantity of a pharmaceutical sold in OTC-products can be a considerable share of the total quantity used, in some cases, e.g. ibuprofen or paracetamol even higher than the amount prescribed. For these reasons, consumption data of pharmaceuticals are not absolute numbers, but merely a qualified estimation. For means of

comparison the national consumption data were normalized in $\text{g}\cdot(\text{person}\cdot\text{year})^{-1}$ considering the total population of the countries. The full dataset can be found in Annex II.

Table 1: Mean annual consumption of selected pharmaceuticals in metric tons for France, Germany, Poland, Spain and the UK (England, Wales). Data available for the period from 1999-2006.

in t/a No. of PPs	Class	France 50	Germany 130	Spain 31	UK 98	Poland 25
Acetylsalicylic acid	Analgesic	638	1125	no data	82	no data
Diclofenac		10	73	2	28	19
Ibuprofen		203	261	108	149	193
Metamizole sodium		no data	164	no data	no data	no data
Paracetamol		2799	367	147	821	186
Ranitidine	Antiulcerative	12	85	20	31	no data
Carbamazepine	Antiepileptic	36	81	no data	40	32
Amoxicillin	Antibiotic	386	99	no data	80	no data
Sulfamethoxazole		20	54	no data	1	7
Troxerutin	Antihypertensive	444	41	no data	no data	no data
Metformin	Antidiabetic	717	518	no data	309	no data
Allopurinol	Urostatic	54	138	no data	24	no data
Iopromide	contrast medium	73	65	no data	no data	no data
Diatrizoate Sodium		no data	54	no data	no data	no data

Table 2: Average annual consumption of selected pharmaceuticals in g per person and year for France, Germany, Poland, Spain and the UK. Data available for the period from 1999-2006

Compound	Class	Annual per capita consumption of PPs (g/cap a)				
		France	Germany	Spain	UK	Poland
Amoxicillin	Antibiotic	6.50	1.20	no data	1.54	no data
Ciprofloxacin		0.21	0.17	0.09	0.12	0.13
Clarithromycin		0.25	0.12	0.13	0.08	0.27
Sulfamethoxazole		0.34	0.65	no data	0.02	0.17
Carbamazepine	Antiepileptic	0.61	0.98	no data	0.77	0.84
Tramadol	Analgesic	0.44	0.30	no data	0.27	no data
Ibuprofen		3.4	3.2	2.6	2.8	5.04
Paracetamol		47.14	4.46	3.60	15.68	4.84
Iopromide	Contrast medium	1.24	0.79	no data	no data	no data
Metformin	Antidiabetic agent	12.1	6.3	no data	5.9	no data

3.2 Exposure data

This compilation of exposure data includes 58400 data points for 178 compounds which were determined in samples from 22 countries. The data points comprise about 4300 measurements of raw wastewater, 15000 data points for treated waste water, 28200 for surface water, 1700 for bank filtrate, 6700 for ground water, 1300 for tap water and 1100 for marine water. Table 3 shows an overview of the number of measurement for several countries. It should be emphasized that a significant share of data on PPs in water samples remains non-published or confidential, e.g. measurements of PPs in drinking water, and was thus not available for this data evaluation.

Table 3: Numbers of measured occurrence data in the WP1 - data compilation for aquatic matrices in different countries

Country	WWTPinf	WWTPeff	SW	BF	GW	DW	MW	Sum
Australia					16			16
Austria	42	90	31		42			205
Belgium	3	3						6
Brazil		12	2					14
Canada	714	1477	4865			30		7086
China	15	15	246			15	180	471
Croatia	135	135						270
Czech Rep.			72					72
Finland	202	202	128					532
France	463	1026	1606	31	60	133	232	3551
Germany	1137	8888	15133	1689	6537	744	17	34145
Greece		135						135
Italy		436	544		12	52		1044
Japan	66	66						132
Korea	141	278	120					539
Norway	25	40					24	89
Romania			64					64
Spain	540	462	432					1434
Sweden	69	282						351
Switzerland	64	431	280					775
UK	150	248	925					1323
USA	559	807	3764		36	313	667	6146
Sum	4325	15033	28212	1720	6703	1287	1120	58400

(WWTPinf=WWTPinfluent, WWTPeff=WWTPeffluent, SW=surface water, BF=bank filtrate, GW=groundwater, DW=drinking water, MW=marine water)

More than half of all measured data available originated from Germany. For all other countries, especially within the EU, significantly less occurrence data was available.

In general, the most extensive data set was available for both wastewater compartments and surface water. Only very few data was available for the other aquatic compartments.

In order to enable a comparison of the literature data, an *average measured environmental concentration* (A-MEC) was defined characterizing the “mean” concentration of a PP in the seven compartments. A-MECs were calculated for all countries for which occurrence data were available. The A-MEC of a pharmaceutical compounds in a specific compartment was calculated as the weighted mean of all data points, reported as statistical median. In those cases where no median was available the mean was used for the calculation of the A-MEC instead. For statistical reasons all values below the limit of detection (LOD) or below the limit of quantification (LOQ) were set to 0. The mathematical expression for the calculation of the weighted mean follows equation 2-1:

$$A - MEC = \frac{\sum_{i=1}^n (\text{Number of samples}_{\text{subset}} \times \text{Median Concentration}_{\text{subset}})}{\sum_{i=1}^m \text{Number of samples}_{\text{total}}} \quad \text{eq. 2-1}$$

4 Results and Discussion of the data evaluation

4.1 MEC/PEC-Comparison

The reliable prediction of environmental concentrations of pollutants is a pre-requisite for an environmental risk assessment (ERA) and is important to understand the potential impact of pharmaceuticals in the environment (Römbke et al. 2001). Tools for predicting environmental concentrations of PPs provide important information for the prioritization of PPs, for environmental monitoring strategies.

In this work, the prediction of concentrations in WWTP influents bases on the Poseidon-Approach given in formula 3-1 (Ternes and Joss 2006b), using consumption data of the pharmaceutical compounds given in Annex II. Excretion data of the unchanged compound were taken from several sources (Besse and Garric 2008; Lienert et al. 2007; Moffat et al. 2004). The equations 3-1, 3-2, and 3-3 below illustrate a method for predicting pharmaceutical concentrations in raw wastewater (WWTP influent, eq. 3-1), treated wastewater (WWTP effluent, eq. 3-2), and surface water (eq. 3-2 and 3-3) based on drug consumption, metabolisation and excretion of the unchanged compound, population figures and elimination rates within WWTPs.

$$PEC_{WWTPin} = \frac{F_{API} \cdot E \cdot 10^9}{365 \cdot Pop \cdot AWW} \quad [\mu\text{g} \cdot \text{L}^{-1}] \quad \text{eq. 3-1}$$

F_{API} : consumption of an active pharmaceutical ingredient per year in a country [kg/a]

E: Fraction excreted including conjugates in urine and faeces

AWW: amount of wastewater per capita and day [L/(cap d)], set to $250 \text{ L} \times \text{cap}^{-1} \times \text{d}^{-1}$

Pop: Population of the country [cap]

The calculations assume that the estimated consumption is evenly distributed over the year and throughout the geographic area and that there is no biodegradation before and in the sewer. However, compounds being readily degraded may suffer transformation during transport in the sewer, which is not accounted for in formula 3-1. Due to the significantly more intense contact with degrading biomass inside the WWTP as compared to during sewer transportation, activity of sewer biomass may be assumed quantitatively negligible for

compounds not being completely degraded within the WWTP (i.e. present in measurable concentrations in the WWTP effluent).

For estimating the PEC of PPs in treated wastewater (WWTP effluent) and surface water, one of the main contributing factors governing the occurrence is the elimination efficiency of pharmaceuticals during wastewater treatment. Average removal rates of PPs in WWTP have been provided by WP 2 (Sebastian Zabczynski). For surface water (SW), the dilution of the WWTP effluent in the receiving water in the receiving water body was furthermore considered. The dilution rate (R_{dilution}) by freshwater depends very much on local conditions. Thus, the available diluting freshwater might comprise rain precipitation as well as inflow, e.g. from a river prior to WWTP discharge, which might originate from another densely populated area and therefore already contain significant amounts of wastewater. On a national level, for most European countries wastewater may be expected to be diluted between 10 and 100 times by the receiving water bodies (Ternes and Joss 2006a). Here, we assume a general dilution factor of 10, as recommended by EMEA (European Medicines Agency 2006), with a background concentration $C_{\text{background}}$ equal to 0. The complete dataset of calculated PEC values are given in Annex III.

$$PEC_{\text{WWTPout}} = PEC_{\text{WWTPin}} \times (1 - \text{removal rate}) \quad [\mu\text{g} \cdot \text{L}^{-1}] \quad \text{eq. 3-2}$$

$$PEC_{\text{SW}} = PEC_{\text{WWTPout}} \times R_{\text{dilution}} + C_{\text{background}} \quad [\mu\text{g} \cdot \text{L}^{-1}] \quad \text{eq. 3-3}$$

Many pharmaceuticals are excreted to a large extent as transformed metabolites and/or conjugated to hydrophilic groups. Conjugates (Phase II) are easily cleaved in municipal WWTPs, causing re-formation of the original molecules (Belfroid et al. 1999; Daughton and Ternes 1999). Therefore, conjugates (Phase II) were considered as parent compounds in the calculation of the PEC values. An example for the re-formation of a pharmaceutical compound from its human phase II metabolite was reported for sulfamethoxazole (Göbel et al. 2005). Resulting concentrations of compounds which are excreted to a high proportion as conjugates might be higher in the WWTP effluent than in the influent. This is due to the cleavage of the phase II metabolites (e.g. acetylated and glucuronidated sulfamethoxazole) during wastewater treatment, releasing the free pharmaceutical, e.g. sulfamethoxazole in the WWTP effluent. In order to consider the formation of phase II metabolites during metabolism and their ready cleavage during wastewater treatment, we applied two different excretion rates E . For the calculation of the PEC_{influent} ($E = 0.20$) the conjugates were not considered, as cleavage occurs mainly during wastewater treatment. The $PEC_{\text{effluent/surface water}}$ was calculated including then additionally the proportion of the conjugates as those are virtually totally

cleaved into the original drug compounds. The calculated PEC values were compared with the A-MEC values obtained for the respective compounds and compartments in four European countries, which are Germany, France, Spain and the UK. In order to ensure the representativeness of the measured values, only those A-MEC values were considered, which comprise at least 20 measurements. For Poland, occurrence data of PPs in environmental waters have not been published so far.

A-MEC values for WWTP influents comprising a sufficient number of single measurements were obtained for Germany and Spain only. It should be pointed out that the excretion of a compound with feces can lead to wide uncertainties in the PEC calculation, depending on the excretion pattern of the respective compound. The share of a compound remaining in the feces will end up in the sewage sludge and not dissolved in the wastewater.

For this, compounds have to be evaluated on a case by case basis depending on their lipophilicity and dissociation behaviour. Another uncertainty may result when the cleavage of conjugates occurs already in the sewer resulting in an underestimation of the influent concentration.

The PECs and their corresponding A-MECs can be differentiated by the resulting ratios of PEC/A-MEC:

Table 4 :Rating of PEC/A-MEC-ratios

Ratio	Color in Tables 4-6	Rating
$0.2 > \text{PEC/A-MEC} < 1$	shaded yellow	PEC acceptable, slightly underestimated
$1 < \text{PEC/A-MEC} < 4$	shaded green	PEC acceptable, slightly overestimated
$4 < \text{PEC/A-MEC} < 8$	Shaded red	PEC significantly overestimated
$8 < \text{PEC/A-MEC}$	Shaded blue	PEC strongly overestimated

In Table 5 - Table 7, the predicted environmental concentrations (PECs) and averaged measured concentrations (A-MECs) of selected pharmaceuticals in WWTP influent, WWTP effluents and surface waters are shown.

Table 5 shows a good agreement between PECs and their corresponding A-MECs for WWTP influent. The PEC values vary with up to a factor of 4 from the A-MECs, showing satisfying agreement. The results also agree well with those reported by (Joss et al. 2006). This illustrates that the concentrations in raw wastewater can be predicted reasonably well

using a rather simple approach, which takes the consumption and human metabolism of a pharmaceutical compound into account.

Among the major factors influencing the PECs and therefore the PEC/A-MEC ratios are the contributions of OTC products. For France, the OTCs were fully included in the consumption data whereas for Germany this was only partly the case and data for Spain, Poland and the UK do not include OTCs at all. Hence the PECs for the latter countries tend to be underestimated where OTCs are concerned. In contrast, some PECs for France may be somewhat overestimated, as it may be assumed that the PPs quantities prescribed/sold are not completely consumed and are therefore not introduced into the wastewater.

As it can be seen in Table 6, the PEC_{effluent} for ibuprofen and paracetamol in France and Germany are strongly overestimated, which hints that the elimination efficiency is higher than considered. For Spain and the UK the estimated effluent concentrations for ibuprofen and paracetamol do match quite well with the measured concentrations. This might be the result of an underestimated consumption, as both compounds are sold in OTC products, and an underestimated elimination efficiency with both errors compensating each other.

For some compounds, e.g. diclofenac and atenolol, PEC_{effluent} match well with the $A-MEC_{\text{effluent}}$, whereas in surface water, the PECs of diclofenac and atenolol are significantly higher than the A-MECs. It can be presumed that this results from the photo degradation of diclofenac (Buser et al. 1998) and the biodegradation of atenolol in rivers and lakes (Schlüsener et al. in preparation).

The iodinated X-ray contrast media represent a particular class of pharmaceutical products. They are widely used for diagnostic purposes and are quickly excreted without major metabolism (Hartwig et al. 1989; Mützel et al. 1989). Consequently, the highest PEC values in the range of 1.2 to 7.3 $\mu\text{g/L}$ in WWTP effluents and 0.12 to 0.73 $\mu\text{g/L}$ in surface water are obtained for iodinated X-ray contrast media. This is mainly due to their high stability in metabolism and wastewater treatment. However, the A-MECs of these compounds are significantly lower. In contrast to drugs used for long-term treatment, diagnostic drugs such as X-ray contrast media are administered to patients in single high doses of up to several hundred gram right before medical examinations, mainly on weekdays. Findings of these pharmaceuticals in the environment are therefore rather irregular, with punctually high values especially during weekdays and drops below the LOQ (Seitz et al. 2006). A reliable monitoring of X-ray contrast media in the environment must therefore take

into account the weekly cycle of administration of these diagnostic drugs (Ternes et al. 2007; Ternes and Hirsch 2000).

With exception of sulfamethoxazole, PEC values of the antibiotics are usually below 1 µg/L in WWTP influents and effluents and below 0.1 µg/L in surface waters. PEC and A-MEC of the macrolides clarithromycin and erythromycin agree very well in the WWTP influents and effluents (Germany), while the PEC are slightly higher than the A-MEC for roxithromycin (Germany and France).

In surface waters, PEC and A-MEC of erythromycin are in very good agreement (Germany and UK), while for all other antibiotics except sulfamethoxazole and trimethoprim, the A-MEC are below the LOQ. The concentrations of sulfamethoxazole and trimethoprim are considerably overestimated by their PEC in all three compartments. An explanation for this discrepancy might be the specific metabolism behaviour of these two compounds. A-MEC of the fluoroquinolone antibiotics ciprofloxacin and ofloxacin are very low compared to their PEC. Sorption is known to be of high relevance for this group of pharmaceuticals (Ternes et al. 2004) as their positively charged groups interact with the negatively charged surfaces of the micro-organisms. This results in strong sorption onto the sludge and eventually in a virtually total removal from the water phase. Fluoroquinolone antibiotics were found in WWTP effluents and surface water in negligible amounts only.

PECs of carbamazepine and of the three beta-blockers atenolol, metoprolol, and sotalol are situated between 1 and 3 µg/L in WWTP influents and effluents, and between 0.1 and 0.3 µg/L in surface water. Comparison of PEC and A-MEC shows a reasonable agreement of the values. Carbamazepine concentration in effluent and surface water tends to be somewhat overestimated.

Table 5: Comparison of PEC/A-MEC values: WWTP influent

Class	Compound	Germany		Spain	
		PEC [µg/L]	A-MEC [µg/L]	PEC [µg/L]	A-MEC [µg/L]
Analgesic	Diclofenac	2.90	2.43	0.24	0.53
	Ibuprofen	5.56	3.51	5.79	21.12
	Naproxen			0.43	0.58
	Paracetamol			25.61	30.97
Antibiotic	Clarithromycin	0.23	0.21		
	Erythromycin	0.23	0.19		
	Roxithromycin	0.47	0.16		
	Sulfamethoxazole	1.43	0.74		
	Trimethoprim	1.07	0.29		
Antiepileptic	Carbamazepine	0.54	1.60		
Beta-blocker	Atenolol	0.61	0.92		
	Metoprolol	1.20	2.05		
	Propranolol	0.19	0.81		
	Sotalol	3.29	1.26		
Tranquilliser	Diazepam	0.01	< LOQ		

Table 6: Comparison of PEC/A-MEC values: WWTP effluent

Class	Compound	Germany		France		Spain		UK	
		PEC [$\mu\text{g/L}$]	A-MEC [$\mu\text{g/L}$]	PEC [$\mu\text{g/L}$]	A-MEC [$\mu\text{g/L}$]	PEC [$\mu\text{g/L}$]	A-MEC [$\mu\text{g/L}$]	PEC [$\mu\text{g/L}$]	A-MEC [$\mu\text{g/L}$]
Analgesic	Diclofenac	2.322	1.344	0.438	0.313	0.194	0.305		
	Ibuprofen	1.112	0.175	1.201	0.101	1.158	1.849	0.997	1.384
	Indomethacin	0.086	0.141						
	Ketoprofen	0.108	0.077	2.193	0.179				
	Naproxen	0.179	0.092	1.826	0.127	0.92	0.091		
	Paracetamol	0.254	<LOQ			0.256	0.28		
Antibiotic	Azithromycin	0.028	<LOQ						
	Clarithromycin	0.126	0.109						
	Ciprofloxacin	0.276	<LOQ	0.329	0.035				
	Erythromycin	0.133	0.252						
	Ofloxacin	0.098	0.01	0.104	0.094				
	Roxithromycin	0.43	0.101	0.798	0.041				
	Sulfamethoxazole	3.503	0.307	1.811	0.206				
	Trimethoprim	0.874	0.07	0.334	0.019				
Antiepileptic	Carbamazepine	3.123	1.187	1.951	0.394				
Beta-blocker	Atenolol	0.4	0.277						
	Metoprolol	1.056	0.842	0.157	0.437				
	Sotalol	1.249	1.109						
Bronchiolytic	Salbutamol	0.01	<LOQ						
Contrast medium	Diatrizoate	7.253	0.312						
	Iopamidol	4.36	0.615						
	Iopromide	5.611	1.051						
	Iomeprol	6.606	0.356						
	Ioxithalamic acid	1.184	0.041						
Lipid regulator	Bezafibrate	1.847	1.16						
Tranquilliser	Diazepam	0.012	<LOQ						

Table 7: Comparison of PEC/A-MEC values: surface water

Class	Compound	Germany		France		Spain		UK	
		PEC [µg/L]	A-MEC [µg/L]	PEC [µg/L]	A-MEC [µg/L]	PEC [µg/L]	A-MEC [µg/L]	PEC [µg/L]	A-MEC [µg/L]
Analgesic	Diclofenac	0.232	0.06	0.044	0.023			0.1415	0.003
	Ibuprofen	0.111	0.011	0.12	0.109			0.0997	0.526
	Indomethacin	0.009	0.006						
	Ketoprofen	0.011	<LOQ	0.219	0.007				
	Naproxen	0.018	0.008	0.183	0.018	0.092	0.012		
	Paracetamol	0.025	0.002	0.269	0.01			0.0894	0.118
Antibiotic	Azithromycin	0.003	<LOQ						
	Ciprofloxacin	0.028	<LOQ						
	Clarithromycin	0.013	<LOQ						
	Erythromycin	0.013	0.026					0.0277	0.032
	Ofloxacin	0.01	<LOQ						
	Roxithromycin	0.043	<LOQ						
	Sulfamethoxazole	0.35	0.03	0.181	0.01			0.0099	0.003
	Trimethoprim	0.087	<LOQ	0.033	0.001			0.0831	0.006
Antiepileptic	Carbamazepine	0.312	0.227	0.195	0.024				
Beta-blocker	Atenolol	0.04	<LOQ	0.09	0.007				
	Metoprolol	0.106	0.025	0.016	0.002				
	Sotalol	0.125	0.044						
Bronchiolytic	Salbutamol	0.001	<LOQ					0.0002	0.115
Contrast medium	Diatrizoate	0.725	0.15						
	Iomeprol	0.661	0.132						
	Iopamidol	0.436	0.22						
	Iopromide	0.561	0.112						
	Ioxithalamic acid	0.118	0.01						
Lipid regulator	Bezafibrate	0.185	0.082	0.223	0.031				
	Gemfibrozil	0.013	0.012						
Tranquilliser	Diazepam	0.001	<LOQ	0.001	<LOQ				

4.2 PPs as indicator substances

The data compilation was further used to propose and verify pharmaceutical residues as environmental indicator substances for the presence of wastewater in the different compartments of the aquatic environment. The presence of human pharmaceuticals points towards a significant proportion of wastewater in surface- and ground waters, such as treated and raw wastewaters. Their presence would allow to specify the contamination sources and to estimate their proportions in the concerned aquatic environment.

4.2.1 Identification of indicators for wastewater originated contamination of the environment

The presence of residues of such human pharmaceuticals in surface water indicates an exposition to wastewater and therefore the potential contamination with a wide range of polar contaminants. In order to identify indicator substances, PPs in the data compilation were evaluated with regards to their removal in wastewater treatment plants.

The Percentage of a compound *i* Not Removed (PNR_i) during wastewater treatment is characterized by the ratio of its measured concentrations in the WWTP effluent and influent:

$$PNR_i = \frac{\text{concentration } i \text{ in WWTP effluent}}{\text{concentration } i \text{ in WWTP influent}}$$

This ratio was calculated from the measured concentrations of each study which reported measurements of PPs in both WWTP effluent and influent. The resulting ratios for each PP were averaged. The complete set of available average removal ratios is given in Annex IV.

Assessment of the occurrence of pharmaceutical products in the wastewater treatment plant influents and effluents allows to identify two different groups of potential environmental indicator substances with respect to their removal behaviour during wastewater treatment.

For determination of the share of treated wastewater, those PPs are chosen which, upon comparison of their environmental concentrations in wastewater treatment plant influents and effluents, are shown not to be removed by usual municipal wastewater treatment. Concentrations of such PPs in the WWTP effluent and influent are similar, leading to a ratio

PNR_i of around 1. Most substances which are not eliminated in wastewater treatment plants, are also persistent in the environment and are not easily removed by degradation or sorption to soil or sediments. Their concentrations in surface waters therefore mainly depend on the dilution of wastewater discharged into the environment, and thus represent the wastewater proportions present in rivers and lakes. Table 8 lists all those PPs with their average ratio PNR_i above 0.7, which are eligible as indicator compounds for the share of treated wastewater. The calculated values of the average PNR_i are most reliable for those PPs, for which large numbers of concentration measurements from different studies have been reported. Therefore, only those PPs have been taken into consideration, for which at least 10 measurements in both influent and effluent are included into the data compilation. Moreover, their average surface water concentrations should be less than 0.1 $\mu\text{g/L}$ in order to ensure a reliable quantification.

Substances of particular interest according to these criteria are the contrast media diatrizoate and iopamidol, the antiepileptic carbamazepine, the antibiotic erythromycin, and the beta-blocker metoprolol. Diatrizoate is especially known for its high persistence in both WWTP and the environment (EU-Project Poseidon 2004). Among the compounds poorly removed in WWTP are furthermore the antibiotics clarithromycin, and azithromycin, the antidepressant fluoxetine, the analgesics phenazone and propyphenazone, and the beta-blocker propranolol. However, the average concentrations of these compounds in surface water are generally below 0.03 $\mu\text{g/L}$ (see Annex II) and therefore close to the method detection limits.

Several metabolites of analgesics and carbamazepine (Table 8 and Annex IV) are among the potential indicator substances. As for all metabolites only very few measurements have been reported (mostly performed within a single study), general conclusions about their utility as environmental indicator compounds cannot be drawn from the present dataset. However, the wide variety of metabolites stable in WWTP illustrated in Table 8 indicates that a closer and more general survey of PP metabolites in WWTP and surface waters might be useful for future strategies of water quality assessment with regard to organic trace pollutants.

Generally, treated wastewater contaminated with some of the above-mentioned PP indicator substances is expected to contain also a large variety of other polar persistent organic compounds, besides the PPs, not being removed during wastewater treatment.

Table 8: Pharmaceutical agents eligible as environmental indicator compounds for the share of treated wastewater (average $PNR_i \approx 1$)

compound	therapeutic class	number of samples		Average PNR_i
		WWTP effluent	WWTP influent	
Propranolol	Beta-blocker	182	47	1.636
Diatrizoate Sodium	contrast medium	10	10	1.121
Clarithromycin	antibiotics	245	120	1.233
AMDOPH	metabolite	12	12	1.091
N-Formyl-4-aminoantipyrine	metabolite	12	12	1.077
Fluoxetine	antidepressant	15	15	1.024
Phenazone	analgesic	178	37	1.015
AMPH	metabolite	12	12	1
Iopamidol	contrast medium	10	10	0.96
Carbamazepine	antiepileptic	401	209	0.957
Erythromycin	antibiotics	215	209	0.963
CBZ-DiOH	metabolite	15	14	0.922
Azithromycin	antibiotics	25	19	0.816
Propyphenazone	analgesic	73	29	0.805
4-Acetaminoantipyrine	metabolite	12	12	0.797
Metoprolol	beta-blocker	208	74	0.771

4.2.2 Identification of indicators for basic removal of polar contaminants in Wastewater treatment

PPs which are completely removed during basic wastewater treatment ($PNR_i \approx 0$) can serve as indicators for the presence of raw or insufficiently treated wastewater in rivers and lakes, e. g. due to WWTP malfunction or overflow events. Table 9 lists all PPs eligible for this type of environmental indicator, with their average ratio PNR_i being below 0.2.

Only for 4 PPs meeting these criteria, more than 10 measurements in both WWTP influents and effluents have been published. These substances are the analgesics ibuprofen and paracetamol, the metabolite salicylic acid, and the lipid regulator bezafibrate. In particular, the analgesics paracetamol and ibuprofen are suggested as indicators for input of widely untreated wastewater. Complete elimination during wastewater treatment was also reported for ofloxacin. However, this compound was discarded as a potential indicator substance, due to its high tendency to sorb onto solid matter.

Table 9: Pharmaceutical agents eligible as environmental indicator compounds for the presence of raw or insufficiently treated wastewater (average $PNR_i < 0.2$)

compound	therapeutic class	number of samples		Average PNR_i
		WWTP effluent	WWTP influent	
Salicylic acid	metabolite	91	88	0.22
Paracetamol	analgesic	57	56	0.21
Ibuprofen	analgesic	384	211	0.151
Bezafibrate	lipid regulator	201	58	0.141

The presence of poorly treated wastewater or even raw wastewater in surface waters might have major consequences for the water quality and the usage of these water bodies, e.g. bathing and swimming, or as drinking water resource due to contamination with pollutants and pathogens.

For both types of indicator substances, those PPs which are used during the whole year in similar quantities are most suitable as environmental indicators. For example, the antiepileptic carbamazepine is consumed by patients regularly and in constant daily doses. This is not necessarily the case for contrast media, which are applied in single high doses before X-ray diagnostics, and are excreted by patients within hours following the examination, thus leading to a more irregular input of these substances into the sewage system. This effect is particularly noted in effluent discharges from small WWTPs serving a limited number of households, and tends to be attenuated in large facilities of major cities.

4.2.3 Input of veterinary PPs

Among the pharmaceuticals most used in animal agriculture are antibiotics of the subclasses of tetracyclines, sulfonamides and macrolides. They are introduced into the environment mainly by land application of animal waste as fertilizer. Through leaching and run-off from agricultural fields and manure storage lagoons, they might directly enter into the surface and ground water compartments without the preliminary cleansing step of a municipal wastewater treatment plant (Alder et al. 2001).

Typical veterinary antibiotics, which are not or only very rarely applied in human medication, are the tetracycline chlortetracycline, the sulfonamides sulfamethazine, sulfadiazine, and sulfathiazole, the macrolides tylosin and spiramycin, and the lincosamide lincomycin. The systematic use of antibiotics for livestock has been severely restricted within the EU. In this respect, the use of the macrolides tylosin and spiramycin as growth promoters for cattle was banned in the EU in 1999, followed by a ban of all antibiotic growth promoters from 1st of January 2006 on. However, policy in other countries, such as the US, Canada, and Australia, is still much less restrictive, and a wider variety of antibiotics is used there for food-producing livestock.

Table 10 shows the average and maximum concentrations of antibiotics for veterinary use measured in surface water and groundwater in different countries worldwide. The most important class of veterinary drugs is that of tetracycline antibiotics (Sarmah et al. 2006), among them chlortetracycline for typically veterinary use, and tetracycline, which is also common in human medication, but is included here due to its prevalent use for livestock. In

fresh manure of cattle, tetracyclines were found in concentrations of several mg/kg (manure) (Bund/Länderausschuss für Chemikaliensicherheit (BLAC) 2003; Hamscher et al. 2005). Due to the fact that tetracyclines are strongly adsorbed to the soil matrix, they are known to persist and accumulate in agricultural soils fertilized with manure, with 100 to 900 µg/kg soil. (Hamscher et al. 2005; Kemper 2008; Sarmah et al. 2006). Tetracyclines are usually not identified in surface water and groundwater, which is in due to the strong adsorption of these drugs to the soil (Bund/Länderausschuss für Chemikaliensicherheit (BLAC) 2003; Hamscher et al. 2005). Therefore, they do not represent suitable indicator compounds in the aquatic environment.

Sulfonamides are used for veterinary purpose in much lower quantities than tetracyclines. However, they are much less accumulated in the soil, and show a higher tendency to leach through soil into the groundwater. The sulfonamide sulfamethazine (sulfadimidine) is the drug most frequently present in the aquatic environment among the veterinary antibiotics. It is detected in surface waters in Canada, the U.S., and China with concentrations up to 0.4 µg/L, and in Germany and France with concentrations up to 0.07 µg/L. Punctual findings of sulfamethazine with concentrations up to 0.24 µg/L are reported for groundwater from areas of highly exposed farmland in Germany (Hamscher et al. 2005; Hirsch et al. 1999), and in several groundwater wells within the surroundings of a confined animal feed operation (CAFO) in the U.S. (Batt et al. 2006). Two other sulfonamides used for veterinary purpose, sulfadiazine and sulfathiazole, are more rarely detected in surface and ground waters than sulfamethazine. Concentrations between 0.1 and 0.5 µg/L are only measured in surface waters in China, while they are generally below 0.016 µg/L in the US and Canada. Occasional findings are reported from the European continent, thus, both sulfonamides were identified with concentrations of 0.02 and 0.05 µg/L in two single groundwater samples from agricultural areas in southern Germany. Sulfadiazine has furthermore been measured at 0.236 µg/L in a single river sample in Italy taken close to a hospital (Perret et al. 2006).

Among the macrolides, only tylosin is exclusively used for veterinary purposes. While tylosin concentrations of up to 0.28 µg/L in surface waters in the U.S. point towards a systematic use in agriculture, its ban as a growth promoter within the European Union in 1999 leads to random findings in river samples in southern Germany and Italy. Two other veterinary macrolides, spiramycin and lincomycin, are also occasionally applied in human medicine. Human medication (e. g. for treatment of toxoplasmosis) might explain the low concentrations of spiramycin measured in surface waters in France and Italy. Lincomycin is

found in surface waters in Italy and Canada in similar concentrations as tylosin in the U. S., indicating a systematic use of this antibiotic for agricultural livestock in these countries (Calamari et al. 2003; Lissemore et al. 2006).

Table 10: Occurrence of antibiotics for veterinary use in surface and ground water.

	Surface water (SW)			Ground water (GW)		
	samples	A-MEC ([$\mu\text{g/L}$])	MAX ([$\mu\text{g/L}$])	samples	A-MEC ([$\mu\text{g/L}$])	MAX ([$\mu\text{g/L}$])
Sulfonamides						
Sulfadiazine						
China	30	0.099	0.336			
Germany	14	0	0	17	0	0
Italy	3	0	0.236			
USA	21	0	0			
Sulfamethazine						
Canada	224	0.002	0.408			
China	30	0.134	0.34			
France	6	0.002	0.002			
Germany	170	0	0.07	124	0	0.24
USA	224	0.096	0.22	18	0.078	0.215
Sulfathiazole						
Canada	136	0.001	0.016			
China	6	0.26	0.52			
USA	36	0	0.01			
Macrolides and lincosamides						
Lincomycin						
Canada	224	0.017	0.355			
Italy	7	0.033	0.249			
USA	24	0	0			
Tylosin						
Canada	136	0	0			
France	6	0	0			
Germany	167	0	0.02	59	0.014	0.05
Italy	8	0.001	0.001			
USA	133	0.031	0.28			
Spiramycin						
France	6	0.004	0.004			
Germany	43	0	0	11	0	0
Italy	22	0.022	0.074			

Consequently, the antibiotics tylosin, sulfamethazine, and lincomycin might in principle be adapted as indicators for veterinary input from agricultural livestock. Table 10 however, shows that so far, only limited numbers of measurements from few countries are available. The values given in Table 10 also illustrate the obvious influence of different registration situations and application practices of veterinary medicine in the different countries, for which measurements are available. Thus, typically veterinary antibiotics of the sulfonamide and macrolide group have been found in surface waters mainly in countries outside Europe, while their findings are rather occasional within the EU due to severe restrictions for their use in livestock. A general statement about veterinary drugs taking into account the specific situation of each country is therefore hardly possible.

Several other antibiotics frequently used for cattle, such as tetracycline, oxytetracycline, erythromycin, trimethoprim and several penicillines are also common human pharmaceuticals. The origin of their environmental occurrence is therefore much more difficult to determine. With the restrictive use of antibiotics for veterinary purposes within the EU, most of these antibiotics found in surface and ground waters are probably of human origin, and are thus introduced into the environment by WWTP effluents rather than veterinary use and subsequent fertilization of agricultural soils with dung and manure.

Due to the different registration situation in the various country, with deviating and/or overlapping use in human and veterinary medicine, no pharmaceutical compounds are fully attributable to veterinary purposes only. Furthermore, systematic exposure data for veterinary compounds is still quite limited not allowing for general conclusions on indicator substances for veterinary purposes within the EU.

4.2.4 Input of PPs from hospitals

The share of contributions from hospitals to the wastewater might be determined by those PPs typically administered to patients during a hospital stay, such as contrast media or cytostatics. However, depending on a country's medical practice, these PPs might also be administered to patients during ambulatory treatment. If hospitals do not specifically take care about separating the excretions of these patients after the treatment, the PPs will be excreted several hours later at the patient's home and mix with the usual household wastewater. Another class of drugs mainly administered to the patients during a hospital stay are the so-called reserve antibiotics, such as vancomycin, which are exclusively applied in the case of severe infections with multi-resistant bacterial strains. Measurements of vancomycin in environmental waters have been performed only in two studies from Germany and France. While the predicted

environmental concentrations (PEC) of this antibiotic are for both countries between 0.10 and 0.17 ng/L in raw wastewater (Table A.III-1), its measured concentrations were generally found to be below the detection limit of the analytical methods.

The currently available dataset does not allow assigning environmental concentrations of pharmaceutical compounds to their application in hospitals only.

4.2.5 Indicators for contamination of ground- and drinking water with wastewater

Ground water is the most common water resource used for drinking water production, which is then treated in order to attain drinking water quality. The presence of residues of human pharmaceuticals in ground and drinking water indicates an exposition to wastewater and therefore a potential contamination with a wide range of polar contaminants and pathogens.

Organic substances which are highly persistent towards transformation processes in the soil and during drinking water production and additionally refrain from sorption onto soil or activated carbon due to their high polarity, are susceptible to break through into the ground water and drinking water supplies. Table 7 gives a list of PPs which have been repeatedly identified in ground water and drinking water. Among them are the X-ray contrast media diatrizoate and iopamidol, which appear to be particularly persistent. They are found in concentrations of several $\mu\text{g/L}$ in ground water and bank filtrate, and still in concentrations of 0.01 to 0.1 $\mu\text{g/L}$ in finished drinking water. Highest concentrations of 3 to 10 $\mu\text{g/L}$ of diatrizoate were systematically measured in groundwater wells which were located in an agricultural field irrigated with treated municipal wastewater (Ternes et al. 2007), illustrating that this compound is hardly eliminated during soil passage. The antiepileptic carbamazepine exhibits a similar persistency in the environment. Its measured environmental concentrations are usually lower than those of diatrizoate and iopamidol. Values between 0.1 and 1 $\mu\text{g/L}$ were measured in ground water and bank filtrate, and traces of carbamazepine are sometimes found in drinking water. The three pharmaceuticals iopamidol, diatrizoate, and carbamazepine therefore represent useful indicator substances for the influence of wastewater in ground and drinking waters. Diatrizoate is suggested as the most suitable tracer compound for contributions of wastewater due to its persistence and high environmental concentrations.

Sulfamethoxazole represents the antibiotic most frequently detected in ground water and bank filtrate with concentrations of 0.01 to 0.08 $\mu\text{g/L}$. Traces of this substance have also repeatedly

been found in drinking water in the range of a few ng/L. Sulfamethoxazole might therefore be a useful tracer in ground and drinking water representing the therapeutic class of antibiotics.

Among the analgesics, phenazone and propyphenazone exhibit the highest environmental persistence. These two compounds are not ubiquitously present in the aquatic environment (Bund/Länderausschuss für Chemikaliensicherheit (BLAC) 2003). However, they have been repeatedly found in concentrations of several hundred ng/L in ground water, bank filtrate, and drinking water especially in the surrounding area of a former drug manufacturing site in Germany (Reddersen et al. 2002). Other analgesics, such as diclofenac, are more rapidly degraded in the environment and are only very occasionally identified in ground and drinking water resources.

Finally, the metabolite clofibrinic acid is known to be highly persistent in the environment and was regularly found in ground water and bank filtrate in concentrations of several µg/L, and in drinking water in concentrations up to 0.2 µg/L. However, the use of the parent drug clofibrate has strongly declined in recent years. Therefore, measured concentrations of clofibrinic acid mainly originate from earlier drug inputs and are not representative for the current contamination of environmental waters.

Table 7: PPs as indicators for wastewater influenced ground and drinking water.

Therapeutic class	compound	country	Ground water			Bank filtrate			Drinking water		
			samples	A-MEC [$\mu\text{g/L}$]	Max [$\mu\text{g/L}$]	samples	A-MEC [$\mu\text{g/L}$]	Max [$\mu\text{g/L}$]	samples	A-MEC [$\mu\text{g/L}$]	Max [$\mu\text{g/L}$]
contrast media	Diatrizoate	Germany	89	1.468	9.6	30	0.011	4	10	0.021	0.085
	Iopamidol	Germany	96	0.064	2.4	30	0	1.4	15	0.011	0.098
antiepileptics	Carbamazepine	Austria	7	0	0						
		Canada							3	0	0
		France	2	0.012	0.023	3	0.053	0.071	8	0	0.043
		Germany	215	0.015	1.1	70	0.082	1	12	0	0.03
		Italy	2	0	0				6	0.005	0.005
		USA							8	0	0
Analgesics	Diclofenac	Austria	7	0	0						
		Canada							3	0	0
		France	2	0	0				7	0.002	0.002
		Germany	143	0	0.93	57	0.003	0.43	58	0	0.006
		Italy	2	0	0				6	0	0
	USA							8	0	0	
	Phenazone	Germany	159	0.234	3.95	116	0.159	1.25	22	0.123	0.4
Propyphenazone	Germany	75	0.133	1.23	131	0.041	1.465	8	0.1	0.12	
Antibiotic	Sulfamethoxazole	China							3	0	0
		France	2	0	0	4	0.011	0.058	2	0	0
		Germany	162	0.006	0.47	20	0.032	0.079			
		Italy	2	0	0				10	0.003	0.08
		USA							14	0.001	0.003
Metabolite	Clofibric acid	France	2	0	0						
		Germany	179	0	11	49	0.007	7.3	151	0.02	0.17
		USA							20	0	0

5 Data gaps

5.1 Availability and comparability of data for environmental exposure

The available data was heterogenic in many aspects. First, the numbers of available measurement data on PPs in the aquatic environment varied greatly between the different countries (Table 3). Furthermore, differences exist concerning the sampling location, the carried out sampling procedure, sample analysis, quality assurance and data evaluation. In detail, samples were frequently taken from sites with a special exposure situation, e.g. receiving waters near WWTPs, vulnerable ground waters infiltrated by wastewater or contaminated river water. Concentrations found in those sites hardly reflect the general exposure situation. Analytical results obtained by using different sampling strategies, e.g. grab samples and composite samples, are of limited comparability. The analytical methods applied for measurement vary concerning the methodology, quality assurance and thus the reliability of the data. For many compounds only few data is available. Finally, the occurrence data is reported using different statistical expression, e.g. median, mean, maximum, percentile values.

5.2 New PP candidates for environmental analysis

For several PPs with a high average annual consumption and correspondingly high predicted environmental concentrations $PEC_{WWTPinf}$, measurements in the aquatic environment have not been reported. Table 8 lists all those compounds whose $PEC_{WWTPinf}$ is higher than 1 $\mu\text{g/L}$ in at least one of the four countries Germany, France, Spain, and UK.

The antidiabetic drug metformin shows by far the highest $PEC_{WWTPinf}$ in all four countries. Measurements in the U. S. have revealed concentrations of this drug of 10 to 26 $\mu\text{g/L}$ in WWTP influents and effluents (Benotti and Brownawell 2007), and up to 0.15 $\mu\text{g/L}$ in surface water (Kolpin et al. 2002). The values are in agreement with the high $PEC_{WWTPinf}$ in the four countries, and therefore, similar concentrations of metformin can be expected for European water bodies. Other compounds with high $PEC_{WWTPinf}$ between 18 $\mu\text{g/L}$ and 82 $\mu\text{g/L}$ especially in France and Germany are the antihypertensive troxerutin, the phlebotropic diosmin, the mucolytic carbocystein, the antiepileptic valproic acid, and the urostatic allopurinol. Measurements in the aquatic environment have not been reported so far for any

of these compounds. In view of their potentially high input, a closer investigation of their occurrence and environmental fate would be desirable.

Table 11: PPs with $PEC_{WWTPinf}$ higher than 1 $\mu\text{g/L}$, for which measurements in the aquatic environment in Europe have not been reported.

Class	Compound	$PEC_{WWTPinf}$ [$\mu\text{g/L}$]							
		Germany		France		Spain		UK	
		PEC_a	PEC_b	PEC_a	PEC_b	PEC_a	PEC_b	PEC_a	PEC_b
Analgesic	Mesalazine	7.925						9.636	
	Antibiotic	Sulfasalazine	5.096	0.51				9.93	0.993
Anticoagulant	Clopidogrel	1.389	0.694			1.253	0.627	1.807	0.904
Antidiabetic	Metformin	69.006	55.205	132.339	105.871			64.678	51.742
Antiepileptics	Valproic acid	7.919	1.98	20.706	5.177			5.55	1.388
Antihypertensive	Captopril	3.173	1.428			0.332	0.149	0.387	0.174
	Irbesartan	1.982				1.4		3.673	
	Lactitol	3.058						0	
	Troxerutin	5.466		82.029					
	Verapamil	7.676	0.23					1.521	0.046
contrast medium	loversol	5.802	5.802						
Diuretic	Torasemide	0.493				9.911		0.002	
Lipid regulator	Atorvastatin	0.633	0.006			0.693	0.007	2.324	0.023
Mucolytic	Carbocistein			42.886				2.323	
Phlebotropic	Diosmin			68.96					
Urostatic	Allopurinol	18.374	5.145	10.015	2.804			5.085	1.424

Furthermore, many pharmaceuticals are extensively metabolized into phase I metabolites. For most metabolites environmental occurrence data is not available.

Table 12: Compounds undergoing major phase I metabolisation

PP	Metabolite	Share excreted
Diclofenac	4'-hydroxydiclofenac	20%
Metoprolol	4-(2-hydroxy-3-isopropylamino-propoxy)phenylacetic acid	65%
Allopurinol	Oxipurinol	70%
Oseltamivir	Oseltamivir hydrolyzed	75%

6 Minutes of the Knappe Workshop

The common workshop of the following 2 work packages (WPs) of the Knappe project took place on Monday, February 18th in Nimes with 35 participants from within and outside the Knappe project:

- WP 1 (Occurrence of PPs in the aquatic environment: towards indicators for contamination with pharmaceuticals)
- WP 2 (Assessment of limits of the current water treatment processes: towards best practices for lowering PPs contamination in the aquatic environment)

In the workshop, the outcomes of both WPs were discussed in three sessions including nine presentations:

Session 1: Analytic methods for pharmaceutical in the environment: Problems and risks

Session 2: Occurrence and exposure scenarios

Session 3: Removal processes

The major outcomes were:

- Modern analytical techniques allow for a very sensitive determination of organic trace pollutants in aquatic compartments. Quality assurance is a key issue for the determination of PPs at environmental level, as matrix effects frequently affect the analytical results.
- Within the different EU-countries, deviations exist in the prescription/consumption behaviour and in the bookkeeping practice for the usage of pharmaceuticals. For example, consumption data are hardly available in Spain and Poland, whereas detailed data exist for France, including even OTC-drugs.
- Modelling of occurrence data is generally feasible for those compounds for which reliable consumption data are available. However, local concentrations might deviate widely from predicted exposure concentrations where non-treated wastewater is discharged or elimination efficiency is low, e.g. due to rainstorm events.
- PPs can be used as indicator substances to determine the wastewater share in surface waters, to determine the input of non or poorly treated wastewater in surface waters,

and in general to determine whether a groundwater or water body is influenced by wastewater.

- Source control measures, such as innovations in prescription practice and urine/feces separation techniques (e.g. in hospitals and public buildings) may lead to an improvement of the current situation, but will not generally solve all problems with anthropogenic compounds in the water cycle.
- The diversity of micro pollutants and transformation products remains a challenge to be tackled.
- Today's wastewater treatment achieves only partial removal of pharmaceuticals and other organic trace pollutants. Treatment practice is very heterogenic, as tertiary treatment is not a common standard in the EU. For successful improvement of WWTPs, sewer systems and rainwater overflow systems should be considered as well. State of the art treatment systems, advanced treatment technologies, such as ozonation or PAC, are an option but the cost-benefit analysis is frequently missing: The precautionary principle seems to be a desirable, but hardly an always feasible way to deal with anthropogenic compounds in the water cycle.

Recommendations and important aspects for future actions:

- Detailed bookkeeping practice on usage of pharmaceuticals in all EU-countries should be installed
- PP-Manufacturers should publish data on fate/WWTP elimination before putting compounds on the market- giving way for measures before the application takes place;
 - If a drug is persistent, then the public has a right to know about that. -
- The installation of new wastewater treatment techniques should consider the current state of the treatment technique, the possibility of state-of-the-art advanced treatment technologies, the sensibility of the receiving water body and the necessity to apply re-used wastewater as water resource within an area.
- Wastewater treatment is not an short term issue and future demands should be identified as early as possible. General changes in wastewater treatment techniques or the sewer system will take decades to take effect on a countrywide scale.

7 List of abbreviations and acronyms

A-MEC	Average measured concentration
BF	Bank filtrate
DDD	Defined daily dose
DW	Drinking water
ERA	Environmental risk assessment
GW	Ground water
MEC	Measured environmental concentration
MW	Marine water
MW	Marine water
OTC	Over the counter = freely available without prescription
PEC	Predicted environmental concentration
PNR_i	Percentage of a compound <i>i</i> not removed in wastewater treatment
PP	Pharmaceutical product
SW	Surface water
TW	Tap water
WP	Work package
WWTP	Wastewater treatment plant
WWTP e	Sewage treatment plants effluents
WWTP i	Sewage treatment plants influent

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9 Annex I: Measured environmental concentrations of pharmaceuticals in the aquatic environment

Table A-I. 1: Averaged environmental concentrations (A-MEC) and maximal concentrations of pharmaceuticals measured in surface water, wastewater treatment plant influent and effluent.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
1-Hydroxyibuprofen									
France	27	0	0						
2,3-Dichlorophenoxyacetic acid									
Canada	9	0.096	0.139				4	0.089	0.103
2-Hydroxyibuprofen									
Canada				8	1.081	1.957	8	0.883	1.563
France	27	0	0.114						
Germany	7	0.032	0.101				10	0.92	5.96
Norway							4	0.485	1.13
4-Acetaminoantipyrine									
Czech Rep.	9	0.25	0.94						
Germany	33	0.335	4.8	12	6.65	8.8	25	2.872	7
Romania	8	1.048	1.56						
4-Aminoantipyrine									
Germany	11	0	0.63	5	0.78	0.78	19	0.095	0.36
4-Chlorobenzoic acid									
France	27	0.002	0.011						
4-hydroxyantipyrin									
Germany	21	0.12	2.4						
6-o-desmethyl naproxen									
France	27	0	0.032						
Acebutolol									
Canada							7	0.308	0.662
Finland	11	0.006	0.014	24	0.3	1.04	24	0.146	0.255
France							2	0.105	0.13
Italy							3	0.04	0.11
Acetylsalicylic acid									
France	52	0.004	0.086				41	0.01	0.212
Germany	69	0	0.34	2	3.2	5	88	0.18	1.51
Romania	8	0.032	0.037						
UK				6	0	0	6	0	0
Alprazolam									
France	27	0	0.002						
Ambroxol									
Czech Rep.	9	0	0						
Germany	33	0.002	0.13				3	0	0
AMDOPH									
Germany	22	0.213	0.35	12	0.55	0.71	25	0.428	0.73
Amityptiline									
France	7	0	0				2	0.003	0.006
UK	12	0	0						

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Amoxicillin									
China	24	0	0						
France				19	0	0	19	0	0
Germany	50	0	0.1				67	0	0.147
Italy	15	0	0				9	0.005	0.005
UK	12	0.035	0.245						
USA	21	0	0						
AMPH									
Germany	22	0.038	0.16	12	0.11	0.15	25	0.074	0.19
Ampicillin									
France	6	0	0				3	0	0
Germany	36	0	0				67	0	0
USA	21	0	0						
Atenolol									
Canada							7	0.987	1.68
Croatia				5	0.395	0.74	5	0.4	1.15
Finland	11	0.022	0.055	24	0.728	1.71	24	0.264	1.18
France	33	0.007	0.1				3	0.57	0.57
Germany	225	0	0.07	22	0.923	2.3	132	0.277	1.8
Italy	15	0.023	0.241				17	0.418	1.168
Spain	17	0.142	0.465	11	1.959	122	5	0.28	1.2
Sweden							24	0.19	0.47
UK	12	0.012	0.06						
USA	12	0.432	0.432	6	3.06	3.06	6	0.879	0.879
Atorvastatin									
Canada	6	0	0.001	3	0.076	0.076	6	0.03	0.037
USA	12	0	0	6	0.201	0.201	6	0	0
Azithromycin									
Croatia				5	0.152	0.3	5	0.096	0.21
France	6	0.005	0.005				3	0.101	0.101
Germany	29	0	0.14				67	0	0.135
Spain	17	0.012	0.068	5	0.16	0.45	5	0.14	0.3
Switzerland				9	0.17	0.38	15	0.16	0.4
Betaxolol									
France							26	0	0
Germany	87	0	0.028	2	0.87	0.87	84	0.024	0.19
Italy							3	0	0
Bezafibrate									
Austria	9	0.008	0.02	7	3.526	9.43	7	0.05	0.13
Canada	196	0.003	0.47	18	0.6	4.7	53	0.202	0.81
Croatia				5	0.023	0.05	5	0	0.01
Finland	8	0.008	0.02	2	0.42	0.42	2	0.011	0.011
France	34	0.031	0.78				5	0.718	1.07
Germany	283	0.082	3.1	17	4.135	7.5	258	1.16	4.8
Italy	31	0.013	0.076				20	0.039	0.91
Spain	20	0.018	0.363	30	0	0	30	0.18	0.34
Bisoprolol									
Canada							7	0.024	0.071
France	6	0.01	0.01				27	0.703	2.838
Germany	317	0	2.9	17	0.074	0.5	200	0.073	2

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Bromazepam									
France	27	0	0.134						
Butalbital									
Germany	18	0	5.3						
Carazolol									
Germany	76	0	0.11	2	0.19	0.19	85	0.002	0.12
Carbamazepine									
Austria	4	0.047	0.133	7	1.258	2.41	7	1.132	1.67
Canada	293	0.017	0.65	29	0.5	1.9	64	0.307	2.3
Croatia				5	0.42	0.95	5	0.41	0.63
Finland	11	0.037	0.08	24	0.288	0.82	24	0.489	2.44
France	89	0.024	1.15	5	0.694	1.333	46	0.394	2.519
Germany	619	0.227	2.5	68	1.6	4	351	1.187	22
Italy	23	0.009	0.345				23	0.286	1.318
Korea	8	0.025	0.061	16	1.84	9.42	25	0.171	0.97
Norway				1	0	0	4	0	0
Romania	8	0.068	0.075						
Spain	22	0.059	0.279	58	0.132	0.95	49	0.168	0.6
Sweden							24	0.44	1.18
UK	14	0.17	0.794						
USA	20	0.075	0.104	13	0.173	0.274	15	0.119	0.187
CBZ-10OH									
Canada	3	0	0	3	0.008	0.008	3	0.009	0.009
CBZ-2OH									
Canada	3	0	0	3	0.121	0.121	3	0.132	0.132
CBZ-3OH									
Canada	3	0	0	3	0.095	0.095	3	0.102	0.102
CBZ-DiH									
Germany	3	0.002	0.004						
CBZ-DiOH									
Canada	3	0.002	0.002	3	1.572	1.572	3	1.325	1.325
Germany	3	0.058	0.14	11	2	3.7	12	2	3.6
CBZ-EP									
Canada	3	0	0	3	0.047	0.047	3	0.052	0.052
Spain				12	0.35	0.5	12	0.16	0.3
Chloramphenicol									
Canada	136	0	0						
China	24	0.084	0.266						
France				19	0	0	19	0	0
Germany	215	0	1.3	8	0	0.19	71	0	0.56
UK	12	0	0						
Chlortetracycline									
Canada	136	0.176	0.192						
France	6	0	0				3	0.056	0.056
Germany	43	0	0				72	0	0
Korea				2	85.98	171	2	45.47	90.9
USA	235	0.15	0.69	3	0.31	0.31	3	0.42	0.42
Cimetidine									
UK	12	0	0.011						
USA				5	0.014	0.014	6	0.012	0.012

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC (µg/L)	MAX (µg/L)	samples	A-MEC (µg/L)	MAX (µg/L)	samples	A-MEC (µg/L)	MAX (µg/L)
Ciprofloxacin									
Canada							16	0.132	0.4
Finland	11	0.008	0.036	24	0.397	4.23	24	0.066	0.13
France	6	0.006	0.006	19	0	0.166	24	0.035	0.101
Germany	55	0	0.028				67	0	0.144
Italy	15	0	0.026				20	0.208	0.514
Sweden				13	0.166	0.3	13	0.023	0.06
USA	128	0.024	0.36	17	0.53	1.4	29	0.262	5.6
Citalopram									
Austria							24	0.054	0.322
Norway				4	0.089	0.612	3	0.062	0.382
Clarithromycin									
Canada							8	0.087	0.536
France	6	0.008	0.075				3	0.117	0.117
Germany	272	0	0.95	114	0.214	1.47	287	0.109	4.5
Italy	15	0.002	0.02				17	0.017	0.073
Switzerland				9	0.38	0.6	18	0.225	0.35
Clenbuterol									
France	7	0	0				2	0.003	0.006
Germany	148	0	0.11	14	0	0	206	0	0.1
Clindamycin									
France	6	0.001	0.001	19	0	0	22	0.001	0.01
Germany	35	0.005	0.03	3	0	0	79	0.011	0.13
USA	10	0	0.14				8	0	1
Clofibric acid									
Austria	4	0.025	0.044						
Canada	196	0.011	0.175	62	0.011	0.22	100	0.03	0.283
Croatia				5	0.072	0.11	5	0.028	0.03
France	27	0	0.014				2	0	0
Germany	291	0.026	0.55	34	0.434	1.2	297	0.235	3.29
Italy	8	0.001	0.006				11	0.064	0.68
Japan				11	0.028	0.028	11	0.014	0.014
Korea				17	1.51	4.38	17	0.31	0.74
Norway				1	0	0	4	0	0
Spain	20	0.007	0.02	30	0.04	2.02	30	0.025	0.12
UK	42	0.01	0.111	15	0.203	0.651	18	0.01	0.044
USA	20	0.038	0.63				2	0	0
Clotrimazole									
France	27	0	0						
Germany	1	0.005	0.005						
UK	18	0.022	0.034	9	0.031	0.033	9	0.014	0.027
Cloxacillin									
France	6	0	0				3	0.01	0.01
Germany	14	0	0				4	0	0
USA	21	0	0	2	0.02	0.02			

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Codeine									
Germany	44	0.009	0.094	11	0.22	0.54	42	0.106	0.9
Romania	8	0.033	0.054						
Spain				18	3.767	11	12	3.7	8.1
UK	12	0.01	0.034						
USA	46	0.012	0.019	5	0.17	0.17	6	0.17	0.17
Cyclophosphamid									
Canada	16	0	0	18	0	0	53	0.001	0.008
Germany	239	0	0.1	14	0	0	130	0	0.15
Italy	16	0	0				17	0.003	0.009
Romania	8	0.023	0.065						
Switzerland	5	0	0	5	0.005	0.011	4	0.003	0.01
UK				6	0	0	6	0	0
Dapsone									
Germany	14	0	0						
Demeclocycline									
Korea				2	1.71	3.15	2	1.365	2.7
USA	36	0	0						
Dextropropoxyphene									
UK	47	0.004	0.682	9	0.027	0.033	14	0.113	0.585
Diatrizoate									
France	6	0.129	0.129				3	2.37	2.37
Germany	594	0.15	100	17	1.941	3.3	106	0.425	15.8
Diazepam									
Belgium				3	0.59	1.18	3	0	0.66
France	43	0	0				5	0	0
Germany	314	0	0.033	32	0	0.1	227	0	0.1
Italy	16	0	0.002				17	0	0
Korea							2	0	0
Romania	8	0.029	0.034						
USA	20	0.001	0.001	8	3.75	5	9	0.003	0.004
Diclofenac									
Austria	9	0.036	0.392	7	2.15	3.55	7	1.844	3
Canada	211	0.015	0.194	70	0.429	2.45	112	0.118	0.895
Croatia				5	0.25	0.54	5	0.215	0.39
Finland	8	0.022	0.055	2	0.35	0.35	2	0.028	0.028
France	85	0.023	0.173	5	3.309	5.218	46	0.313	0.92
Germany	563	0.06	1.8	44	2.43	28	382	1.344	10
Greece							6	0.07	0.89
Italy	25	0.01	0.158				8	0.68	5.45
Japan				11	0.251	0.251	11	0.145	0.145
Korea	8	0.003	0.007	17	2.59	9.87	26	1.301	10.96
Norway				1	0	0	4	0	0.03
Spain	20	0.021	0.06	56	0.531	3.6	47	0.305	2.2
Sweden							24	0.29	1.48
UK	49	0.003	0.568	9	0.997	1.036	15	0.34	2.349
USA	42	0.003	0.009	8	0.087	0.116	30	0	0.033
Dicloxacillin									
France	6	0	0				3	0	0
Germany	57	0	0				63	0	0

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Dihydrocodeine									
Germany	36	0.008	0.079	6	0.1	0.33	38	0.026	0.3
Dilantin									
Korea	8	0.004	0.009				9	0.036	0.181
USA	14	0.076	0.088	8	0.329	0.402	6	0.287	0.287
Diltiazem									
Canada	6	0	0						
UK	12	0	0.001						
USA				5	0.057	0.057	6	0.053	0.053
Dimethylaminophenazone									
France							2	0.215	0.43
Germany	168	0.001	0.34	14	0.137	0.96	92	0.013	1
Italy							3	0	0
Doxepin									
France	7	0	0				2	0	0
Doxycycline									
Canada	136	0.007	0.073				8	0.038	0.046
France	6	0	0	19	0	0	22	0.01	0.073
Germany	35	0	0				56	0	0
Korea				2	0.11	0.22	2	0.015	0.03
Sweden				10	0.083	2.48	10	0.227	0.915
USA	151	0.001	0.02	3	10	10	3	10.9	10.9
Enalapril									
Italy	15	0	0.001				9	0	0
USA	12	0	0	6	0.035	0.035	6	0.001	0.001
Erythromycin									
Canada	224	0.003	0.051				8	0.08	0.838
China	24	0.245	0.636						
Croatia				5	0	0	5	0	0
France	6	0.025	0.075				3	0.35	0.35
Germany	301	0.026	1.7	98	0.189	1.51	278	0.252	6
Italy	15	0.003	0.016				17	0.043	0.353
Korea	8	0.003	0.005				9	0.12	0.294
Spain	21	0.033	0.2	11	0.069	0.25	5	0.15	0.28
Switzerland				9	0.07	0.19	18	0.068	0.199
UK	37	0.032	1.022	9	0.113	0.141	15	0.157	1.842
USA	148	0.101	1209	101	0.332	3.9	102	0.111	1.1
Etofibrate									
Germany	63	0	0				20	0	0
Fenofibrate									
Canada				36	0	0	39	0	0
France	33	0.005	0.025				5	0.214	0.31
Germany	121	0	0				20	0	0.03
Italy							3	0.16	0.16
USA				5	0	0	6	0	0
Fenofibric acid									
Brazil	2	0.06	0.54				2	0.07	0.4
France	27	0	0.21						
Germany	145	0.014	0.28	2	1.1	1.1	166	0.223	1.2

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Fenoprofen									
Canada	25	0	0	44	0	0	78	0	0.217
France							2	0.235	0.28
Germany	43	0	0				59	0	0
Italy	15	0.004	0.022				8	0.938	5.4
Fenoterol									
Germany	76	0	0.061				83	0	0.06
Flucloxacillin									
France	6	0	0				3	0	0
Germany							51	0	0.023
Flumequine									
France				19	0.006	0.025	19	0.017	0.035
USA	21	0	0						
Fluoxetine									
Canada							19	0.011	0.099
Croatia				5	0	0	5	0	0
France	27	0	0.004	5	0.209	1.236			
Korea	8	0	0				9	0.002	0.002
Norway				4	0.002	0.002	3	0.001	0.001
Spain	10	0	0						
UK	6	0.02	0.034						
USA	27	0.001	0.002	13	0.239	0.6	17	0.207	0.56
Fluvoxamine									
Norway				4	0.002	0.004	3	0	0.001
Furazolidone									
Germany	14	0	0						
Furosemide									
France	27	0	0.039						
Italy	15	0.004	0.255				17	0.589	2.102
Fusidine									
France				19	0	0.07	19	0	0
Gabapentin									
UK	12	0.046	0.098						
Gemfibrozil									
Canada	299	0.004	58	62	0.479	36.53	104	0.436	2.09
Croatia				5	0.155	0.36	5	0.12	0.32
France	85	0.007	0.086				46	0.06	1.34
Germany	206	0.012	0.51				105	0.318	1.5
Italy	8	0.001	0.044				3	0.84	4.76
Korea	8	0.007	0.009	16	0	0	25	0.003	0.017
Spain	17	0.035	0.497						
Sweden							24	0.56	2.07
USA	142	0.045	0.79	8	3.73	4.77	29	0.027	0.234
Hydrochlorothiazide									
Italy	15	0.006	0.256				17	0.488	1.253
Hydrocodone									
Germany	37	0.002	0.028				28	0	0.4
Korea	8	0.002	0.002				9	0.033	0.07
USA	8	3.113	4.15	7	0.055	0.07	9	0.012	0.068

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Ibuprofen									
Austria				7	1.642	3.17	7	0.012	0.035
Canada	211	0.018	6.4	70	15.4	75.8	112	1.37	24.6
Croatia				5	0.516	0.9	5	0.266	0.8
Finland	8	0.023	0.069	2	13.1	13.1	2	0.026	0.026
France	91	0.109	5.6	5	0.097	2.191	46	0.101	1.82
Germany	407	0.011	0.53	25	3.512	14	293	0.175	3.7
Italy	33	0.014	0.201				25	1.526	95
Japan				11	1.966	1.966	11	0.04	0.04
Korea	8	0.028	0.038	17	0.3	0.58	26	0.065	0.31
Norway							4	0.235	0.68
Romania	8	0.073	0.115						
Spain	20	0.055	0.289	58	21.12	168	49	1.849	28
Sweden							24	0.11	7.11
UK	108	0.526	5.044	15	16.89	33.764	33	1.384	27.256
USA	150	0.154	5.85	2	35.48	68.7	34	0.084	1.25
Ifosfamid									
Canada				18	0	0	18	0	0
Germany	224	0	0.18	12	0	0.04	122	0	2.9
Switzerland	5	0	0	5	0.005	5	4	0	0.006
Imipramine									
France	7	0	0				2	0	0
Indomethacin									
Canada	152	0	0.15	44	0.211	0.64	82	0.1	0.507
Croatia				5	0	0	5	0	0
France	6	0	0				3	0	0
Germany	394	0.006	0.22	5	0	0.95	190	0.141	0.6
Spain	10	0	0.01						
UK	2	0.001	0.002						
USA	23	0	0.048				20	0.012	0.029
Iohexol									
France	6	0.115	0.115				3	1.64	1.64
Germany	498	0.074	0.5	4	9	9	4	1	7
Iomeprol									
France	6	0.14	0.411				3	1.59	1.59
Germany	583	0.132	0.89	17	3.095	10	72	0.356	10
Iopamidol									
France	6	0.456	0.456				3	8.03	8.03
Germany	596	0.22	2.8	17	2.059	9	85	0.615	15
Iopanoic acid									
France	6	0	0				3	0	0
Iopromide									
Austria				7	0.036	0.18	7	0	0
France	10	0.004	0.017				3	0.25	0.25
Germany	601	0.112	4	19	8.816	22	86	1.051	20
Korea	8	0.134	0.361				9	2.359	4.03
USA	8	0.004	0.009	2	0.008	0.017	3	0.012	0.012
Iothalamic acid									
France	6	0	0				3	0	0
Germany	50	0.01	0.19	6	0.18	0.18	20	0.042	0.64

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Ioxaglic acid									
France	6	0.039	0.039				3	0.58	0.58
Ioxithalamic acid									
France	6	0.036	0.438				3	0.44	0.44
Germany	50	0.01	0.08	6	0.17	0.17	34	0.041	0.21
Josamycin									
France				19	0	0	19	0.019	0.27
Ketoprofen									
Canada	69	0.021	0.079	70	1.545	5.7	112	0.048	0.409
Croatia				5	0.451	0.97	5	0.318	0.62
Finland	8	0.013	0.028	2	2	2	2	0.032	0.032
France	85	0.007	0.04	5	4.1	10.8	46	0.179	1.62
Germany	382	0	0.12	8	0.07	0.19	218	0.077	0.38
Italy	15	0.002	0.026				8	0.438	2.1
Japan				11	0.979	0.979	11	0.445	0.445
Spain	17	0	0.144	5	0.23	0.96	5	0.2	0.75
USA	23	0	0	5	1	1	28	0.002	0.031
Labetalol									
Canada							7	0.081	0.175
Lansoprazole									
Croatia				5	0	0	5	0	0
Spain	10	0	0						
Lincomycin									
Canada	224	0.017	0.355						
Italy	15	0.03	0.249				9	0.03	0.03
USA	24	0	0	6	0	0			
Lorazepam									
France	27	0	0.015	5	0.133	0.221			
Meclocycline									
Canada	136	0	0						
Korea				2	0.785	1.07	2	0.275	0.37
USA	15	0.03	0.11						
Meclofenamic acid									
Brazil							10	0	0
Canada	9	0.107	0.115				4	0.084	0.09
Germany	49	0	0				10	0	0
UK	2	0	0						
Mefenamic acid									
Croatia				5	0.005	0.005	5	0.007	0.01
Japan				11	0.221	0.221	11	0.062	0.062
Spain	10	0.002	0.003						
UK	78	0.03	0.242	15	0.172	0.363	27	0.186	0.396
Meprobamate									
Korea	8	0	0				9	0.005	0.006
USA	14	0.263	0.306	8	1.166	1.44	6	1.27	1.27
Metamizole sodium									
Spain				12	14	24	12	4.9	7.5
Metformin									
USA	84	0.11	0.15	5	26	26	6	11	11

Table A.I-1: continued

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Methicillin									
France	6	0	0				3	0	0
Germany	14	0	0				4	0	0
Metoprolol									
Canada							7	0.244	0.402
Croatia				5	0	0	5	0	0
Finland	11	0.049	0.116	24	1.094	1.46	24	0.802	1.6
France	33	0.002	0.07				29	0.437	1.774
Germany	335	0.025	2.2	22	2.05	7.2	232	0.842	9.12
Italy							3	0.01	0.1
Spain	13	0	0.014	30	0.02	0.09	30	0.01	0.14
Sweden							24	0.08	0.39
UK	12	0.03	0.155						
USA	23	0.131	0.571				20	0.282	2.269
Metronidazole									
France				19	0	0	19	0.011	0.039
Germany	16	0.003	0.044						
Spain				6	5.9	9.4			
UK	12	0	0						
Mevastatin									
Croatia				5	0	1.17	5	0.383	0.8
Spain	10	0	0	5	0.55	1.25	5	0.35	0.85
Mezlocillin									
France	6	0	0				3	0	0
Germany	21	0	0.012				51	0	0.02
Miconazole									
UK	6	0.008	0.009						
Minocycline									
Korea				2	4.64	8.9	2	0	0
USA	36	0	0						
NA873									
Czech Rep.	9	0	0						
Germany	32	0.007	0.059						
Nadolol									
Canada							7	0.056	0.076
Germany	76	0	0				83	0.009	0.14
Nafcillin									
France	6	0	0				3	0	0
Germany	14	0	0				4	0	0

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Naproxen									
Austria	5	0.013	0.382						
Canada	299	0.019	4.5	70	13.52	611	112	2.616	33.9
Croatia				5	0.099	0.19	5	0.108	0.16
Finland	8	0.015	0.032	2	4.9	4.9	2	0.043	0.043
France	85	0.018	0.275	5	0.207	9.4	46	0.127	2.667
Germany	201	0.008	0.39	14	0.577	1.3	194	0.092	0.94
Italy	15	0	0.022				8	1.154	5.22
Japan				11	0.276	0.276	11	0.099	0.099
Korea	8	0.011	0.018				9	0.105	0.483
Spain	27	0.012	0.247	39	0.582	8.62	39	0.091	0.45
Sweden							24	0.41	2.15
USA	64	0.022	0.195	8	19.58	22.5	40	0.637	24.6
N-Formyl-4-aminoantipyrine									
Czech Rep.	9	0	0.8						
Germany	33	0.201	6.5	12	1.3	1.9	25	0.838	2
Nifedipine									
Canada	6	0	0						
Germany	11	0	0	5	0	0	19	0	0.089
USA				5	0	0	6	0	0
Nordazepam									
France	7	0	0.002				2	0.004	0.008
Norfloracin									
Canada							16	0.042	0.112
China	24	0.081	0.251						
Finland	11	0	0	24	0.081	0.96	24	0	0.11
France				19	0	0.059	21	0.037	0.24
Italy							3	0.06	0.07
Sweden				13	0.135	0.319	13	0.024	0.071
USA	151	0.091	0.12	15	0.054	0.25	9	0.113	0.33
Norfluoxetine									
Canada							11	0	0
Ofloxacin									
Canada							16	0.136	0.548
China	24	0.044	0.108						
Croatia				5	0	0	5	0	0
Finland	11	0	0.005	24	0.072	0.35	24	0.014	0.03
France	6	0.005	0.005	19	0	0	24	0.094	0.51
Germany	21	0	0.06	3	0	0.22	54	0.01	0.19
Italy	7	0.033	0.306				20	0.584	1.081
Spain	17	0.033	0.146						
Sweden				10	0.153	0.287	10	0.045	0.12
USA	24	0.088	0.109	6	0.435	1	8	0.255	0.35
o-Hydroxy Atorvastatin									
USA	12	0.004	0.004	6	0.196	0.196	6	0	0
Omeprazole									
Germany	11	0	0	5	0	0	19	0	0
Italy	16	0	0				17	0	0

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Oxacillin									
France	6	0	0				3	0	0
Germany	57	0	0				71	0	0.03
USA	21	0	0						
Oxazepam									
France	27	0.038	0.814	5	0.674	1.574			
Germany	11	0.09	0.4	11	0.48	0.86	12	0.32	0.63
Oxolinic acid									
France				19	0	0	19	0	0
USA	21	0	0						
Oxytetracycline									
Canada	136	0	0						
France	6	0	0	19	0	0	22	0.009	0.063
Germany	35	0	0				56	0	0.02
Italy	8	0	0.019				8	0	0
Korea				2	11.93	23.62	2	3.265	6.53
USA	238	0.12	0.34	9	15.67	47	3	4.2	4.2
Paracetamol									
Canada	16	0	3.6				16	0	9
Croatia				5	10.19	26.09	5	2.102	5.99
Czech Rep.	9	0.015	0.106						
France	34	0.01	0.463				2	5.704	11.3
Germany	77	0.002	0.066				49	0	6
Korea	8	0.033	0.073	16	0.07	0.26	25	0.041	0.16
Spain	13	0.037	0.25	56	30.97	246	47	0.28	6.2
UK	92	0.118	1.388	15	4.199	69.57	30	0.055	0.218
USA	8	0.001	0.002	7	48.96	61	9	0.574	0.86
Paroxetine									
Croatia				5	0	0	5	0	0
Norway				4	0.002	0.012	3	0.001	0.002
Spain	10	0	0						
Penicillin G									
France	6	0	0				3	0	0
Germany	57	0	0				71	0	0
USA	24	0	0	6	0	0			
Penicillin V									
France	6	0	0				3	0	0
Germany	49	0	0.02				55	0	0.013
USA	24	0	0	6	0	0			
Pentobarbital									
Germany	18	0.445	5.4						
Pentoxifylline									
Canada	16	0	0				35	0.011	0.045
Germany	99	0	0.26						
Korea	8	0.002	0.002				9	0.003	0.004
Romania	8	0.209	0.299						
USA	8	0	0	2	0	0	3	0.002	0.002

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Phenazon									
Canada	16	0	0	18	0	0	34	0	0
Czech Rep.	9	0	0.035						
France							2	0	0
Germany	493	0.031	2.5	32	0.171	0.45	264	0.088	0.9
Italy							3	0	0.37
USA				5	0.029	0.029	6	0.013	0.013
Phenobarbital									
Germany	18	0	1.5						
p-Hydroxy Atorvastatin									
USA	12	0.005	0.005	6	0.28	0.28	6	0	0
Pindolol									
France	6	0.01	0.01				3	0	0
Germany	14	0	0						
Piperacillin									
France	6	0	0				3	0	0
Germany	21	0	0				51	0	0.04
Piroxicam									
Germany	40	0	0				32	0	0
Pravastatin									
Canada	3	0	0	3	0.117	0.117	3	0.059	0.059
Croatia				5	0	0	5	0	0
Spain	10	0	0						
Propranolol									
Canada	6	0	0				7	0.03	0.05
Croatia				5	0.168	0.29	5	0.29	0.47
France	33	0.002	0.04				29	0.366	1.111
Germany	257	0.002	0.59	28	0.814	10	223	0.072	0.8
Italy							3	0.01	0.09
Spain	20	0	0.063	41	0.212	6.5	35	0.033	0.52
UK	62	0.02	0.215	9	0.07	0.119	15	0.23	0.373
USA	22	0	0.074				19	0.009	0.2
Propyphenazon									
Croatia				5	0	0	5	0	0
Czech Rep.	9	0.008	0.069						
France	6	0	0				3	0	0
Germany	313	0.042	0.88	24	0.135	0.25	95	0.074	0.99
Spain	17	0	0.059	5	0.5	0.85	5	0.2	0.45
Ranitidine									
Croatia				5	0.188	0.29	5	0.135	0.2
Italy	15	0.001	0.038				17	0.282	0.61
Spain	17	0.019	0.142	6	0.98	1.7			
UK	12	0	0						
USA	84	0.01	0.01	5	0.33	0.33	6	0.062	0.062
Rifampin									
France				19	0	0	19	0	0.009
Risperidone									
USA	12	0	0	6	0	0	6	0	0

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Roxithromycin									
Austria				7	0.187	0.5	7	0.098	0.23
Canada	139	0.001	0.002				11	0.006	0.018
China	24	0.041	0.169						
France	11	0.013	0.395	19	0	0	22	0.041	0.14
Germany	303	0	0.56	117	0.163	1	292	0.101	1.7
Switzerland				9	0.02	0.04	18	0.011	0.031
USA	140	0.037	0.18	3	1.5	1.5	3	0.87	0.87
Salbutamol									
Canada							7	0.007	0.01
France	7	0	0				2	0	0
Germany	323	0	0.19	16	0.026	0.21	208	0	0.17
Italy	15	0.001	0.002				17	0.008	0.018
UK	72	0.115	0.471	6	0.113	0.141	18	0.109	0.17
USA				5	13	13	6	8.1	8.1
Salicylic acid									
Canada	31	0.079	17	52	11.1	27.8	75	0.385	35
France	27	0.008	0.613						
Germany	35	0.025	4.1				36	0	0.14
Italy	15	0.036	0.205				5	6.2	12
Korea				16	23.92	88.99	16	2.43	6.73
Spain	3	0.013	0.019	30	0	0	30	0.045	0.19
Secobarbital									
Germany	18	0	0.1						
Sertraline									
Norway				4	0.002	0.016	3	0.002	0.002
Simvastatin									
Canada	3	0	0	3	0.004	0.004	3	0.001	0.001
France	3	0	0				3	0	0
Germany	48	0	0				7	0	0
UK	12	0	0						
USA	12	0.001	0.001	6	5	5	6	0	0
Simvastatin hydroxy acid									
USA	12	0	0	6	0.01	0.01	6	0	0
Sotalol									
Canada							7	0.264	0.429
Croatia				5	0.167	0.2	5	0.185	0.21
Finland	11	0.041	0.086	24	0.706	3.28	24	0.26	1.12
France	6	0.063	0.063				3	0.87	0.87
Germany	225	0.044	0.95	22	1.255	3.526	132	1.109	6.5
Spain	10	0	0.07						
Spiramycin									
France	6	0.004	0.004	19	0	0.158	22	0.318	4
Germany	43	0	0				67	0	0.04
Italy	15	0.005	0.074				17	0.043	0.161
Sulfachlorpyridazine									
Canada	224	0.003	0.02						
Korea				2	4.045	6.53	2	0.03	0.06
USA	36	0	0						

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Sulfadiazine									
Canada							8	0.019	0.019
China	30	0.099	0.336	3	0	0	3	0	0
Germany	14	0	0						
Italy	3	0	0.236						
USA	21	0	0						
Sulfadimethoxine									
Canada	136	0.001	0.056						
Italy	3	0.028	0.074						
Korea				2	6.345	12.23	2	0	0
USA	15	0	0.04						
Sulfamerazine									
Canada	136	0	0						
Greece							24	0	0
Korea				2	2.49	3.45	2	0	0
USA	36	0	0.06						
Sulfamethazine									
Canada	224	0.002	0.408				8	0.363	0.363
China	30	0.134	0.34	3	0.58	0.58	3	0	0
France	6	0.002	0.002	19	0	0.002	22	0	0.004
Germany	170	0	0.07				59	0	0.2
Greece							24	0	0
Korea				2	50.62	97.23	2	0	0
USA	224	0.096	0.22	8	0.112	0.3	3	0.36	0.36
Sulfamethoxazole									
Canada	136	0.003	0.009				8	0.243	0.871
China	30	0.101	0.33	3	0.64	0.64	3	0.56	0.56
Croatia				5	0.59	0.87	5	0.39	0.82
France	38	0.01	0.24	19	0.225	5.4	24	0.206	0.34
Germany	308	0.03	0.48	25	0.742	9	103	0.307	4.7
Greece							6	0.194	0.4
Italy	21	0.003	0.402				20	0.123	0.317
Korea	8	0.02	0.036	2	0.225	0.45	11	0.118	0.407
Spain	17	0.015	0.169	5	0.45	0.96	5	0.4	0.8
Sweden				10	0.302	0.674	10	0.248	0.304
Switzerland				9	0.09	0.15	15	0.09	0.35
UK	36	0.003	0.06	9	0	0	14	0	0.132
USA	257	0.135	1.9	30	0.782	2.8	44	0.389	6
Sulfapyridine									
China	6	0	0	3	0	0	3	0	0
Greece							24	0	0
Italy	3	0.066	0.121						
UK	12	0.009	0.039						
Sulfathiazole									
Canada	136	0.001	0.016						
China	6	0.26	0.52	3	0.35	0.35	3	0	0
Greece							24	0	0
Korea				2	584.62	1158.68	2	2.225	4.27
USA	36	0	0.01						

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Tamoxifen									
UK	20	0.053	0.212	9	0.153	0.215	9	0.199	0.369
Terbutaline									
France	7	0	0				2	0	0
Germany	176	0	0.03	14	0.053	0.37	142	0.002	0.6
Tetracycline									
Canada	136	0	0				8	0.151	0.977
France	6	0	0	19	0	0	22	0.009	0.066
Germany	35	0	0				56	0	0
Korea				2	0.545	0.98	2	0.705	1.41
USA	245	0.038	0.11	11	13.46	48	19	0.646	3.6
Thiamphenicol									
France				19	0	0	19	0	0
Timolol									
Canada							7	0	0
Germany	68	0.002	0.068				29	0	0.07
Tramadol									
Germany	4	0.025	0.052						
UK	12	0.358	2.108						
Trimethoprim									
Canada	224	0.002	0.015				19	0.205	0.344
Croatia				5	1.172	4.22	5	0.29	0.31
France	33	0.001	0.014	19	0.026	1.05	24	0.019	0.17
Germany	299	0	0.2	23	0.291	1.1	203	0.07	1.5
Greece							6	0.12	0.3
Italy							3	0.04	0.13
Korea	8	0.004	0.005				9	0.053	0.188
Spain	17	0.02	0.069	11	0.186	0.65	5	0.11	0.23
Sweden				13	0.52	1.86	37	0.284	1.88
Switzerland				9	0.29	0.44	15	0.07	0.31
UK	54	0.006	0.569	9	0.263	0.3	12	0.238	0.322
USA	242	0.076	0.8	30	1.652	7.9	41	0.238	2.4
Tylosin									
Canada	136	0	0						
France	6	0	0	19	0	0	22	0	0
Germany	167	0	0.02				143	0	0.09
Italy	8	0	0.003				8	0.001	0.001
USA	133	0.031	0.28	105	0.153	1.5	99	0.046	0.72
Valsartan									
UK	12	0.012	0.133						
Vancomycin									
France	6	0	0				3	0	0
Germany	21	0	0				51	0	0
Venlafaxine									
Austria							24	0	0.206
Warfarin									
USA				5	0.17	0.17	6	0	0
Xylometazolin									
Czech Rep.	9	0	0						
Germany	32	0.001	0.009						

Table A.I-1: continued.

	Surface water (SW)			STP influent			STP effluent		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Zolpidem									
France	27	0	0.004	5	0.06	1.119			

Table A-I. 2: Averaged environmental concentrations (A-MEC) and maximal concentrations of pharmaceuticals measured in ground water, bank filtrate, drinking water, and marine water.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
1-Hydroxyibuprofen												
France	2	0	0							8	0	0
2-Hydroxyibuprofen												
France	2	0	0							8	0	0.563
Norway										12	0	0.002
4-Chlorobenzoic acid												
France	2	0	0							8	0	0.035
4-hydroxyantipyrin												
Germany	42	0	0	84	0	0						
6-o-desmethyl naproxen												
France	2	0	0							8	0	0.161
Acetylsalicylic acid												
France							7	0	0.001			
Germany							55	0	0			
Alprazolam												
France	2	0	0							8	0	0
Ambroxol												
Germany	42	0	0	84	0	0						
AMDOPH												
Germany	2	1.2	1.2				2	0.9	0.9			
Amitriptyline												
France							7	0	0			
Amoxicillin												
China										20	0	0
Germany	16	0	0.1									
AMPH												
Germany							2	0.03	0.03			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Ampicillin												
Germany	10	0	0									
Atenolol												
France	2	0	0							8	0.016	0.245
Germany	103	0	0	32	0	0						
USA							6	0	0			
Atorvastatin												
USA							6	0	0			
Azithromycin												
Germany	10	0	0									
Betaxolol												
Germany	29	0	0									
Bezafibrate												
Austria	7	0.004	0.023									
France	2	0	0							8	0.003	0.026
Germany	66	0	0.19	49	0	0.11	55	0	0.027			
Italy	2	0	0				6	0.001	0.002			
Bisoprolol												
Germany	117	0	0.074	32	0	0.11						
Bromazepam												
France	2	0.117	0.161							8	0	0.356
Carazolol												
Germany	23	0	0									
Carbamazepine												
Austria	7	0	0									
Canada							3	0	0			
France	2	0.012	0.023	3	0.053	0.071	8	0	0.043	8	0.329	0.997
Germany	215	0.015	1.1	70	0.082	1	12	0	0.03			
Italy	2	0	0				6	0.005	0.005			
USA							8	0	0	44	0.005	0.078

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Chloramphenicol												
China										20	0	0
Germany	98	0	0	10	0	0						
Chlortetracycline												
Germany	58	0	0									
USA							6	0	0			
Cimetidine												
USA										44	0	0.067
Ciprofloxacin												
Germany	10	0	0									
USA							6	0	0			
Clarithromycin												
Germany	152	0	0	12	0	0						
Clenbuterol												
France							7	0	0			
Germany	87	0	0	32	0	0						
Clofibric acid												
France	2	0	0							8	0	0
Germany	179	0	11	49	0.007	7.3	151	0.02	0.17	15	0	0.019
USA							20	0	0			
Clotrimazole												
France	2	0	0							8	0	0
Cloxacillin												
Germany	37	0	0									
Codeine												
Germany	1	0	0									
USA										44	0.005	0.105
Cyclophosphamid												
Germany	85	0	0	32	0	0	12	0	0			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Dapsone												
Germany	6	0	0									
Demeclocycline												
USA							6	0	0			
Diatrizoate												
Germany	89	1.468	9.6	30	0.011	4	10	0.021	0.085			
Diazepam												
France	2	0	0				7	0	0	8	0	0.004
Germany	95	0	0	32	0	0	12	0	0			
USA							8	0	0			
Diclofenac												
Austria	7	0	0									
Canada							3	0	0			
France	2	0	0				7	0.002	0.002	8	0.032	0.101
Germany	143	0	0.93	57	0.003	0.43	58	0	0.006			
Italy	2	0	0				6	0	0			
USA							8	0	0			
Dicloxacillin												
Germany	53	0	0									
Dihydrocodeine												
Germany	1	0	0									
Dilantin												
USA							8	0.001	0.001			
Diltiazem												
Canada							3	0	0			
USA										44	0.001	0.013
Dimethylaminophenazone												
Germany	33	0.024	0.4				4	0	0			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Doxepin												
France							7	0	0			
Doxycycline												
Germany	37	0	0									
USA							6	0	0			
Enalapril												
USA							6	0	0			
Erythromycin												
China										20	0.003	0.005
Germany	152	0	0	12	0	0						
USA							8	0	0.005			
Etofibrate												
Germany	7	0	0				12	0	0			
Fenofibrate												
France	2	0	0							8	0	0.027
Germany	33	0	0				12	0	0			
USA										38	0	0
Fenofibric acid												
France	2	0	0							8	0	0
Germany	31	0	0.598				57	0	0.042			
Fenoprofen												
Germany	7	0	0									
Fenoterol												
Germany	3	0	0									
Flumequine												
USA							6	0.002	0.002			
Fluoxetine												
France	2	0	0							8	0	0
USA							13	0	0	17	0	0.007

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Furazolidone												
Germany	6	0	0									
Furosemide												
France	2	0	0							8	0.01	0.118
Gemfibrozil												
Canada							3	0	0			
France	2	0	0				7	0	0	8	0	0.018
Germany	22	0	0				55	0	0			
Italy	2	0	0				6	0	0.001			
USA							8	0	0.002			
Hydrocodone												
Germany	1	0	0									
USA							2	0	0	38	0.002	0.025
Ibuprofen												
Austria	7	0	0									
Canada							3	0.003	0.003			
France	2	0	0	3	0	0	8	0	0.001	8	0	0.021
Germany	101	0	0	30	0	0.2	58	0	0.003	2	0	0
Italy	2	0	0				6	0	0			
Norway										12	0	0.001
USA							22	0.082	1.35			
Ifosfamid												
Germany	85	0	0	32	0	0	12	0	0			
Imipramine												
France							7	0	0			
Indomethacin												
Germany	88	0	0	49	0	0.005	55	0	0			
Iodipamide												
Germany	8	0.01	0.01									

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Iohexol												
Germany	32	0.002	0.01				2	0.039	0.04			
Iomeprol												
Germany	59	0.001	0.01	30	0	0.16	2	0.086	0.092			
Iopamidol												
Germany	96	0.064	2.4	30	0	1.4	15	0.011	0.098			
Iopanoic acid												
Germany	8	0.01	0.01									
Iopromide												
Austria	7	0.002	0.01									
France				4	0	0	2	0	0			
Germany	96	0.001	0.21	30	0	0.04	15	0.01	0.086			
USA							2	0.002	0.005			
Iothalamic acid												
Germany	24	0.003	0.072				10	0	0.01			
Ioxaglic acid												
Germany	8	0.01	0.01									
Ioxithalamic acid												
Germany	42	0.002	0.049				10	0	0			
Ketoprofen												
France	2	0	0				7	0	0.003	8	0	0
Germany	94	0	0	30	0	0	25	0	0			
USA										38	0	0
Lincomycin												
USA							6	0	0			
Lorazepam												
France	2	0	0							8	0.013	0.013
Meprobamate												
USA							8	0.006	0.008			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Metformin												
USA										44	0	0.092
Methicillin												
Germany	37	0	0									
Metoprolol												
France	2	0	0							8	0.005	0.118
Germany	126	0	0.065	36	0	0.03						
Metronidazole												
Germany	6	0	0									
Minocycline												
USA							6	0	0			
NA873												
Germany	42	0	0	84	0	0						
Nadolol												
Germany	21	0	0									
Nafcillin												
Germany	37	0	0									
Naproxen												
Canada							6	0	0			
France	2	0	0				7	0	0	8	0.011	0.214
Germany	77	0	0.14	30	0	0						
USA							10	0	0			
Nifedipine												
Canada							3	0	0			
USA										41	0	0.004
Nordazepam												
France							7	0	0			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Norfloxacin												
China										20	0.011	0.028
USA							12	0	0			
Ofloxacin												
China										20	0.008	0.016
o-Hydroxy Atorvastatin												
USA							6	0	0			
Oxacillin												
Germany	53	0	0									
Oxazepam												
France	2	0.002	0.003							8	0.519	2.183
Oxolinic acid												
USA							6	0.003	0.004			
Oxytetracycline												
Germany	48	0	0									
USA							6	0	0			
Paracetamol												
France	2	0	0				7	0.01	0.211	8	0.013	0.162
Germany	42	0	0	84	0	0						
USA							2	0	0	44	0.018	0.188
Penicillin G												
Germany	48	0	0									
Penicillin V												
Germany	43	0	0									
Pentoxifylline												
Germany	13	0	0									
USA							2	0	0			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Phenazon												
Germany	159	0.234	3.95	116	0.159	1.25	22	0.123	0.4			
USA										38	0	0
p-Hydroxy Atorvastatin												
USA							6	0	0			
Pindolol												
Germany	6	0	0									
Piroxicam												
Germany	49	0	0									
Propranolol												
Canada							3	0	0			
France	2	0	0							8	0.021	0.224
Germany	141	0	0.096	32	0	0						
Propyphenazon												
Germany	75	0.133	1.23	131	0.041	1.465	8	0.1	0.12			
Ranitidine												
USA										44	0	0
Risperidone												
USA							6	0	0			
Roxithromycin												
Austria	7	0.004	0.01									
China										20	0.006	0.031
France				4	0	0	2	0	0			
Germany	152	0	0	12	0	0						
USA							6	0	0.001			
Salbutamol												
France							7	0	0			
Germany	93	0	0	32	0	0						
USA										17	0	0

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Salicylic acid												
Canada							3	0.004	0.004			
France	2	0.037	0.043									
Simvastatin												
Germany	6	0	0									
USA							6	0	0			
Simvastatin hydroxy acid												
USA							6	0	0			
Sotalol												
Germany	102	0	0.56	40	0	0.37						
Spiramycin												
Germany	11	0	0									
Sulfachlorpyridazine												
USA							6	0	0			
Sulfadiazine												
China							3	0	0	20	0	0
Germany	17	0	0.05									
Italy							4	0	0			
Sulfadimethoxine												
Italy							4	0	0.011			
USA	18	0.05	0.068				6	0	0			
Sulfamerazine												
USA							6	0	0			
Sulfamethazine												
China							3	0	0	20	0	0
Germany	124	0	0.24									
USA	18	0.078	0.215				6	0	0			

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Sulfamethoxazole												
China							3	0	0	20	0	0
France	2	0	0	4	0.011	0.058	2	0	0	8	0.028	0.24
Germany	162	0.006	0.47	20	0.032	0.079						
Italy	2	0	0				10	0.003	0.08			
USA							14	0.001	0.003	44	0.006	0.081
Sulfapyridine												
China							3	0	0			
Italy							4	0	0			
Sulfathiazole												
China							3	0	0			
Germany	11	0	0.02									
Terbutaline												
France							7	0	0			
Germany	76	0	0	16	0	0						
Tetracycline												
Germany	48	0	0									
USA							6	0	0			
Timolol												
Germany	20	0	0									
Trimethoprim												
France	2	0	0							8	0	0
Germany	162	0	0.04	20	0	0						
USA							14	0	0	44	0.005	0.125
Tylosin												
Germany	59	0	0									
USA							6	0	0.004			
Warfarin												
USA										44	0	0.005

Table A.I-2: continued.

	Ground water (GW)			Bank filtrate (BF)			Drinking water (DW)			Marine coastal water (MW)		
	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])	samples	A-MEC ([µg/L])	MAX ([µg/L])
Xylometazolin												
Germany	42	0	0	84	0	0						
Zolpidem												
France	2	0	0							8	0	0.005

10 Annex II: Consumption of PPs in 5 European countries

Table A-II. 1: Annual consumption of pharmaceuticals in g per year and person for France, Germany, Poland, Spain and the UK (Average of 1999-2006).

Compound	Therapeutic Class	Annual per capita consumption of PPs (g/a)				
		Germany	France	Spain	UK/Wales	Poland
Amoxicillin	Antibiotic	1.198	6.496		1.535	
Ampicillin		0.131			0.039	
Azithromycin		0.041	0.069		0.008	0.048
Chloramphenicol		0.004			0.002	
Chlortetracycline		0.003			0	
Ciprofloxacin		0.172	0.205	0.091	0.124	0.126
Clarithromycin		0.118	0.254	0.132	0.077	0.271
Clindamycin		0.146			0.011	0.113
Dapsone		0.001			0.002	
Dicloxacillin		0.001				
Doxycycline		0.137	0.105		0.027	
Erythromycin		0.257			0.536	0.166
Flucloxacillin		0.028			0.558	
Flumequine		0.008				
Furazolidone		0				
Josamycin				0.216		
Metronidazole		0.095	0.616		0.178	
Mezlocillin		0.083				
Minocycline		0.009				
Norfloxacin		0.037			0.008	0.079
Ofloxacin		0.066	0.07		0.005	0.023
Oxacillin		0.003				
Oxytetracycline		0.025			0.476	
Penicillin G		0.082			0	
Penicillin V		1.05			0.443	
Piperacillin		0.001			0	
Roxithromycin		0.086	0.16		0	0.049
Spiramycin		0.005	0.007		0	
Sulfadiazine		0.031			0	
Sulfamerazine		0.011				
Sulfamethoxazole		0.652	0.337		0.018	0.171
Sulfasalazine		0.465			0.906	
Tetracycline	0.017			0.028	0.085	
Trimethoprim	0.147	0.056		0.14		
Vancomycin	0.011	0.015		0		
Atenolol	Beta-blocker	0.139	0.309		0.636	0.125
Betaxolol		0.004			0	
Bisoprolol		0.037	0.036		0.012	
Carazolol		0				
Diltiazem		0.129		0.136	0.427	
Metoprolol		0.995	0.148		0.036	0.393
Nadolol		0.003	0.016		0.001	
Pindolol		0.149	0.075		0	
Propranolol		0.065	0.21		0.143	0.01
Sotalol		0.283			0.061	0.032

Table A-II. 1: continued.

Compound	Therapeutic Class	Annual per capita consumption of PPs (g/a)				
		Germany	France	Spain	UK/Wales	Poland
Carbamazepine	Antiepileptics	0.983	0.614		0.767	0.838
Gabapentin		0.202		0.046	0.75	
Phenobarbital		0.007				
Valproic acid		0.723	1.889		0.506	
Atorvastatin	Lipid regulator	0.058		0.051	0.212	
Bezafibrate		0.382	0.462		0.146	0.007
Fenofibrate		0.169	1.446		0.052	0.18
Gemfibrozil		0.072			0.017	0.007
Pravastatin		0.016		0.024	0.039	
Simvastatin		0.065	0.117	0.023	0.257	0.028
Acetylsalicylic acid	Analgesic	13.665	10.749		1.564	
Celecoxib		0.074		0.048	0.08	
Codeine		0.094			0.302	
Dextropropoxyphene			0.875		0.861	
Diclofenac		0.883	0.167	0.059	0.538	0.506
Hydrocodone		0				
Ibuprofen		3.172	3.425	2.641	2.843	5.036
Indomethacin		0.041			0.02	0.022
Ketoprofen		0.018	0.366	0.005	0.025	0.337
Mesalazine		0.723			0.879	
Metamizole sodium		1.99				
Naproxen		0.063	0.643	0.259	0.615	1.009
Paracetamol		4.456	47.143	3.595	15.683	4.839
Phenazon		0.352				
Piroxicam		0.008	0.034	0.011	0.004	
Propyphenazon		0.44				
Rofecoxib		0.022		0.005	0	
Tramadol	0.3	0.436		0.272		
Diatrizoate Sodium	contrast medium	0.662				
Iohexol		0.098				
Iomeprol		0.603				
Iopamidol		0.398				
Iopromide		0.788	1.236			
Ioxithalamic acid		0.108				
Ioversol		0.529				
Cyclophosphamid	Cytostatic	0.007	0.005		0	
Ifosfamid		0.002	0.002			
Tamoxifen		0.009				
Amitryptiline	Antidepressant	0.081			0.061	
Citalopram		0.024				
Doxepin		0.065				
Fluoxetine			0.063	0.034	0.06	
Paroxetine		0.007		0.04	0.028	
Sertraline		0.03		0.067	0.085	
Venlafaxine		0.082		0.027	0.147	
Alprazolam	Tranquilliser	0.121				
Bromazepam		0.004	0.044			
Diazepam		0.011	0.008		0.012	
Lorazepam		0.984	0.01		0.001	
Oxazepam		0.012	0.104		0.002	

Table A-II. 1: continued.

Compound	Therapeutic Class	Annual per capita consumption of PPs (g/a)				
		Germany	France	Spain	UK/Wales	Poland
Amlodipine	Antihypertensive	0.018		0.013	0.058	
Captopril		0.29		0.024	0.035	
Enalapril		0.056				
Irbesartan		0.181		0.102	0.335	
Lactitol		0.279			0	
Nifedipine		0.097				
Troxerutin		0.499	7.485			
Valsartan		0.101		0.127	0.15	
Verapamil		0.7			0.139	
Zopiclone	Sedative	0.003	0.033		0.012	
Zolpidem		0.004	0.056		0.001	
Risperidone	Antipsychotic	0.001				
Cimetidine	Antiulcerative	0.009				
Lansoprazole		0.007		0.012	0.157	
Omeprazole		0.081		0.063	0.14	
Pantoprazole		0.061		0.018	0.02	
Ranitidine		1.038	0.196	0.484	0.599	
Furosemide	Diuretic	0.341	0.359		0.281	
Hydrochlorothiazide		0.201				
Torsemide		0.045		0.723	0	
Clenbuterol	Bronchiolytic	0				
Fenoterol		0.003			0	
Salbutamol		0.01			0.002	0.004
Terbutaline		0.002			0.008	
Theophylline		1.457			0.177	
Ambroxol	Mucolytic	0.15				
Carbocistein			3.913		0.212	
Xylometazolin	Vasoconstrictor	0.007			0	
Pentoxifylline	Vasodilator	0.953			0.018	
Dihydrocodeine	Antitussive	0.013			0.205	
Clotrimazole	Antifungal	0.057			0.011	
Miconazole		0.107			0.008	
Nimodipine	Nootropic	0.001		0.033	0	
Piracetam		1.249			0.022	
Clopidogrel	Anticoagulant	0.127		0.091	0.165	
Allopurinol	Urostatic	1.677	0.914		0.464	
Metformin	Antidiabetic	6.297	12.076		5.902	
Diosmin	Phlebotropic		6.293			

Table A-II. 2: Average annual consumption of pharmaceuticals in metric tons for France, Germany, Poland, Spain and the UK. Data available for the period from 1999-2006 were averaged.

Compound	Therapeutic Class	Total annual consumption (t/a)				
		Germany	France	Spain	UK/Wales	Poland
Amoxicillin	Antibiotic	98.57	385.612		80.321	
Ampicillin		10.758			2.06	
Azithromycin		3.351	4.073		0.405	1.858
Chloramphenicol		0.32			0.104	
Chlortetracycline		0.28			0	
Ciprofloxacin		14.186	12.186	3.746	6.506	4.847
Clarithromycin		9.729	15.105	5.391	4.027	10.397
Clindamycin		12.048			0.571	4.348
Dapsone		0.076			0.079	
Dicloxacillin		0.104				
Doxycycline		11.252	6.243		1.407	
Erythromycin		21.124			28.031	6.367
Flucloxacillin		2.345			29.213	
Flumequine		0.668				
Furazolidone		0.015				
Josamycin				12.802		
Metronidazole		7.798	36.545		9.338	
Mezlocillin		6.868				
Minocycline		0.713				
Norfloxacin		3.04			0.393	3.031
Ofloxacin		5.4	4.137		0.276	0.895
Oxacillin		0.216				
Oxytetracycline		2.032			24.904	
Penicillin G		6.742			0.007	
Penicillin V		86.398			23.186	
Piperacillin		0.063			0.002	
Roxithromycin		7.096	9.5		0	1.878
Spiramycin		0.402	0.42		0	
Sulfadiazine		2.55			0.007	
Sulfamerazine		0.923				
Sulfamethoxazole		53.693	20.015		0.965	6.579
Sulfasalazine		38.275			47.426	
Tetracycline	1.396			1.49	3.256	
Trimethoprim	12.13	3.346		7.337		
Vancomycin	0.912	0.918		0.016		
Atenolol	Beta-blocker	11.421	18.337		33.274	4.819
Betaxolol		0.354			0.006	
Bisoprolol		3.01	2.113		0.636	
Carazolol		0.001				
Diltiazem		10.656		5.561	22.345	
Metoprolol		81.907	8.786		1.905	15.102
Nadolol		0.213	0.938		0.042	
Pindolol		12.275	4.476		0.004	
Propranolol		5.362	12.487		7.478	0.403
Sotalol		23.288			3.213	1.23

Table A-II.2: continued

Compound	Therapeutic Class	Total annual consumption (t/a)				
		Germany	France	Spain	UK/Wales	Poland
Carbamazepine	Antiepileptics	80.892	36.438		40.152	32.168
Gabapentin		16.592		1.868	39.237	
Phenobarbital		0.6				
Valproic acid		59.478	112.162		26.508	
Atorvastatin	Lipid regulator	4.753		2.074	11.1	
Bezafibrate		31.454	27.426		7.66	0.273
Fenofibrate		13.896	85.835		2.723	6.905
Gemfibrozil		5.963			0.902	0.274
Pravastatin		1.354		0.979	2.067	
Simvastatin		5.318	6.943	0.925	13.458	1.06
Acetylsalicylic acid	Analgesic	1124.786	638.106		81.863	
Celecoxib		6.12		1.956	4.205	
Codeine		7.72			15.822	
Dextropropoxyphene				51.963	45.04	
Diclofenac		72.676	9.896	2.419	28.15	19.448
Hydrocodone		0.007				
Ibuprofen		261.055	203.312	108.253	148.787	193.387
Indomethacin		3.402			1.06	0.855
Ketoprofen		1.479	21.697	0.21	1.296	12.933
Mesalazine		59.524			46.017	
Metamizole sodium		163.778				
Naproxen		5.186	38.166	10.626	32.161	38.761
Paracetamol		366.809	2798.538	147.348	820.834	185.806
Phenazon		29.003				
Piroxicam		0.669	2.008	0.452	0.215	
Propyphenazon		36.243				
Rofecoxib		1.792		0.186	0	
Tramadol	24.69	25.897		14.229		
Diatrizoate Sodium	contrast medium	54.481				
Iohexol		8.053				
Iomeprol		49.616				
Iopamidol		32.744				
Iopromide		64.841	73.4			
Ioxithalamic acid		8.895				
Ioversol		43.581				
Cyclophosphamid	Cytostatic	0.538	0.282		0.017	
Ifosfamid		0.187	0.121			
Tamoxifen		0.78				
Amitryptiline	Antidepressant	6.676			3.214	
Citalopram		1.958				
Doxepin		5.385				
Fluoxetine			3.74	1.38	3.115	
Paroxetine		0.578		1.631	1.489	
Sertraline		2.445		2.758	4.43	
Venlafaxine		6.787		1.109	7.677	
Alprazolam	Tranquilliser	10				
Bromazepam		0.29	2.604			
Diazepam		0.888	0.463		0.649	
Lorazepam		81	0.585		0.04	
Oxazepam		0.97	6.195		0.124	

Table A-II.2: continued

Compound	Therapeutic Class	Total annual consumption (t/a)				
		Germany	France	Spain	UK/Wales	Poland
Amlodipine	Antihypertensive	1.448		0.513	3.011	
Captopril		23.833		0.992	1.85	
Enalapril		4.607				
Irbesartan		14.89		4.188	17.54	
Lactitol		22.967			0.001	
Nifedipine		7.97				
Troloxerutin		41.058	444.339			
Valsartan		8.283		5.187	7.83	
Verapamil		57.655			7.264	
Zopiclone	Sedative	0.265	1.948		0.65	
Zolpidem		0.327	3.344		0.058	
Risperidone	Antipsychotic	0.109				
Cimetidine	Antiulcerative	0.72		0.49	8.221	
Lansoprazole		0.543		2.571	7.326	
Omeprazole		6.708		0.757	1.068	
Pantoprazole		5				
Ranitidine		85.409	11.656	19.831	31.344	
Furosemide	Diuretic	28.086	21.288		14.732	
Hydrochlorothiazide		16.514				
Torasemide		3.7		29.654	0.008	
Clenbuterol	Bronchiolytic	0.001			0	0.17
Fenoterol		0.217			0.109	
Salbutamol		0.852			0.411	
Terbutaline		0.131			9.258	
Theophylline		119.896				
Ambroxol	Mucolytic	12.37				
Carbocistein			232.308		11.093	
Xylometazolin	Vasoconstrictor	0.572			0.001	
Pentoxifylline	Vasodilator	78.418			0.926	
Dihydrocodeine	Antitussive	1.069			10.74	
Clotrimazole	Antifungal	4.662			0.591	
Miconazole		8.8			0.397	
Nimodipine	Nootropic	0.12		1.349	0.004	
Piracetam		102.784			1.174	
Clopidogrel	Anticoagulant	10.432		3.749	8.632	
Allopurinol	Urostatic	138.008	54.247		24.286	
Metformin	Antidiabetic	518.303	716.858		308.888	
Diosmin	Phlebotropic		373.544			

11 Annex III: Predicted environmental concentrations (PEC) in raw sewage water and surface water

Table A-III. 1: Predicted environmental concentrations (PEC) of pharmaceuticals in raw sewage water (WWTP influent) calculated for France, Germany, Poland, Spain and the UK from the consumption data given in Annex I (PECa: PEC calculated without excreted PP fraction (E=1), PECb: PEC calculated with excreted PP fraction).

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PP in WWTP influent [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb
Acetylsalicylic acid	Analgesic	149.752		117.801				17.141			
Celecoxib		0.815				0.654		0.88			
Codeine		1.028	0.565					3.313	1.822		
Dextropropoxyphene				9.593	0.48			9.431	0.472		
Diclofenac		9.676	2.903	1.827	0.548	0.808	0.243	5.894	1.768	5.55	1.665
Hydrocodone		0.001	0								
Ibuprofen		34.756	13.555	37.533	14.638	36.18	14.11	31.154	12.15	55.19	21.524
Indomethacin		0.453	0.136					0.222	0.067	0.244	0.073
Ketoprofen		0.197	0.148	4.005	3.004	0.07	0.053	0.271	0.204	3.691	2.768
Mesalazine		7.925						9.636			
Metamizole sodium		21.805									
Naproxen		0.69	0.083	7.046	0.846	3.551	0.426	6.734	0.808	11.062	1.328
Paracetamol		48.836	25.395	516.638	268.652	49.246	25.608	171.874	89.374	53.027	27.574
Phenazon		3.861									
Piroxicam		0.089	0.009	0.371	0.037	0.151	0.015	0.045	0.005		
Propyphenazon		4.825									
Rofecoxib		0.239				0.062		0			
Tramadol		3.287	0.986	4.781	1.434			2.979	0.894		
Clopidogrel		Anticoagulant	1.389	0.694			1.253	0.627	1.807	0.904	
Clotrimazole	Antifungal	0.621						0.124			
Miconazole		1.172	0.598					0.083	0.042		
Ambroxol	Mucolytic	1.647	1.318								
Carbocistein				42.886				2.323			

Table A-III.1: continued.

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PPs in WWTP influent [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb
Amoxicillin	Antibiotic	13.123	9.843	71.188	53.391			16.818	12.614		
Ampicillin		1.432	0.43					0.431	0.129		
Azithromycin		0.446	0.277	0.752	0.466			0.085	0.053	0.53	0.329
Chloramphenicol		0.043	0.038					0.022	0.02		
Chlortetracycline		0.037	0.006					0	0		
Ciprofloxacin		1.889	1.454	2.25	1.732	1.252	0.964	1.362	1.049	1.383	1.065
Clarithromycin		1.295	0.233	2.789	0.502	1.802	0.324	0.843	0.152	2.967	0.534
Clindamycin		1.604	0.209					0.12	0.016	1.241	0.161
Dapsone		0.01	0.006					0.017	0.01		
Dicloxacillin		0.014	0.008								
Doxycycline		1.498	0.599	1.153	0.461			0.295	0.118		
Erythromycin		2.812	2.756					5.869	5.752	1.817	1.781
Flucloxacillin		0.312						6.117			
Flumequine		0.089									
Furazolidone		0.002									
Josamycin				2.363	0.473						
Metronidazole		1.038	0.208	6.747	1.349			1.955	0.391		
Mezlocillin		0.914									
Minocycline		0.095									
Norfloxacin		0.405	0.255					0.082	0.052	0.865	0.545
Ofloxacin		0.719	0.611	0.764	0.649			0.058	0.049	0.255	0.217
Oxacillin		0.029									
Oxytetracycline		0.271						5.215			
Penicillin G		0.898	0.709					0.001	0.001		
Penicillin V		11.503						4.855			
Piperacillin		0.008	0.008					0	0		
Roxithromycin	0.945	0.472	1.754	0.877			0	0	0.536	0.268	
Spiramycin	0.053		0.078				0				

Table A-III.1: continued.

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PPs in WWTP influent [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb
Sulfadiazine	Antibiotic	0.34	0.17					0.001	0.001		
Sulfamerazine		0.123	0.074								
Sulfamethoxazole		7.149	1.430	3.695	0.739			0.202	0.040	1.878	0.376
Sulfasalazine		5.096	0.51					9.93	0.993		
Tetracycline		0.186	0.108					0.312	0.181	0.929	0.539
Trimethoprim		1.615	1.066	0.618	0.408			1.536	1.014		
Vancomycin		0.121	0.096	0.169	0.134			0.003	0.003		
Amitriptyline	Antidepressant	0.889	0.018								
Citalopram		0.261	0.253					0.673	0.653		
Doxepin		0.717	0								
Fluoxetine				0.69	0.304	0.461	0.203	0.652	0.287		
Paroxetine		0.077	0.002			0.545	0.016	0.312	0.009		
Sertraline		0.326	0.046			0.922	0.129	0.928	0.13		
Venlafaxine		0.904				0.371		1.607			
Phenobarbital	Antiepileptic	0.08	0.034								
Carbamazepine		10.77	0.538	6.727	0.336			8.407	0.420	9.18	0.459
Gabapentin		2.209				0.624		8.216			
Valproic acid		7.919	1.98	20.706	5.177			5.55	1.388		
Amlodipine	Antihypertensive	0.193	0.073			0.172	0.065	0.63	0.24		
Captopril		3.173	1.428			0.332	0.149	0.387	0.174		
Enalapril		0.613	0.227								
Irbesartan		1.982				1.4		3.673			
Lactitol		3.058						0			
Nifedipine		1.061									
Troxerutin		5.466		82.029							
Valsartan		1.103				1.734		1.64			
Verapamil		7.676	0.23					1.521	0.046		
Risperidone	Antipsychotic	0.015									

Table A-III.1: continued.

Compound	Class	Predicted environmental concentrations (PEC) of PPs in WWTP influent [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb
Atenolol	Beta-blocker	1.521	0.608	3.385	1.354			6.967	2.787	1.375	0.550
Betaxolol		0.047	0.007					0.001	0		
Bisoprolol		0.401	0.24	0.39	0.234			0.133	0.08		
Carazolol		0									
Diltiazem		1.419	0.057			1.859	0.074	4.679	0.187		
Metoprolol		10.905	1.2	1.622	0.178			0.399	0.044	4.31	0.474
Nadolol		0.028	0.027	0.173	0.166			0.009	0.008		
Pindolol		1.634	0.409	0.826	0.207			0.001	0		
Propranolol		0.714	0.186	2.305	0.599			1.566	0.407	0.115	0.03
Sotalol		3.101	3.287					0.673	0.713	0.351	0.372
Clenbuterol	Bronchiolytic	0									
Fenoterol		0.029	0.022					0	0		
Salbutamol		0.113	0.099					0.023	0.02	0.048	0.042
Terbutaline		0.017	0.017					0.086	0.086		
Theophylline		15.963	2.075					1.939	0.252		
Diatrizoate sodium	contrast medium	7.253	7.253								
Iohexol		1.072	1.072								
Iomeprol		6.606	6.606								
Iopamidol		4.36	4.36								
Iopromide		8.633	8.633	13.55	13.55						
Ioversol		5.802	5.802								
Ioxithalamic acid		1.184	1.184								
Cyclophosphamid	Cytostatic	0.072	0.018	0.052	0.013			0.004	0.001		
Ifosfamid		0.025		0.022							
Tamoxifen		0.104									
Furosemide	Diuretic	3.739	3.739	3.93	3.93			3.085	3.085		
Hydrochlorothiazide		2.199	2.199								
Torasemide		0.493				9.911		0.002			

Table A-III.1: continued.

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PPs in WWTP influent [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb	PECa	PECb
Nimodipine	Nootropic	0.016				0.451		0.001			
Piracetam		13.684						0.246			
Atorvastatin	Lipid regulator	0.633	0.006			0.693	0.007	2.324	0.023		
Bezafibrate		4.188	2.931	5.063	3.544			1.604	1.123	0.078	0.054
Fenofibrate		1.85	0.463	15.846	3.961			0.57	0.143	1.971	0.493
Gemfibrozil		0.794	0.286					0.189	0.068	0.078	0.028
Pravastatin		0.18	0.09			0.327	0.164	0.433	0.216		
Simvastatin		0.708	0.007	1.282	0.013	0.309	0.003	2.818	0.028	0.303	0.003
Zolpidem	Sedative	0.044	0	0.617	0.006			0.012	0		
Zopiclone		0.035	0.007	0.36	0.076			0.136	0.029		
Alprazolam	Tranquilliser	1.331	0.359								
Bromazepam		0.039	0.001	0.481	0.01						
Diazepam		0.118	0.013	0.085	0.009			0.136	0.015		
Lorazepam		10.784	8.088	0.108	0.081			0.008	0.006		
Oxazepam		0.129	0.116	1.144	1.029			0.026	0.023		
Cimetidine	Antiulcerative	0.096	0.072								
Lansoprazole		0.072	0			0.164	0	1.721	0		
Omeprazole		0.893	0.009			0.859	0.009	1.534	0.015		
Pantoprazole		0.666	0.007			0.253	0.003	0.224	0.002		
Ranitidine		11.371	7.278	2.152	1.377	6.628	4.242	6.563	4.2		
Allopurinol	Urostatic	18.374	5.145	10.015	2.804			5.085	1.424		
Xylometazolin	Vasoconstrictor	0.076						0			
Metformin	Antidiabetic	69.006	55.205	132.339	105.871			64.678	51.742		
Pentoxifylline	Vasodilator	10.44	0.104					0.194	0.002		
Clofibric acid	Metabolite		0.067								
Salicylic acid				136.27		107.199				15.599	
Dihydrocodeine	Antitussive	0.142						2.249			
Diosmin	Phlebotropic			68.96							

Table A-III. 2: Predicted environmental concentrations (PEC) of pharmaceuticals in surface water (SW) calculated for France, Germany, Poland, Spain and the UK from the consumption data given in Annex I. (PEC_a: PEC calculated without excreted PP fraction (E=1), PEC_b: PEC calculated with excreted PP fraction).

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PPs in surface water [µg/L]									
		Germany		France		Spain		UK/Wales		Poland	
		PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b
Diclofenac	Analgesic	0.774	0.232	0.146	0.044	0.065	0.019	0.472	0.141	0.444	0.133
Ibuprofen		0.695	0.271	0.751	0.293	0.724	0.282	0.623	0.243	1.104	0.43
Indomethacin		0.029	0.009					0.014	0.004	0.015	0.005
Ketoprofen		0.014	0.011	0.292	0.219	0.005	0.004	0.02	0.015	0.269	0.202
Naproxen		0.025	0.018	0.254	0.183	0.128	0.092	0.242	0.175	0.398	0.287
Paracetamol		0.733	0.381	7.75	4.03	0.739	0.384	2.578	1.341	0.795	0.414
Azithromycin	Antibiotic	0.004	0.003	0.008	0.005			0.001	0.001	0.005	0.003
Ciprofloxacin		0.036	0.028	0.043	0.033	0.024	0.018	0.026	0.02	0.026	0.02
Clarithromycin		0.07	0.013	0.151	0.027	0.097	0.018	0.046	0.008	0.16	0.029
Erythromycin		0.166	0.163					0.346	0.339	0.107	0.105
Norfloxacin		0.032	0.02					0.007	0.004	0.069	0.044
Ofloxacin		0.012	0.01	0.012	0.01			0.001	0.001	0.004	0.003
Roxithromycin		0.086	0.043	0.16	0.08			0	0	0.049	0.024
Sulfamethoxazole		0.693	0.68	0.358	0.351			0.02	0.019	0.182	0.178
Trimethoprim		0.132	0.087	0.051	0.033			0.126	0.083		
Carbamazepine	Antiepileptics	1.077	0.312	0.673	0.195			0.841	0.244	0.918	0.266
Gabapentin		0.002				0.001		0.008			
Valproic acid		0.008	0.002	0.021	0.005			0.006	0.001		
Atenolol	Beta-blocker	0.1	0.04	0.223	0.089			0.46	0.184	0.091	0.036
Metoprolol		0.96	0.106	0.143	0.016			0.035	0.004	0.379	0.042
Sotalol		0.118	0.125					0.026	0.027	0.013	0.014
Salbutamol	Bronchiolytic	0.001	0.001					0	0	0	0
Diatrizoate Sodium	contrast medium	0.725	0.725								
Iomeprol		0.661	0.661								
Iopamidol		0.436	0.436								
Iopromide		0.561	0.561	0.881	0.881						
Ioxithalamic acid		0.118	0.118								

Table A-III.2: continued.

Compound	Therapeutic Class	Predicted environmental concentrations (PEC) of PPs in surface water [$\mu\text{g/L}$]									
		Germany		France		Spain		UK/Wales		Poland	
		PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b	PEC _a	PEC _b
Diazepam	Tranquilliser	0.011	0.001	0.008	0.001			0.012	0.001		
Bezafibrate	Lipid regulator	0.264	0.185	0.319	0.223			0.101	0.071	0.005	0.003
Gemfibrozil		0.036	0.013					0.008	0.003	0.004	0.001
Clofibrate	Metabolite		0.005								

12 Annex IV: Removal behaviour of PPs in sewage treatment plants (WWTP)

Table A-IV. 1: Number of measured samples and average removal of PPs in wastewater treatment plants

compound	number of samples		PNRi
	STP effluent	STP influent	
Flumequine	19	19	2.8
Dextropropoxyphene	9	9	2.1
Propranolol	182	47	1.6
Doxycycline	15	15	1.3
Tamoxifen	9	9	1.3
Clarithromycin	245	120	1.2
Diatrizoate	10	10	1.1
CBZ-10OH	3	3	1.1
CBZ-2OH	3	3	1.1
AMDOPH	12	12	1.1
N-Formyl-4-aminoantipyrine	12	12	1.1
Mefenamic acid	37	31	1.1
CBZ-3OH	3	3	1.1
Fluoxetine	15	15	1.0
Phenazon	178	37	1.0
AMPH	12	12	1.0
Erythromycin	215	209	1.0
Iopamidol	10	10	1.0
Carbamazepine	401	209	1.0
Chlortetracycline	5	5	0.9
Ioxithalamic acid	6	6	0.9
Diltiazem	6	5	0.9
CBZ-DiOH	15	14	0.9
Meprobamate	6	6	0.9
Cimetidine	6	5	0.9
2-Hydroxyibuprofen	8	8	0.8
Azithromycin	25	19	0.8
Propyphenazon	73	29	0.8
Demeclocycline	2	2	0.8
4-Acetaminoantipyrine	12	12	0.8
CBZ-EP	15	15	0.8
Iothalamic acid	6	6	0.8
Metoprolol	208	74	0.8
Gemfibrozil	80	77	0.7
Sertraline	3	4	0.7
Codeine	28	28	0.7
Citalopram	3	4	0.7
Roxithromycin	257	133	0.7
Sotalol	112	51	0.7
Indomethacin	49	46	0.7
Oxazepam	12	11	0.7
Diclofenac	447	231	0.6

Fehler! Verweisquelle konnte nicht gefunden werden.: **continued.**

compound	number of samples		PNRi
	STP effluent	STP influent	
Sulfamethoxazole	129	103	0.6
Mevastatin	5	5	0.6
Dilantin	10	10	0.6
Dimethylaminophenazone	2	2	0.6
Cyclophosphamid	4	5	0.6
Dihydrocodeine	10	6	0.6
Tetracycline	13	13	0.6
Trimethoprim	234	105	0.5
Salbutamol	20	13	0.5
Atenolol	123	62	0.5
Clofibric acid	289	112	0.5
Pravastatin	3	3	0.5
Acebutolol	24	24	0.5
Iopromide	72	29	0.5
4-Aminoantipyrine	5	5	0.5
Ranitidine	11	10	0.5
Clotrimazole	9	9	0.5
Iomeprol	60	17	0.4
Metformin	6	5	0.4
Paroxetine	3	4	0.4
Sulfamethazine	8	8	0.4
Ketoprofen	237	111	0.4
Carazolol	2	2	0.4
Naproxen	329	156	0.4
Meclocycline	2	2	0.4
Metamizole sodium	12	12	0.4
Fenofibric acid	2	2	0.3
Tylosin	99	99	0.3
Norfloxacin	46	46	0.3
Bisoprolol	2	2	0.3
Ciprofloxacin	48	48	0.3
Terbutaline	2	2	0.3
Atorvastatin	9	9	0.2
Ofloxacin	34	34	0.2
Salicylic acid	91	88	0.2
Paracetamol	57	56	0.2
Betaxolol	2	2	0.2
Oxytetracycline	5	5	0.2
Ibuprofen	384	211	0.2
Bezafibrate	201	58	0.1
Simvastatin	9	9	0.1
Hydrocodone	6	5	0.1
Iohexol	4	4	0.1
Enalapril	6	6	0.0
Sulfachlorpyridazine	2	2	0.0
Sulfathiazole	5	5	0.0
Diazepam	9	9	0.0
Minocycline	2	2	0.0

Fehler! Verweisquelle konnte nicht gefunden werden.: **continued.**

compound	number of samples		PNRi
	STP effluent	STP influent	
p-Hydroxy Atorvastatin	6	6	0.0
Phenobarbital	4	4	0.0
Ifosfamid	4	5	0.0
Fluvoxamine	3	4	0.0
Sulfadimethoxine	2	2	0.0
o-Hydroxy Atorvastatin	6	6	0.0
Sulfamerazine	2	2	0.0
Warfarin	6	5	0.0
Gabapentin	4	4	0.0
Valproic acid	4	4	0.0
Simvastatin hydroxy acid	6	6	0.0

13 Annex V: References of the data compilation

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