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Analysis of pharmaceuticals and hormones in samples from WWTPs and receiving waters

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Summary

A screening study was performed on selected pharmaceuticals and hormones. A total of 103 pharmaceuticals were analysed in 25 samples from a national program and 41 samples from a regional program. In addition, three hormones were analysed in 25 samples. The sampling programs were focused on samples from waste water treatment plants (WWTPs) and their receiving waters. Biota samples (perch) were also included in the study.

45 pharmaceuticals were detected in the effluent of at least one WWTP, in levels that ranged from low ng/L up to 8.8 µg/L, with a median concentration of 52 ng/L. Caffeine was detected in highest concentrations followed by the beta-blocker metoprolol (1.8 µg/l). In WWTP sludge, 31 substances were detected. The antibiotic ciprofloxacine often dominated and was found in all sludge samples in the range 800-1800 µg/Kg dw. 44 pharmaceuticals were detected in surface water samples in the range from low ng/L up to 480 ng/L. Measured surface water concentrations were compared to critical environmental concentrations, i.e. the water concentration that is expected to cause a pharmacological effect in fish. This evaluation showed that eight pharmaceuticals in these samples may cause a pharmacological response in fish exposed to these waters. In biota (perch muscle) 17 substances were detected in concentrations up to 150 µg/Kg.

Concentrations of hormones in WWTP effluents were <0.12 -0.76 ng/L for β-estradiol, <0.23–25 ng/L for estrone and <0.38–23 ng/L for ethinyl estradiol. Hormone measurements in perch bile suggested increased concentrations due to influence from WWTP emissions. Concentrations of hormones in three WWTP sludge's were 2–7 ng/g dw for β-estradiol, 2–36 ng/g dw for estrone and 46–62 ng/g dw for ethinyl estradiol.

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Summary

A screening study was performed on selected pharmaceuticals and hormones. The selection of pharmaceuticals was based on ecotoxicological criteria, primarily potency and potential to bioconcentrate. Additional pharmaceuticals, that have been part of previous screening programs, were also included. A total of 103 pharmaceuticals were analysed in 25 samples from a national program and 41 samples from a regional program. In addition, three hormones were analysed in 25 samples.

The sampling programs were focused on the importance of diffuse emissions of pharmaceuticals from urban areas reflected in samples from waste water treatment plants (WWTPs) and their receiving waters. Biota samples (perch) were also included in the study.

With the two sample programs taken together, 45 pharmaceuticals out of the 103 were detected in the effluent of at least one WWTP, in levels that ranged from low ng/L up to 8.8 µg/L, with a median concentration of 52 ng/L. Caffeine was detected in highest concentrations followed by the beta-blocker metoprolol (1.8 µg/l).

In WWTP sludge, 31 substances were detected. The antibiotic ciprofloxacine often dominated and was found in all sludge samples in the range 800-1800 µg/Kg dw.

Of the 103 pharmaceuticals included 44 were detected in surface water samples in the range from low ng/L up to 480 ng/L. Measured surface water concentrations were compared to critical environmental concentrations, i.e. the water concentration that is expected to cause a pharmacological effect in fish. This evaluation showed that eight pharmaceuticals in these samples may cause a pharmacological response in fish exposed to these waters.

In biota (perch muscle) 17 substances were detected in concentrations up to 150 µg/Kg. Highest concentrations, in the same range as what has been measured previously in similar studies, were found in fish from Kyrkviken in Arvika and Varnumsviken in Kristinehamn, both from the regional sample program.

Concentrations of hormones in WWTP effluents were <0.12 -0.76 ng/L for β-estradiol, <0.23–25 ng/L for estrone and <0.38–23 ng/L for ethinyl estradiol.

Hormone measurements in perch bile suggested increased concentrations due to influence from WWTP emissions.

Concentrations of hormones in three WWTP sludge's were 2–7 ng/g dw for β-estradiol, 2–36 ng/g dw for estrone and 46–62 ng/g dw for ethinyl estradiol.

Sammanfattning

En screeningundersökning av läkemedelssubstanser och hormoner har utförts. Urvalet av läkemedel i studien gjordes utifrån ekotoxikologiska kriterier, främst potens och potential att biokoncentrera. Detta urval komplementerades med några läkemedel som ingått i tidigare screeningundersökningar. Totalt 103 läkemedel analyserades i 25 prover i ett nationellt provprogram och 41 prover i ett regionalt program. Dessutom analyserades tre hormoner i 25 prover.

Screeningundersökningen fokuserade på betydelsen av diffusa emissioner från tätbebyggda områden med betoning på utgående avloppsvatten från avloppsreningsverk (ARV) och recipienter till dessa. Biotaprover (abborre) ingick också.

Med de två provprogrammen tagna tillsammans, detekterades 45 av de 103 läkemedlen i utgående vatten från åtminstone ett ARV, i koncentrationer upp till 8.8 µg/l. Mediankoncentrationen var 52 ng/l. Koffein hittades i högst halter följt av betablockeraren metoprolol (1.8 µg/l).

I reningsverksslam hittades 31 substanser. Ciprofloxacin, ett antibiotikum, var ofta dominerande och fanns i alla slam i koncentrationsintervallet 800-1800 µg/Kg ts.

Av läkemedlen uppmättes 44 i ytvatten (låga ng/L upp till 480 ng/l) och de uppmätta halterna jämfördes med kritiska miljökoncentrationer; dvs. den vattenkoncentration som förväntas orsaka en farmakologisk respons i fisk. Denna jämförelse visade att åtta av läkemedlen uppmättes i halter som sannolikt kan orsaka en farmakologisk respons i fisk som exponeras för detta vatten.

I biotaproverna (muskel från abborre) detekterades 17 substanser i koncentrationer upp till 150 µg/Kg. De högsta koncentrationerna, som var i nivå med vad som uppmätts i likande studier, hittades i fisk från Kyrkviken, Arvika och Varnumsviken, Kristinehamn, båda från det regionala provprogrammet.

Koncentrationen av hormoner i utgående vatten från avloppreningsverk var <0,12 -0,76 ng/l för β-estradiol, <0,23–25 ng/l för estrone and <0,38–23 ng/l för ethinyl estradiol.

Resultatet av mätning av hormoner i galla från abborre kan tolkas som att påverkan från avloppsvatten gett upphov till högre halter.

Hormonkoncentrationer i tre reningsverksslam var 2–7 ng/g ts för β-estradiol, 2–36 ng/g ts för estrone och 46–62 ng/g ts för ethinyl estradiol.

1 Introduction

As an assignment from the Swedish Environment Protection Agency, a screening study concerning pharmaceuticals has been performed. The national sample program was supplemented with a regional program where five county administrative boards participated. Concentrations of pharmaceuticals were measured in samples from waste water treatment plants (WWTPs) (influents, effluents, sludge), receiving waters and fish muscle. The work was in part a follow-up on an earlier screening study (Fick et al., 2011).

In addition, after method development work, concentrations of hormones (ethinyl estradiol, β-estradiol, estrone) were analysed in WWTP effluents, receiving waters, sludge and fish bile.

The screening study has been carried out by Swedish Environmental Research Institute (IVL) together with Umeå University (UmU). The chemical analyses of pharmaceuticals were undertaken at UmU. Hormones were analysed at IVL.

2 Pharmaceuticals as environmental pollutants

2.1 Background

Pharmaceuticals are increasingly used for human and animal applications and can be detected in aquatic systems globally, due to the worldwide usage and the incomplete removal in waste water treatment plants (WWTPs), or a complete lack of WWTPs, (Hughes et al., 2013; Kookana et al., 2014; Lishman et al., 2006; Loos et al., 2013, 2009; Verlicchi et al., 2012). Surface water concentrations of pharmaceuticals usually range from low µg l^{-1} close to point sources to low ng l^{-1}, with clear correlations to population densities, volume of the receiving water body and technologies used in WWTPs (Deo, 2014; Fatta-Kassinos et al., 2011; Hughes et al., 2013; Sim et al., 2011). However many pharmaceuticals are highly potent and have pharmacological effect at low concentrations and studies have shown that exposed wildlife have conserved drug targets which can cause pharmacological action via high-affinity interactions (Gunnarsson et al., 2008; LaLone et al., 2013; Brown et al., 2014). Several laboratory studies on aquatic organisms have shown that various pharmaceuticals can cause negative effects on growth, behavior, development and reproduction (Brodin et al., 2013; Fent et al., 2006; Kidd et al., 2007; Lange et al., 2009; Santos et al., 2010; Zeilinger et al., 2009). One effect that has been studied in detail is reproductive disorders in fish and it has been shown for example that ethinyl estradiol causes severe reproductive disorders at low ng/L concentrations (Lange et al. 2001; Kidd et al. 2007). Levonorgestrel, a synthetic gestagen which is commonly used in oral contraceptives, was shown to inhibit reproduction in fathead minnow at concentrations below 1 ng/L (Zeilinger et al. 2009).

Since raw sewage and wastewater effluent is a major source of the pharmaceuticals detected in the environment, a lot of researchers has studied the characteristics of the removal processes in laboratory, semi and full scale (Castiglioni et al., 2006; Lindberg et al., 2014, 2005; Loos et al., 2013; Verlicchi et al., 2012; Vieno et al., 2007).

2.2 Selection of pharmaceuticals to include in the screening

There is a wide range of pharmaceuticals available globally, e.g. to date there are more than 6000 pharmaceuticals on the global market (Martindale 2011). Therefore various prioritization approaches are used in order to select which pharmaceuticals that should be included in monitoring schemes. Several prioritisation and ranking schemes, based on different types of data, have been proposed (Berninger and Brooks 2010, Besse and Garric 2008, Brooks et al 2009, Christen et al 2010, Cooper et al 2008, Fick et al 2010, Huggett et al. 2003, Kools et al 2008, Kostich et al 2010, Kumar et al 2010), however the usefulness of many models is limited due to lack of appropriate data and/or the requirement of a substantial portion of expert judgement and/or case-by-case assessment. One useful approach was suggested by Huggett et al. (Huggett et al. 2003) and has been named the fish plasma model (FPM). The FPM compares the human therapeutic plasma concentration (HTPC) for a pharmaceutical to a theoretical fish plasma steady state concentration (FssPC). The comparison results in a ratio of two concentrations (HTPC/FssPC) where a lower ratio equals a higher risk. This risk is actually thought to reflect the likelihood for a pharmacological (but not necessarily adverse) response in fish, assuming that orthologs to the human drug targets are functionally conserved in fish. The FPM is thus based on pharmacological data as well as on sales statistics and physicochemical properties (logP). One major benefit of this model is that it enables theoretical risks to be calculated for the great majority of pharmaceuticals, since human therapeutic plasma concentrations are readily available in the literature.

Selection of pharmaceuticals included in the screening was based on this concept. All pharmaceuticals on sale in Sweden where ranked according to their concentration ratios and the selection of pharmaceuticals were then based on this ranking. In addition, antibiotics and some pharmaceuticals that have been included in previous screening programs were also included.

2.3 Hormones

Two of the hormones included in the screening, β-estradiol and estrone, are naturally produced whereas ethinyl estradiol is a contraceptive of anthropogenic origin (Gunnarsson et al. 2009).

In the review by Jarošová and co-workers (2014), observed concentrations of estrogens from a number, mainly European, countries are given. Furthermore, the authors compares established, as well as suggest new, Estrogenic Equivalency Factors (EEFs), for estimation of a sample's 17β-estradiol equivalent (cEEQ). The highest estrogenic potential of waste water effluent has been attributed to estrogenic steroids (Desbrow et al. 1998, Korner 2001). This methodology is analogous to dioxin toxicity estimation using toxic equivalency factors (TEFs) and 2,3,7,8-TCDD toxic equivalents (TEQs) (van den Berg et al. 1998, 2006). The EEFs used are 1, 0.13 and 1.09 for β-estradiol, estrone and ethinyl estradiol, respectively.

There are a number of studies which have observed adverse effects in fish residing close to WWTP effluent sites. These observations have been seen in a wide geographical spread over the globe, e.g. in the US (Iwanowicz et al 2009), the UK (Jobling et al. 2006), France (Hinfray et al. 2010, Sanchez et al. 2011) and Canada (Tetrault et al. 2011). There has also been shown that there is a relationship between urban WWTP and intersex among fish that could not be found in fish from rural, agricultural, background sites (Tetrault et al. 2011). A review by Wise and co-workers (2011) lists sources and environmental pathways of estrogens and ethinyl estradiol in particular. Furthermore, the study argues that ethinyl estradiol has a limited input to the total estrogenic potential of (US) drinking water but also concludes that ethinyl estradiol might have local negative effects in surface waters, e.g. close to WWTPs.

3 Sampling strategy and study sites

3.1 National sampling program

A sampling strategy was developed in order to determine concentrations of pharmaceuticals in the environment and in wastewater treatment plants (WWTPs). The sampling program was focused on diffuse emissions from urban areas and distribution from WWTPs and their receiving waters. The program also included samples from non-urban areas without direct impact of WWTPs. Biota samples (fish) from surface water that receive sewage effluent as well as samples from locations not affected by sewage effluent were also included. Individual samples, including sampling dates, are listed in Appendix 1.

The measurements from the WWTPs included effluent and sludge. Surface water samples upstream and at several locations downstream Kungsängsverket, Uppsala, were analysed.

The sampling program is summarized in Table 1.

Table 1 Samples included in the national sampling program.

Type	WWTP effluent	WWTP sludge	Surface water	Biota	Total
Background areas					
Lakes			2	2	4
Urban areas					
Stockholm, Henriksdal WWTP	3	1			4
Umeå, Öhn WWTP	3	1			4
Uppsala, Kungsängsv. WWTP	3	1			4
Uppsala			6	3	9
Total	9	3	8	5	25

3.2 Regional sampling program

In addition to the national sampling program Swedish county administrative boards had the opportunity to collect and send samples for analysis. Several administrative counties participated and samples included effluent and sludge from municipal WWTPs, surface water and biota, Table 2. Individual samples are listed in Appendix 2.

Table 2 Samples included in the regional sampling program.

Type	WWTP Influent	WWTP Effluent	WWTP Sludge	Surface water	Biota	Ground water	Total
WWTPs	3	12	9				24
Rivers and lakes				9	7	1	17
Total	3	12	9	9	7	1	**41**

4 Methods

4.1 Sampling

Surface waters were sampled directly into 1 litre polyethene (PE) bottles at approximately 0.5 m depth using a telescopic bottle holder.

The staff at the different WWTPs collected influent and effluent water samples in 1 litre PE bottles and de-watered sludge from the anaerobic chambers into PE jars. The samples were stored frozen (-18°C) until analysis.

Fish were caught using fishing net and stored frozen. Perch was chosen because it is one of the most stationary fish species in the investigated areas. Fish muscle was dissected from the dorsal muscle using solvent washed scalpels. A composite sample from around ten individuals from each site was prepared. Bile for analysis of hormones was prepared from individuals that were grouped together in same sex samples according to Appendix 11.

4.2 Analysis of pharmaceuticals

4.2.1 Chemicals

All pharmaceutical reference standards were classified as analytical grade (>98%). Sulphuric acid (99.999%) were purchased from Sigma-Aldrich (Steinheim, Germany) and ethyl acetate (Analytical reagent, 99.8%) were purchased from Labscan Ltd., (Dublin, Ireland). $^{2}H_{6}$ -amitriptyline, $^{2}H_{10}$-carbamazepine, $^{13}C_{3}{}^{15}N$-ciprofloxacin , $^{2}H_{5}$-fluoxetine, $^{13}C_{6}$-sulfamethoxazole, , $^{13}C^{2}H_{3}$-tramadol and $^{13}C_{3}$-trimethoprim were bought from Cambridge Isotope Laboratories (Andover, MA, USA). $^{2}H_{5}$-oxazepam, $^{2}H_{7}$-promethazine, $^{2}H_{4}$-risperidone, and $^{13}C_{2}{}^{15}N$-tamoxifen were bought from Sigma-Aldrich (Steinheim, Germany). Methanol and acetonitrile were purchased in LC/MS grade quality (Lichrosolv - hypergrade, Merck, Darmstadt, Germany). The purified water was prepared by an Milli-Q Gradient ultrapure water system (Millipore, Billerica, USA), equipped with a UV radiation source. The buffering of the mobile phases was performed by addition of 1ml of formic acid (Sigma-Aldrich, Steinheim, Germany) to 1 L of solvent.

4.2.2 Sample preparation

All water samples (incoming sewage, treated effluent, surface and ground water) (250 mL) were filtered through a 0.45 µm membrane filter (MF, Millipore, Sundbyberg, Sweden) and acidified to pH 3 using sulfuric acid. Then 50 ng of each of the 12 isotopically labelled pharmaceuticals used as internal and surrogate standards were added to each sample. Solid phase extraction (SPE) columns (Oasis HLB, 200mg, Waters Corporation, Milford, MA, USA) were pre-conditioned and equilibrated with 5.0 mL of methanol and 5.0 mL of de-ionized water. Samples were applied to the SPE columns at a flow rate of 5 mL min^{-1}. Water with 5 % methanol was used to wash the SPE column before eluting with 5 mL of methanol. Eluates were collected in 10 mL vials, evaporated to 20 µL under a gentle air stream, and dissolved in 5 % acetonitrile in water to a final volume of 1.0 mL.

Sludge samples were first freeze dried and 0.1 g (dry weight) were used for extraction. Before extraction 50 ng of each internal and surrogate standard were added to the sludge. Extraction was sequentially performed first using 1.5 ml ethylacetate and methanol (1:1 mixture) followed by 1.5 ml methanol and water (7:3 mixture) with 5% triethylamine. Samples were homogenized for four minutes at 42 000 oscillations per minute, using a Mini Beadbeater (Biospec. Bartlesville, USA) with zirconium beads and then centrifuged at 14 000 revolutions per minute for 10 min. This protocol was followed for both eluent mixtures and the supernatants were combined, evaporated to 20 µL and reconstituted in 1 ml water and acetonitrile (95:5 mixture) with 0.1% formic acid.

Fish muscle samples (0.1 g) were extracted sequentially after addition of 50 ng of each internal and surrogate standard. Three sequential extractions were done; 1.5 ml methanol and water (7:3) with 0.1% formic acid; 1.5 ml acetonitrile and 1.5 ml acetonitrile. Samples were homogenized for four minutes at 42 000 oscillations per minute, using a Mini Beadbeater (Biospec. Bartlesville, USA) with zirconium beads and then centrifuged at 14 000 revolutions per minute for 10 min. This protocol was followed for all three eluent mixtures individually and the supernatants were combined, evaporated to 20 µL and reconstituted in 1 ml water and acetonitrile (95:5 mixture) with 0.1% formic acid.

4.2.3 Instrumental analysis

The same methodology as that reported by Grabic et al. (2012) was used. In short, a triple stage quadrupole MS/MS TSQ Quantum Ultra EMR (Thermo Fisher Scientific, San Jose, CA, USA) coupled with an Accela LC pump (Thermo Fisher Scientific, San Jose, CA, USA) and a PAL HTC autosampler (CTC Analytics AG, Zwingen, Switzerland) were used as analytical system. Sample (20 µL) was loaded onto a Hypersil GOLD aQ TM column (50 mm x 2.1 mm ID, 5 µm particles, Thermo Fisher Scientific, San Jose, CA, USA) preceded by a guard column (2 mm×2.1 mm i.d, 5 µm particles) of the same packing material and from the same manufacturer. A gradient of methanol and acetonitrile in water (all solvents buffered by 0.1% formic acid) was used for elution of analytes. The elution conditions were programed as follows: 200 µL min^{-1} 10% methanol in water for 1 min, isocratically, followed by a gradient change to 30/10/60 water/ acetonitrile / methanol at a flow of 250 µL min^{-1} in 8 min. Then the column was washed by ACN/ methanol 60/40 at a flow of 300 µl min^{-1} in 9 minutes. These parameters were held for 1 min and then switched to the starting conditions and held for 4 min before the next run.

Heated electrospray (HESI) and atmospheric pressure photo ionization (APPI) in positive and negative mode was used for ionisation of target compounds. Both first and third quadrupole were operated at resolution 0.7 FMWH, and two or three SRM transitions were monitored for each analyte. The setting of key parameters, SRM transitions, absolute recoveries, etc is stated in Grabic et al. (2012).

Samples were quantified using internal standard method. Several calibration standards covering all concentration range were measured before, in the middle and at the end of sample sequences. The maximum difference between results at quantification and qualification mass transition was set to 30% as criterion for positive identification.

4.2.4 Quality control

Possible memory effects were evaluated by a blank injection of Milli-Q water after standard samples of varying concentrations. Field and laboratory blank samples were included in each batch. Standards were analyzed in a wide concentration range (0.005 ng ml^{-1} to 5000 ng ml^{-1}) and were used for evaluating the linearity, sensitivity - quantification limit (LOQ) defined as 10 times the standard deviation of the blank, reproducibility of retention, precision as repeatability, and column stability. Method recoveries were determined by spiking the standard solution to matrix at the following concentration levels: milliQ water (100 ng L^{-1}), surface water (100 ng L^{-1}) and sewage effluent (1000 ng L^{-1}). Analyte addition was made with the criteria that the spiking would be at a level at least three times the original concentration in surface water and sewage effluent, respectively.

4.3 Analysis of hormones

4.3.1 Sample preparation

The method for extraction of estrogens from water was taken from Gunnarsson et al. 2009 with minor differences. The pH was adjusted to 2 instead of 4 with hydrochloric acid; a primary secondary amine (PSA) clean-up column was used instead in lieu of an amine column; a carbonate buffer was used rather than a potassium hydroxide buffer and slightly different reaction times during the derivatization and finally, a second derivatization step was undertaken.

The water samples were spiked with surrogate standard, [2D5]β-Estradiol (100 µL, 108 ng/mL) and allowed to equilibrate overnight. Prior to the extraction, methanol (20 mL) was added to the samples and the pH adjusted to approximately pH 2 by the addition of hydrochloric acid (concentrated, 0.2–1.2 mL). The samples were applied on SPE columns (ENV+, 500 mg, 6 mL cartridge) using a vacuum manifold with a flow rate of approximately 2 mL/min after cleaning/activation of the columns using methyl-tert-butyl ether (MtBE; 6mL), methanol (6 mL) MQ-water at pH≈2 (6 mL). After the samples were applied to the SPE-columns, the cartridges were dried under vacuum. Subsequently, the columns were rinsed with methanol/MQ-water (4 : 6, 6 mL), MQ-water at pH≈2 (6 mL) and a solution of NH4(aq)/methanol/MQ-water (2 : 10 : 88,6 mL). The columns were then eluted with methanol/MtBE (1 : 9, 12 mL), the solvent evaporated with gentle flow of nitrogen and moderate heat and the samples were re-dissolved in ethyl acetate/methanol (8 : 2, 2 mL). The samples were filtered through a PSA column (500 mg, 6 mL) which had been conditioned with water saturated ethyl acetate (4 mL) and ethyl acetate/methanol (8 : 2, 4 mL). The test tubes were subsequently rinsed with ethyl acetate/methanol (8 : 2, 2 mL). The samples were subsequently derivatized as described below.

The methods employed for analysis of fish bile were based on the work by Budzinkski *et al.* 2006. (incubation) and Pettersson *et al.* 2007 (extraction). The samples were pooled in a polypropylene test tube and the sample vials rinsed twice with a sodium acetate buffer (0.5 mL, 0.01 M, pH 5) and sodium acetate buffer was added to a total of 5 mL in each test tube. Internal standard, [$^2D_5$]β-Estradiol (100 µL, 108 ng/mL), was added to the samples. The enzymatic hydrolysis was perfomed utilizing an aqueous suspension of β-glucuronidase from *Helix pomatia* H-3AF (30 µL, Sigma-Aldrich) and incubated at 55^{o}C for 3 hours. Following the incubation, 1.5 g sodium chloride was added to the samples before the extraction using a mixture of n-hexane/MtBE (2 : 1, 5 mL) twice. The samples were subsequently derivatized as described below.

Freeze dried sludge samples (0.25 g, dry weight) were spiked with [$^2D_5$]β-Estradiol (10 µL, 1.04 µg/mL) as internal standard and were left to equilibrate (3 h). After equilibration, the samples were transferred to the polytetrafluoroethylene extraction tubes of a Milestone Ethos One, high performance microwave digestive system and methanol (13 mL) was added to the samples which were extracted at 110°C for 25 minutes. Once the samples had cooled to ambient temperature, the supernatant was collected and reduced in volume to 2 mL using a gentle flow of nitrogen and moderate heat. The samples were diluted with MQ-water at pH≈2 (3 mL). The samples were purified using first an ENV+ and then a PSA column as described for water samples, with the exception that the sample volume was 5 mL prior to the ENV+ column. The extract following the PSA column was dissolved in ethyl acetate/n-hexane (4 : 6, 1.5 mL) and applied to a silica gel column (6% deactivation with water, 1 g, 6 mL cartridge) after conditioning with ethyl acetate/n-hexane (4 : 6, 25 mL). The samples were eluted with ethyl acetate/n-hexane (4 : 6, 18.5 mL). The extracts were reduced in volume to approximately 0.5 mL using a gentle flow of nitrogen and moderate heat and sodium sulfate (0.1 g) was added to the samples to remove any residual water. The dried samples were transferred to a new test tube and the sodium sulfate was washed with n-hexane (1.5 mL). The samples were subsequently derivatized as described below.

Prior to derivatization n-undecane (50 µL) was added as a “keeper” and the sample extracts were reduced in volume to approximately 0.1 mL using a gentle flow of nitrogen and moderate heat. A carbonate buffer (1 M, 1 mL) and 10% pentafluorobenzoyl chloride in toluene (PFBzCl, 10 µL) were added to the samples which were agitated (5 minutes). Another addition of 10% PFBzCl in toluene (10 µL) was performed and the samples were agitated once more (5 minutes). The samples were extracted by inversion (3 minutes) with n-hexane (2 mL) and re-extracted by inversion (3 min) with n-hexane (2 mL). The extracts were combined and the volume reduced with a gentle flow of nitrogen and moderate heat to 0.05 mL. N-Methyl-N-(trimethylsilyl)trifluoroacetamide (MSTFA, 50 µL) and anhydrous pyridine (50 µL) were added and the samples heated (60°C, 1.5 h). The samples were subsequently once more reduced in volume to approximately 0.05 mL with a gentle flow of nitrogen before transfer to vials and volume adjustment with n-hexane to 0.5 mL as final volume.

The aim was to create a pentafluorobenzoyl ester of the phenolic functional group of the analytes. A subsquent conjugation of the the alcohol group of β-estradiol and ethinyl estradiol (estrone lacks an alcohol group) with MSTFA created di-substituted analytes, i.e. pentafluorobenzoyl ester, trimethylsilyl ether derivatives of β-estradiol and ethinyl estradiol. The reason for the second conjugation was to improve the GC/MS peak shape thereby improving the response, and lower the quantification limit of β-estradiol. During derivatization of standards it was noted that the derivatization with MSTFA took longer time for ethinyl estradiol than for β-estradiol .This became even more pronounced when actual samples were analysed, to the point that ethinyl estradiol in most of the samples remained close to non-silylated due to unknow matrix dependent effects. Hence, only β-estradiol was analysed as a pentafluorobenzoyl ester, trimethylsilyl ether derivative.

4.3.2 Instrumental analysis

The analysis was performed on an Agilent 7890A GC coupled to an Agilent 7000A GC/MS triple quad using a splittless injection of 1 µL on a 30m × 250 µm × 0.25 µm DB-5MS capillary column from Agilent J&W. The injector was set to 250°C and the oven programed to an initial temperature of 80°C which was held for 1 minute. The temperature was increased by 50°C/min to 290°C and subsequently by 5°C/min to 315°C, which was held for 3.8 minutes. A gas carrier flow was kept constant at 1.5 mL/min during the analysis. The mass spectrometer was operated in the negative chemical ionization mode with methane as the reagent gas using single ion monitoring of the following m/z; 464, 538, 543 and 490 for the analytes; estrone, β-estradiol, $[^2D_5]$β-estradiol and ethinyl estradiol, respectively.

5 Results and discussion

5.1 Pharmaceuticals, national program

No pharmaceuticals were detected in the laboratory blank samples and in the blank injections of Milli-Q water. Limit of quantification of the used methods are presented in Appendix 3 and 4. The results of the measurements of the pharmaceuticals are presented in detail in Appendix 5-9 where the concentrations of the individual pharmaceuticals are given. All results from the regional sampling program are presented in Appendix 10.

5.1.1 Background areas

Two background locations were included in the screening, Lake Tärnan and Krycklan Study Catchment. Lake Tärnan is a lake with no connection to effluent from WWTPs but receives direct anthropogenic contamination from people in the region. Krycklan Study Catchment study area (KSC) is located near Umeå in northern Sweden and covers an area of ~67 km² with no known point sources of pollution (Laudon et al., 2004). Both surface water and biota (perch) samples were taken at both locations.

Seven pharmaceuticals were detected in the surface water from Lake Tärnan in the 0.23 -41 ng/L range (sample N1, Appendix 5). Three pharmaceuticals were detected at a 10 to 40 ng/L range and they were all antibiotics or non-steroid anti-inflammatory agents (NSAIDs), which correlate well with previous studies (e.g. Fick et al 2011). Lake Tärnan receives a diffuse direct contamination which produces a pattern that differs from the concentrations in treated effluent. For example common painkillers, e.g. paracetamol, that are removed to a large extent in WWTPs, can be found in relatively high amounts in diffuse contaminated locations , which has been seen in previous Swedish screening studies (Andersson et al. 2006; Remberger et al. 2009, Fick et al 2011). Trace amounts of one pharmaceutical were detected in fish from Lake Tärnan (sample N2, Appendix 8).

No pharmaceuticals were detected in either the water or the biota sample from the Krycklan Study Catchment study area which is consistent with the lack of anthropogenic pollution.

5.1.2 Sewage treatment plants

5.1.2.1 WWTP effluents

Levels of pharmaceuticals were measured on three consecutive days in treated effluent water to the WWTP in Stockholm (Henriksdal), Umeå (Ön) and Uppsala (Kungsängsverket). These three WWTPs are all relatively large, treating water from approximately 835 000, 100 000 and 160 000 person equivalents respectively. A difference in the treatment process among the WWTPs is that Umeå lacks a dedicated nitrogen-removal stage, which also makes the overall residence time shorter.

Of the 101 pharmaceuticals included in this study 42 were detected in the WWTP effluent of at least one WWTP, see Appendix 6. Levels ranged from low ng/L up to 1500 ng/L; with a median concentration of 51 ng/L. Metoprolol was the pharmaceutical that was detected in highest amounts, up to 1500 ng/L. Maximum, minimum and median concentrations of all detected pharmaceuticals in the studied WWTP effluents are shown in Figure 1. Measured levels in this study correlate to measured levels in the literature (e.g. Santos et al 2010; Gros et al. 2011, Loos et al 2013, Lindberg et al 2014) as well as to the levels reported by the Swedish environmental protection agency (SEPA 2008) and previous national screening studies (Andersson et al. 2006; Woldegiorgis et al. 2007; Remberger et al. 2009, Fick et al 2011).

5.1.2.2 WWTP sludge

Levels of pharmaceuticals in digested dewatered sludge from all three WWTPs were measured and the results are presented in Figure 2 and Appendix 7. Thirty-one pharmaceuticals were detected at levels from low ng/Kg up to mg/Kg. The pharmaceutical that was detected at the highest level, 1.3 mg/Kg, was ciprofloxacin, an antibiotic, and similar levels have been detected previously in a Swedish screening study (Lindberg et al. 2005; SEPA 2008). Measured concentrations correlate to previously published levels (Lindberg et al. 2005; Andersson et al. 2006; Woldegiorgis et al. 2007; SEPA 2008; Jelic et al. 2011).

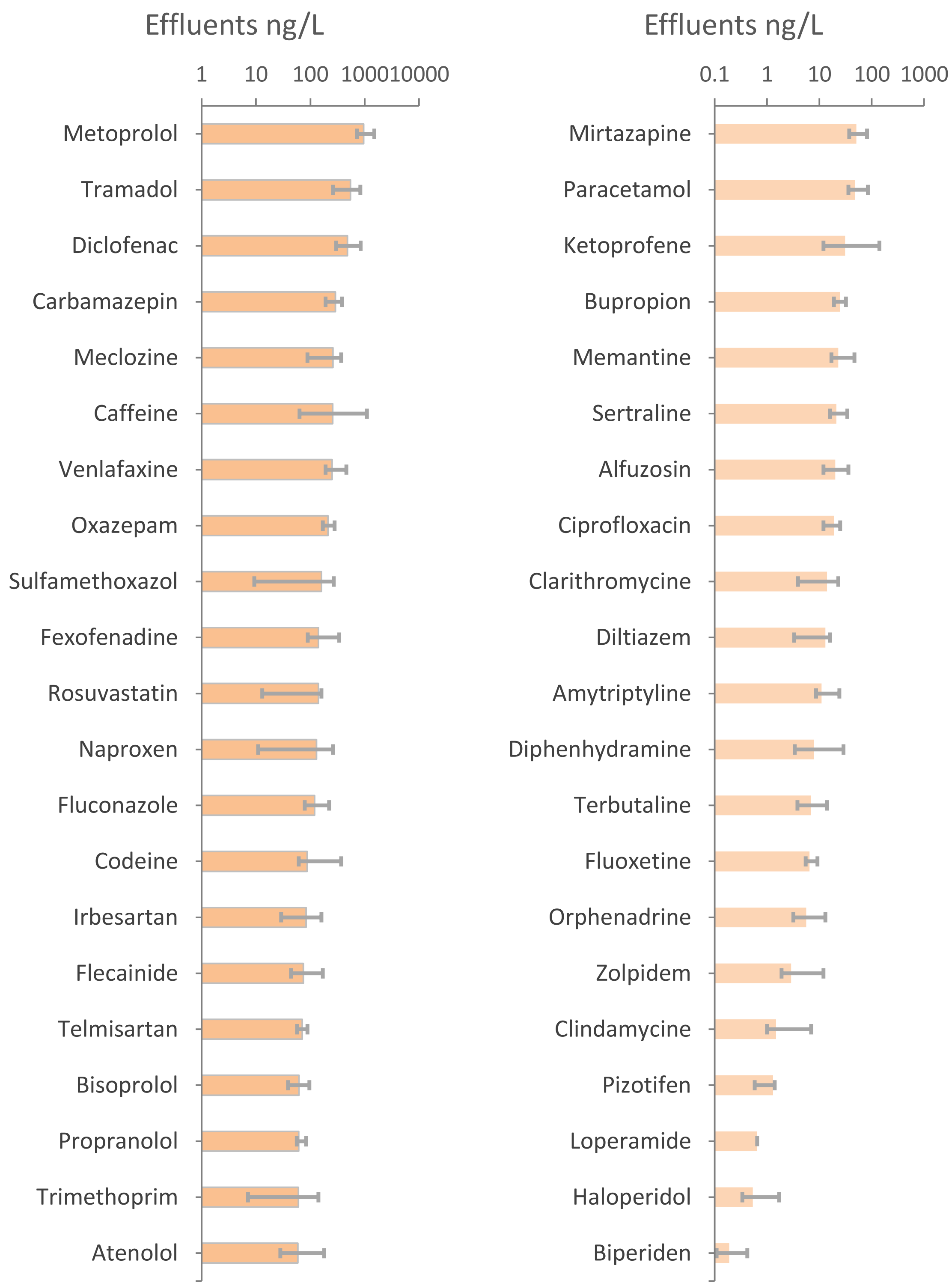

Figure 1 Minimum, median and maximum concentrations of pharmaceuticals in WWTP effluents in three Swedish WWTPs (n=9).

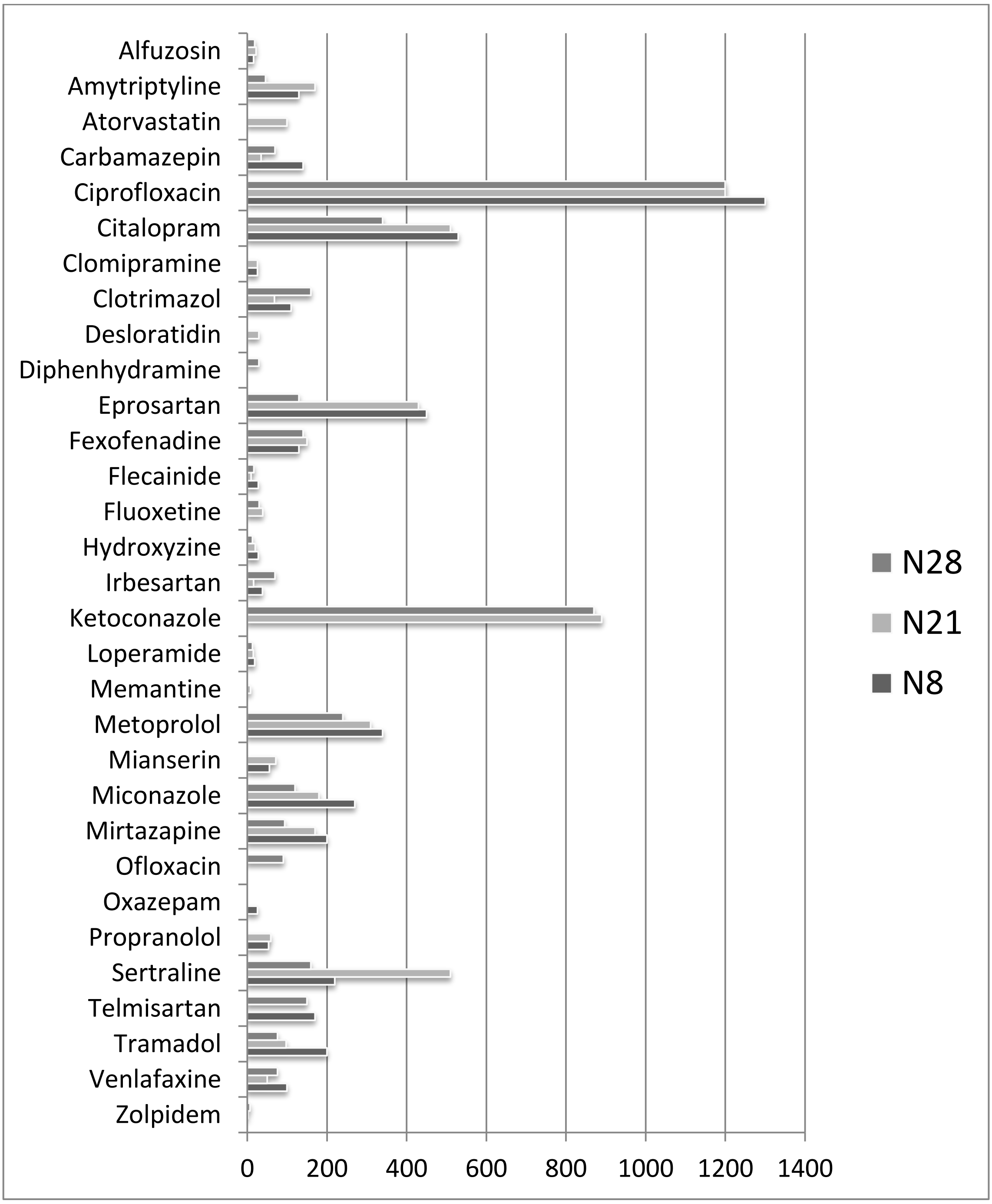

Figure 2 Detected pharmaceuticals (µg/Kg) in dewatered digested sludge from the WWTP Kungsängsverket, Uppsala (N8), Ön, Umeå (N21) and Henriksdal, Stockholm (N25).

5.1.3 Recieving waters

Of the 101 pharmaceuticals included in this study forty-one were detected in the surface water samples in the range of low ng/L up to 350 ng/L, Figure 3 (Appendix 5). Detected levels are comparable with the lower ranges found in a European-wide survey that included samples from 122 Rivers in 27 European countries (Loos et al. 2009) and levels found in previous screening studies (Andersson et al. 2006; Woldegiorgis et al. 2007; Remberger et al. 2009; Daneshvar et al. 2010, Fick et al 2011). A total of 8 surface samples were analysed, two samples (N1 and N3) were taken at background areas in Södermanland and Västerbotten County (see 5.1. Background areas) and 6 samples were taken downstream of the WWTP Kungsängsverket (Uppsala) (N10-14) and in an adjacent lake (N9) not receiving treated effluent. Kungsängsverket WWTP receives hospital wastewater and discharges the treated effluent in a small river. Samples N10-N14 can therefore be considered to be effluent-dominated surface water samples.

The effluent from WWTP Kungsängsverket, Uppsala, discharges into River Fyrisån. Surface water was sampled upstream the sewage effluent discharge point,-1.7 km (N9), and at five points downstream; 5 m (N10), 150 m (N11), 3.5 km (N12), 4.6 km (N13) and 5.5 km (N14). Concentrations of pharmaceuticals clearly increased in the first downstream sample and then sequentially decreased in the following samples Figure 3). The annual average flow in Fyrisån is 8.6 m^3/s and the average effluent flow from WWTP Kungsängsverket is 2 200 m^3/h (Uppsala vatten, 2011), i.e. a mean dilution factor of 14.

One way to evaluate the pharmaceuticals potential to cause adverse effects at given water concentrations is to compare the measured levels to the corresponding critical environmental concentration (CEC) values for each pharmaceutical (Fick et al. 2010). CEC is calculated as the water concentration that would elevate the plasma concentration in exposed fish to a level equal to the human therapeutic plasma concentration. Concentration ratios (CEC to measured concentration) of 1 or below indicate that the measured level of that pharmaceutical is expected to cause a pharmacological effect in fish. However, it should be stressed that concentration ratios only reflect the probability for pharmacological interactions to occur, and not whether the interactions would be adverse or not.

A total of 159 observations of pharmaceuticals in surface water were made in this study, distributed between 42 pharmaceuticals and 7 samples (Appendix 9). Out of these 159 observations, 6 (3.8 %) had a concentration ratio below 1, i.e. the water concentration of the specific pharmaceutical in these samples are expected to cause a pharmacological response in fish exposed to these waters and 12 (7.5 %) had a concentration ratio between 1 and 10, Figure 4.

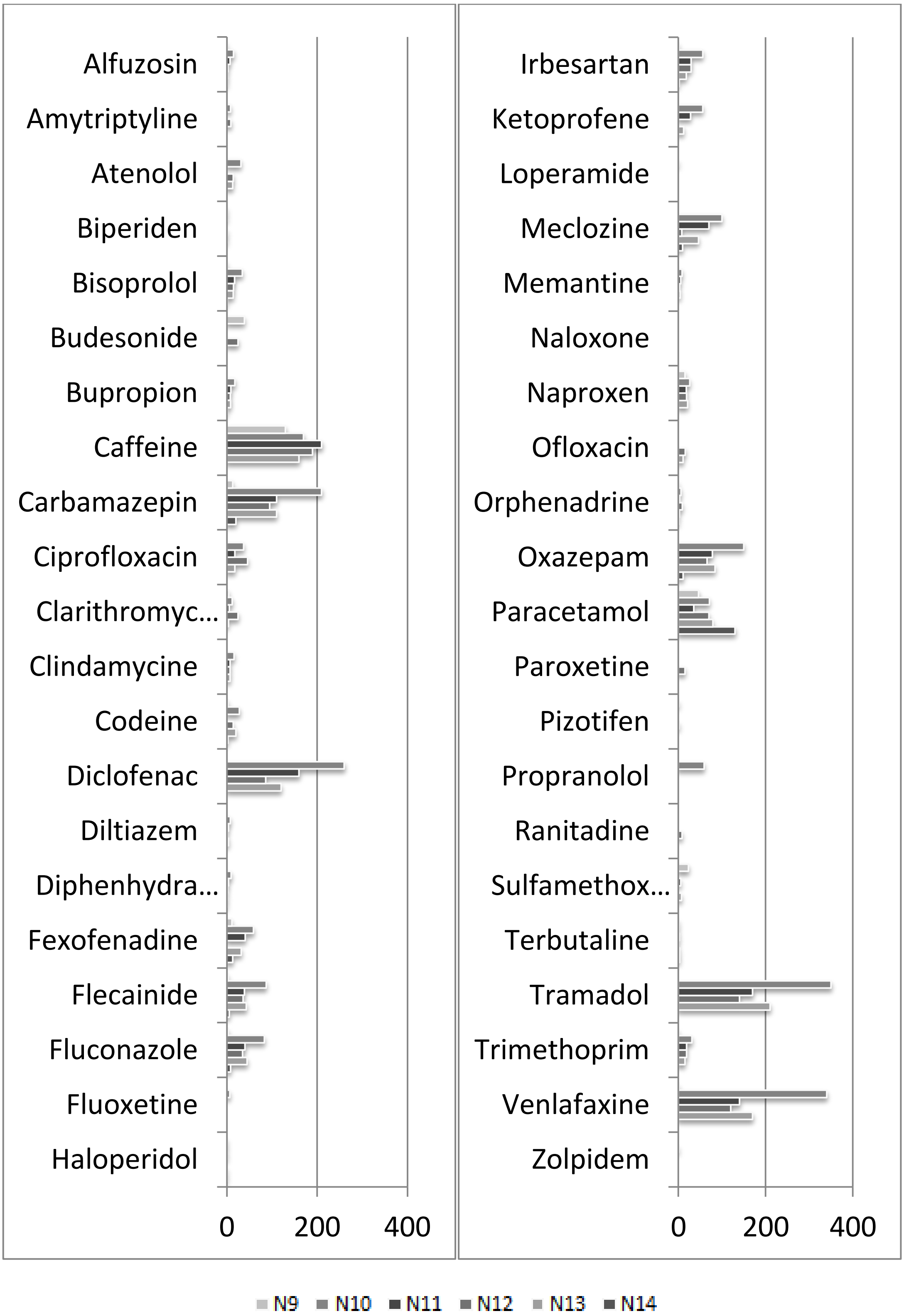

Figure 3 Detected pharmaceuticals (ng/L) in surface water samples from Uppsala (N9 – N14).

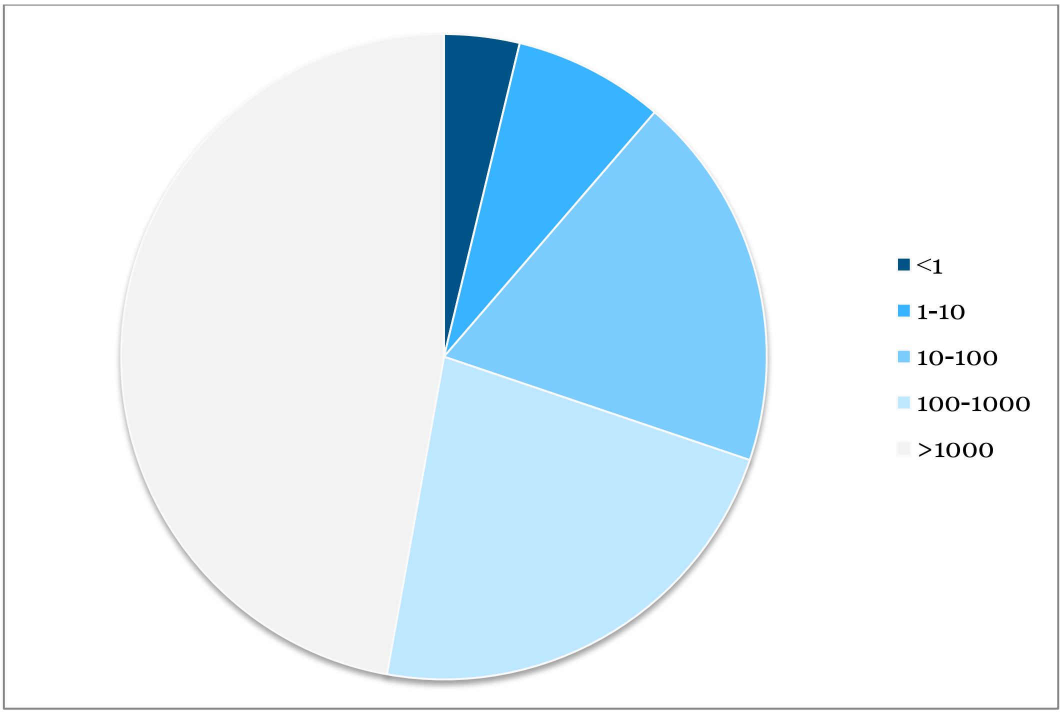

Figure 4 Histogram of concentration ratios in surface water samples N1, N3, N9 – N14. Number of observations in each class are; <1 = 6 (3.8%), 1-10 = 12 (7,5%), 11-100 = 30 (19%), 101-1000 = 36 (23%), >1000 = 75 (47%).

Two pharmaceuticals were detected with a concentration ratio below 1, i.e. levels above their CEC value, all measured in the most polluted surface water samples, the hypertension drug irbesartan (at site N10) and the antihistamine meclozine (at sites N10-14).

Six additional pharmaceuticals were detected at concentration ratios in the range 1-10; amytriptyline, budesonide, bupropion, haloperidol, paroxetine and pizotifen. All observations of pharmaceuticals with a concentration ratio < 10 were made in the effluent dominated samples. Some of these observations were close to the LOQ and the results should not be extrapolated too far, but these findings suggest that diffuse anthropogenic sources can cause elevated levels of pharmaceuticals, at specific sites, that could cause adverse effects.

It should be emphasized that the pharmaceuticals that were included in this screening were selected based on their potential to be present in Swedish surface waters in concentrations close to their CEC values.

5.1.4 Biota

Samples were taken from perch caught in; Lake Tärnan (N2), Krycklan (N4), Valloxen (N15) and in river Fyrisån downstream WWTP Kungsängsverket, Uppsala (N16, 17) (Appendix 9).

Valloxen was used as a regional reference lake in the Uppsala area. The surface area is 2.8 km^2. The lake is not influenced by municipal WWTP effluents. However, there are several bathing sites and the water quality may be affected by private properties with more or less efficient onsite wastewater treatment.

Only one pharmaceutical, the anti-psychotic risperidone, was detected in the biota (perch) samples, (Appendix 8).

Only two of these samples were taken from effluent dominated surface water but these results differ markedly from previous studies (e.g. Fick et al 2011) and also from two of the samples in the regional sampling program (R25, R27) where more pharmaceuticals were found. Several studies have detected pharmaceuticals in biota exposed to effluent dominated rivers (Huerta et al., 2012; Zenker et al., 2014). Perch was chosen in this study because it is one of the most stationary fish species in this region but it cannot be excluded that the sampled fish recently migrated from less exposed sites.

5.2 Pharmaceuticals, regional program

Three influents, ten effluents and eleven sludge samples from WWWP s were analysed in the regional program. The results did not differ substantially from the results from the national program, or the previous screening study in 2010 (Fick et al 2011).

In the influents, 48 out of 101 pharmaceuticals were detected (median concentration 99 ng/L). Paracetamol was detected in the highest amount (up to 110 µg/L).

In the effluents, 45 out of 101 pharmaceuticals were detected (median concentration 51 ng/L). As in the national program highest concentrations were found for metoprolol, up to 1800 ng/L. The list of detected substances was almost the same as for the national samples, one exception being budesonide, found in five of the regional effluents.

In sludge 33 out of 101 pharmaceuticals were detected (median concentration 98 ng/kg d w). Ciprofloxacin was detected in the highest amount (up to 1.8 µg/kg), which was similar to the results in the national program.

Nine surface waters were analysed and 39 out of 101 pharmaceuticals were detected with a median concentration of 3.2 ng/L. High levels of diclofenac (480 ng(L) was measured in one of the samples (R24 Kyrkviken, Arvika).

Seven perch samples were analysed and 17 out of 101 pharmaceuticals were detected with a median concentration of 11 ng/L. In two of the biota samples (R25 Kyrkviken, Arvika and R27 Varnumsviken, Kristinehamn), 14 and 13 pharmaceuticals, respectively, were detected at levels that were similar to previous studies where fish exposed to effluent dominated surface waters were analysed (Fick et al 2011, Huerta et al 2012, Zenker at al 2014) . One of the samples (R34) was a marine sample and in this sample only risperidone was detected.

One groundwater sample was analysed and 9 out of 101 pharmaceuticals were detected at trace levels with a median concentration of 0.54 ng/L.

5.3 Hormones

5.3.1 Water

The effluent waters (24 h composite samples from three consecutive days) from WWTPs in Uppsala, Umeå and Stockholm (Henriksdal) were analysed for hormones, see Figure 5. cEEQ (see 2.3) were estimated and is shown in the same figure. Concentrations of estrone were 1.6 – 2.7 ng/L and 16 – 25 ng/L in effluents from Uppsala and Umeå respectively, but <0.4 ng/L in all samples from Stockholm. The synthetic hormone ethinyl estradiol showed concentrations similar to estrone: 1.0 – 1.2 in Uppsala, 20 – 23 in Umeå and <0.4 – 0.96 in Stockholm. β-Estradiol was detected only in the effluents from Umeå (0.45–0.76 ng/L).

Thus concentrations were higher in effluents from Umeå than from Uppsala or Stockholm. A difference in the treatment process among the WWTPs is that Umeå lacks a dedicated nitrogen-removal stage, which also makes the overall residence time shorter. As concentrations in influents to the WWTPs were not measured, we do not know if such differences affected the effluent concentrations.

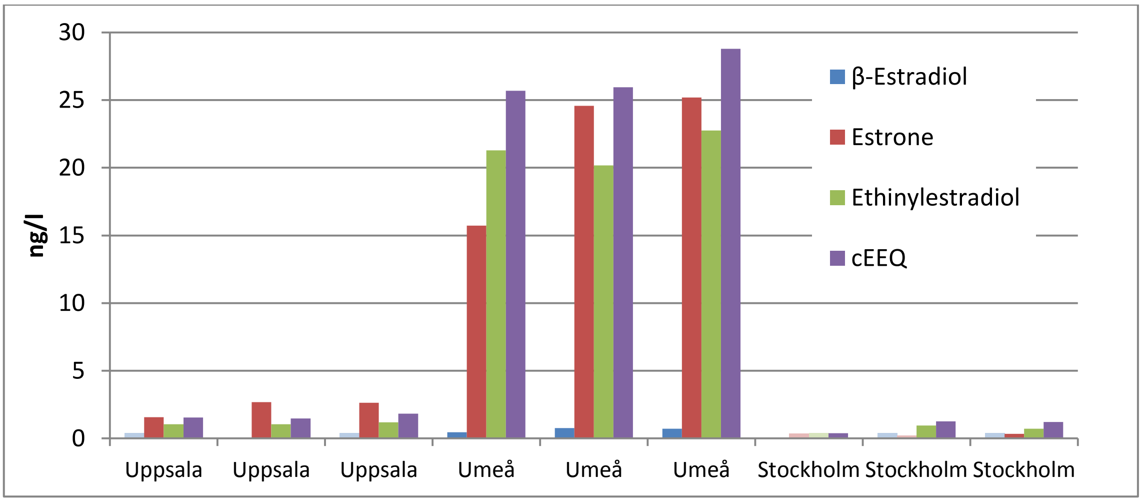

Figure 5 Concentrations of hormones and cEEQ in effluent waters. Note that pale bars indicate detection but not quantification of the respective analyte and are set to LOQ of the sample.

Ethinyl estradiol could also be detected in the receiving water Fyrisån downstream Uppsala WWTP (0.36 and 0.27 ng/L), but not upstream (Figure 6). Estrone was detected at somewhat higher concentrations (<LOQ–1.2 ng/L), but also upstream of the WWTP discharge point (0.59 ng/L).

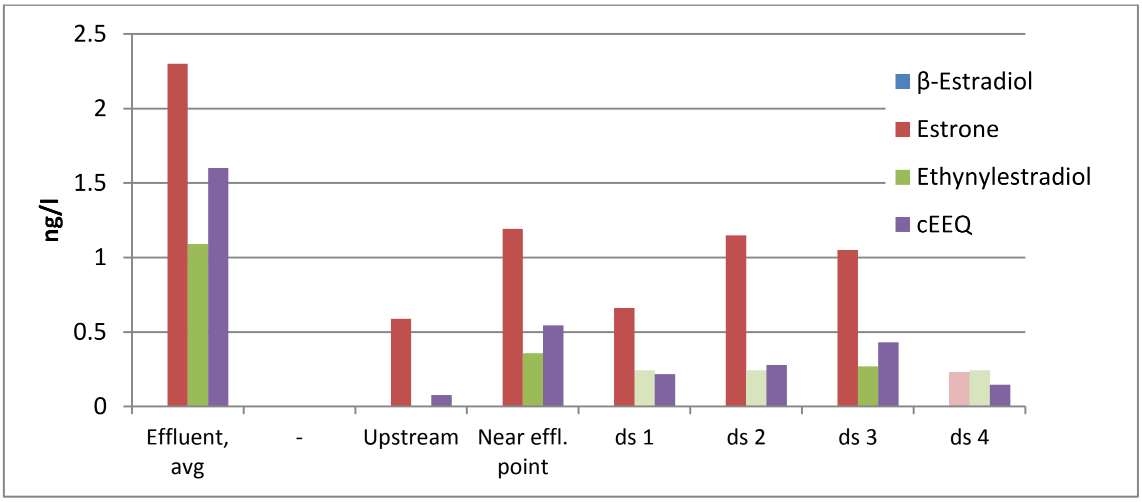

Figure 6 Concentrations of hormones in effluent from Uppsala WWTP (average of three samples) and in the receiving water Fyrisån upstream, close to, and at 150 m (ds 1), 3.5 km (ds 2), 4.6 km (ds 3) and 5.5 km (ds 4) downstream the effluent point.). Note that pale bars indicate detection but not quantification of the respective analyte and are set to LOQ of the sample.

When the concept of Estrogenic Equivalency Factors (EEF) (see 2.3) is applied on the results, it becomes clear that ethinyl estradiol governs the total estrogenic load and that estrone becomes less important due to its lower EEF, 0.13, compared to 1 and 1.09 for β-estradiol and ethinyl estradiol, respectively. However, the abundance of estrone in effluent water still contributes significantly to the total cEEQ.

5.3.2 Fish bile

Bile from perch (*Perca fluviatilis*) collected at three different sites, in the regional reference lake Valloxen, in River Fyrisån near the effluent point from Uppsala WWTP and in the river 4.6 km downstream, were analysed as pooled same sex samples, i.e. male and female samples were pooled from each site. Sample details and results are given in Appendix 11 and Figure 7.

The concentrations of the natural hormones β-estradiol and estrone in bile from near the effluent discharge point were 22–47 ng/g and 28–50 ng/g respectively, and at the site “downstream 3” 140–290 ng/g and 100–160 ng/g, respectively. In Lake Valloxen only estrone (2.6 ng/g) was detected above LOQ, and only in female fish.

At the two WWTP influenced sites the concentration of the synthetic hormone ethinyl estradiol was in the range 2.3–7.7 ng/g. Ethinyl estradiol was not detected above LOQ in lake Valloxen, Figure 8.

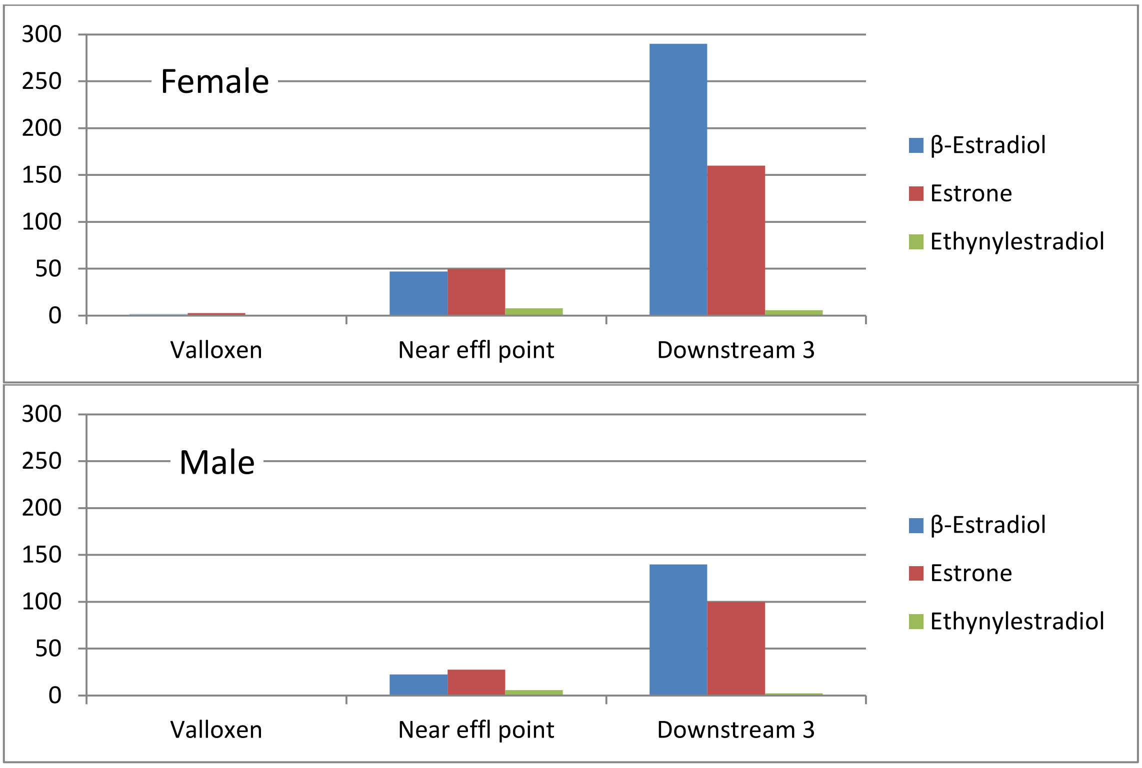

Figure 7 Hormones in bile from female and male perch from three different sites (see text). Note that pale bars indicate detection but not quantification of the respective analyte and are set to LOQ of the sample.

Concidering cEEQ, it becomes clear that β-estradiol governs the total estrogenic load and that estrone becomes less important due to its lower EEF, 0.13, compared to 1 and 1.09 for β-estradiol and ethinyl estradiol, respectively. However, the abundance of estrone in fish bile still contributes significantly to the total EEQ.

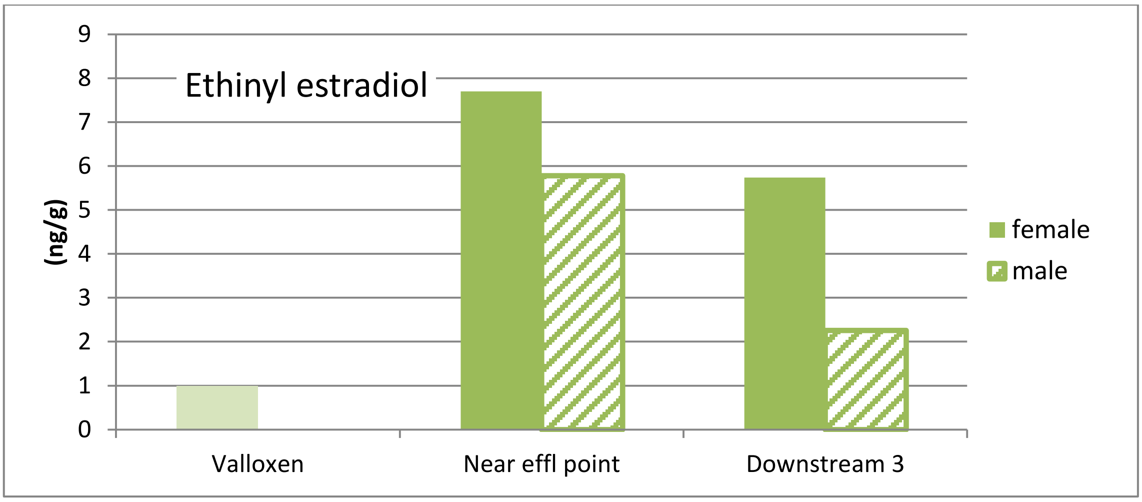

Figure 8 Ethinyl estradiol in bile from female and male perch from three different sites (see text). Note that pale bars indicate detection but not quantification of the analyte and are set to LOQ of the sample.

In conclusion, the reference site had the lowest concentrations for all analytes, suggesting that the elevated concentrations of hormones, natural and anthropogenic at the other investigated sites, might be due to emissions from the WWTP.

Sludge

Hormones were analysed in sludge from WWTPs in Uppsala, Umeå and Stockholm (Henriksdal), (Figure 9).

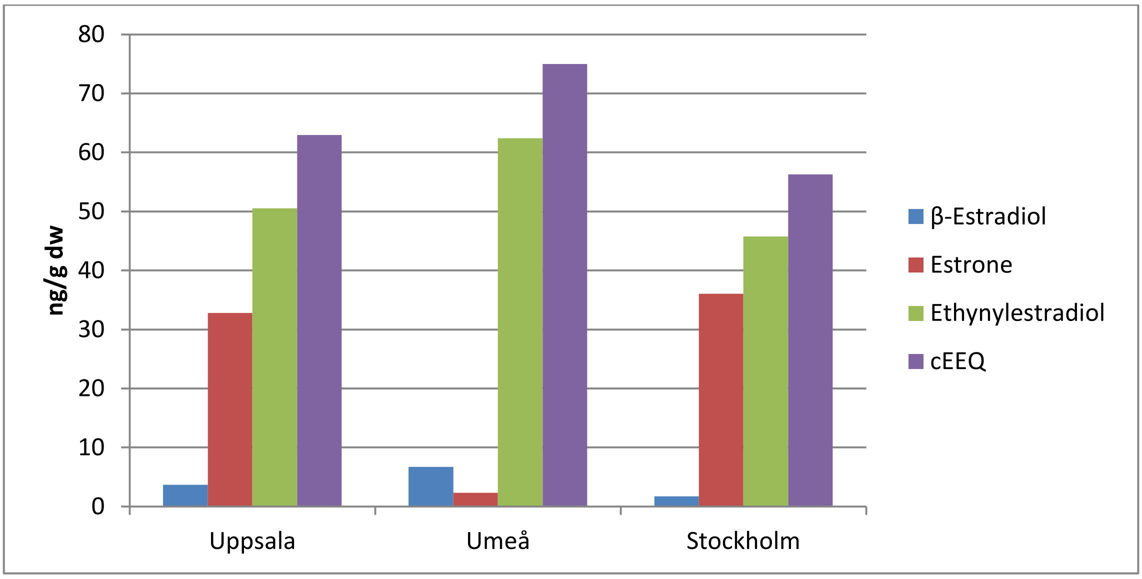

Figure 9 Concentrations of hormones in sludge.

The ethinyl estradiol concentrations in the three sludge samples were all in the range 46–62 ng/g dw; the β-estradiol concentrations were lower, 2–7 ng/g dry weight, with the highest concentration in Umeå.

The estrone concentration in sludge from Umeå, 2 ng/g dw, was lower than in sludge from Uppsala and Stockholm, 36 and 33 ng/g dw, respectively.

Concidering cEEQ, it becomes clear that ethinyl estradiol governs the total estrogenic load in the sludge samples.

The different treatment process in Umeå, mentioned above as a proposed explanation for the relatively high hormone concentrations in the effluent, may also affect the water/sludge distribution of estrogens and/or transformation thereof which is documented to be of a complex nature (Colucci et al. 2001, Prater et al. 2015).

6 Conclusions

- Several of the pharmaceuticals in the screening (44%) were detected in WWTP effluent with a median concentration of 52 ng/L.
- Several pharmaceuticals were detected in high levels in sewage sludge.
- 44 of the pharmaceuticals were detected in the surface water samples; in the range low ng/L to 480 ng/L. The highest levels were found in close proximity to discharge points of WWTPs. In this study 8 out of 103 pharmaceuticals were detected at such levels that they may cause a pharmacological response in fish exposed to these waters.
- In biota (perch) 17 pharmaceuticals were detected in concentrations up to 150 µg/kg. The highest concentrations were similar to what has been found previously in similar studies.
- The analytical method allowed detection of hormones at low concentrations (LOD < 0.2 ng/L) in both effluent and surface waters, in fish bile (LOD < 1 ng/g) and in sludge (LOD <1 –< 10 ng/g dw).
- Hormone concentrations were higher in effluents from Umeå than from Uppsala or Stockholm. In the corresponding sludge samples no such differences were found, in fact the estrone concentration was lower in Umeå compared to the other two.
- The results from the hormone measurements in fish bile suggested increased concentrations due to influence from WWTP emissions.

Suggestions for further studies:

As some of the pharmaceuticals were found in lakes with no load from WWTP effluents, at environmental relevant concentrations, a need for further studies of lakes affected by private sewers only, was identified.

Since high levels of several pharmaceuticals were detected in the sludge samples both in this study and in previous studies, it would be interesting to investigate the mobility of pharmaceuticals in this matrix.

7 Acknowledgement

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Appendix 1 Sample table, National sample program

ID UmU	Municipality	Site	Matrix	Sampling date	Coord. RT90	
N1	Vallentuna	Tärnan	Surface water	2014-09-10	6608704	164490
N2	Vallentuna	Tärnan	Fish	2014-09-09	6608704	164490
N3	Umeå	Krycklan	Surface water	2014-10-10		
N4	Umeå	Krycklan	Fish	2014-10-10		
N5	Uppsala	Uppsala WWTP	Effluent	2014-09-02	6637475	1603969
N6	Uppsala	Uppsala WWTP	Effluent	2014-09-03	6637475	1603969
N7	Uppsala	Uppsala WWTP	Effluent	2014-09-04	6637475	1603969
N8	Uppsala	Uppsala WWTP	Sludge	2014-09-03	6637475	1603969
N9	Uppsala	U-a upstream	Surface water	2014-08-28	6638717	1602928
N10	Uppsala	U-a near effl. point	Surface water	2014-08-28	6637288	1603795
N11	Uppsala	U-a downstream 1 (150 m)	Surface water	2014-08-28	6637143	1603849
N12	Uppsala	U-a downstream 2 (3.5 km)	Surface water	2014-08-28	6636722	1603894
N13	Uppsala	U-a downstream 3 (4.6 km)	Surface water	2014-08-28	6634020	1604660
N14	Uppsala	U-a downstream 4 (5.5 km)	Surface water	2014-08-28	6631097	1604232
N15	Uppsala	U-a Valloxen	Fish	2014-08-29	6624246	1612705
N16	Uppsala	U-a near effl. point	Fish	2014-08-29	6637288	1603795
N17	Uppsala	U-a downstream 3 (4.6 km)	Fish	2014-08-29	6634020	1604660
N18	Umeå	Umeå WWTP	Effluent	2014-08-19	6475757	1387219
N19	Umeå	Umeå WWTP	Effluent	2014-08-20	6475757	1387219
N20	Umeå	Umeå WWTP	Effluent	2014-08-21	6578812	1631124
N21	Umeå	Umeå WWTP	Sludge	2014-08-20	6578812	1631124
N22	Stockholm	Henriksdal WWTP	Effluent	2014-09-03	6578812	1631124
N23	Stockholm	Henriksdal WWTP	Effluent	2014-09-05	7085160	1720924
N24	Stockholm	Henriksdal WWTP	Effluent	2014-09-06	7085160	1720924
N25	Stockholm	Henriksdal WWTP	Sludge	2014-09-04	7085160	1720924

Appendix 2 Sample table, Regional sample program

ID UmU	County	Municipality	Site	Matrix	Sampling date	Coord. RT90	
R1	Gotland	Gotland	Visby WWTP	Effluent	2014-07-22		
R2	Gotland	Gotland	Åminne	Surface water	2014-07-22	6391405	1676247
R3	Gotland	Gotland	Raw water, Åminne WW	Ground water	2014-08-27		
R4	Jämtland	Östersund	Göviken WWTP	Effluent	2014-10-08		
R5	Jämtland	Östersund	Göviken WWTP	Sludge	2014-10-08		
R6	Jämtland	Östersund	Storsjön, effl. point Gövikens WWTP	Surface water	2014-09-23	7009798	1440743
R7	Jämtland	Åre	Åre WWTP	Effluent	2014-09-25		
R8	Jämtland	Åre	Åre WWTP	Sludge	2014-09-25		
R9	Jämtland	Åre	Åresjön, effl point Åre WWTP	Surface water	2014-09-23	7033373	1365932
R10	Jönköping	Jönköping	Simsholmen WWTP	Influent	2014-08-21		
R11	Jönköping	Jönköping	Simsholmen WWTP	Effluent	2014-08-21		
R12	Jönköping	Jönköping	Simsholmen WWTP	Sludge	2014-08-19		
R13	Jönköping	Värnamo	Värnamo WWTP	Influent	2014-08-12		
R14	Jönköping	Värnamo	Värnamo WWTP	Effluent	2014-08-12		
R15	Jönköping	Eksjö	Eksjö WWTP	Effluent	2014-09-03		
R16	Jönköping	Tranås	Tranås WWTP	Influent	2014-10-07		
R17	Jönköping	Tranås	Tranås WWTP	Effluent	2014-10-07		
R18	Jönköping	Tranås	Tranås WWTP	Sludge	2014 v 27-41		
R19	Jönköping	Nässjö	Nässjö WWTP	Effluent	2014-09-05 - 07		
R20	Jönköping	Nässjö	Nässjö WWTP	Sludge	2014 v 24-36		
R21	Jönköping	Hultsfred	Hultsfred WWTP	Effluent	2014-09-09		
R22	Värmland	Kristinehamn	Fiskartorpet WWTP	Effluent	2014-09-23		
R23	Värmland	Kristinehamn	Fiskartorpet WWTP	Sludge	2014-09-23		
R24	Värmland	Arvika	Kyrkviken	Surface water	2014-09-30	6618525	1318936
R25	Värmland	Arvika	Kyrkviken	Fish, perch muscle	2014-09-30	6618298	1319406
R26	Värmland	Kristinehamn	Varnumsviken	Surface water	2014-10-02	6578732	1401169
R27	Värmland	Kristinehamn	Varnumsviken	Fish, perch muscle	2014-10-02	6579704	1401904
R28	Värmland	Säffle	Säffle WWTP	Sludge	2014-09-02		
R29	Östergötland	Norrköping	Slottshagen WWTP	Effluent	2014-08-13		
R30	Östergötland	Norrköping	Slottshagen WWTP	Sludge	2014-08-18		
R31	Östergötland	Linköping	Nykvarn WWTP	Effluent	2014-08-07		
R32	Östergötland	Linköping	Nykvarn WWTP	Sludge	2014-08-07		
R33	Östergötland	Finspång	Dovern, downstream Finspång	Fish, perch muscle	2014-09-15	6502580	1503010
R34	Östergötland	Norrköping	Pampusfjärden, Bråviken	Fish, perch muscle	2014-09-15	6500750	1529200
R35	Östergötland	Norrköping	Glan, downstream Skärblacka	Fish, perch muscle	2014-09-15	6496860	1516170
R36	Östergötland	Linköping	Roxen, downstream Linköping	Fish, perch muscle	2014-09-15	6480119	1489361
R37	Östergötland	Boxholm	Västra Sommen	Fish, perch muscle	2014-09-15	6434750	1455200
R38	Östergötland	Motala	Boren	Surface water	2014-10-27	6493147	1469315
R39	Östergötland	Linköping	Roxen	Surface water	2014-10-27	6480119	1489361
R40	Östergötland	Norrköping	Glan	Surface water	2014-10-27	6496735	1516214
R41	Östergötland	Boxholm	Sommen	Surface water	2014-10-27	6447279	1454997

Appendix 3. Limit of quantification in surface, sewage and drinking water of the used analytical method

Name	LOQ	Name	LOQ	Name	LOQ
	ng/L		ng/L		ng/L
Alfuzosin	0,1	Dihydroergotamine	50	Mirtazapine	10
Alprazolam	10	Diltiazem	0,5	Naloxone	1
Amiodarone	50	Diphenhydramine	0,05	Naproxen	10
Amytriptyline	5	Donepezil	0,5	Nefazodone	0,5
Atenolol	5	Duloxetine	1	Norfloxacin	10
Atorvastatin	50	Eprosartan	5	Ofloxacin	10
Atracurium	0,5	Erythromycine	50	Orphenadrine	0,1
Azelastine	5	Fenofibrate	10	Oxazepam	5
Azithromycine	5	Fentanyl	0,5	Oxytetracycline	50
Beclomethasone	10	Fexofenadine	5	Paracetamol	10
Biperiden	0,1	Finasteride	10	Paroxetine	10
Bisoprolol	0,1	Flecainide	0,1	Perphenazine	10
Bromocriptine	5	Fluconazole	0,5	Pizotifen	0,5
Budesonide	10	Flunitrazepam	10	Promethazine	10
Buprenorphine	10	Fluoxetine	5	Propranolol	50
Bupropion	0,1	Flupentixol	5	Ranitadine	5
Caffeine	50	Fluphenazine	10	Repaglinide	0,5
Carbamazepin	1	Flutamide	5	Risperidone	0,1
Chlorpromazine	5	Glibenclamide	10	Rosuvastatin	10
Chlorprothixene	10	Glimepiride	10	Roxithromycine	50
Cilazapril	1	Haloperidol	0,1	Sertraline	10
Ciprofloxacin	10	Hydroxyzine	0,5	Sotalol	0,5
Citalopram	5	Ibuprofen	180	Sulfamethoxazol	5
Clarithromycine	1	Irbesartan	0,5	Tamoxifen	5
Clemastine	0,5	Ketoconazole	50	Telmisartan	50
Clindamycine	1	Ketoprofene	10	Terbutaline	0,5
Clomipramine	0,5	Levomepromazine	50	Tetracycline	50
Clonazepam	5	Loperamide	0,5	Tramadol	50
Clotrimazol	1	Maprotiline	5	Trihexyphenidyl	0,1
Codeine	0,5	Meclozine	5	Trimethoprim	0,1
Cyproheptadine	5	Memantine	0,5	Venlafaxine	0,5
Desloratidin	0,5	Metoprolol	5	Verapamil	10
Diclofenac	10	Mianserin	1	Zolpidem	0,5
Dicycloverine	5	Miconazole	5		

Appendix 4. Limit of quantification in sludge samples of the used analytical method.

Name	LOQ	Name	LOQ	Name	LOQ
	µg/Kg		µg/Kg		µg/Kg
Alfuzosin	0,1	Dihydroergotamine	50	Mirtazapine	10
Alprazolam	10	Diltiazem	0,5	Naloxone	1
Amiodarone	50	Diphenhydramine	0,05	Naproxen	10
Amytriptyline	5	Donepezil	0,5	Nefazodone	0,5
Atenolol	5	Duloxetine	1	Norfloxacin	10
Atorvastatin	50	Eprosartan	5	Ofloxacin	10
Atracurium	0,5	Erythromycine	50	Orphenadrine	0,1
Azelastine	5	Fenofibrate	10	Oxazepam	5
Azithromycine	5	Fentanyl	0,5	Oxytetracycline	50
Beclomethasone	10	Fexofenadine	5	Paracetamol	10
Biperiden	0,1	Finasteride	10	Paroxetine	10
Bisoprolol	0,1	Flecainide	0,1	Perphenazine	10
Bromocriptine	5	Fluconazole	0,5	Pizotifen	0,5
Budesonide	10	Flunitrazepam	10	Promethazine	10
Buprenorphine	10	Fluoxetine	5	Propranolol	50
Bupropion	0,1	Flupentixol	5	Ranitadine	5
Caffeine	50	Fluphenazine	10	Repaglinide	0,5
Carbamazepin	1	Flutamide	5	Risperidone	0,1
Chlorpromazine	5	Glibenclamide	10	Rosuvastatin	10
Chlorprothixene	10	Glimepiride	10	Roxithromycine	50
Cilazapril	1	Haloperidol	0,1	Sertraline	10
Ciprofloxacin	10	Hydroxyzine	0,5	Sotalol	0,5
Citalopram	5	Ibuprofen	180	Sulfamethoxazol	5
Clarithromycine	1	Irbesartan	0,5	Tamoxifen	5
Clemastine	0,5	Ketoconazole	50	Telmisartan	50
Clindamycine	1	Ketoprofene	10	Terbutaline	0,5
Clomipramine	0,5	Levomepromazine	50	Tetracycline	50
Clonazepam	5	Loperamide	0,5	Tramadol	50
Clotrimazol	1	Maprotiline	5	Trihexyphenidyl	0,1
Codeine	0,5	Meclozine	5	Trimethoprim	0,1
Cyproheptadine	5	Memantine	0,5	Venlafaxine	0,5
Desloratidin	0,5	Metoprolol	5	Verapamil	10
Diclofenac	10	Mianserin	1	Zolpidem	0,5
Dicycloverine	5	Miconazole	5		

Appendix 5. Results, surface water from Vallentuna (N1), Krycklan (N3) and Uppsala (N9-14).

	N1	N3	N9	N10	N11	N12	N13	N14
	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L
Name								
Alfuzosin	0,23	<LOQ	0,31	15	7,1	2,6	1,4	0,8
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	<LOQ	<LOQ	8,1	<LOQ	9,1	<LOQ	<LOQ
Atenolol	<LOQ	<LOQ	<LOQ	31	<LOQ	14	13	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	0,13	0,13	<LOQ	1,2	0,11	<LOQ
Bisoprolol	<LOQ	<LOQ	0,86	34	17	15	14	0,44
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	39	<LOQ	<LOQ	25	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	<LOQ	<LOQ	<LOQ	18	9	7,5	8,4	0,24
Caffeine	<LOQ	<LOQ	130	170	210	190	160	<LOQ
Carbamazepin	<LOQ	<LOQ	13	210	110	95	110	20
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	37	<LOQ	<LOQ	37	18	46	18	<LOQ
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clarithromycine	<LOQ	<LOQ	4,2	12	5,4	25	3,3	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	<LOQ	<LOQ	<LOQ	16	6,9	7,1	6,9	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Codeine	1,6	<LOQ	2,6	28	<LOQ	14	20	2,7
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	<LOQ	<LOQ	<LOQ	260	160	86	120	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	<LOQ	<LOQ	<LOQ	7,5	3,5	1,2	3,7	<LOQ
Diphenhydramine	<LOQ	<LOQ	<LOQ	9,7	3,5	1,6	1,3	0,13
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	<LOQ	<LOQ	11	59	41	<LOQ	32	13
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	<LOQ	<LOQ	2,8	87	39	36	43	5,5
Fluconazole	0,55	<LOQ	3	83	40	35	45	8,3
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	<LOQ	<LOQ	6,5	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	0,36	<LOQ	0,73	0,51	0,15	<LOQ	0,34	0,48
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Irbesartan	<LOQ	<LOQ	1,3	56	29	29	18	1,5

	N1	N3	N9	N10	N11	N12	N13	N14
	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L
Name								
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ketoprofene	<LOQ	<LOQ	<LOQ	56	28	<LOQ	12	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	<LOQ	<LOQ	<LOQ	0,54	<LOQ	<LOQ	<LOQ	<LOQ
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	<LOQ	<LOQ	<LOQ	100	70	7,7	46	9,7
Memantine	<LOQ	<LOQ	<LOQ	8,5	5,1	3	4,2	<LOQ
Metoprolol	<LOQ	<LOQ	<LOQ	<LOQ	260	<LOQ	<LOQ	<LOQ
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mirtazapine	<LOQ	<LOQ	<LOQ	20	<LOQ	<LOQ	<LOQ	<LOQ
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	15	<LOQ	15	26	18	19	21	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	16	11	<LOQ
Orphenadrine	<LOQ	<LOQ	0,35	6,1	2,7	9,2	2,1	0,8
Oxazepam	<LOQ	<LOQ	<LOQ	150	78	66	84	11
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	41	<LOQ	46	71	35	70	79	130
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	15	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	0,89	<LOQ	<LOQ	1,9	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	<LOQ	<LOQ	<LOQ	59	<LOQ	<LOQ	<LOQ	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	8,5	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Rosuvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	<LOQ	23	<LOQ	5,1	<LOQ	7	<LOQ
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Terbutaline	3,7	<LOQ	1,1	1,2	2,3	0,61	2,8	2,8
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	<LOQ	<LOQ	<LOQ	350	170	140	210	<LOQ
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	<LOQ	<LOQ	0,25	31	19	19	15	<LOQ
Venlafaxine	<LOQ	<LOQ	0,99	340	140	120	170	<LOQ
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Zolpidem	<LOQ	<LOQ	<LOQ	0,88	<LOQ	<LOQ	<LOQ	<LOQ

Appendix 6. Results, effluent from WWTPs in Uppsala[a] (N5-N7), Umeå [b] (N18-20) and Stockholm [c] (N22-24).

	N5	N6	N7	N18	N19	N20	N22	N23	N24
	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L
Name									
Alfuzosin	36	20	17	17	12	28	21	25	20
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	24	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	11	8,7	<LOQ
Atenolol	60	59	53	150	130	180	46	34	28
Atorvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	0,14	0,19	0,42	<LOQ	0,11	<LOQ	0,28
Bisoprolol	59	42	39	82	84	96	74	61	62
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	32	25	23	25	19	20	27	24	25
Caffeine	<LOQ	63	63	1100	970	450	<LOQ	63	<LOQ
Carbamazepin	380	290	330	290	200	320	280	220	190
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	25	22	12	21	19	22	13	16	15
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clarithromycine	16	7,5	14	15	23	14	13	19	3,9
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	3,4	1,5	1,5	<LOQ	1,4	7	1	<LOQ	1,2
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Codeine	87	66	80	250	270	370	97	63	61
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	680	490	360	580	410	840	480	350	300
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	9,5	5,6	3,3	12	14	16	13	15	14
Diphenhydramine	14	7,9	6,4	3,5	3,4	6,5	29	26	23
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	110	120	140	230	220	340	140	89	93
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	170	160	170	48	44	56	92	74	72
Fluconazole	150	120	120	210	160	220	110	83	79
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	8	<LOQ	9,2	<LOQ	6,4	<LOQ	6,6	5,5	5,5
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	1,7	0,34	<LOQ	0,34	0,97	0,94	0,61	0,46	0,44
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	N5	N6	N7	N18	N19	N20	N22	N23	N24
	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L
Name									
Irbesartan	83	84	68	44	29	54	160	130	120
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ketoprofene	31	18	<LOQ	100	76	140	23	<LOQ	12
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	<LOQ	0,65	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	280	220	88	300	170	370	320	260	250
Memantine	19	17	23	47	32	42	21	23	24
Metoprolol	950	710	740	1300	1100	1500	990	810	780
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mirtazapine	81	53	51	50	37	51	57	42	41
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	14	11	<LOQ	260	130	230	<LOQ	<LOQ	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Orphenadrine	7,4	7,3	13	4	4,8	5,6	5,9	3,2	4,2
Oxazepam	280	250	240	170	170	210	240	200	180
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	48	36	46	83	45	84	74	84	43
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	0,58	<LOQ	1,4	1,3	<LOQ	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	57	<LOQ	<LOQ	65	56	83	<LOQ	<LOQ	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Rosuvastatin	<LOQ	<LOQ	<LOQ	150	130	160	13	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	16	<LOQ	34	20	23	27	20	21
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	<LOQ	120	220	<LOQ	270	200	73	9,3
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	88	57	<LOQ	<LOQ	<LOQ	<LOQ	71	<LOQ	<LOQ
Terbutaline	6,1	3,8	7	14	7,1	8,1	6,4	7,8	5,5
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	680	510	550	790	580	830	370	290	260
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	62	53	60	100	84	140	22	12	7,1
Venlafaxine	460	400	370	230	200	250	260	220	190
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Zolpidem	1,9	2	2,3	3,4	2,1	2,9	3,4	3,5	12

[a] WWTP Kungsängsverket

[b] WWTP Ön

[c] WWTP Henriksdal

Appendix 7. Results, dewatered digested sludge from WWTPs in Uppsala[a] (N8), Umeå[c] (N21) and Stockholm[b] (N25).

	N8	N21	N25
	µg/Kg dw	µg/Kg dw	µg/Kg dw
Name			
Alfuzosin	16	22	19
Alprazolam	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ
Amytriptyline	130	170	46
Atenolol	<LOQ	<LOQ	<LOQ
Atorvastatin	<LOQ	100	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	<LOQ
Bisoprolol	<LOQ	<LOQ	<LOQ
Bromocriptine	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ
Bupropion	<LOQ	<LOQ	<LOQ
Caffeine	<LOQ	<LOQ	<LOQ
Carbamazepin	140	35	70
Chlorpromazine	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ
Ciprofloxacin	1300	1200	1200
Citalopram	530	510	340
Clarithromycine	<LOQ	<LOQ	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ
Clindamycine	<LOQ	<LOQ	<LOQ
Clomipramine	26	26	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ
Clotrimazol	110	68	160
Codeine	<LOQ	<LOQ	<LOQ
Cyproheptadine	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	29	<LOQ
Diclofenac	<LOQ	<LOQ	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ
Diltiazem	<LOQ	<LOQ	<LOQ
Diphenhydramine	<LOQ	<LOQ	29
Donepezil	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ
Eprosartan	450	430	130
Erythromycine	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ
Fexofenadine	130	150	140
Finasteride	<LOQ	<LOQ	<LOQ
Flecainide	28	10	17
Fluconazole	<LOQ	<LOQ	<LOQ
Flunitrazepam	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	39	30
Flupentixol	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ
Haloperidol	<LOQ	<LOQ	<LOQ
Hydroxyzine	28	20	13

	N8	N21	N25
	µg/Kg dw	µg/Kg dw	µg/Kg dw
Name			
Ibuprofen	<LOQ	<LOQ	<LOQ
Irbesartan	38	16	70
Ketoconazole	<LOQ	890	870
Ketoprofene	<LOQ	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ
Loperamide	19	15	13
Maprotiline	<LOQ	<LOQ	<LOQ
Meclozine	<LOQ	<LOQ	<LOQ
Memantine	<LOQ	8,6	<LOQ
Metoprolol	340	310	240
Mianserin	56	72	<LOQ
Miconazole	270	180	120
Mirtazapine	200	170	94
Naloxone	<LOQ	<LOQ	<LOQ
Naproxen	<LOQ	<LOQ	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	91
Orphenadrine	<LOQ	<LOQ	<LOQ
Oxazepam	26	<LOQ	<LOQ
Oxytetracycline	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	<LOQ	<LOQ
Paroxetine	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ
Propranolol	54	59	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ
Risperidone	<LOQ	<LOQ	<LOQ
Rosuvastatin	<LOQ	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ
Sertraline	220	510	160
Sotalol	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	<LOQ	<LOQ
Tamoxifen	<LOQ	<LOQ	<LOQ
Telmisartan	170	<LOQ	150
Terbutaline	<LOQ	<LOQ	<LOQ
Tetracycline	<LOQ	<LOQ	<LOQ
Tramadol	200	98	76
Trihexyphenidyl	<LOQ	<LOQ	<LOQ
Trimethoprim	<LOQ	<LOQ	<LOQ
Venlafaxine	100	50	76
Verapamil	<LOQ	<LOQ	<LOQ
Zolpidem	<LOQ	2,1	7,1

[a] WWTP Kungsängsverket

[b] WWTP Ön

[c] WWTP Henriksdal

Appendix 8. Results, perch muscle from Vallentuna (N2), Krycklan (N4) and Uppsala (N15-17).

	N2	N4	N15	N16	N17
	µg/Kg	µg/Kg	µg/Kg	µg/Kg	µg/Kg
Name					
Alfuzosin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atenolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bisoprolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Caffeine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Carbamazepin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clarithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Codeine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diphenhydramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Irbesartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	N2	N4	N15	N16	N17
	µg/Kg	µg/Kg	µg/Kg	µg/Kg	µg/Kg
Name					
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ketoprofene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Memantine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Metoprolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mirtazapine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Orphenadrine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Oxazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	5,5	<LOQ	7,7	1,2	2
Rosuvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Terbutaline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Venlafaxine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Zolpidem	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

Appendix 9. Calculated concentration ratios (CR) in Vallentuna (N1) and Uppsala (N9-14). See 2.2 and 5.3 for aditional information.

	N1	N9	N10	N11	N12	N13	N14
Name							
Alfuzosin	4300	3200	67	140	380	710	1200
Amytriptyline			**5,9**		**5,3**		
Atenolol			26000		57000	61000	
Biperiden		720	720		77	850	
Bisoprolol		4000	100	200	230	250	7900
Budesonide		**2,2**			**3,4**		
Bupropion			**6,4**	13	15	14	480
Caffeine							
Carbamazepin		26000	1600	3100	3600	3100	17000
Ciprofloxacin	510000		510000	1100000	410000	1100000	
Clarithromycine		1700	600	1300	290	2200	
Clindamycine			8200	19000	19000	19000	
Codeine	17000	10000	950		1900	1300	9900
Diclofenac			18	28	53	38	
Diltiazem			3700	8000	23000	7500	
Diphenhydramine			210	580	1300	1600	16000
Fexofenadine		1800	340	490		630	1600
Flecainide		700	23	50	55	46	360
Fluconazole							
Fluoxetine			75				
Haloperidol		**8,9**	13	43		19	14
Irbesartan		38	**0,89**	1,7	1,7	2,8	33
Ketoprofene			870	1700		4100	
Loperamide			12				
Meclozine			**0,04**	**0,057**	**0,52**	**0,087**	**0,41**
Memantine			260	440	740	530	
Naloxone							
Naproxen	55000	55000	32000	46000	44000	40000	
Ofloxacin					1687500	2454545	
Orphenadrine		4700	270	610	180	780	2100
Oxazepam			200	390	470	370	2800
Paracetamol	590000	520000	340000	690000	340000	300000	180000
Paroxetine					**1,9**		
Pizotifen		**9,6**			**4,5**		
Propranolol			34				
Ranitadine					27000		
Sulfamethoxazol		4300000		19000000		14000000	
Terbutaline		2200	2100	1100	4100	880	880
Tramadol			14	28	34	23	
Trimethoprim		13000000	110000	170000	170000	220000	
Venlafaxine		6173,737	18	44	51	36	
Zolpidem			1100				

Appendix 10. Results from the regional screening program, samples R1-R41.

	R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12
	ng/L	ng/L	ng/L	ng/L	µg/kg dw	ng/L	ng/L	µg/kg dw	ng/L	ng/L	ng/L	µg/kg dw
Name												
Alfuzosin	12	0,65	0,28	24	65	0,82	<LOQ	35	0,12	16	10	27
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	<LOQ	<LOQ	51	76	<LOQ	<LOQ	160	<LOQ	<LOQ	<LOQ	94
Atenolol	87	<LOQ	<LOQ	360	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	390	200	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	<LOQ	0,56	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	2,1	<LOQ	<LOQ
Bisoprolol	110	<LOQ	<LOQ	150	<LOQ	0,36	<LOQ	<LOQ	<LOQ	220	71	<LOQ
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	32	<LOQ	<LOQ	18	<LOQ	0,11	<LOQ	<LOQ	<LOQ	12	5,8	<LOQ
Caffeine	130	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	150000	650	<LOQ
Carbamazepin	380	3,4	<LOQ	340	34	<LOQ	<LOQ	<LOQ	<LOQ	350	330	120
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	17	<LOQ	<LOQ	40	1800	13	<LOQ	950	<LOQ	160	23	990
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	530	<LOQ	<LOQ	110	<LOQ	<LOQ	<LOQ	380
Clarithromycine	3	<LOQ	<LOQ	5,2	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	20	2,2	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	3	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	74	<LOQ	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	60	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	42
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	180	<LOQ	<LOQ	22	<LOQ	<LOQ	<LOQ	93
Codeine	160	0,65	0,88	540	<LOQ	0,9	<LOQ	<LOQ	0,52	250	150	<LOQ
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	440	<LOQ	<LOQ	520	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	26	300	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	9	<LOQ	<LOQ	24	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	12	6,6	<LOQ
Diphenhydramine	10	<LOQ	0,062	4,2	<LOQ	0,065	<LOQ	<LOQ	0,061	1,9	3,3	<LOQ
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	180	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	200
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	290	<LOQ	<LOQ	120	98	<LOQ	<LOQ	32	<LOQ	130	83	71
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	140	<LOQ	0,15	47	<LOQ	0,12	<LOQ	6	<LOQ	79	47	<LOQ
Fluconazole	110	0,53	<LOQ	72	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	71	51	<LOQ
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	5,1	<LOQ	<LOQ	10	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12
	ng/L	ng/L	ng/L	ng/L	µg/kg dw	ng/L	ng/L	µg/kg dw	ng/L	ng/L	ng/L	µg/kg dw
Name												
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	0,47	<LOQ	0,11	0,63	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	18	0,32	<LOQ
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	20
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	270	<LOQ	<LOQ
Irbesartan	92	<LOQ	<LOQ	77	24	<LOQ	<LOQ	34	<LOQ	47	41	22
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	520	<LOQ	<LOQ	<LOQ	750
Ketoprofene	21	<LOQ	<LOQ	44	<LOQ	<LOQ	84	<LOQ	<LOQ	89	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	0,77	<LOQ	<LOQ	0,5	14	<LOQ	<LOQ	14	<LOQ	<LOQ	<LOQ	17
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	25
Meclozine	550	<LOQ	<LOQ	240	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	44	170	<LOQ
Memantine	40	<LOQ	0,57	11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	45	27	<LOQ
Metoprolol	1100	<LOQ	<LOQ	1500	<LOQ	7,9	<LOQ	<LOQ	<LOQ	1300	620	<LOQ
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	360	<LOQ	<LOQ	17	<LOQ	<LOQ	<LOQ	300
Mirtazapine	60	<LOQ	<LOQ	57	270	<LOQ	<LOQ	36	<LOQ	46	39	190
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	85	<LOQ	<LOQ	110	<LOQ	13	74	<LOQ	<LOQ	530	<LOQ	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Orphenadrine	6,8	<LOQ	<LOQ	6,9	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	11	5,9	<LOQ
Oxazepam	240	<LOQ	<LOQ	240	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	210	210	<LOQ
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	32	<LOQ	64	<LOQ	<LOQ	<LOQ	<LOQ	16	62000	230	<LOQ
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	27	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	11	<LOQ	<LOQ
Propranolol	63	<LOQ	<LOQ	99	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	52	60
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	38	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Rosuvastatin	<LOQ	<LOQ	<LOQ	110	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	200	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	26	<LOQ	<LOQ	31	750	<LOQ	<LOQ	120	<LOQ	<LOQ	19	460
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	36	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	410	26	5,3	370	<LOQ	12	<LOQ	<LOQ	25	310	51	<LOQ
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	73	<LOQ	<LOQ	<LOQ	<LOQ
Terbutaline	18	<LOQ	0,82	14	<LOQ	0,7	<LOQ	<LOQ	0,97	7,3	10	<LOQ
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	120	<LOQ	<LOQ
Tramadol	560	<LOQ	<LOQ	770	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	780	420	62
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	23	<LOQ	0,54	86	<LOQ	0,5	<LOQ	<LOQ	<LOQ	79	46	<LOQ
Venlafaxine	280	1,2	<LOQ	240	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	340	170	<LOQ
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	22	<LOQ	<LOQ	<LOQ	35
Zolpidem	3	<LOQ	<LOQ	2,1	14	<LOQ	<LOQ	<LOQ	<LOQ	1,2	1,1	<LOQ

	R14	R13	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24
	ng/L	ng/L	ng/L	ng/L	ng/L	µg/kg dw	ng/L	µg/kg dw	ng/L	ng/L	µg/kg dw	ng/L
Name												
Alfuzosin	31	17	19	33	23	29	12	31	15	19	62	0,32
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	31	<LOQ	<LOQ	<LOQ	98	<LOQ	85	29	24	160	<LOQ
Atenolol	390	620	110	690	350	<LOQ	220	<LOQ	140	170	<LOQ	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	130	<LOQ	82	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	0,67	0,13	1,8	<LOQ	<LOQ	0,2	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bisoprolol	270	530	89	280	130	<LOQ	120	<LOQ	45	66	<LOQ	0,58
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	<LOQ	1000	50	<LOQ	38	<LOQ	23	17	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	23	35	<LOQ	1,9	5,6	<LOQ	1,8	<LOQ	0,97	6,6	<LOQ	<LOQ
Caffeine	2400	160000	490	140000	240	<LOQ	8800	<LOQ	<LOQ	52	<LOQ	200
Carbamazepin	1000	1100	230	560	470	120	270	74	550	220	<LOQ	12
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	16	230	<LOQ	220	19	1300	<LOQ	810	14	<LOQ	900	21
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	400	<LOQ	470	<LOQ	<LOQ	540	<LOQ
Clarithromycine	16	25	2,5	150	59	<LOQ	36	<LOQ	19	26	<LOQ	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	1,1	44	1,5	29	1,5	<LOQ	1,3	<LOQ	1,3	1,8	<LOQ	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	82	<LOQ	55	<LOQ	<LOQ	62	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	68	<LOQ	36	<LOQ	<LOQ	40	<LOQ
Codeine	460	710	31	380	170	<LOQ	88	<LOQ	19	48	<LOQ	2,7
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	27	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	630	<LOQ	370	3000	920	<LOQ	260	<LOQ	710	410	<LOQ	480
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	42	37	6,6	13	4,7	<LOQ	38	<LOQ	1,6	21	19	<LOQ
Diphenhydramine	5,2	1,5	<LOQ	6,3	3,4	<LOQ	7,4	<LOQ	3	<LOQ	<LOQ	<LOQ
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	270	<LOQ	<LOQ	220	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	230	220	73	100	56	110	46	43	210	66	<LOQ	6,8
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	200	270	100	160	110	30	110	15	83	170	18	1,8
Fluconazole	150	240	19	57	44	<LOQ	21	<LOQ	130	65	<LOQ	2,4
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	<LOQ	8,4	24	18	<LOQ	11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	2,1	17	1,3	15	0,41	<LOQ	1,2	16	0,21	1,4	12	0,2
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	24	<LOQ	25	<LOQ	<LOQ	22	<LOQ
Ibuprofen	<LOQ	300	<LOQ	370	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	R14	R13	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24
	ng/L	ng/L	ng/L	ng/L	ng/L	µg/kg dw	ng/L	µg/kg dw	ng/L	ng/L	µg/kg dw	ng/L
Name												
Irbesartan	110	120	44	180	130	62	73	23	82	120	44	1,2
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1400	<LOQ	560	<LOQ	<LOQ	<LOQ	<LOQ
Ketoprofene	82	140	18	110	100	<LOQ	36	<LOQ	34	<LOQ	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	25	0,76	9,6	<LOQ	<LOQ	15	<LOQ
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	410	85	89	42	120	<LOQ	66	<LOQ	210	320	<LOQ	16
Memantine	24	25	6,1	22	16	<LOQ	15	<LOQ	19	9,5	<LOQ	2
Metoprolol	1500	2200	640	2600	1500	550	1200	<LOQ	1800	1000	<LOQ	41
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	75	<LOQ	50	<LOQ	<LOQ	18	<LOQ
Mirtazapine	47	39	25	88	42	200	26	110	61	42	85	<LOQ
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	600	1100	<LOQ	1200	1200	<LOQ	190	<LOQ	58	<LOQ	<LOQ	20
Nefazodone	<LOQ	1,5	<LOQ	0,76	<LOQ	<LOQ	0,94	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Orphenadrine	7,2	11	3,9	<LOQ	4,8	<LOQ	7,5	<LOQ	<LOQ	4,1	<LOQ	<LOQ
Oxazepam	360	360	170	320	320	48	160	<LOQ	480	390	62	13
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	71000	45	110000	68	<LOQ	290	<LOQ	<LOQ	77	<LOQ	15
Paroxetine	<LOQ	26	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	6,9	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	2,3	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	99	<LOQ	<LOQ	55	<LOQ	<LOQ	53	94	<LOQ	67	<LOQ	<LOQ
Ranitadine	<LOQ	91	<LOQ	44	<LOQ	<LOQ	9,8	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Rosuvastatin	270	510	27	140	36	<LOQ	61	<LOQ	290	<LOQ	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	<LOQ	42	19	14	370	30	160	13	19	490	<LOQ
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	130	250	<LOQ	170	180	<LOQ	81	<LOQ	260	100	<LOQ	38
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	57	<LOQ	67	<LOQ	<LOQ	240	<LOQ	67	<LOQ	120	100	<LOQ
Terbutaline	9,1	13	4,8	14	5	<LOQ	8,9	<LOQ	8,1	4,9	<LOQ	7,1
Tetracycline	<LOQ	130	<LOQ	180	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	1400	2000	380	1000	950	240	500	69	820	580	<LOQ	<LOQ
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	72	98	57	59	45	<LOQ	57	<LOQ	37	130	<LOQ	2,6
Venlafaxine	200	180	160	680	450	120	320	<LOQ	370	180	<LOQ	0,9
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	27	<LOQ
Zolpidem	1,8	1,8	0,77	1,1	2,5	7,5	2,1	<LOQ	<LOQ	3,3	<LOQ	<LOQ

	R25	R26	R27	R28	R29	R30	R31	R32	R33	R34	R35	R36
	µg/kg wet weight	ng/L	µg/kg wet weight	µg/kg dw	ng/L	µg/kg dw	ng/L	µg/kg dw	µg/kg wet weight	µg/kg wet weight	µg/kg wet weight	µg/kg wet weight
Name												
Alfuzosin	<LOQ	<LOQ	<LOQ	41	15	20	12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	<LOQ	<LOQ	420	26	410	6,6	160	<LOQ	<LOQ	<LOQ	<LOQ
Atenolol	<LOQ	14	<LOQ	<LOQ	350	<LOQ	400	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	180	<LOQ	110	<LOQ	190	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	12	<LOQ	38	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	11	0,53	31	<LOQ	<LOQ	<LOQ	0,77	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bisoprolol	<LOQ	1	<LOQ	<LOQ	59	<LOQ	76	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	29	<LOQ	<LOQ	<LOQ	<LOQ	35	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	<LOQ	0,18	<LOQ	<LOQ	11	<LOQ	17	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Caffeine	<LOQ	92	<LOQ	<LOQ	80	<LOQ	2200	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Carbamazepin	<LOQ	6,9	<LOQ	<LOQ	230	98	480	100	<LOQ	<LOQ	<LOQ	<LOQ
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	10	<LOQ	20	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	<LOQ	180	<LOQ	920	<LOQ	800	26	1100	<LOQ	<LOQ	<LOQ	<LOQ
Citalopram	<LOQ	<LOQ	<LOQ	230	<LOQ	320	<LOQ	480	<LOQ	<LOQ	<LOQ	<LOQ
Clarithromycine	6,2	<LOQ	<LOQ	<LOQ	16	<LOQ	13	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clemastine	<LOQ	<LOQ	30	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	<LOQ	<LOQ	<LOQ	<LOQ	11	<LOQ	2,7	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	450	<LOQ	53	<LOQ	73	<LOQ	<LOQ	<LOQ	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	150	580	<LOQ	98	<LOQ	130	<LOQ	<LOQ	<LOQ	<LOQ
Codeine	<LOQ	3,2	<LOQ	<LOQ	140	<LOQ	200	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	<LOQ	51	<LOQ	<LOQ	490	<LOQ	590	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	8,3	<LOQ	32	<LOQ	7,9	<LOQ	17	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diphenhydramine	<LOQ	0,089	<LOQ	<LOQ	7,8	<LOQ	6,5	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	1300	<LOQ	340	<LOQ	340	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	11	<LOQ	<LOQ	<LOQ	180	240	230	410	<LOQ	<LOQ	<LOQ	<LOQ
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	10	2,8	19	64	55	19	170	42	<LOQ	<LOQ	<LOQ	<LOQ
Fluconazole	<LOQ	2,4	<LOQ	<LOQ	65	<LOQ	110	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	<LOQ	<LOQ	<LOQ	7,2	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	8,4	0,87	48	<LOQ	0,25	<LOQ	1,8	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Hydroxyzine	11	<LOQ	<LOQ	<LOQ	<LOQ	43	<LOQ	54	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	R25	R26	R27	R28	R29	R30	R31	R32	R33	R34	R35	R36
	µg/kg wet weight	ng/L	µg/kg wet weight	µg/kg dw	ng/L	µg/kg dw	ng/L	µg/kg dw	µg/kg wet weight	µg/kg wet weight	µg/kg wet weight	µg/kg wet weight
Name												
Irbesartan	<LOQ	2,8	<LOQ	160	40	<LOQ	88	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1500	<LOQ	770	<LOQ	<LOQ	<LOQ	<LOQ
Ketoprofene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	27	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	3,4	1,7	39	79	<LOQ	39	<LOQ	32	<LOQ	<LOQ	<LOQ	2,1
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	<LOQ	<LOQ	23	<LOQ	280	<LOQ	200	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Memantine	<LOQ	<LOQ	<LOQ	<LOQ	23	<LOQ	34	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Metoprolol	<LOQ	<LOQ	<LOQ	<LOQ	1100	<LOQ	1500	150	<LOQ	<LOQ	<LOQ	<LOQ
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	170	<LOQ	150	<LOQ	280	<LOQ	<LOQ	<LOQ	<LOQ
Mirtazapine	<LOQ	<LOQ	<LOQ	360	51	190	71	310	<LOQ	<LOQ	<LOQ	<LOQ
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	<LOQ	16	<LOQ	<LOQ	<LOQ	<LOQ	120	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Nefazodone	5,4	<LOQ	50	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	3
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Orphenadrine	<LOQ	1,2	<LOQ	<LOQ	10	<LOQ	5,9	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Oxazepam	<LOQ	<LOQ	<LOQ	<LOQ	310	<LOQ	300	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	94	<LOQ	<LOQ	40	<LOQ	270	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	82	<LOQ	62	<LOQ	<LOQ	<LOQ	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Repaglinide	12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	6,8	<LOQ	26	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1,7	1,2	0,11	1,5
Rosuvastatin	<LOQ	<LOQ	<LOQ	<LOQ	12	<LOQ	68	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	<LOQ	<LOQ	1800	18	320	16	560	<LOQ	<LOQ	<LOQ	<LOQ
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	140	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	150	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Terbutaline	<LOQ	0,84	<LOQ	<LOQ	11	<LOQ	7,3	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	<LOQ	<LOQ	<LOQ	<LOQ	630	190	810	60	<LOQ	<LOQ	<LOQ	<LOQ
Trihexyphenidyl	6,5	<LOQ	18	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	<LOQ	<LOQ	<LOQ	<LOQ	26	<LOQ	60	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Venlafaxine	<LOQ	<LOQ	<LOQ	<LOQ	300	<LOQ	260	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Zolpidem	<LOQ	<LOQ	<LOQ	<LOQ	2,4	<LOQ	2,1	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	R37	R38	R39	R40	R41
	µg/kg wet weight	ng/L	ng/L	ng/L	ng/L
Name					
Alfuzosin	<LOQ	0,14	0,99	0,29	0,17
Alprazolam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amiodarone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Amytriptyline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atenolol	<LOQ	<LOQ	37	<LOQ	<LOQ
Atorvastatin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Atracurium	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azelastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Azithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Beclomethasone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Biperiden	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bisoprolol	<LOQ	0,16	15	<LOQ	<LOQ
Bromocriptine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Budesonide	<LOQ	<LOQ	16	<LOQ	<LOQ
Buprenorphine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Bupropion	<LOQ	0,12	5,9	0,13	0,18
Caffeine	<LOQ	<LOQ	300	66	59
Carbamazepin	<LOQ	2,2	84	6,3	3,2
Chlorpromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Chlorprothixene	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Cilazapril	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ciprofloxacin	<LOQ	<LOQ	17	<LOQ	<LOQ
Citalopram	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clarithromycine	<LOQ	<LOQ	3,3	<LOQ	<LOQ
Clemastine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clindamycine	<LOQ	<LOQ	27	<LOQ	<LOQ
Clomipramine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clonazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Codeine	<LOQ	1,6	28	1,5	0,77
Cyproheptadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Desloratidin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diclofenac	<LOQ	56	120	<LOQ	<LOQ
Dicycloverine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Dihydroergotamine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Diltiazem	<LOQ	<LOQ	6,9	<LOQ	<LOQ
Diphenhydramine	<LOQ	0,07	0,98	<LOQ	0,22
Donepezil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Duloxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Eprosartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fenofibrate	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fentanyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fexofenadine	<LOQ	<LOQ	15	<LOQ	<LOQ
Finasteride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flecainide	<LOQ	0,23	36	0,84	0,47
Fluconazole	<LOQ	0,87	28	0,85	<LOQ
Flunitrazepam	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluoxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flupentixol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Fluphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Flutamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glibenclamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glimepiride	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Haloperidol	<LOQ	0,14	0,27	0,39	0,5
Hydroxyzine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Irbesartan	<LOQ	<LOQ	12	<LOQ	<LOQ
Ketoconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

	R37	R38	R39	R40	R41
	µg/kg wet weight	ng/L	ng/L	ng/L	ng/L
Name					
Ketoprofene	<LOQ	<LOQ	41	<LOQ	<LOQ
Levomepromazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Loperamide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Maprotiline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Meclozine	<LOQ	<LOQ	61	<LOQ	<LOQ
Memantine	<LOQ	<LOQ	6,2	<LOQ	<LOQ
Metoprolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mianserin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Miconazole	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Mirtazapine	<LOQ	<LOQ	11	<LOQ	<LOQ
Naloxone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Naproxen	<LOQ	12	140	<LOQ	<LOQ
Nefazodone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ofloxacin	<LOQ	<LOQ	<LOQ	21	<LOQ
Orphenadrine	<LOQ	<LOQ	0,55	<LOQ	<LOQ
Oxazepam	<LOQ	<LOQ	60	<LOQ	<LOQ
Oxytetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Paracetamol	<LOQ	23	39	41	34
Paroxetine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Perphenazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Pizotifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Promethazine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Ranitadine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Repaglinide	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Risperidone	1,1	<LOQ	<LOQ	<LOQ	<LOQ
Rosuvastatin	<LOQ	<LOQ	25	<LOQ	<LOQ
Roxithromycine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sertraline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sotalol	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Sulfamethoxazol	<LOQ	13	<LOQ	<LOQ	44
Tamoxifen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Telmisartan	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Terbutaline	<LOQ	0,52	9,7	0,59	1,6
Tetracycline	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	<LOQ	<LOQ	170	<LOQ	<LOQ
Trihexyphenidyl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Trimethoprim	<LOQ	0,15	23	6,1	0,22
Venlafaxine	<LOQ	<LOQ	61	0,71	1,1
Verapamil	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Zolpidem	<LOQ	<LOQ	0,75	<LOQ	<LOQ

Appendix 11. Hormones

Hormones in water, results

ID IVL	ID UmU	Site	Unit	β-Estradiol	Estrone	Ethinyl estradiol
3379	N1	Lake Tärnan	ng/L	< 0.12	< 0.069	< 0.072
3361	N5	Uppsala WWTP	ng/L	< 0.40	1.6	1.1
3362	N6	Uppsala WWTP	ng/L	< 0.12	2.7	1.0
3363	N7	Uppsala WWTP	ng/L	< 0.40	2.6	1.2
3330	N9	Uppsala, upstream	ng/L	< 0.12	0.59	< 0.072
3331	N10	Uppsala, close to effl. point	ng/L	< 0.12	1.2	0.36
3332	N11	Uppsala, downstr 1	ng/L	< 0.12	0.66	< 0.24
3333	N12	Uppsala, downstr 2	ng/L	< 0.12	1.1	< 0.24
3334	N13	Uppsala, downstr 3	ng/L	< 0.12	1.1	0.27
3335	N14	Uppsala, downstr 4	ng/L	< 0.12	< 0.23	< 0.24
3325	N18	Umeå WWTP	ng/L	0.45	16	21
3326	N19	Umeå WWTP	ng/L	0.76	25	20
3327	N20	Umeå WWTP	ng/L	0.71	25	23
3369	N22	Henriksdal WWTP*	ng/L	< 0.19	< 0.37	< 0.38
3370	N23	Henriksdal WWTP	ng/L	< 0.40	< 0.23	0.96
3371	N24	Henriksdal WWTP	ng/L	< 0.40	0.34	0.72
		LOD	ng/L	< 0.12	< 0.069	< 0.072
		LOQ	ng/L	< 0.40	< 0.23	< 0.24
		*LOD sample 3369	ng/L	< 0.19	< 0.11	< 0.11
		*LOQ sample 3369	ng/L	< 0.63	< 0.37	< 0.38

Hormones in fish bile, results

All fish were caught 2014-08-29.

Site	Sex	# of indivi-duals	Age	Tot sample weight (g)	Unit	β-Estradiol	Estrone	Ethinyl estradiol
Valloxen	male	1	6+	0.10	ng/g	< 0.79	< 0.70	< 0.39
Valloxen	female	2	4+, 4+	0.13	ng/g	< 2.0	2.6	< 1.0
Near effl point	male	3	2+, 4+, 4+	0.15	ng/g	22	28	5.8
Near effl point	female	3	2+, 2+, 4+	0.24	ng/g	47	50	7.7
Downstr 3	male	2	1+, 1+	0.20	ng/g	140	100	2.3
Downstr 3	female	3	1+, 3+, 3+	0.37	ng/g	290	160	5.7
				LOD	ng/g	0.21-0.79	0.18-0.70	0.10-0.39
				LOQ	ng/g	0.69-2.65	0.61-2.34	0.31-1.30

Hormones in sludge, results

ID IVL	ID UmU	Site	Unit	β-Estradiol	Estrone	Ethinyl estradiol
3364	N8	Uppsala WWTP	ng/g dw	3.7	33	51
3329	N21	Umeå WWTP	ng/g dw	6.7	2.3	62
3372	N25	Stockholm, Henriksdal WWTP	ng/g dw	1.7	36	46
		LOD	ng/g dw	0.47-0.59	0.55-0.59	10-11
		LOQ	ng/g dw	1.6-1.7	1.8-2.0	34-36

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