

Supporting information for:

Hospital Wastewater Treatment by Membrane Bioreactor: Performance and Efficiency for Organic Micropollutant Elimination

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1. Analyzed micropollutants

Table S1. Alphabetical list of analyzed micropollutants

| Compound | CAS number ^(supplier) | Description |
|--|---------------------------------------|---|
| 4-Acetamidoantipyrine | 83-15-8 ^(S-A) | 3 rd metabolite of Aminopyrine / Metamizole |
| 4-Aminoantipyrine | 83-07-8 ^(R) | 2 nd metabolite of Aminopyrine / Metamizole |
| 4-Dimethylaminoantipyrine (Aminopyrine) ¹ | 58-15-1 ^(R) | analgesic / antipyretic |
| 4-Formylaminoantipyrine | 1672-58-8 ^(S-A) | 4 th (final) metabolite of Aminopyrine / Metamizole |
| 4-Methylaminoantipyrine | 519-98-2 ^(H) | active substance of Aminopyrine / Metamizole - analgesic, N02BB02 |
| 4/5-Methylbenzotriazole (2 isomers) ² | 136-85-6, 29878-31-7 ^(S-A) | corrosion inhibitors |
| Atenolol | 29122-68-7 ^(S-A) | beta blocking agent |
| Atenolol acid (Metoprolol acid) | 56392-14-4 ^(TRC) | metabolite of Atenolol / Metoprolol |
| Azithromycin | 83905-01-5 ^(S-A) | macrolide antibacterial |
| Benzotriazole | 95-14-7 ^(S-A) | corrosion inhibitor |
| Bezafibrate | 41859-67-0 ^(S-A) | lipid modifying agent |
| Carbamazepine | 298-46-4 ^(S-A) | antiepileptic |
| Cilastatin | 82009-34-5 ^(TRC) | enzyme inhibitor (used with Imipenem - antibacterial, J01DH51) |
| Ciprofloxacin | 85721-33-1 ^(F) | fluoroquinolone antibacterial |
| Clarithromycin | 81103-11-9 ^(IDC) | macrolide antibacterial |
| Clindamycin | 18323-44-9 ^(S-A) | lincosamide antibacterial |
| Clofibrac acid | 882-09-7 ^(S-A) | metabolite of Clofibrate - lipid modifying agent, C10AB01 |
| Cyclophosphamide | 50-18-0 ^(S-A) | cytostatic |
| D617 | 34245-14-2 ^(TRC) | metabolite of Verapamil |
| Dexamethasone | 50-02-2 ^(S-A) | corticosteroid |
| Diatrizoate (Amidotriazoic, or diatrizoic acid) | 117-96-4 ^(BS) | iodinated X-ray contrast medium |
| Diazepam | 439-14-5 ^(Ro) | anxiolytic |
| Diclofenac | 15307-86-5 ^(S-A) | antiinflammatory / antirheumatic |
| Erythromycin ³ | 114-07-8 ^(S-A) | macrolide antibacterial |
| Fluconazole | 86386-73-4 ^(E) | antimycotic |
| Fluoxetine | 54910-89-3 ^(TRC) | antidepressant |
| Furosemide | 54-31-9 ^(S-A) | diuretic |
| Gabapentin | 60142-96-3 ^(TRC) | antiepileptic |
| Hydrochlorothiazide | 58-93-5 ^(S-A) | diuretic |
| Ifosfamide | 3778-73-2 ^(S-A) | cytostatic |
| Indometacin | 53-86-1 ^(S-A) | antiinflammatory / antirheumatic |
| Iohexol | 66108-95-0 ^(F) | iodinated X-ray contrast medium |
| Iomeprol | 78649-41-9 ^(BG) | iodinated X-ray contrast medium |
| Iopamidol | 62883-00-5 ^(BG) | iodinated X-ray contrast medium |
| Iopromide | 73334-07-3 ^(BS) | iodinated X-ray contrast medium |
| Ioxitalamic acid | 28179-44-4 ^(BG) | iodinated X-ray contrast medium |
| Levetiracetam | 102767-28-2 ^(TRC) | antiepileptic |
| Lidocaine | 137-58-6 ^(S-A) | anesthetic, local |
| Mefenamic acid | 61-68-7 ^(S-A) | antiinflammatory / antirheumatic |
| Methylprednisolone | 83-43-2 ^(F) | corticosteroid |
| Metoprolol | 37350-58-6 ^(S-A) | beta blocking agent |
| Metronidazole | 443-48-1 ^(R) | imidazole antibacterial |
| Morphine | 57-27-2 ^(L) | analgesic (opioid) |
| N4-Acetylsulfamethoxazole | 21312-10-7 ^(S-A) | metabolite of Sulfamethoxazole |
| Naproxen | 22204-53-1 ^(S-A) | antiinflammatory / antirheumatic |

¹ 4-Dimethylaminoantipyrine (Aminophenazone, or aminopyrine) is not used in Switzerland due to severe side effects (agranulocytosis)

² Methylbenzotriazole measured in this study is a sum of 4-Methylbenzotriazole and 5-Methylbenzotriazole (mixture called Tolyltriazole)

³ Erythromycin measured in this study is a sum of Erythromycin and Erythromycin-H₂O

table continues

Table S1. Alphabetical list of analyzed micropollutants (*continued*)

| Compound | CAS number <small>(supplier)</small> | Description |
|-----------------------------|--------------------------------------|--|
| Norfloxacin | 70458-96-7 ^(R) | fluoroquinolone antibacterial |
| Oseltamivir | 196618-13-0 ^(Ro) | antiviral |
| Oseltamivir carboxylate | 187227-45-8 ^(Ro) | active substance of Oseltamivir |
| Oxazepam | 604-75-1 ^(L) | anxiolytic |
| Paracetamol (Acetaminophen) | 103-90-2 ^(S-A) | analgesic / antipyretic |
| Phenazone (Antipyrine) | 60-80-0 ^(E) | analgesic / antipyretic |
| Primidone | 125-33-7 ^(S-A) | antiepileptic (barbiturate) |
| Propranolol | 525-66-6 ^(S-A) | beta blocking agent |
| Ranitidine | 66357-35-5 ^(S-A) | acid disorders - alimentary system |
| Ritalinic acid | 19395-41-6 ^(S-A) | metabolite of Methylphenidate (Ritalin) - psychostimulant, N06BA04 |
| Ritonavir | 155213-67-5 ^(TRC) | antiviral |
| Roxithromycin | 80214-83-1 ^(S-A) | macrolide antibacterial |
| Sotalol | 3930-20-9 ^(S-A) | beta blocking agent |
| Sulfadiazine | 68-35-9 ^(S-A) | sulfonamide antibacterial |
| Sulfamethoxazole | 723-46-6 ^(S-A) | sulfonamide antibacterial |
| Sulfapyridine | 144-83-2 ^(R) | sulfonamide antibacterial |
| Thiopental | 76-75-5 ^(TRC) | anesthetic, general (barbiturate) |
| Tramadol | 27203-92-5 ^(F) | analgesic (opioid) |
| Trimethoprim | 738-70-5 ^(S-A) | antibacterial |
| Valsartan | 137862-53-4 ^(TRC) | angiotensin II receptor antagonist |
| Venlafaxine | 93413-69-5 ^(TRC) | antidepressant |
| Verapamil | 152-11-4 ^(S-A) | calcium channel blocker |

List of suppliers:

| | |
|-------|---|
| (BG) | courtesy of Byk Gulden, Singen, Germany |
| (BS) | courtesy of Bayer Schering Pharma, Berlin, Germany |
| (CDN) | CDN Isotopes INC., Pointe-Claire, Canada |
| (E) | Dr. Ehrenstorfer GmbH, Augsburg, Germany |
| (F) | Fluka, Sigma-Aldrich, Buchs, Switzerland |
| (H) | in-house synthesis (hydrolysis of metamizole) |
| (IDC) | IDC, Abbott Laboratories, Zug, Switzerland |
| (L) | Lipomed AG, Arlesheim, Switzerland |
| (R) | Riedel-de Haen Laborchemikalien GmbH & Co., Seelze, Germany |
| (Ro) | courtesy of F. Hoffmann-La Roche Ltd, Basel, Switzerland |
| (S-A) | Sigma-Aldrich, Seelze, Germany |
| (TRC) | Toronto Research Chemicals, North York, Canada |

Table S2. Alphabetical list of isotope labelled internal standards

| Internal standard | Analyte | Supplier ¹ |
|---------------------------------------|---|----------------------------|
| 5-Methylbenzotriazole-D6 | 4/5-Methylbenzotriazole ² | Toronto Research Chemicals |
| Atenolol-D7 | Atenolol, 4-Methylaminoantipyrine | Toronto Research Chemicals |
| Atenolol acid-D5 | Atenolol acid, Metronidazole | Toronto Research Chemicals |
| Azithromycin-D3 | Azithromycin | Toronto Research Chemicals |
| Benzotriazole-D4 | Benzotriazole | Toronto Research Chemicals |
| Bezafibrate-D4 | Bezafibrate | Dr. Ehrenstorfer GmbH |
| Carbamazepine-C13,D2 | Carbamazepine | Toronto Research Chemicals |
| Clarithromycin-N-methyl-D3 | Clarithromycin, Roxithromycin | Toronto Research Chemicals |
| Clofibric acid-D4 | Clofibric acid, Thiopental | Toronto Research Chemicals |
| Cyclophosphamide-D4 | Cyclophosphamide, 4/5-Methylbenzotriazole ² , Ifosfamide | Toronto Research Chemicals |
| Diatrizoate-D6 (Amidotrizoic acid-D6) | Diatrizoate | Toronto Research Chemicals |
| Diazepam-D5 | Diazepam | Lipomed AG |
| Diclofenac-D4 | Diclofenac | Toronto Research Chemicals |
| Erythromycin-13C2 | Erythromycin | Toronto Research Chemicals |
| Fluconazol-D4 | Fluconazol | Dr. Ehrenstorfer GmbH |
| Fluoxetine-D5 | Fluoxetine, Erythromycin-H ₂ O | Toronto Research Chemicals |
| Furosemide-D5 | Furosemide | Toronto Research Chemicals |
| Gabapentin-D4 | Gabapentin | Toronto Research Chemicals |
| Hydrochlorothiazide-13C-D2 | Hydrochlorothiazide | Toronto Research Chemicals |
| Indometacin-D4 | Indometacin | Toronto Research Chemicals |
| Iohexol-D5 | Iohexol | Toronto Research Chemicals |
| lomeprol-D3 | lomeprol | Toronto Research Chemicals |
| lopamidol-D3 | lopamidol | Toronto Research Chemicals |
| lopromide-D3 | lopromide | Toronto Research Chemicals |
| Ioxitalamic acid-D4 | Ioxitalamic acid | Toronto Research Chemicals |
| Levetiracetam-D3 | Levetiracetam, 4-Formylaminoantipyrine | Toronto Research Chemicals |
| Lidocaine-D10 | Lidocaine, 4-Dimethylaminoantipyrine | Toronto Research Chemicals |
| Mefenamic acid-D3 | Mefenamic acid | Toronto Research Chemicals |
| Methylprednisolone-D4 | Methylprednisolone, Dexamethasone | Toronto Research Chemicals |
| Metoprolol-D7 | Metoprolol | Toronto Research Chemicals |
| Morphine-D3 | Morphine | Lipomed AG |
| N-Acetylsulfamethoxazole-D5 | N-Acetylsulfamethoxazole | Toronto Research Chemicals |
| Naproxen-D4 | Naproxen | CDN |
| Oxazepam-D5 | Oxazepam | Lipomed AG |
| Paracetamol-D4 (Acetaminophen-D4) | Paracetamol | Toronto Research Chemicals |
| Phenazone-D3 (Antipyrine-D3) | Phenazone | Toronto Research Chemicals |
| Primidone-D5 | Primidone | Toronto Research Chemicals |
| Propranolol-D7 | Propranolol, D617 | Toronto Research Chemicals |
| Ranitidine-D6 | Ranitidine | Toronto Research Chemicals |
| Ritalinic acid-D10 | Ritalinic acid, Cilastatin, Oseltamivir carboxylate | Toronto Research Chemicals |
| Ritonavir-D6 | Ritonavir | Toronto Research Chemicals |
| Sotalol-D6 .HCl | Sotalol | Dr. Ehrenstorfer GmbH |
| Sulfadiazine-D4 | Sulfadiazine, 4-Aminoantipyrine, Sulfapyridine ² | Toronto Research Chemicals |
| Sulfamethoxazole-D4 | Sulfamethoxazole | Dr. Ehrenstorfer GmbH |
| Sulfapyridine-D4 | Sulfapyridine ² | Toronto Research Chemicals |
| Tramadol-D6 | Tramadol, 4-Acetamidoantipyrine | Toronto Research Chemicals |
| Trimethoprim-D9 | Trimethoprim | Dr. Ehrenstorfer GmbH |
| Valsartan-D3 | Valsartan | Toronto Research Chemicals |
| Venlafaxine-D6 | Venlafaxine, Clindamycin, Oseltamivir | Toronto Research Chemicals |
| Verapamil-D6 | Verapamil | Toronto Research Chemicals |

¹ See Table S1 for supplier's location² Internal standard not available before March 2010

Table S3. Classification of analyzed pharmaceuticals and industrial chemicals

| | Compound | ATC code | Description |
|---|---------------------------------|----------|---|
| ANTIINFECTIVES | | | |
| <i>Antibacterials</i> | Azithromycin | J01FA10 | macrolide antibacterial |
| | Ciprofloxacin | J01MA02 | fluoroquinolone antibacterial |
| | Clarithromycin | J01FA09 | macrolide antibacterial |
| | Clindamycin | J01FF01 | lincosamide antibacterial |
| | Erythromycin ¹ | J01FA01 | macrolide antibacterial |
| | Metronidazole | J01XD01 | imidazole antibacterial |
| | Norfloxacin | J01MA06 | fluoroquinolone antibacterial |
| | Roxithromycin | J01FA06 | macrolide antibacterial |
| | Sulfadiazine | J01EC02 | sulfonamide antibacterial |
| | Sulfamethoxazole | J01EC01 | sulfonamide antibacterial |
| | Sulfapyridine | J01EB04 | sulfonamide antibacterial |
| | Trimethoprim | J01EA01 | antibacterial |
| <i>Antimycotics</i> | Fluconazole | J02AC01 | antimycotic |
| <i>Antivirals</i> | Oseltamivir | J05AH02 | antiviral |
| | Ritonavir | J05AE03 | antiviral |
| <i>Metabolites</i> | N4-Acetylsulfamethoxazole | | metabolite of Sulfamethoxazole |
| | Oseltamivir carboxylate | | active substance of Oseltamivir |
| ANTIINFLAMMATORY PREPARATIONS | | | |
| <i>Non-steroidal antiinflammatory</i> | Diclofenac | M01AB05 | NSAID / antirheumatic |
| | Indometacin | M01AB01 | NSAID / antirheumatic |
| | Mefenamic acid | M01AG01 | NSAID / antirheumatic |
| | Naproxen | M01AE02 | NSAID / antirheumatic |
| ANTINEOPLASTICS | | | |
| <i>Cytostatics</i> | Cyclophosphamide | L01AA01 | cytostatic |
| | Ifosfamide | L01AA06 | cytostatic |
| CARDIOVASCULAR SYSTEM PREPARATIONS | | | |
| <i>Diuretics</i> | Furosemide | C03CA01 | diuretic |
| | Hydrochlorothiazide | C03AA03 | diuretic |
| <i>Beta blocking agents</i> | Atenolol | C07AB03 | beta blocking agent |
| | Metoprolol | C07AB02 | beta blocking agent |
| | Propranolol | C07AA05 | beta blocking agent |
| | Sotalol | C07AA07 | beta blocking agent |
| <i>Calcium channel blocker</i> | Verapamil | C08DA01 | calcium channel blocker |
| <i>Angiotensin II receptor antagonist</i> | Valsartan | C09CA03 | angiotensin II receptor antagonist |
| <i>Lipid modifying agent</i> | Bezafibrate | C10AB02 | lipid modifying agent |
| <i>Metabolites</i> | Atenolol acid (Metoprolol acid) | | metabolite of Atenolol / Metoprolol |
| | Clofibric acid | | metabolite of Clofibrate - lipid modifying agent, C10AB01 |
| | D617 | | metabolite of Verapamil |
| CONTRAST MEDIA | | | |
| <i>X-ray contrast media</i> | Diatrizoate (Diatrizoic acid) | V08AA01 | iodinated X-ray contrast medium |
| | Iohexol | V08AB02 | iodinated X-ray contrast medium |
| | Iomeprol | V08AB10 | iodinated X-ray contrast medium |
| | Iopamidol | V08AB04 | iodinated X-ray contrast medium |
| | Iopromide | V08AB05 | iodinated X-ray contrast medium |
| | Ioxitalamic acid | V08AA05 | iodinated X-ray contrast medium |

¹ Erythromycin measured in this study is a sum of Erythromycin and Erythromycin-H₂O

table continues

Table S3. Classification of analyzed pharmaceuticals and industrial chemicals (*continued*)

| Compound | ATC code | Description |
|------------------------------------|--|--|
| HORMONAL PREPARATIONS | | |
| | Dexamethasone | H02AB02 corticosteroid |
| | Methylprednisolone | H02AB04 corticosteroid |
| NERVOUS SYSTEM PREPARATIONS | | |
| <i>Anesthetics</i> | Lidocaine | N01BB02 anesthetic, local |
| | Thiopental | N01AF03 anesthetic, general (barbiturate) |
| <i>Analgesics / antipyretics</i> | 4-Dimethylaminoantipyrine ² | N02BB03 analgesic / antipyretic |
| | Morphine | N02AA01 analgesic (opioid) |
| | Paracetamol (Acetaminophen) | N02BE01 analgesic / antipyretic |
| | Phenazone (Antipyrine) | N02BB01 analgesic / antipyretic |
| | Tramadol | N02AX02 analgesic (opioid) |
| <i>Antiepileptics</i> | Carbamazepine | N03AF01 antiepileptic |
| | Gabapentin | N03AX12 antiepileptic |
| | Levetiracetam | N03AX14 antiepileptic |
| | Primidone | N03AA03 antiepileptic (barbiturate) |
| <i>Psycholeptics</i> | Diazepam | N05BA01 anxiolytic |
| | Oxazepam | N05BA04 anxiolytic |
| <i>Psychoanaleptics</i> | Fluoxetine | N06AB03 antidepressant |
| | Venlafaxine | N06AX16 antidepressant |
| <i>Metabolites</i> | 4-Acetamidoantipyrine | 3 rd metabolite of Aminopyrine / Metamizole |
| | 4-Aminoantipyrine | 2 nd metabolite of Aminopyrine / Metamizole |
| | 4-Formylaminoantipyrine | 4 th (final) metabolite of Aminopyrine / Metamizole |
| | 4-Methylaminoantipyrine | active substance of Aminopyrine / Metamizole - analgesic, N02BB02 |
| | Ritalinic acid | metabolite of Methylphenidate (Ritalin) - psychostimulant, N06BA04 |
| OTHER PHARMACEUTICALS | | |
| | Cilastatin | enzyme inhibitor (used with Imipenem - antibacterial, J01DH51) |
| | Ranitidine | A02BA02 acid disorders - alimentary system |
| INDUSTRIAL CHEMICALS | | |
| | Benzotriazole | corrosion inhibitor |
| | 4/5-Methylbenzotriazole (2 isomers) ³ | corrosion inhibitor |

² 4-Dimethylaminoantipyrine (Aminophenazone, or aminopyrine) is not used in Switzerland due to severe side effects (agranulocytosis)

³ Methylbenzotriazole measured in this study is a sum of 4-Methylbenzotriazole and 5-Methylbenzotriazole (mixture called Tolyltriazole)

Table S4. Structures and properties of analyzed micropollutants (JChem for Excel, ChemAxon)

| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|--|--|---|------------|---------------------|--|
| 4-Acetamidoantipyrene | | C ₁₃ H ₁₅ N ₃ O ₂ | 245.1170 | 0.15 | CC(=O)NC=C2C(=O)N(c1ccc(cc1)N(C)C)C=2C |
| 4-Aminoantipyrene | | C ₁₁ H ₁₃ N ₃ O | 203.1059 | 0.33 | c(ccc1N(N(C=2C)C)C(=O)C2N)cc1 |
| 4-Dimethylaminoantipyrene (Aminopyrene) ² | | C ₁₃ H ₁₇ N ₃ O | 231.1366 | 1.15 | c(ccc1N(N(C=2C)C)C(=O)C2N(C)C)cc1 |
| 4-Formylaminoantipyrene | | C ₁₂ H ₁₃ N ₃ O ₂ | 231.1008 | 0.11 | O=C2C(=O)C(=O)C(NC)N2c1cccc1 |
| 4-Methylaminoantipyrene | | C ₁₂ H ₁₅ N ₃ O | 217.1215 | 0.77 | CNC1=C(C)N(C)N(C1=O)C2=CC=CC=C2 |
| 4-Methylbenzotriazole 5-Methylbenzotriazole | | C ₇ H ₇ N ₃ | 133.0635 | 1.81 | Cc1cccc2[nH]nnc12 Cc1cccc2[nH]nnc12 |
| Atenolol | | C ₁₄ H ₂₂ N ₂ O ₃ | 266.1625 | 0.43 | CC(C)NCC(O)COc1ccc(cc1)CC(N)=O |
| Atenolol acid (Metoprolol acid) | | C ₁₄ H ₂₁ N ₁ O ₄ | 267.1465 | -4.17 | CC(C)NCC(O)COc1ccc(cc1)CC(=O)O |

Table S4. Structures and properties of analyzed micropollutants (continued)

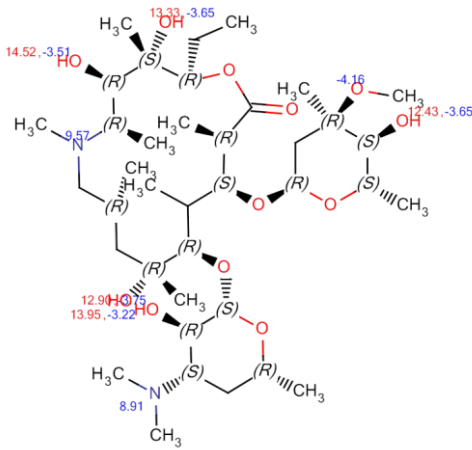
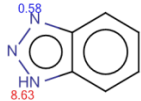
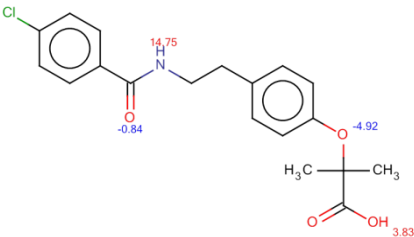
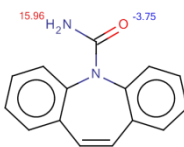
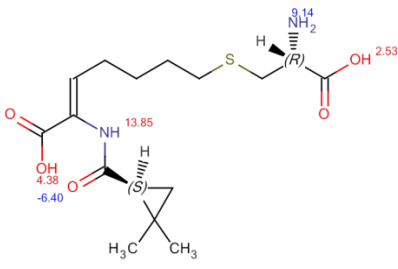
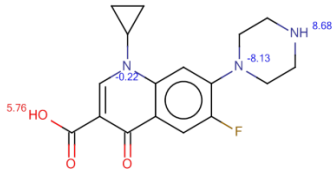
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|---------------|---|--|------------|---------------------|--|
| Azithromycin |  | C ₃₈ H ₇₂ N ₂ O ₁₂ | 748.5080 | 2.44 | CC[C@H]1OC(=O)[C@H](C)[C@@H](O[C@@H]2C[C@@](C)(OC)[C@@H](O)[C@H](C)O2)C(C)[C@@H](O)[C@@H]3O[C@H](C)C[C@@H](C[C@@H]3O)N(C)C[C@@](C)(O)C[C@@H](C)CN(C)[C@H](C)[C@@H](O)[C@]1(C)O |
| Benzotriazole |  | C ₆ H ₅ N ₃ | 119.0478 | 1.30 | c12c(nn[nH]1)cccc2 |
| Bezafibrate |  | C ₁₉ H ₂₀ ClNO ₄ | 361.1075 | 3.99 | c1(C(NCCc2ccc(OC(=O)C(C)cc2)=O)c(C)cc1 |
| Carbamazepine |  | C ₁₅ H ₁₂ N ₂ O | 236.0944 | 2.77 | N1(c2c(ccc2)C=Cc2c1cccc2)C(N)=O |
| Cilastatin |  | C ₁₆ H ₂₆ N ₂ O ₅ S | 358.1562 | -1.39 | [H][C@](N)(CSCCCC=C(/N C(=O)[C@@]1([H])CC1(C)C(C(=O)=O)C(O)=O |
| Ciprofloxacin |  | C ₁₇ H ₁₈ F ₁ N ₃ O ₃ | 331.1327 | -1.38 | C(C1)C1N(C=C(C(=O)O)-c(cc(c3F)N(CC N4)CC4)c2c3 |

Table S4. Structures and properties of analyzed micropollutants (continued))

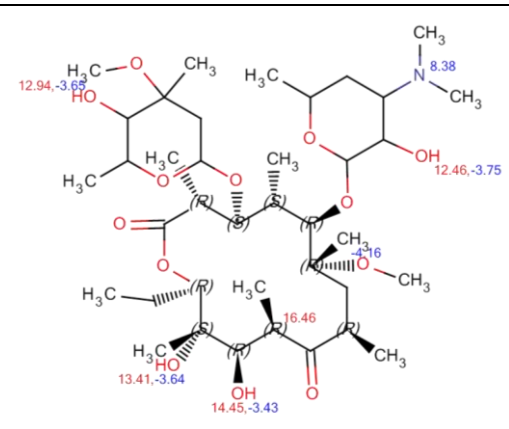
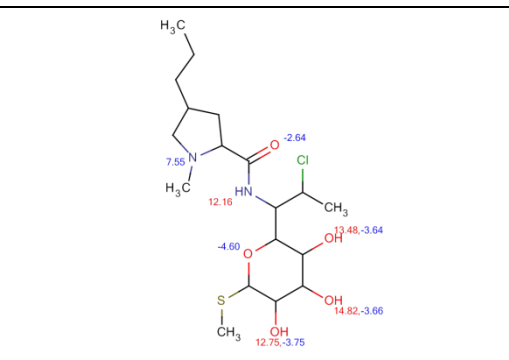
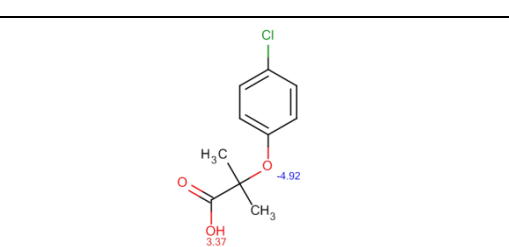
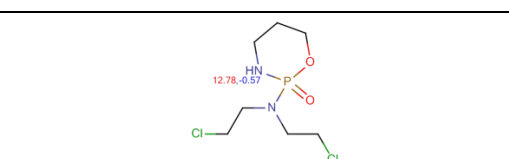
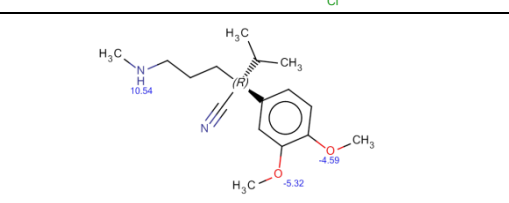
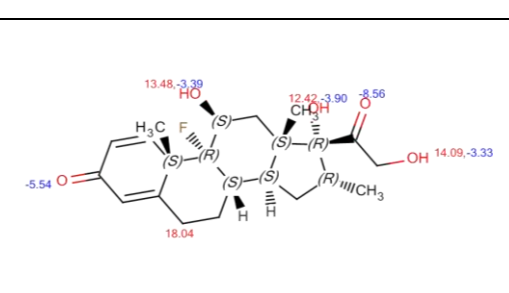
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|------------------|---|--|------------|---------------------|---|
| Clarithromycin |  | C ₃₈ H ₆₉ NO ₁₃ | 747.4763 | 3.24 | <chem>CC[C@H]1OC(=O)[C@H](C)[C@@H](OC2CC(C)(OC)C(O)C(C)O2)[C@H](C)[C@@H](OC3OC(C)CC(C3O)N(C)C)[C@@](C)(C)[C@H](C)C(=O)[C@H](C)[C@@H](O)[C@]1(C)O)O</chem> |
| Clindamycin |  | C ₁₈ H ₃₃ ClN ₂ O ₅ S ₁ | 424.1799 | 1.04 | <chem>S(C)C(OC(C1O)C(NC(=O)C(N(C)C2)CC2C)CC(C1)C)C(O)C1O</chem> |
| Clofibric acid |  | C ₁₀ H ₁₁ ClO ₃ | 214.0391 | 2.90 | <chem>CC(C)(OC1=C(C=C(Cl)C=C1)C(O)=O</chem> |
| Cyclophosphamide |  | C ₇ H ₁₅ Cl ₂ N ₂ O ₂ P | 260.0248 | 0.10 | <chem>C1CCN(CCCl)P1(=O)NCCC</chem> |
| D617 |  | C ₁₇ H ₂₆ N ₂ O ₂ | 290.1994 | 2.96 | <chem>CNCCC[C@@](C#N)(C(C)C)c1ccc(OC)c(O)C)c1</chem> |
| Dexamethasone |  | C ₂₂ H ₂₉ FO ₅ | 392.1999 | 1.68 | <chem>[H][C@@]12[C@@H](C)[C@@](O)(C(=O)C)O[C@@]1(C)C[C@H](O)[C@@]3(F)[C@@]2([H])CCC4=CC(=O)C=C[C@]34C</chem> |

Table S4. Structures and properties of analyzed micropollutants (continued))

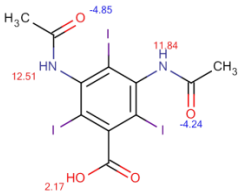
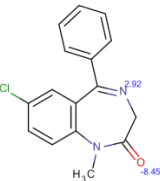
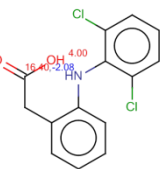
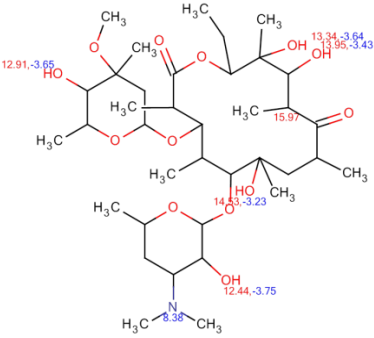
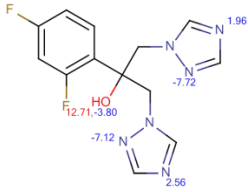
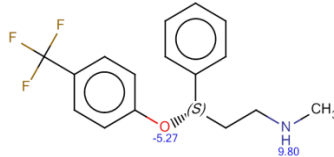
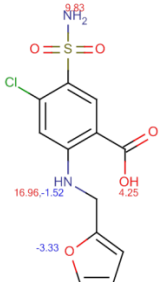
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|---------------------------|---|---------------|------------|---------------------|---|
| Diatrizoate |  | C11H9I3N2O4 | 613.7691 | 0.29 | CC(=O)NC1=C(I)C(C(O)=O)=C(I)C(NC(C)=O)=O)=C1I |
| Diazepam |  | C16H13ClN2O | 284.0716 | 3.08 | CN1C2=C(C=C(Cl)C=C2)C(=NCC1=O)C3=CC=CC=C3 |
| Diclofenac |  | C14H11Cl2N1O2 | 295.0161 | 4.26 | c1c(c(ccc1)Nc1c(cccc1Cl)Cl)CC(=O)O |
| Erythromycin ¹ |  | C37H67NO13 | 733.4607 | 2.60 | O(C(C(O)C1(O)C(C)C)C(C1)OC(C(C(=O)OC(C(O)(C(O)C2C)C)CC)C(C(C)C(C(O)(CC(C2=O)C)OC(O)C(C3)C)C(O)C3N(C)C |
| Fluconazole |  | C13H12F2N6O | 306.1035 | 0.56 | OC(CN1C=NC=N1)(CN2C=N)C=C(F)C=C(F)C=C3 |
| Fluoxetine |  | C17H18F3NO | 309.1335 | 4.17 | c1([C@@H](O)c2ccc(C(F)(F)F)cc2)CCNC)c3ccccc3 |
| Furosemide |  | C12H11ClN2O5S | 330.0077 | 1.75 | NS(=O)(=O)C1=CC(Cl)=CC(C(=O)O)N1C2=CC=CO2 |

Table S4. Structures and properties of analyzed micropollutants (continued)

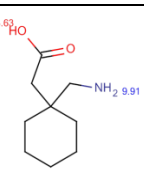
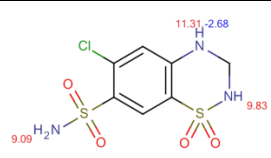
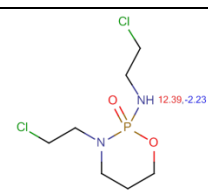
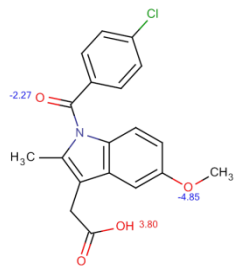
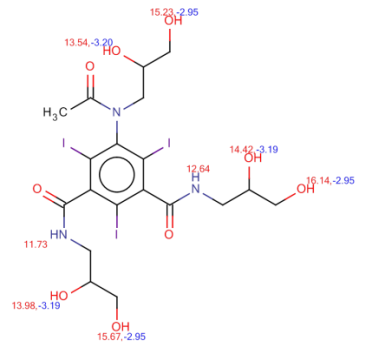
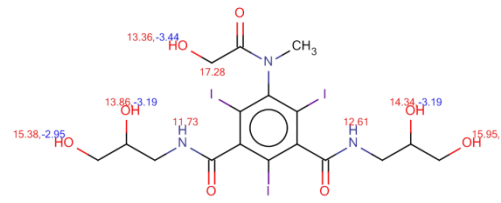
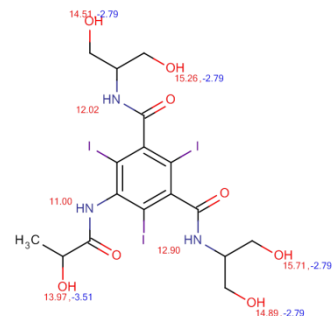
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|---------------------|---|---------------|------------|---------------------|---|
| Gabapentin |  | C9H17NO2 | 171.1259 | -1.51 | NCC1(CC(O)=O)CCCC1 |
| Hydrochlorothiazide |  | C7H8ClN3O4S2 | 296.9645 | -0.58 | NS(=O)(=O)C1=CC2=C(NCN S2(=O)=O)C=C1Cl |
| Ifosfamide |  | C7H15Cl2N2O2P | 260.0248 | 0.10 | C1CCN(P(OC1)(=O)NCCCl)C=C1 |
| Indometacin |  | C19H16ClNO4 | 357.0768 | 3.53 | COC1=CC2=C(C=C1)N(C(=O)C3=CC=C(Cl)C=C3)C(C)=C2C(=O)O |
| Iohexol |  | C19H26I3N3O9 | 820.8798 | -1.95 | OCC(O)CNC(=O)c1c(I)c(N(CC(O)CO)C(C)=O)c(I)c(c1I)C(=O)NCC(O)CO |
| Iomeprol |  | C17H22I3N3O8 | 776.8535 | -1.45 | Ic1c(c(I)c(c(I)c1N(C)C(=O)C(=O)NCC(O)CO)C(=O)NCC(O)CO |
| Iopamidol |  | C17H22I3N3O8 | 776.8535 | -2.04 | CC(O)C(=O)N(C1=C(I)C(C(=O)NC(CO)CO)=C(I)C(C(=O)NC(CO)CO)=C1)C |

Table S4. Structures and properties of analyzed micropollutants (continued)

| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|--------------------|--|--|------------|---------------------|--|
| Iopromide | | C ₁₈ H ₂₄ I ₃ N ₃ O ₈ | 790.8692 | -1.74 | <chem>c1(c(c(c(I)c(c1)NC(COC)=O)C(NC[C@@H](CO)O)=O)I)C(N[C[C@@H](CO)O)C)=O</chem> |
| Ioxitalamic acid | | C ₁₂ H ₁₁ I ₃ N ₂ O ₅ | 643.7797 | 0.74 | <chem>CC(=O)NC1=C(I)C(C(O)=O)=C(I)C(C(=O)NCCO)=C1I</chem> |
| Levetiracetam | | C ₈ H ₁₄ N ₂ O ₂ | 170.1055 | -0.59 | <chem>[H]C(CC)(N1CCC1=O)C(N)=O</chem> |
| Lidocaine | | C ₁₄ H ₂₂ N ₂ O | 234.1732 | 1.54 | <chem>CCN(CC)CC(=O)NC1=C(C)C=CC=C1C</chem> |
| Mefenamic acid | | C ₁₅ H ₁₅ N ₁ O ₂ | 241.1097 | 5.40 | <chem>c1(c(cccc1)C(O)=O)Nc1c(c(ccc1)C)C</chem> |
| Methylprednisolone | | C ₂₂ H ₃₀ O ₅ | 374.2093 | 1.56 | <chem>[H][C@@]12CC[C@]1(O)C(=O)CO[C@@]1(C)C[C@@H](O)[C@@]3([H])[C@@]2([H])C[C@]1([H])(C)C4=CC(=O)C=C[C@]34C</chem> |
| Metoprolol | | C ₁₅ H ₂₅ N ₁ O ₃ | 267.1829 | 1.76 | <chem>COCC1=CC=C(COC1)CNC(C)C=C1</chem> |

Table S4. Structures and properties of analyzed micropollutants (continued)

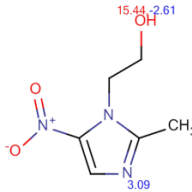
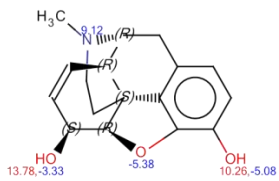
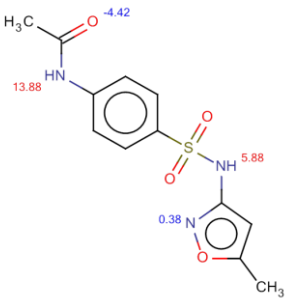
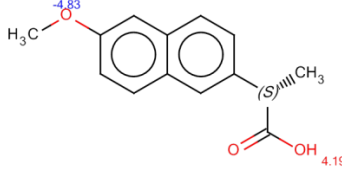
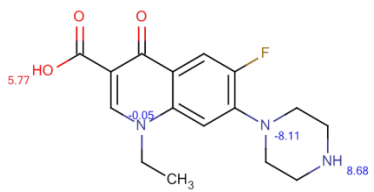
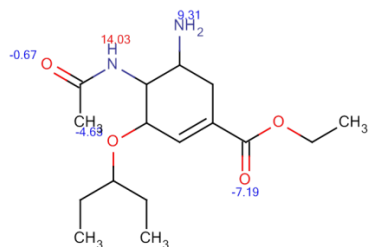
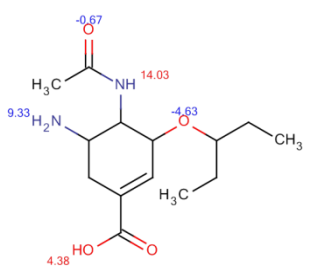
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|---------------------------|---|--|------------|---------------------|---|
| Metronidazole |  | C ₆ H ₉ N ₃ O ₃ | 171.0638 | -0.46 | <chem>CC1=NC=C(N1CCO)[N+](O)=O</chem> |
| Morphine |  | C ₁₇ H ₁₉ NO ₃ | 285.1359 | 0.89 | <chem>c12[C@]34[C@@H]5[C@H]([N@](C)CC4)Cc2ccc(c1O[C@H]3[C@@H](O)C=C5)O</chem> |
| N4-Acetylsulfamethoxazole |  | C ₁₂ H ₁₃ N ₃ O ₄ S | 295.0621 | 0.86 | <chem>c1(ccc(cc1)NC(C)=O)S(Nc1cc(C)on1)(=O)=O</chem> |
| Naproxen |  | C ₁₄ H ₁₄ O ₃ | 230.0937 | 2.99 | <chem>c12c(cc(OC)cc2)ccc(c1)[C@@H](C(O)=O)C</chem> |
| Norfloxacin |  | C ₁₆ H ₁₈ F ₁ N ₃ O ₃ | 319.1327 | -1.48 | <chem>CCN1C=C(C(O)=O)C(=O)C2=CC(F)=C(C=C12)N3CCNCC3</chem> |
| Oseltamivir |  | C ₁₆ H ₂₈ N ₂ O ₄ | 312.2044 | 1.16 | <chem>CCOC(=O)C1=CC(OC(CC)C)C(NC(C)=O)C(N)C1</chem> |
| Oseltamivir carboxylate |  | C ₁₄ H ₂₄ N ₂ O ₄ | 284.1731 | -2.07 | <chem>CCC(CC)OC1C=C(CC(N)C1NC(C)=O)C(O)=O</chem> |

Table S4. Structures and properties of analyzed micropollutants (continued)

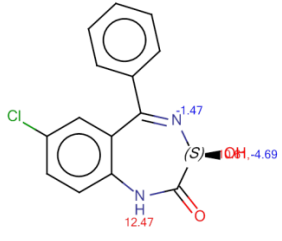
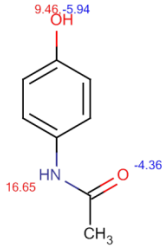
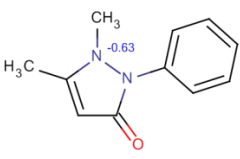
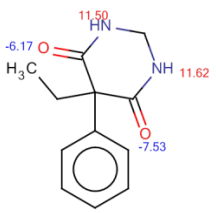
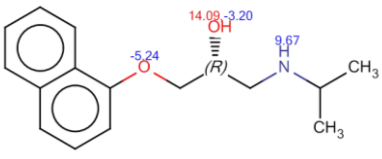
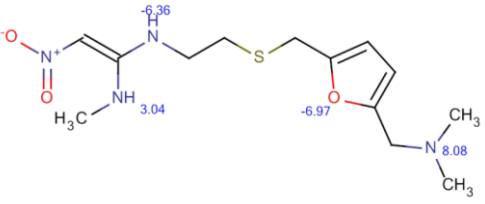
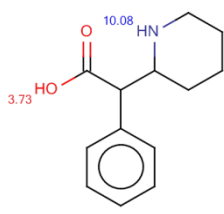
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|-----------------------------|---|---|------------|---------------------|---|
| Oxazepam |  | C ₁₅ H ₁₁ ClN ₂ O ₂ | 286.0480 | 2.92 | <chem>c12C(c3ccccc3)=N[C@@H](O)C(Nc1ccc(c2)Cl)=O</chem> |
| Paracetamol (Acetaminophen) |  | C ₈ H ₉ N ₁ O ₂ | 151.0628 | 0.91 | <chem>CC(=O)NC1=CC=C(O)C=C1</chem> |
| Phenazone (Antipyrine) |  | C ₁₁ H ₁₂ N ₂ O | 188.0944 | 1.22 | <chem>CN1N(C(=O)C=C1C)C2=CC=CC=C2</chem> |
| Primidone |  | C ₁₂ H ₁₄ N ₂ O ₂ | 218.1050 | 1.12 | <chem>c1(ccccc1)C2(C(=O)NCNC2=O)CC</chem> |
| Propranolol |  | C ₁₆ H ₂₁ NO ₂ | 259.1567 | 2.58 | <chem>c12c(OC[C@@H](CNC(C)C)O)cccc1cccc2</chem> |
| Ranitidine |  | C ₁₃ H ₂₂ N ₄ O ₃ S | 314.1407 | 0.98 | <chem>CN1C(NCCSC1=CC=C(CN(C)C)O1)=C/[N+](O1)=O</chem> |
| Ritalinic acid |  | C ₁₃ H ₁₇ NO ₂ | 219.1254 | -0.49 | <chem>c(ccc1C(C(=O)O)C(NCC2)CC2)cc1</chem> |

Table S4. Structures and properties of analyzed micropollutants (continued)

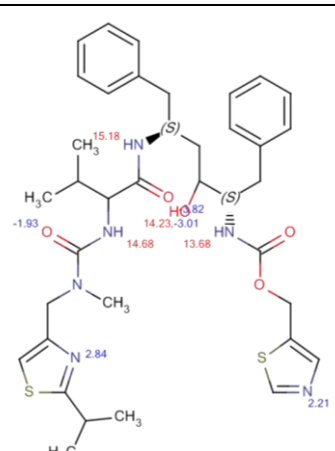
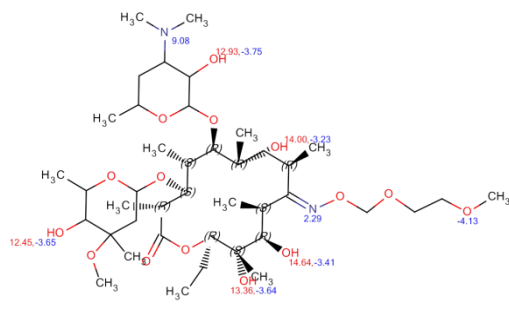
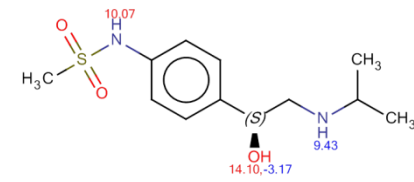
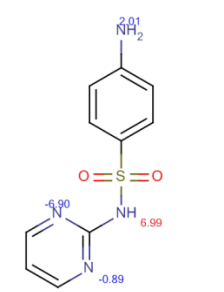
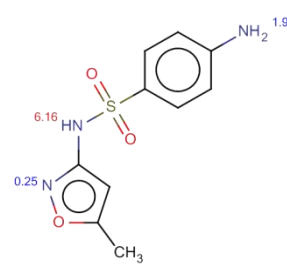
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log Kow (uncharged) | Smile |
|------------------|---|------------------|------------|---------------------|--|
| Ritonavir |  | C37H48N6 O5S2 | 720.3128 | 5.22 | <chem>CC(C)C(NC(=O)N(C)CC1=CSC(=N1)C(C)C(=O)N[C@H](CC(O)[C@H](CC2=CC=C(C=C2)NC(=O)OCC3=CN=C(S3)CC4=CC=CC=C4</chem> |
| Roxithromycin |  | C41H76N2 O15 | 836.5240 | 3.00 | <chem>CC[C@H]1OC(=O)[C@H](C)[C@@H](OC2CC(C)(OC)C(O)C(C)O2)[C@H](C)[C@@H](OC2OC(C)CC(C2)N(C)C)[C@](C)(O)C[C@H](C)\C(=N/OCOCOC)[C@H](C)[C@@H](O)[C@]1(C)O</chem> |
| Sotalol |  | C12H20N2 O3S | 272.1189 | -0.41 | <chem>c1([C@@H](CNC(C)C)O)ccc(NS(C)(=O)=O)cc1</chem> |
| Sulfadiazine |  | C10H10N4 O2S | 250.0519 | 0.39 | <chem>NC1=CC=C(C=C1)S(=O)(=O)NC2=NC=CC=N2</chem> |
| Sulfamethoxazole |  | C10H11N3 O3S1 | 253.0516 | 0.79 | <chem>c1(S(Nc2cc(C)on2)(=O)=O)cc(N)cc1</chem> |

Table S4. Structures and properties of analyzed micropollutants (continued)

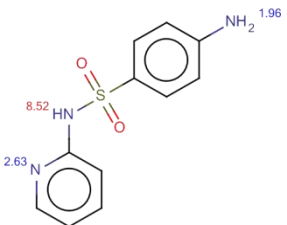
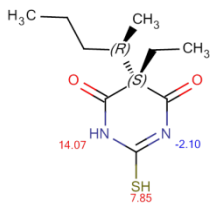
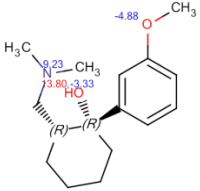
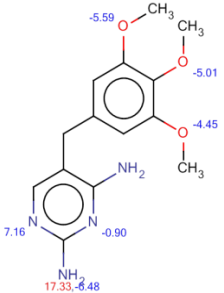
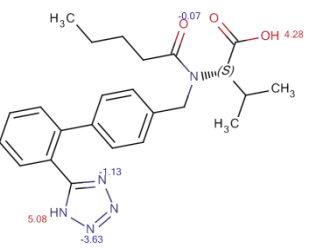
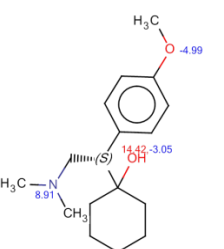
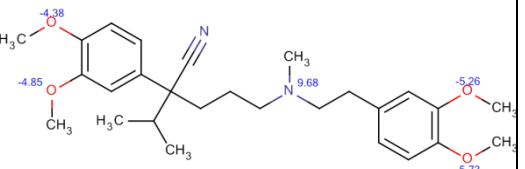
| Compound | Structure / pKa (red acidic, blue basic) | Formula | Exact Mass | Log K _{ow} (uncharged) | Smile |
|---------------|---|--|------------|---------------------------------|---|
| Sulfapyridine |  | C ₁₁ H ₁₁ N ₃ O ₂ S ₁ | 249.0566 | 1.01 | <chem>c1(S(Nc2cccn2)(=O)=O)ccc(N)cc1</chem> |
| Thiopental |  | C ₁₁ H ₁₈ N ₂ O ₂ S | 242.1089 | 2.77 | <chem>C1([C@@](C(N=C(N1)S)=O)([C@@H](CC(C)C)C)C)C)=O</chem> |
| Tramadol |  | C ₁₆ H ₂₅ NO ₂ | 263.1885 | 2.45 | <chem>COC1=CC=C(C(=C1)[C@@]2(O)CCCC[C@@H]2CN(C)C)C</chem> |
| Trimethoprim |  | C ₁₄ H ₁₈ N ₄ O ₃ | 290.1373 | 1.28 | <chem>c1(Cc2c(nc(N)nc2)N)cc(c(OC)c(c1)OC)OC</chem> |
| Valsartan |  | C ₂₄ H ₂₉ N ₅ O ₃ | 435.2270 | 4.51 | <chem>CCCCC(=O)N(CC1=CC=C(C=C1)C2=C(C=CC=C2)C3=N(N=NN3)[C@@H](C(C)C)C(O)=O</chem> |
| Venlafaxine |  | C ₁₇ H ₂₇ NO ₂ | 277.2036 | 2.74 | <chem>C1CCCC(C1)([C@@H](c1ccc(cc1)OC)CN(C)C)O</chem> |
| Verapamil |  | C ₂₇ H ₃₈ N ₂ O ₄ | 454.2826 | 5.04 | <chem>COC1=C(OC)C=CC(C(C)C)C(C#N)CCCN(CCC2=CC(OC)C=C2)C=C1</chem> |

Table S5. Speciation and Log D_{ow} values of analyzed micropollutants (JChem for Excel, ChemAxon)

| Compound | Strongest Basic pK _a | Strongest Acidic pK _a | Speciation at pH 1 - 14 | | | | | | | | | | | | Log D _{ow} | | | | | | | | |
|---------------------------|---------------------------------|----------------------------------|-------------------------|------|------|------|------|------|-------|---|---|----|----|----|---------------------|----|-------|-------|-------|-------|-------|-------|-------|
| | | | pH 4 | pH 5 | pH 6 | pH 7 | pH 8 | pH 9 | pH 10 | | | | | | | | | | | | | | |
| 4-Acetamidoantipyrine | (-) | 12.52 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| 4-Aminoantipyrine | (-) | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.33 | 0.33 | 0.33 | 0.33 | 0.33 | 0.33 | 0.33 |
| 4-Dimethylaminoantipyrine | 3.46 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.04 | 1.14 | 1.15 | 1.15 | 1.15 | 1.15 | 1.15 |
| 4-Formylaminoantipyrine | (-) | 12.66 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.10 |
| 4-Methylaminoantipyrine | 1.22 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.77 | 0.77 | 0.77 | 0.77 | 0.77 | 0.77 | 0.77 |
| 4/5-Methylbenzotriazole | 1.01 | 8.86 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.81 | 1.81 | 1.81 | 1.81 | 1.76 | 1.45 | 0.77 |
| Atenolol | 9.67 | 14.08 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.82 | -2.80 | -2.68 | -2.14 | -1.24 | -0.33 | 0.26 |
| Atenolol acid | 9.67 | 3.54 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.59 | -3.42 | -4.05 | -4.17 | -3.80 | -3.03 | -2.46 |
| Azithromycin | 9.57 | 12.43 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -4.54 | -4.41 | -3.64 | -1.99 | -0.08 | 1.55 | 2.29 |
| Benzotriazole | 0.58 | 8.63 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.30 | 1.30 | 1.30 | 1.29 | 1.21 | 0.80 | 0.11 |
| Bezafibrate | (-) | 3.83 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 3.59 | 2.79 | 1.83 | 0.97 | 0.55 | 0.47 | 0.46 |
| Carbamazepine | (-) | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 2.77 | 2.77 | 2.77 | 2.77 | 2.77 | 2.77 | 2.77 |
| Cilastatin | 9.14 | 2.53 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.44 | -2.00 | -2.91 | -3.86 | -4.58 | -4.99 | -5.53 |
| Ciprofloxacin | 8.68 | 5.76 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.68 | -1.62 | -1.46 | -1.38 | -1.43 | -1.68 | -1.92 |
| Clarithromycin | 8.38 | 12.46 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.21 | 0.10 | 0.89 | 1.84 | 2.71 | 3.15 | 3.23 |
| Clindamycin | 7.55 | 12.16 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.19 | -1.47 | -0.52 | 0.38 | 0.91 | 1.02 | 1.03 |
| Clofibric acid | (-) | 3.37 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 2.18 | 1.27 | 0.32 | -0.38 | -0.60 | -0.63 | -0.63 |
| Cyclophosphamide | (-) | 12.78 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 |
| D617 | 10.54 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.28 | -0.28 | -0.26 | -0.10 | 0.50 | 1.42 | 2.31 |
| Dexamethasone | (-) | 12.42 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.68 | 1.68 | 1.68 | 1.68 | 1.68 | 1.68 | 1.68 |
| Diatrizoate | (-) | 2.17 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.54 | -2.46 | -3.06 | -3.22 | -3.23 | -3.24 | -3.24 |
| Diazepam | 2.92 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 3.04 | 3.07 | 3.08 | 3.08 | 3.08 | 3.08 | 3.08 |
| Diclofenac | (-) | 4.00 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 3.96 | 3.21 | 2.26 | 1.37 | 0.85 | 0.74 | 0.73 |
| Erythromycin | 8.38 | 12.44 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.85 | -0.54 | 0.25 | 1.20 | 2.06 | 2.50 | 2.58 |
| Fluconazole | 2.56 | 12.71 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.55 | 0.56 | 0.56 | 0.56 | 0.56 | 0.56 | 0.56 |
| Fluoxetine | 9.80 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.93 | 0.94 | 1.04 | 1.50 | 2.38 | 3.31 | 3.96 |
| Furosemide | (-) | 4.25 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.56 | 0.93 | 0.00 | -0.93 | -1.58 | -1.81 | -2.10 |
| Gabapentin | 9.91 | 4.63 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.88 | -1.61 | -1.52 | -1.51 | -1.51 | -1.55 | -1.80 |
| Hydrochlorothiazide | (-) | 9.09 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.58 | -0.58 | -0.58 | -0.58 | -0.61 | -0.82 | -1.60 |
| Ifosfamide | (-) | 12.39 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.09 |
| Indometacin | (-) | 3.80 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 3.12 | 2.31 | 1.35 | 0.50 | 0.08 | 0.01 | 0.00 |
| Iohexol | (-) | 11.73 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.95 | -1.95 | -1.95 | -1.95 | -1.95 | -1.95 | -1.96 |
| Iomeprol | (-) | 11.73 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.45 | -1.45 | -1.45 | -1.45 | -1.45 | -1.45 | -1.45 |
| Iopamidol | (-) | 11.00 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.04 | -2.04 | -2.04 | -2.04 | -2.04 | -2.05 | -2.08 |
| Iopromide | (-) | 11.09 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.74 | -1.74 | -1.74 | -1.74 | -1.75 | -1.75 | -1.78 |
| Ioxitalamic acid | (-) | 2.13 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.12 | -2.04 | -2.63 | -2.77 | -2.79 | -2.79 | -2.79 |
| Levetiracetam | (-) | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.59 | -0.59 | -0.59 | -0.59 | -0.59 | -0.59 | -0.59 |
| Lidocaine | 7.75 | 13.78 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.77 | -1.14 | -0.21 | 0.72 | 1.35 | 1.52 | 1.54 |
| Mefenamic acid | (-) | 3.89 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 5.04 | 4.25 | 3.30 | 2.42 | 1.97 | 1.88 | 1.87 |
| Methylprednisolone | (-) | 12.58 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.56 | 1.56 | 1.56 | 1.56 | 1.56 | 1.56 | 1.56 |
| Metoprolol | 9.67 | 14.09 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.48 | -1.47 | -1.34 | -0.81 | 0.09 | 1.01 | 1.59 |
| Metronidazole | 3.09 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.51 | -0.46 | -0.46 | -0.46 | -0.46 | -0.46 | -0.46 |
| Morphine | 9.12 | 10.26 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.30 | -2.23 | -1.83 | -0.99 | -0.03 | 0.74 | 0.89 |
| N4-Acetylsulfamethoxazole | 0.38 | 5.88 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.85 | 0.81 | 0.55 | 0.10 | -0.06 | -0.08 | -0.09 |
| Naproxen | (-) | 4.19 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 2.77 | 2.11 | 1.18 | 0.25 | -0.36 | -0.52 | -0.54 |
| Norfloxacin | 8.68 | 5.77 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.79 | -1.73 | -1.56 | -1.48 | -1.52 | -1.78 | -2.03 |

LEGEND:

1 cathionic at pH 1

6 zwitterionic at pH 6

14 anionic at pH 14

table continues

Table S5 Speciation and Log D_{ow} values of analyzed micropollutants (*continued*)

| Compound | Strongest Basic pK _a | Strongest Acidic pK _a | Speciation at pH 1 - 14 | | | | | | | | | | | | | Log D _{ow} | | | | | | | |
|-------------------------|---------------------------------|----------------------------------|-------------------------|------|------|------|------|------|-------|---|---|----|----|----|----|---------------------|-------|-------|-------|-------|-------|-------|-------|
| | | | pH 4 | pH 5 | pH 6 | pH 7 | pH 8 | pH 9 | pH 10 | | | | | | | | | | | | | | |
| Oseltamivir | 9.31 | 14.03 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.87 | -1.85 | -1.69 | -1.07 | -0.16 | 0.68 | 1.08 |
| Oseltamivir carboxylate | 9.33 | 4.38 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.37 | -2.13 | -2.08 | -2.07 | -2.09 | -2.22 | -2.66 |
| Oxazepam | (-) | 10.61 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 2.92 | 2.92 | 2.92 | 2.92 | 2.92 | 2.91 | 2.83 |
| Paracetamol | (-) | 9.46 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.91 | 0.91 | 0.91 | 0.91 | 0.89 | 0.78 | 0.27 |
| Phenazone | (-) | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 |
| Primidone | (-) | 11.50 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.12 | 1.12 | 1.12 | 1.12 | 1.12 | 1.12 | 1.11 |
| Propranolol | 9.67 | 14.09 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.66 | -0.64 | -0.52 | 0.02 | 0.92 | 1.83 | 2.42 |
| Ranitidine | 8.08 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -2.46 | -1.96 | -1.09 | -0.13 | 0.64 | 0.93 | 0.98 |
| Ritalinic acid | 10.08 | 3.73 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.63 | -0.51 | -0.49 | -0.49 | -0.50 | -0.52 | -0.71 |
| Ritonavir | 2.84 | 13.68 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 5.20 | 5.22 | 5.22 | 5.22 | 5.22 | 5.22 | 5.22 |
| Roxithromycin | 9.08 | 12.45 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.50 | -0.40 | 0.06 | 0.93 | 1.89 | 2.66 | 2.95 |
| Sotalol | 9.43 | 10.07 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -3.19 | -3.18 | -3.04 | -2.48 | -1.58 | -0.71 | -0.41 |
| Sulfadiazine | 2.01 | 6.99 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.38 | 0.38 | 0.35 | 0.13 | -0.33 | -0.52 | -0.55 |
| Sulfamethoxazole | 1.97 | 6.16 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.78 | 0.76 | 0.60 | 0.14 | -0.11 | -0.15 | -0.15 |
| Sulfapyridine | 2.63 | 8.52 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 0.99 | 1.01 | 1.01 | 1.00 | 0.91 | 0.53 | 0.16 |
| Thiopental | (-) | 7.85 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 2.77 | 2.77 | 2.77 | 2.72 | 2.43 | 1.90 | 1.67 |
| Tramadol | 9.23 | 13.80 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -1.04 | -0.98 | -0.59 | 0.24 | 1.20 | 2.02 | 2.38 |
| Trimethoprim | 7.16 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.18 | -0.11 | 0.27 | 0.92 | 1.23 | 1.28 | 1.28 |
| Valsartan | (-) | 4.28 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 4.31 | 3.49 | 1.92 | 0.46 | -0.36 | -0.60 | -0.63 |
| Venlafaxine | 8.91 | 14.42 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | -0.75 | -0.62 | -0.07 | 0.84 | 1.78 | 2.48 | 2.70 |
| Verapamil | 9.68 | (-) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 1.54 | 1.57 | 1.76 | 2.42 | 3.36 | 4.28 | 4.87 |

LEGEND:

1 cathionic at pH 1

6 zwitterionic at pH 6

14 anionic at pH 14

2. Analytical method

Analytical Hardware. The instrumentation hardware for on-line SPE-HPLC-MS/MS consisted of a triple quadrupole mass spectrometer detector TSQ Quantum Ultra (Thermo Fisher Scientific, USA), an HTC PAL auto-sampler with a 100 µL side-port Hamilton syringe, a large volume dispenser module (10-mL dispenser syringe with 10-mL loop, CTC Analytics AG, Switzerland), a quaternary pump (Rheos Allegro, Flux instruments, Switzerland), a binary pump (Surveyor, Thermo/Finnigan), an isocratic pump (Rheos 2000, Flux instruments, Switzerland), an HPLC column thermostat (Jones, Omnilab, Switzerland), two six-port valves, and an 18-mL loop for sample enrichment. The SPE cartridge was prepared in house by filling an empty cartridge (stainless steel, 20 × 2.1 mm, BGB Analytik AG, Germany) with 13 mg Isolute ENV⁺ (70 µm, Separtis GmbH) and 7 mg Oasis HLB (15 µm, Waters). One SPE cartridge was used for up to 200 samples (a new SPE cartridge for each measurement sequence). The analytical HPLC column (Atlantis T3, 150 × 3 mm, 3 µm, Waters) was equipped for each sequence with a fresh in-line filter (0.5 µm pore size, BGB Analytik AG, Germany).

On-line SPE-HPLC-MS/MS. Positions of the valves and the pump flow schemes were as described in Stoob et al.⁽¹⁾. The combination of two six-port valves enabled a flow scheme with separate processes running simultaneously in three time steps. Time $t=0$ min: a chromatographic run started with the organic mobile phase (methanol) eluting the SPE cartridge containing the sample enriched during the previous chromatographic run, while simultaneously the sample loop was washed. Time $t=11$ min: a new acidified sample was loaded by an auto-sampler to an 18-mL sample loop, while the chromatographic run continued and the eluted SPE cartridge was washed (methanol, acetonitrile) and preconditioned (nanopure water with 0.1% formic acid). Time $t=20.5$ min: the sample from the loop was directed onto the SPE cartridge to be enriched, while the dispenser syringe was washed. For the chromatographic gradient, an aqueous fraction of HPLC mobile phase (HPLC-grade water with 0.1% formic acid) joined the SPE eluent just before the HPLC column, forming together a mixture with a flow rate of 400 $\mu\text{L}/\text{min}$ containing initially 7.5% methanol. After 8 min, a gradient of methanol was raised up to 95%; the analysis time was 43 minutes. Electrospray ionization in polarity switching mode (ESI +/-) was used. MS/MS data were acquired in time selective reaction monitoring (SRM) mode (271 transitions per run) with a cycle time of 1.000 s. Source parameters and substance specific MS/MS parameters are listed in Table S6.

Quality Control. Each sample was measured in two or three dilutions to achieve a concentration within the calibration range for each compound and to assure reliability of the measurement. For quality control purposes, each sample dilution was measured twice, one calibration standard was regularly injected after 20-40 samples throughout the measuring sequence, and multiple blank (nanopure water) and blind (nanopure water with internal standards) samples were included. Results of clindamycin, D617, metronidazole, oseltamivir, and oseltamivir carboxylate, for which no matching internal standards were available, were corrected according to their relative recoveries.

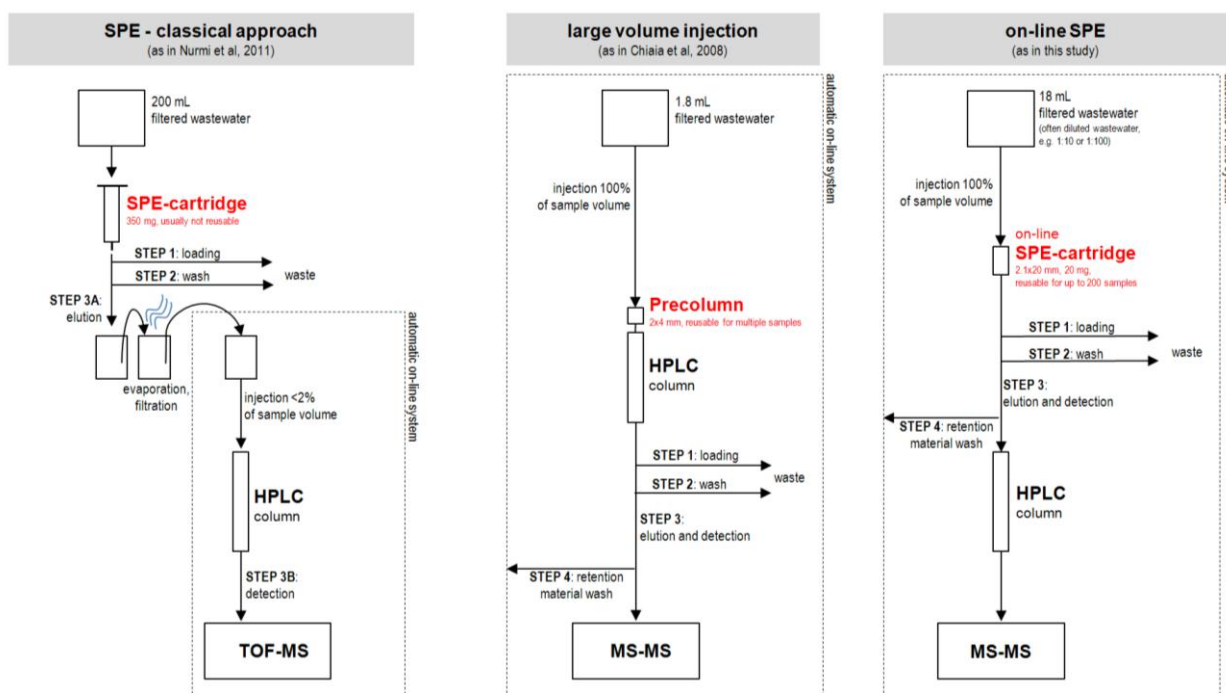


Figure S1 Comparison of classical SPE⁽²⁾ experimental set-up with large volume injection⁽³⁾ and on-line SPE.

Table S6. Substance specific MS/MS settings.

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|-------------------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| 4-Acetamidoantipyrine_F2 | 246 | 204 | 1 | 13 | 63 | 10.5 | 18 |
| 4-Acetamidoantipyrine_F1 | 246 | 228 | 1 | 13 | 63 | 10.5 | 18 |
| 4- Aminoantipyrine_F2 | 204 | 159 | 1 | 11 | 51 | 10.6 | 18 |
| 4- Aminoantipyrine_F1 | 204 | 56.1 | 1 | 18 | 51 | 10.6 | 18 |
| 4- Dimethylaminoantipyrine | 232 | 111 | 1 | 16 | 48 | 10.5 | 19 |
| 4- Dimethylaminoantipyrine_F1 | 232 | 97.1 | 1 | 16 | 48 | 10.5 | 19 |
| 4- Formylaminoantipyrine_F2 | 232 | 77.1 | 1 | 34 | 51 | 11 | 18 |
| 4- Formylaminoantipyrine_F1 | 232 | 214 | 1 | 11 | 51 | 11 | 18 |
| 4- Formylaminoantipyrine_f3 | 232 | 204 | 1 | 12 | 51 | 11 | 18 |
| 4-Methylaminoantipyrine_F2 | 218 | 187 | 1 | 6 | 60 | 10.5 | 13.6 |
| 4-Methylaminoantipyrine_F1 | 218 | 56.1 | 1 | 19 | 60 | 10.5 | 13.6 |
| 4-Methylaminoantipyrine_f3 | 218 | 159 | 1 | 12 | 60 | 10.5 | 13.6 |
| 4/5-Methylbenzotriazole_F2 | 134 | 79.1 | 1 | 17 | 80 | 17 | 25 |
| 4/5-Methylbenzotriazole_F1 | 134 | 77 | 1 | 22 | 80 | 17 | 25 |
| 5-Methylbenzotriazole-d6_F2 | 140 | 85 | 1 | 20 | 80 | 17 | 25 |
| 5-Methylbenzotriazole-d6_F1 | 140 | 81 | 1 | 28 | 80 | 17 | 25 |
| Atenolol_F1 | 267 | 190 | 1 | 18 | 93 | 9 | 13.4 |
| Atenolol_F2 | 267 | 225 | 1 | 16 | 93 | 9 | 13.4 |
| D7-Atenolol_F2 | 274 | 226 | 1 | 16 | 93 | 9 | 12.9 |
| D7-Atenolol_F1 | 274 | 190 | 1 | 18 | 93 | 9 | 12.9 |
| Atenolol acid_F2 | 268 | 191 | 1 | 17 | 81 | 10.9 | 14.6 |
| Atenolol acid_F1 | 268 | 145 | 1 | 24 | 81 | 10.9 | 14.6 |
| Atenolol acid_f3 | 268 | 226 | 1 | 16 | 81 | 10.9 | 14.6 |
| Atenolol acid-D5 | 273 | 196 | 1 | 17 | 81 | 10.9 | 14.6 |
| Atenolol acid-D5_F1 | 273 | 150 | 1 | 24 | 81 | 10.9 | 14.6 |
| Atenolol acid-D5_f3 | 273 | 231 | 1 | 16 | 81 | 10.9 | 14.6 |
| Azithromycin_F2 | 750 | 158 | 1 | 32 | 135 | 14.9 | 24 |
| Azithromycin_F1 | 750 | 591 | 1 | 22 | 135 | 14.9 | 24 |
| D3-Azithromycin_F2 | 753 | 158 | 1 | 32 | 135 | 14.9 | 24 |
| D3-Azithromycin_F1 | 753 | 594 | 1 | 22 | 135 | 14.9 | 24 |
| Benzotriazole_F2 | 120 | 92 | 1 | 12 | 70 | 12.5 | 19 |
| Benzotriazole_F1 | 120 | 65.1 | 1 | 15 | 70 | 12.5 | 19 |
| D4-Benzotriazole_F2 | 124 | 96 | 1 | 12 | 70 | 12.5 | 19 |
| D4-Benzotriazole_F1 | 124 | 69.1 | 1 | 15 | 70 | 12.5 | 19 |
| Bezafibrate_F2 | 362 | 139 | 1 | 17 | 109 | 29.8 | 33 |
| Bezafibrate_F1 | 362 | 316 | 1 | 10 | 109 | 29.8 | 33 |
| D4-Bezafibrate_F2 | 366 | 143 | 1 | 17 | 109 | 29.8 | 32.7 |
| D4-Bezafibrate_F1 | 366 | 320 | 1 | 10 | 109 | 29.8 | 32.7 |
| Carbamazepine_F2 | 237 | 192 | 1 | 22 | 91 | 25 | 31 |
| Carbamazepine_F1 | 237 | 194 | 1 | 17 | 91 | 25 | 31 |
| Carbamazepine-13C,d2_F2 | 240 | 194 | 1 | 17 | 91 | 25 | 31 |
| Carbamazepine-13C,d2_F1 | 240 | 195 | 1 | 22 | 91 | 25 | 31 |
| Cilastatin_F2 | 359 | 202 | 1 | 15 | 92 | 14 | 21 |
| Cilastatin_F1 | 359 | 97 | 1 | 22 | 92 | 14 | 21 |
| Ciprofloxacin_F2 | 332 | 245 | 1 | 23 | 112 | 12 | 20 |
| Ciprofloxacin_F1 | 332 | 288 | 1 | 17 | 112 | 12 | 20 |

table continues

Table S6. Substance specific MS/MS settings (continued)

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|-------------------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| Ciprofloxacin-D8_F2 | 340 | 249 | 1 | 23 | 112 | 12 | 20 |
| Ciprofloxacin-D8_F1 | 340 | 296 | 1 | 17 | 112 | 12 | 20 |
| Clarithromycin_F2 | 749 | 158 | 1 | 22 | 118 | 27.3 | 32 |
| Clarithromycin_F1 | 749 | 590 | 1 | 15 | 118 | 27.3 | 32 |
| D3-Clarithromycin-N-methyl_F2 | 752 | 161 | 1 | 22 | 118 | 27.3 | 32 |
| D3-Clarithromycin-N-methyl_F1 | 752 | 593 | 1 | 15 | 118 | 27.3 | 32 |
| Clindamycin_F2 | 425 | 377 | 1 | 15 | 97 | 18.8 | 24 |
| Clindamycin Cl | 427 | 126 | 1 | 33 | 97 | 18.8 | 24 |
| Clindamycin_F1 | 425 | 126 | 1 | 33 | 97 | 18.8 | 24 |
| Clofibric acid_F2 | 213 | 85 | 0 | 11 | 80 | 29.4 | 32.6 |
| Clofibric acid Cl | 215 | 129 | 0 | 18 | 80 | 29.4 | 32.6 |
| Clofibric acid_F1 | 213 | 127 | 0 | 18 | 80 | 29.4 | 32.6 |
| D4-Clofibric acid_F1 | 217 | 131 | 0 | 18 | 80 | 29.4 | 32.6 |
| D4-Clofibric acid_F2 | 217 | 85 | 0 | 11 | 80 | 29.4 | 32.6 |
| D4-Clofibric acid Cl | 219 | 133 | 0 | 18 | 80 | 29.4 | 32.6 |
| Cyclophosphamid_F2 | 261 | 233 | 1 | 9 | 85 | 18 | 26 |
| Cyclophosphamid Cl | 263 | 140 | 1 | 16 | 85 | 18 | 26 |
| Cyclophosphamid_F1 | 261 | 140 | 1 | 16 | 85 | 18 | 26 |
| Cyclophosphamid_F2 | 261 | 142 | 1 | 14 | 85 | 18 | 26 |
| Cyclophosphamid_F3 | 261 | 63 | 1 | 33 | 85 | 18 | 26 |
| Cyclophosphamid-D4_F2 | 265 | 235 | 1 | 9 | 85 | 18 | 26 |
| Cyclophosphamid-D4_F1 | 265 | 140 | 1 | 16 | 85 | 18 | 26 |
| D617_F2 | 291 | 248 | 1 | 17 | 96 | 17.2 | 28 |
| D617_F1 | 291 | 260 | 1 | 16 | 96 | 17.2 | 28 |
| Dexamethasone_F2 | 393 | 355 | 1 | 11 | 83 | 28.9 | 33 |
| Dexamethasone_F1 | 393 | 373 | 1 | 5 | 83 | 28.9 | 33 |
| Diatrizoat- NH4_F2 | 632 | 233 | 1 | 46 | 86 | 10.8 | 18 |
| Diatrizoate- NH4_F1 | 632 | 361 | 1 | 27 | 86 | 10.8 | 18 |
| Diatrizoate-D6- NH4_F2 | 638 | 239 | 1 | 46 | 86 | 10.8 | 18 |
| Diatrizoate-D6- NH4_F1 | 638 | 367 | 1 | 27 | 86 | 10.8 | 18 |
| Diazepam_F2 | 285 | 154 | 1 | 26 | 107 | 28 | 32.7 |
| Diazepam_F1 | 285 | 193 | 1 | 31 | 107 | 28 | 32.7 |
| Diazepam-d5_F2 | 290 | 154 | 1 | 26 | 107 | 28 | 32.7 |
| Diazepam-d5_F1 | 290 | 198 | 1 | 31 | 107 | 28 | 32.7 |
| Diclofenac_F2 | 296 | 215 | 1 | 17 | 80 | 30.9 | 33.9 |
| Diclofenac Cl | 298 | 216 | 1 | 34 | 80 | 30.9 | 33.9 |
| Diclofenac_F1 | 296 | 214 | 1 | 34 | 80 | 30.9 | 33.9 |
| D4-Diclofenac_F2 | 302 | 219 | 1 | 17 | 80 | 30.9 | 33.7 |
| D4-Diclofenac Cl | 304 | 221 | 1 | 34 | 80 | 30.9 | 33.7 |
| D4-Diclofenac_F1 | 302 | 218 | 1 | 34 | 80 | 30.9 | 33.7 |
| Erythromycin_F2 | 735 | 158 | 1 | 23 | 125 | 23.9 | 32 |
| Erythromycin_F1 | 735 | 576 | 1 | 14 | 125 | 23.9 | 32 |
| 13C2-Erythromycin_F2 | 738 | 160 | 1 | 23 | 125 | 23.9 | 32 |
| 13C2-Erythromycin_F1 | 738 | 579 | 1 | 14 | 125 | 23.9 | 32 |
| Erythromycin-H2O_F2 | 717 | 158 | 1 | 33 | 113 | 25.7 | 32 |
| Erythromycin-H2O_F1 | 717 | 558 | 1 | 10 | 113 | 25.7 | 32 |
| Fluconazole_F2 | 307 | 238 | 1 | 16 | 96 | 15 | 21 |
| Fluconazole_F1 | 307 | 220 | 1 | 17 | 96 | 15 | 21 |

table continues

Table S6. Substance specific MS/MS settings (*continued*)

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|------------------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| Fluconazole-d4_F2 | 311 | 242 | 1 | 16 | 96 | 15 | 21 |
| Fluconazole-d4_F1 | 311 | 223 | 1 | 17 | 96 | 15 | 21 |
| Fluoxetine_F2 | 310 | 91.1 | 1 | 80 | 62 | 25.3 | 31 |
| Fluoxetine_F1 | 310 | 44.1 | 1 | 14 | 62 | 25.3 | 31 |
| Fluoxetine_f3 | 310 | 42.1 | 1 | 40 | 62 | 25.3 | 31 |
| Fluoxetine-d5_F2 | 315 | 42.1 | 1 | 40 | 62 | 25.3 | 31 |
| Fluoxetine-d5_F1 | 315 | 44.1 | 1 | 14 | 62 | 25.3 | 31 |
| Furosemide Cl | 331 | 287 | 0 | 17 | 70 | 21 | 28 |
| Furosemide_F2 | 329 | 205 | 0 | 23 | 70 | 21 | 28 |
| Furosemide_F1 | 329 | 285 | 0 | 16 | 70 | 21 | 28 |
| Furosemide-d5 | 334 | 206 | 0 | 23 | 70 | 21 | 28 |
| Furosemide-d5 Cl | 336 | 292 | 0 | 17 | 70 | 21 | 28 |
| Furosemide-d5_F1 | 334 | 290 | 0 | 16 | 70 | 21 | 28 |
| Gabapentin_F2 | 172 | 137 | 1 | 15 | 84 | 10.9 | 13.8 |
| Gabapentin- D4 | 176 | 140 | 1 | 15 | 84 | 10.9 | 13.8 |
| Gabapentin- D4_F1 | 176 | 158 | 1 | 14 | 84 | 10.9 | 13.8 |
| Gabapentin_F1 | 172 | 154 | 1 | 12 | 84 | 10.9 | 13.8 |
| Gabapentin_f3 | 172 | 67.1 | 1 | 32 | 84 | 10.9 | 13.8 |
| Hydrochlorothiazid_F1 | 296 | 269 | 0 | 18 | 88 | 10.9 | 14.7 |
| Hydrochlorothiazid_F2 | 296 | 205 | 0 | 22 | 88 | 10.9 | 14.7 |
| Hydrochlorothiazid 13C,d2_F2 | 299 | 206 | 0 | 22 | 88 | 10.9 | 14.7 |
| Hydrochlorothiazid 13C,d2_F1 | 299 | 270 | 0 | 18 | 88 | 10.9 | 14.7 |
| Ifosfamide_F2 | 261 | 92 | 1 | 22 | 78 | 17 | 25 |
| Ifosfamide_F1 | 261 | 154 | 1 | 23 | 78 | 17 | 25 |
| Indometacin_F2 | 358 | 111 | 1 | 45 | 88 | 29 | 34.1 |
| Indometacin_F1 | 358 | 139 | 1 | 18 | 88 | 29 | 34.1 |
| Indometacin-d4_F2 | 362 | 115 | 1 | 45 | 88 | 29 | 34.1 |
| Indometacin-d4_F1 | 362 | 143 | 1 | 18 | 88 | 29 | 34.1 |
| Iohexol_F2 | 822 | 603 | 1 | 28 | 162 | 9.5 | 14 |
| Iohexol_F1 | 822 | 804 | 1 | 19 | 162 | 9.5 | 14 |
| Iohexol-d5_F2 | 827 | 608 | 1 | 28 | 162 | 9.5 | 14 |
| Iohexol-d5_F1 | 827 | 809 | 1 | 19 | 162 | 9.5 | 14 |
| lomeprol_F2 | 778 | 687 | 1 | 23 | 146 | 9 | 14.5 |
| lomeprol_F1 | 778 | 405 | 1 | 41 | 146 | 9 | 14.5 |
| lomeprol-d3_F2 | 781 | 690 | 1 | 23 | 146 | 9 | 14.5 |
| lomeprol-d3_F1 | 781 | 408 | 1 | 41 | 146 | 9 | 14.5 |
| lopamidol_F2 | 778 | 387 | 1 | 41 | 139 | 7.5 | 12 |
| lopamidol_F1 | 778 | 559 | 1 | 21 | 139 | 7.5 | 12 |
| lopamidol-d3_F2 | 781 | 390 | 1 | 41 | 139 | 7.5 | 12 |
| lopamidol-d3_F1 | 781 | 562 | 1 | 21 | 139 | 7.5 | 12 |
| lopromide_F2 | 792 | 573 | 1 | 25 | 140 | 9.5 | 15 |
| lopromide_F1 | 792 | 300 | 1 | 60 | 140 | 9.5 | 15 |
| lopromid-D3_F2 | 795 | 576 | 1 | 25 | 140 | 9.5 | 15 |
| lopromid-D3_F1 | 795 | 300 | 1 | 60 | 140 | 9.5 | 15 |
| loxitalamic_acid_F2 | 645 | 429 | 1 | 28 | 122 | 10.3 | 17 |
| loxitalamic_acid_F1 | 645 | 302 | 1 | 45 | 122 | 10.3 | 17 |
| loxitalamic_acid-d4_F2 | 649 | 429 | 1 | 28 | 122 | 10.3 | 17 |

table continues

Table S6. Substance specific MS/MS settings (*continued*)

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|---------------------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| Ioxitalamic_acid-d4_F1 | 649 | 302 | 1 | 45 | 122 | 10.3 | 17 |
| Levertiracetam_F2 | 171 | 154 | 1 | 5 | 56 | 8 | 18 |
| Levertiracetam_F1 | 171 | 126 | 1 | 14 | 56 | 8 | 18 |
| Levertiracetam-D3_F2 | 174 | 157 | 1 | 5 | 56 | 8 | 18 |
| Levertiracetam-D3_F1 | 174 | 129 | 1 | 14 | 56 | 8 | 18 |
| Lidocaine_F2 | 235 | 58.1 | 1 | 34 | 74 | 11.4 | 19 |
| Lidocaine_F1 | 235 | 86.1 | 1 | 17 | 74 | 11.4 | 19 |
| Lidocaine_f3 | 235 | 30.2 | 1 | 42 | 74 | 11.4 | 19 |
| Lidocaine-d10_F2 | 245 | 64.1 | 1 | 34 | 74 | 11.4 | 19 |
| Lidocaine-d10_F1 | 245 | 96.2 | 1 | 17 | 74 | 11.4 | 19 |
| Lidocaine-d10_f3 | 245 | 32.2 | 1 | 42 | 74 | 11.4 | 19 |
| Mefenamic acid_F2 | 242 | 209 | 1 | 25 | 80 | 30 | 36 |
| Mefenamic acid_F1 | 242 | 224 | 1 | 15 | 80 | 30 | 36 |
| D3-Mefenamic acid_F2 | 245 | 212 | 1 | 28 | 80 | 30 | 36 |
| D3-Mefenamic acid_F1 | 245 | 227 | 1 | 19 | 80 | 30 | 36 |
| Methylprednisolone_F2 | 375 | 339 | 1 | 7 | 82 | 29 | 33 |
| Methylprednisolone_F1 | 375 | 357 | 1 | 7 | 82 | 29 | 33 |
| Methylprednisolone-d4_F2 | 379 | 343 | 1 | 7 | 82 | 29 | 33 |
| Methylprednisolone-d4_F1 | 379 | 361 | 1 | 7 | 82 | 29 | 33 |
| Metoprolol_F2 | 268 | 191 | 1 | 15 | 91 | 12.8 | 19 |
| Metoprolol_F1 | 268 | 159 | 1 | 17 | 91 | 12.8 | 19 |
| Metoprolol_f3 | 268 | 133 | 1 | 21 | 91 | 12.8 | 19 |
| D7-Metoprolol_F2 | 275 | 133 | 1 | 21 | 91 | 12.7 | 19 |
| D7-Metoprolol_F1 | 275 | 159 | 1 | 17 | 91 | 12.7 | 19 |
| D7-Metoprolol_f3 | 275 | 191 | 1 | 15 | 91 | 12.7 | 19 |
| Metronidazole_F2 | 172 | 82.1 | 1 | 24 | 71 | 10.7 | 25 |
| Metronidazole_F1 | 172 | 128 | 1 | 14 | 71 | 10.7 | 25 |
| Morphine_F2 | 286 | 201 | 1 | 24 | 100 | 6.12 | 12.4 |
| Morphine_F1 | 286 | 165 | 1 | 38 | 100 | 6.12 | 12.4 |
| Morphine-d3_F2 | 289 | 201 | 1 | 24 | 100 | 6.12 | 12.4 |
| Morphine-d3_F1 | 289 | 165 | 1 | 38 | 100 | 6.12 | 12.4 |
| N4-Acetylsulfamethoxazol_F2 | 296 | 198 | 1 | 17 | 103 | 17.3 | 22 |
| N4-Acetylsulfamethoxazol_F1 | 296 | 134 | 1 | 23 | 103 | 17.3 | 22 |
| d5-N4-Acetylsulfamethoxazole_F2 | 301 | 203 | 1 | 17 | 103 | 17.3 | 22 |
| d5-N4-Acetylsulfamethoxazole_F1 | 301 | 139 | 1 | 23 | 103 | 17.3 | 22 |
| Naproxen_F1 | 231 | 185 | 1 | 15 | 126 | 26 | 33.5 |
| Naproxen_F2 | 231 | 170 | 1 | 21 | 126 | 26 | 33.5 |
| Naproxen- D4_F2 | 235 | 170 | 1 | 56 | 126 | 26 | 33.5 |
| Naproxen- D4_F1 | 235 | 189 | 1 | 15 | 126 | 26 | 33.5 |
| Norfloxacin_F2 | 320 | 276 | 1 | 13 | 105 | 11.8 | 22 |
| Norfloxacin_F1 | 320 | 302 | 1 | 17 | 105 | 11.8 | 22 |
| Norfloxacin-D5_F2 | 325 | 281 | 1 | 17 | 105 | 11.8 | 22 |
| Norfloxacin-D5_F1 | 325 | 307 | 1 | 17 | 105 | 11.8 | 22 |
| Oseltamivir_F1 | 313 | 166 | 1 | 17 | 95 | 18.8 | 31 |
| Oseltamivir_F2 | 313 | 120 | 1 | 33 | 95 | 18.8 | 31 |
| Oseltamivir carboxylate_F2 | 285 | 120 | 1 | 32 | 91 | 13 | 24 |
| Oseltamivir carboxylate_F1 | 285 | 138 | 1 | 18 | 91 | 13 | 24 |

table continues

Table S6. Substance specific MS/MS settings (*continued*)

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|-----------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| Oxazepam_F2 | 287 | 269 | 1 | 14 | 76 | 27 | 31.4 |
| Oxazepam_F1 | 287 | 241 | 1 | 23 | 76 | 27 | 31.4 |
| Oxazepam-Cl_F2 | 289 | 271 | 1 | 14 | 76 | 27 | 31.4 |
| Oxazepam-Cl_F1 | 289 | 243 | 1 | 23 | 76 | 27 | 31.4 |
| Oxazepam-d5_F2 | 292 | 274 | 1 | 14 | 76 | 27 | 31.4 |
| Oxazepam-d5_F1 | 292 | 246 | 1 | 23 | 76 | 27 | 31.4 |
| Paracetamol_F2 | 152 | 93 | 1 | 16 | 80 | 8 | 18 |
| Paracetamol_F1 | 152 | 110 | 1 | 9 | 80 | 8 | 18 |
| Paracetamol_f3 | 152 | 65.1 | 1 | 26 | 80 | 8 | 18 |
| D4-Paracetamol_F2 | 156 | 97 | 1 | 16 | 80 | 8 | 18 |
| D4-Paracetamol_F1 | 156 | 114 | 1 | 9 | 80 | 8 | 18 |
| Phenazone_F2 | 189 | 131 | 1 | 17 | 95 | 13 | 19 |
| Phenazone_F1 | 189 | 77 | 1 | 37 | 95 | 13 | 19 |
| D3-Phenazone_F2 | 192 | 131 | 1 | 17 | 95 | 13 | 19 |
| D3-Phenazone_F1 | 192 | 77 | 1 | 37 | 95 | 13 | 19 |
| Primidone_F2 | 219 | 91 | 1 | 27 | 88 | 15 | 22 |
| Primidone_F1 | 219 | 162 | 1 | 11 | 88 | 15 | 22 |
| Primidone-d5_F2 | 224 | 93 | 1 | 27 | 88 | 15 | 22 |
| Primidone-d5_F1 | 224 | 167 | 1 | 11 | 88 | 15 | 22 |
| Propranolol_F2 | 260 | 155 | 1 | 23 | 89 | 15 | 25 |
| Propranolol_F1 | 260 | 183 | 1 | 17 | 89 | 15 | 25 |
| D7-Propranolol_F2 | 267 | 161 | 1 | 23 | 89 | 15 | 25 |
| D7-Propranolol_F1 | 267 | 189 | 1 | 17 | 89 | 15 | 25 |
| Ranitidine_F2 | 315 | 130 | 1 | 26 | 81 | 8 | 17 |
| Ranitidine_F1 | 315 | 176 | 1 | 17 | 81 | 8 | 17 |
| Ranitidine-d6_F2 | 321 | 130 | 1 | 26 | 81 | 8 | 17 |
| Ranitidine-d6_F1 | 321 | 176 | 1 | 17 | 81 | 8 | 17 |
| Ritalinic acid_F2 | 220 | 56.1 | 1 | 41 | 69 | 12.7 | 18 |
| Ritalinic acid_F1 | 220 | 84.1 | 1 | 19 | 69 | 12.7 | 18 |
| Ritalinic acid_f3 | 220 | 91.1 | 1 | 39 | 69 | 12.7 | 18 |
| Ritalinic acid-d10_F2 | 230 | 61.1 | 1 | 41 | 69 | 12.7 | 18 |
| Ritalinic acid-d10_F1 | 230 | 93.2 | 1 | 19 | 69 | 12.7 | 18 |
| Ritonavir_F2 | 721 | 268 | 1 | 27 | 95 | 29 | 34.3 |
| Ritonavir_F1 | 721 | 140 | 1 | 53 | 95 | 29 | 34.3 |
| Ritonavir_f3 | 721 | 197 | 1 | 37 | 95 | 29 | 34.3 |
| Ritonavir-d6_F2 | 727 | 274 | 1 | 27 | 95 | 29 | 34.3 |
| Ritonavir-d6_F1 | 727 | 146 | 1 | 53 | 95 | 29 | 34.3 |
| Ritonavir-d6_f3 | 727 | 203 | 1 | 37 | 95 | 29 | 34.3 |
| Roxithromycin_F2 | 838 | 158 | 1 | 33 | 130 | 27 | 32 |
| Roxithromycin_F1 | 838 | 679 | 1 | 15 | 130 | 27 | 32 |
| Sotalol_F2 | 273 | 213 | 1 | 15 | 87 | 10.1 | 13.1 |
| Sotalol_F1 | 273 | 255 | 1 | 11 | 87 | 10.1 | 13.1 |
| D6-Sotalol_F2 | 279 | 214 | 1 | 15 | 87 | 10.1 | 13 |
| D6-Sotalol_F1 | 279 | 261 | 1 | 11 | 87 | 10.1 | 13 |
| Sulfadiazine_F2 | 251 | 108 | 1 | 21 | 80 | 9.5 | 15.8 |
| Sulfadiazine_F1 | 251 | 156 | 1 | 14 | 80 | 9.5 | 15.8 |
| d4-Sulfadiazine_F2 | 255 | 96 | 1 | 24 | 80 | 9.5 | 15.8 |

table continues

Table S6. Substance specific MS/MS settings (continued)

| | m/z | | ESI pos→ 1 neg→ 0 | Collision energy (V) | Tube lens voltage (V) | Acquisition (min) | |
|------------------------|-------------------|-----------------|-------------------------|----------------------------|-----------------------------|-------------------|-----------|
| | Precursor mass | Product mass | | | | Start time | Stop time |
| d4-Sulfadiazine_F1 | 255 | 160 | 1 | 19 | 80 | 9.5 | 15.8 |
| Sulfamethoxazole_F2 | 254 | 92 | 1 | 24 | 94 | 12 | 20 |
| Sulfamethoxazole_F1 | 254 | 156 | 1 | 15 | 94 | 12 | 20 |
| d4-Sulfamethoxazole_F2 | 258 | 96 | 1 | 24 | 94 | 12 | 20 |
| d4-Sulfamethoxazole_F1 | 258 | 160 | 1 | 15 | 94 | 12 | 20 |
| Sulfapyridine_F2 | 250 | 184 | 1 | 13 | 87 | 9.5 | 22 |
| Sulfapyridine_F1 | 250 | 156 | 1 | 14 | 87 | 9.5 | 22 |
| Sulfapyridine-d4_F2 | 254 | 96 | 1 | 29 | 87 | 9.5 | 22 |
| Sulfapyridine-d4_F1 | 254 | 160 | 1 | 16 | 87 | 9.5 | 22 |
| Sulfapyridine-d4_f3 | 254 | 188 | 1 | 18 | 87 | 9.5 | 22 |
| Thiopental_F2 | 241 | 198 | 0 | 12 | 53 | 26 | 36 |
| Thiopental_F1 | 241 | 58 | 0 | 21 | 53 | 26 | 36 |
| Tramadol_F2 | 264 | 42.1 | 1 | 78 | 62 | 12.7 | 20 |
| Tramadol_F1 | 264 | 58.1 | 1 | 16 | 62 | 12.7 | 20 |
| Tramadol_f3 | 264 | 246 | 1 | 9 | 62 | 12.7 | 20 |
| Tramadol-d6_F2 | 270 | 45.2 | 1 | 78 | 62 | 12.7 | 20 |
| Tramadol-d6_F1 | 270 | 64.1 | 1 | 16 | 62 | 12.7 | 20 |
| Tramadol-d6_f3 | 270 | 252 | 1 | 9 | 62 | 12.7 | 20 |
| Trimethoprim_F2 | 291 | 261 | 1 | 14 | 98 | 10.9 | 14.6 |
| Trimethoprim_F1 | 291 | 230 | 1 | 10 | 98 | 10.9 | 14.6 |
| D9-Trimethoprim_F2 | 300 | 264 | 1 | 14 | 98 | 10.9 | 13.7 |
| D9-Trimethoprim_F1 | 300 | 234 | 1 | 10 | 98 | 10.9 | 13.7 |
| Valsartan_F2 | 436 | 291 | 1 | 18 | 85 | 30.1 | 33.2 |
| Valsartan_F1 | 436 | 207 | 1 | 27 | 85 | 30.1 | 33.2 |
| Valsartan-d3_F2 | 439 | 294 | 1 | 18 | 85 | 30.1 | 33.2 |
| Valsartan-d3_F1 | 439 | 207 | 1 | 27 | 85 | 30.1 | 33.2 |
| Venlafaxin_F2 | 278 | 260 | 1 | 10 | 63 | 16.5 | 26 |
| Venlafaxin_F1 | 278 | 58.1 | 1 | 18 | 63 | 16.5 | 26 |
| Venlafaxin-d6_F2 | 284 | 266 | 1 | 10 | 63 | 16.5 | 26 |
| Venlafaxin-d6_F1 | 284 | 58.1 | 1 | 18 | 63 | 16.5 | 26 |
| Verapamil_F2 | 455 | 150 | 1 | 37 | 108 | 21.5 | 30 |
| Verapamil_F1 | 455 | 165 | 1 | 27 | 108 | 21.5 | 30 |
| Verapamil_f3 | 455 | 303 | 1 | 24 | 108 | 21.5 | 30 |
| Verapamil-d6_F2 | 461 | 150 | 1 | 37 | 108 | 21.5 | 30 |
| Verapamil-d6_F1 | 461 | 165 | 1 | 27 | 108 | 21.5 | 30 |
| Verapamil-d6_f3 | 461 | 309 | 1 | 24 | 108 | 21.5 | 30 |

Source parameters:

Ion Transfer Capillary Temperature: 350 °C
 Spray Voltage: 3800 V (ESI+), 3000 V (ESI-)
 Sheath Gas Pressure: 50 bar
 Aux Gas Pressure: 10 bar

Table S7. Quality control (137 measurements, all matrices, campaign August 2009). To fail QC criteria, F1/F2 (the ratio of quantifier and qualifier transitions) exceeded 20% tolerance of deviation from F1/F2 ratio in calibration standards and Δt_R (the difference between retention time of an internal standard and analyte in the same sample) differed from Δt_R in calibration standards by more than 0.15 min.

| | Matching internal standard | Known and constant concentration of calibration standards | QC in matrix failed (#failed / #>LOQ) | | Calibration curve r^2 (file 090915) | Calibr. range | Precision | Uncertainty (confidence level 95%) | QC label |
|-------------------------------------|----------------------------|---|---------------------------------------|--------------|---------------------------------------|---------------|-----------|------------------------------------|----------|
| | | | F1/F2 | Δt_R | | | | | |
| 4-Acetamidoantipyrine | - | - | 0 / 120 | 19 / 120 | 0.8278 | 1 - 2'500 | 39% | 99% | c |
| 4-Aminoantipyrine | - | - | 8 / 84 | 5 / 84 | 0.9840 | 250 - 40'000 | 83% | 172% | d |
| 4-Dimethylaminoantipyrine | - | - | n.d. | n.d. | 0.9647 | 50 - 2'500 | 16% | 57% | c |
| 4-Formylaminoantipyrine | - | - | 4 / 132 | 24 / 132 | 0.9826 | 1 - 2'500 | 18% | 74% | c |
| 4-Methylaminoantipyrine | - | - | 14 / 56 | 10 / 56 | 0.9680 | 500 - 40'000 | 84% | 178% | d |
| 4/5-Methylbenzotriazole (2 isomers) | - ^a | yes | 1 / 137 | 4 / 137 | 0.3967 | 5 - 10'000 | 65% | 133% | d |
| Atenolol | yes | yes | 11 / 87 | 0 / 87 | 0.9964 | 10 - 2'500 | 4% | 12% | a |
| Atenolol acid | yes | yes | 7 / 137 | 0 / 137 | 0.9978 | 5 - 2'500 | 6% | 13% | a |
| Azithromycin | yes | yes | 6 / 35 | 1 / 35 | 0.9918 | 5 - 2'500 | 9% | 22% | b |
| Benzotriazole | yes | yes | 0 / 137 | 0 / 137 | 0.9946 | 50 - 2'500 | 7% | 17% | b |
| Bezafibrate | yes | yes | 4 / 60 | 0 / 60 | 0.9993 | 1 - 2'500 | 3% | 8% | a |
| Carbamazepine | yes | yes | 0 / 133 | 0 / 133 | 0.9996 | 1 - 2'500 | 7% | 15% | b |
| Cilastatin | - | yes | 5 / 23 | 1 / 23 | 0.9554 | 25 - 2'500 | 28% | 60% | c |
| Ciprofloxacin | yes | (?) | 0 / 127 | 1 / 127 | 0.9961 | 50 - 2'500 | 18% | 55% | c |
| Clarithromycin | - | yes | 4 / 124 | 0 / 124 | 0.9976 | 1 - 2'500 | 4% | 10% | a |
| Clindamycin | - | yes | 5 / 124 | 0 / 124 | 0.9077 | 5 - 2'500 | 26% | 53% | c |
| Clofibric acid | yes | yes | n.d. | n.d. | 0.9935 | 5 - 2'500 | 6% | 19% | b |
| Cyclophosphamide | yes | yes | 3 / 73 | 7 / 73 | 0.9971 | 5 - 2'500 | 4% | 13% | a |
| D617 | - | yes | 5 / 85 | 10 / 85 | 0.9939 | 1 - 2'500 | 11% | 26% | b |
| Dexamethasone | - | yes | n.d. | n.d. | 0.9954 | 5 - 2'500 | 5% | 11% | a |
| Diatrizoate | yes | yes | 0 / 121 | 0 / 121 | 0.9967 | 250 - 40'000 | 39% | 82% | c |
| Diazepam | yes | yes | 2 / 10 | 0 / 10 | 0.9961 | 1 - 2'500 | 3% | 9% | a |
| Diclofenac | yes | yes | 14 / 115 | 0 / 115 | 0.9986 | 1 - 2'500 | 6% | 15% | b |
| Erythromycin | yes | - | 16 / 20 | 0 / 20 | 0.9991 | 5 - 2'500 | 3% | 42% | c |
| Erythromycin-H2O | - | - | 0 / 22 | 0 / 22 | 0.9833 | 5 - 2'500 | 15% | 51% | c |

table continues

Table S7. Quality control (continued)

| | Matching internal standard | Known and constant concentration of calibration standards | QC in matrix failed (#failed / #>LOQ) | | Calibration curve r ² (file 090915) | Calibr. range | Precision | Uncertainty (confidence level 95%) | QC label |
|---------------------------|----------------------------|---|---------------------------------------|-----------------|--|---------------|-----------|------------------------------------|----------|
| | | | F1/F2 | Δt _R | | | | | |
| Fluconazole | yes | yes | 0 / 136 | 0 / 136 | 0.9993 | 5 - 2'500 | 2% | 7% | a |
| Fluoxetine | yes | yes | n.d. | n.d. | 0.9968 | 1 - 2'500 | 6% | 26% | b |
| Furosemide | yes | yes | 13 / 99 | 0 / 99 | 0.9962 | 5 - 2'500 | 8% | 23% | b |
| Gabapentin | yes | yes | 9 / 116 | 0 / 116 | 0.9976 | 250 - 2'500 | 7% | 21% | b |
| Hydrochlorothiazide | yes | yes | 26 / 137 | 0 / 137 | 0.9974 | 5 - 2'500 | 4% | 10% | a |
| Ifosfamide | - | yes | 0 / 4 | 0 / 4 | 0.9872 | 1 - 2'500 | 6% | 17% | b |
| Indometacin | yes | yes | 7 / 91 | 0 / 91 | 0.9988 | 1 - 2'500 | 3% | 11% | a |
| Iohexol | yes | yes | 7 / 7 | 4 / 7 | 0.9943 | 100 - 30'000 | 32% | 64% | c |
| lomeprol | yes | yes | 21 / 104 | 1 / 104 | 0.9849 | 100 - 40'000 | 70% | 141% | d |
| lopamidol | yes ^b | yes | 97 / 137 | 81 / 137 | 0.9542 | 250 - 40'000 | 187% | 375% | d |
| lopromide | yes | yes | 10 / 128 | 1 / 128 | 0.9905 | 100 - 40'000 | 44% | 90% | c |
| loxitalamic acid | yes | yes | 55 / 129 | 60 / 129 | 0.9843 | 250 - 40'000 | 25% | 61% | c |
| Levetiracetam | yes | yes | 7 / 63 | 0 / 63 | 0.9987 | 10 - 2'500 | 4% | 11% | a |
| Lidocaine | yes | yes | 0 / 129 | 0 / 129 | 0.9913 | 5 - 2'500 | 4% | 10% | a |
| Mefenamic acid | yes | yes | 3 / 122 | 0 / 122 | 0.9986 | 1 - 2'500 | 4% | 12% | a |
| Methylprednisolone | yes | yes | n.d. | n.d. | 0.9985 | 5 - 2'500 | 3% | 9% | a |
| Metoprolol | yes | yes | 0 / 109 | 0 / 109 | 0.9993 | 25 - 2'500 | 2% | 7% | a |
| Metronidazole | - | yes | 8 / 113 | 12 / 113 | 0.9658 | 25 - 2'500 | 27% | 55% | c |
| Morphine | yes | yes | 23 / 54 | 22 / 54 | 0.9986 | 25 - 2'500 | 11% | 24% | b |
| N4-Acetylsulfamethoxazole | yes | yes | 5 / 137 | 1 / 137 | 0.9987 | 1 - 2'500 | 4% | 11% | a |
| Naproxen | yes ^b | yes | n.d. | n.d. | 0.9866 | 100 - 2'500 | 23% | 74% | c |
| Norfloxacin | yes ^b | (?) | 52 / 89 | 0 / 89 | 0.9895 | 500 - 2'500 | 13% | 49% | c |
| Oseltamivir | yes | yes | 10 / 67 | 22 / 67 | 0.9194 | 5 - 2'500 | 27% | 55% | c |
| Oseltamivir carboxylate | - | yes | 29 / 51 | 2 / 51 | 0.9984 | 25 - 2'500 | 8% | 17% | b |
| Oxazepam | yes | yes | 0 / 137 | 0 / 137 | 0.9989 | 1 - 2'500 | 3% | 9% | a |
| Paracetamol | yes | yes | 0 / 54 | 0 / 54 | 0.9839 | 50 - 5'000 | 12% | 29% | b |
| Phenazone | yes | (?) | 1 / 121 | 7 / 121 | 0.9997 | 5 - 2'500 | 5% | 42% | c |

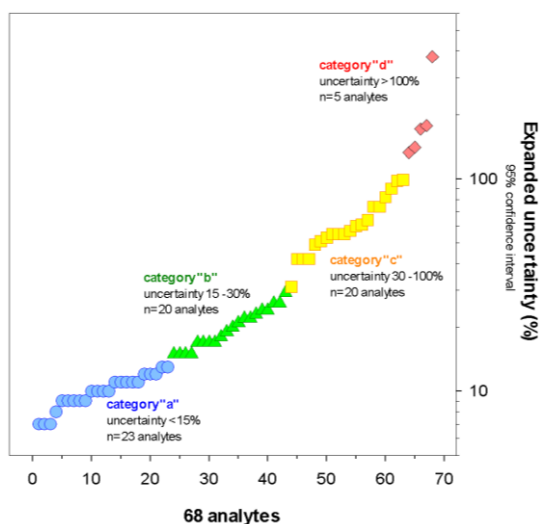
table continues

Table S7. Quality control (continued)

| | Matching internal standard | Known and constant concentration of calibration standards | QC in matrix failed (#failed / #>LOQ) | | Calibration curve r ² (file 090915) | Calibr. range | Precision | Uncertainty (confidence level 95%) | QC label |
|------------------|----------------------------|---|---------------------------------------|-----------------|--|---------------|-----------|------------------------------------|----------|
| | | | F1/F2 | Δt _R | | | | | |
| Primidone | yes | yes | 10 / 75 | 7 / 75 | 0.9998 | 5 - 2'500 | 2% | 15% | b |
| Propranolol | yes | yes | 2 / 52 | 1 / 52 | 0.9869 | 5 - 2'500 | 11% | 24% | b |
| Ranitidine | yes | yes | 4 / 93 | 0 / 93 | 0.9941 | 10 - 2'500 | 6% | 15% | b |
| Ritalinic acid | yes | yes | 64 / 136 | 18 / 136 | 0.9979 | 5 - 2'500 | 5% | 18% | b |
| Ritonavir | yes | yes | 3 / 56 | 0 / 56 | 0.9922 | 1 - 2'500 | 9% | 20% | b |
| Roxithromycin | - | yes | 12 / 31 | 2 / 31 | 0.9943 | 1 - 2'500 | 11% | 22% | b |
| Sotalol | yes | yes | 8 / 98 | 0 / 98 | 0.9981 | 25 - 2'500 | 3% | 7% | a |
| Sulfadiazine | yes | yes | 0 / 10 | 0 / 10 | 0.9992 | 5 - 2'500 | 4% | 11% | a |
| Sulfamethoxazole | yes | yes | 0 / 137 | 0 / 137 | 0.9987 | 5 - 2'500 | 4% | 10% | a |
| Sulfapyridine | - a | yes | 4 / 47 | 15 / 47 | 0.9962 | 5 - 2'500 | 11% | 42% | c |
| Thiopental | - | yes | one transition | 4 / 21 | 0.9956 | 5 - 2'500 | 42% | 98% | c |
| Tramadol | yes | yes | 1 / 105 | 0 / 105 | 0.9997 | 5 - 2'500 | 4% | 9% | a |
| Trimethoprim | yes | yes | 18 / 51 | 1 / 51 | 0.9912 | 25 - 2'500 | 15% | 31% | c |
| Valsartan | yes | yes | 6 / 137 | 2 / 137 | 0.9994 | 1 - 2'500 | 2% | 17% | b |
| Venlafaxin | yes | yes | 16 / 91 | 3 / 91 | 0.9964 | 5 - 2'500 | 5% | 12% | a |
| Verapamil | yes | yes | 0 / 20 | 0 / 20 | 0.9987 | 5 - 2'500 | 4% | 9% | a |

a i.s. available since March 2010
 b low intensity of internal standard

| | |
|---------------------------|-----------------------------|
| Uncertainty less than 14% | a (best) |
| Uncertainty 15 – 29% | b (good) |
| Uncertainty 30 – 100% | c (high uncertainty) |
| Uncertainty above 100% | d (semiquantitative) |



Calculation of precision, uncertainty, relative recoveries, and LOQs

1. Precision

The instrumental intraday precision of the online SPE-HPLC/MS/MS measurements is reported in Table S7. It was estimated from 18 data points of a reference standard with known concentration (1000 ng/L and 2500 ng/L) over a time period of one month (August 2009, 3 sequences, one analyst) according to the EURACHEM / CITAC Guide⁽⁴⁾. Standard deviations for 1000 ng/L and 2500 ng/L standards were calculated:

$$SD_{1000} = \sqrt{\frac{\sum(x-1000)^2}{(n_{1000}-1)}} \quad SD_{2500} = \sqrt{\frac{\sum(x-2500)^2}{(n_{2500}-1)}}$$

Pooled relative standard deviation RSD_{pool} was calculated from relative standard deviations for each of the two standard concentrations and number of data points n for the respective standard concentration.

$$RSD_{pool} = \sqrt{\frac{(RSD_{1000}^2 \cdot (n_{1000} - 1)) + (RSD_{2500}^2 \cdot (n_{2500} - 1))}{(n_{1000} - 1) + (n_{2500} - 1)}}$$

$$(rel U_{precision}) = RSD_{pool}$$

2. Uncertainty

Expanded uncertainty with confidence level of 95% is reported in Table S7. It was calculated according to the EURACHEM / CITAC Guide⁽⁴⁾ from combined relative overall uncertainty, which comprises:

- instrumental intraday precision (as above)
- bias (method relative recovery)
- other uncertainty contributions

2.1. Bias

The bias of the analytical procedure was investigated during the in-house validation study using spiked samples (relative recoveries: all matrices, all dilutions, various spiking concentrations, various sequences, three analysts).

If the relative recovery was in the range 75-125% (majority of compounds), reported value was not corrected for recovery and the uncertainty was calculated from mean recovery, coverage factor k ($k=2$ for 95% confidence interval), standard deviation SD and number of data points n , as follows:

$$U_{biasA} = \sqrt{\left(\frac{1 - \text{mean recovery}}{k}\right)^2 + \left(\frac{SD}{\sqrt{n}}\right)^2}$$

If the reported value was corrected for relative recovery (clindamycin, D617, metronidazole, oseltamivir, oseltamivir carboxylate), the uncertainty was calculated:

$$U_{biasB} = \frac{SD}{\sqrt{n}}$$

$$(rel U_{bias}) = U_{bias} / (\text{mean recovery})$$

2.2. Other uncertainty contributions

Other uncertainties were estimated:

- (rel U_{o1}) reference material purity, gravimetric/volumetric devices:
2% (as calculated by A. Goebel ⁽⁵⁾)
- (rel U_{o2}) calibration standard stock solution stability:
0.5% estimated for stable compounds
20% estimated for less stable compounds
- (rel U_{o3}) nonlinearity in detector response
estimated negligible
- (rel U_{o4}) sample homogeneity
estimated negligible

$$rel U_{other} = \sqrt{(rel U_{o1})^2 + (rel U_{o2})^2}$$

2.3. Calculation of combined relative overall uncertainty

$$rel U_{combined} = \sqrt{(rel U_{precision})^2 + (rel U_{bias})^2 + (rel U_{other})^2}$$

2.4. Calculation of expanded uncertainty

According to desired confidence level, respective coverage factor k is used:

| confidence level | coverage factor k |
|------------------|---------------------|
| approx. 68% | 1 |
| approx. 95% | 2 |
| 99% | 2.58 |
| 99.7% | 3 |

Expanded uncertainty was obtained by multiplying combined standard uncertainty ($rel U_{combined}$) by a coverage factor (k).

$$(rel U) = k \cdot (rel U_{combined})$$

3. Relative recoveries

Relative recoveries are reported in Table S9 and were calculated from the samples of a given matrix and dilution spiked with 1000 ng/L of analyte.

3.1. Example of relative recoveries calculation (Atenolol, SP-1, dilution 1:10)

Recoveries for atenolol in SP-1 matrix diluted 1:10 were calculated from the following measured concentrations

Composite 7, SP-1, dilution 1:10 (average of 2 injections): 365 ng/L (C_0)
Composite 7, SP-1, dilution 1:10, spiked 1000 ng/L (average of 2 injections): 1383 ng/L (C_{spike})

as follows:

$$\% \text{ relative recoveries} = 100\% \cdot (C_{spike} - C_0) / C_{theor.spike}$$

$$\% \text{ relative recoveries} = 100\% \cdot (1383 - 365) / 1000 = 102\%$$

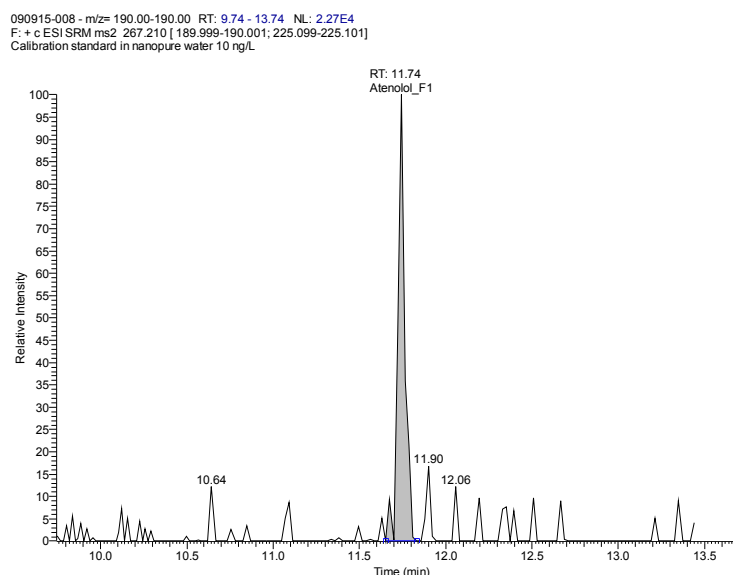
4. Limits of quantification (LOQ)

Limits of quantification are not constant values and can vary from one sequence to another. Estimated limits of quantification for each matrix, dilution, and transition are reported in Table S10. LOQs were estimated:

- from signal-to-noise ratio of a low concentration calibration standard (S/N = 10), multiplied by a matrix factor (ion suppression or enhancement factor)
- or (values marked ^a) by extrapolation from signal-to-noise ratio of an unspiked sample peak intensity, whenever it was not possible to obtain a matrix factor due to high concentrations in matrix prior to spiking.

4.1. Example of LOQ estimation using a matrix factor (*Atenolol_F1*, SP-1, dilution 1:10)

From chromatograms of calibration standards in nanopure water, a concentration with a peak having a signal-to-noise ratio of 10:1 was chosen. It represents the LOQ in nanopure water (LOQ_{nanopure}). In case of *atenolol_F1* it was 10 ng/L.



The matrix factor was calculated from the following peak areas

| | |
|---|------------|
| 1000 ng/L in nanopure water (average of 2 standards): | 4 111 388 |
| 1000 ng/L spiked in SP-1 dilution 1:10 (average of 2 injections): | 12 867 910 |
| unspiked SP-1 dilution 1:10 (average of 2 injections): | 3 577 611 |

as follows:

| | |
|----------------------------------|------------------------------------|
| 1000 ng/L in SP-1 dilution 1:10: | 12 867 910 - 3 577 611 = 9 290 249 |
| matrix factor: | 9 290 249 / 4 111 388 = 2.26 |

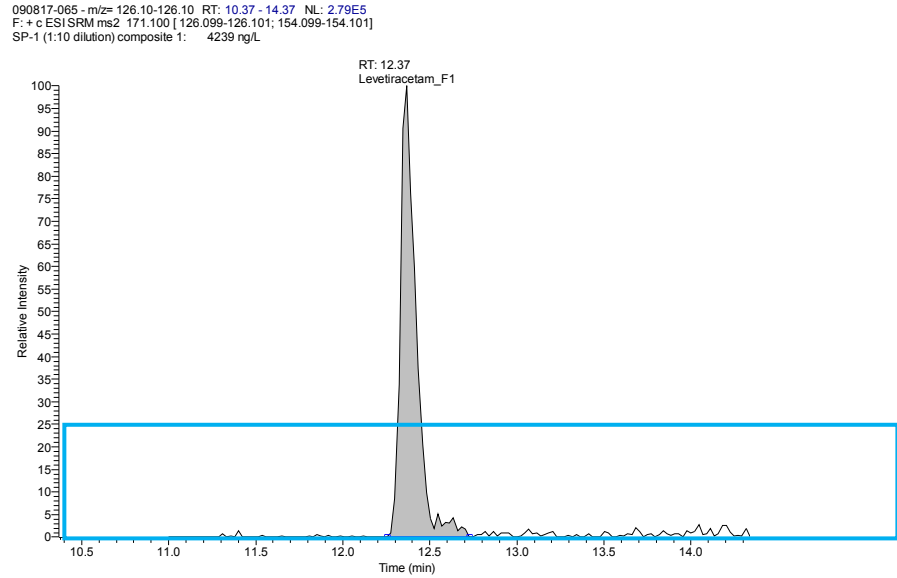
The matrix factor reflects the change of analyte peak intensity caused by the fact that co-eluting matrix compounds are influencing ionization of the analyte during the electrospray ionization. The consequence is either ion suppression (when the peak area in matrix is smaller than in nanopure water, and the matrix factor is <1) or ion enhancement (when the peak area in matrix is bigger than in nanopure water, and the matrix factor is >1).

$$LOQ_{matrix} = (LOQ_{nanopure} / matrix\ factor) * dilution\ factor$$

$$LOQ_{matrix} = (10 / 2.26) * 10 = 44\ ng/L$$

4.2. Example of LOQ estimation using extrapolation of sample peak intensity (*Levetiracetam_F1, SP-1, dilution 1:10*)

A chromatogram of an unspiked sample in the desired matrix and dilution with as low concentration as possible was looked for. In case of levetiracetam_F1 in SP-1 and dilution 1:10 the following chromatogram of Composite 1 sample with a concentration around 4000 ng/L was used:



In this chromatogram the signal-to-noise ratio is more than 10 but there is no sample with lower concentration of levetiracetam available. A rough estimation of the baseline noise was done by zooming in, giving a noise at around 2.5 % of the intensity. Therefore, a peak with a signal-to-noise of 10 has around 25% of the intensity of the peak. Therefore, LOQ is estimated as 25% of the peak, so at 1000 ng/L.

Table S8 Sample matrices

| | |
|----------------------|-------------------------------------|
| Hospital wastewater | |
| SP-1 | wastewater from hospital sewer |
| SP-2 | MBR influent (sedimentation tank) |
| SP-3 | MBR permeate |
| SP-4 | PAC effluent |
| SP-5 | O ₃ effluent |
| SP-6 | biofilter effluent |
| SP-7 | UV and UV/TiO ₂ effluent |
| Municipal wastewater | |
| WWTP-in | WWTP influent |
| WWTP-eff | WWTP effluent |

Table S9. Relative recoveries determined by spiking 1000 ng/L (campaign August 2009). Sample matrices are described in Table S8

| | Matrix: | | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|-------------------------------------|-------------------------|------|--------|------|--------|--------|-------------|--------|-------|--------|------|--------|------|-------|-------|---------|------|----------|----|
| | Sample dilution factor: | | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| 4-Acetamidoantipyrine | H.bckg | 95% | H.bckg | 56% | 126% | 106% | 72% | 82% | 78% | 64% | 81% | 302% | 103% | 70% | 84% | <10% | 110% | | |
| 4-Aminoantipyrine | H.bckg | 102% | H.bckg | 98% | H.bckg | H.bckg | 80% | H.bckg | <10% | H.bckg | 126% | H.bckg | <10% | 266% | 126% | <10% | 67% | | |
| 4-Dimethylaminoantipyrine | 160% | 116% | 163% | 127% | 250% | 173% | 108% | <10% | 14% | 209% | 121% | <10% | 11% | 100% | 118% | 14% | 96% | | |
| 4-Formylaminoantipyrine | 126% | 106% | 98% | 97% | H.bckg | 100% | 102% | 115% | 93% | 102% | 105% | 121% | 93% | 72% | 91% | 94% | 90% | | |
| 4-Methylaminoantipyrine | H.bckg | 135% | H.bckg | 125% | 40% | 112% | 108% | <10% | 22% | 64% | 195% | <10% | 13% | >300% | >300% | <10% | 174% | | |
| 4/5-Methylbenzotriazole (2 isomers) | H.bckg | 138% | H.bckg | 135% | H.bckg | H.bckg | 145% | H.bckg | 182% | H.bckg | 213% | H.bckg | 227% | 145% | 142% | 177% | 154% | | |
| Atenolol | 102% | 115% | 108% | 103% | 114% | 117% | 114% | 101% | 107% | 114% | 103% | 110% | 107% | 107% | 103% | 94% | 105% | | |
| Atenolol acid | 105% | 115% | 106% | 111% | 119% | 99% | 109% | 101% | 100% | 112% | 119% | 107% | 109% | 113% | 104% | 107% | 101% | | |
| Azithromycin | 113% | 153% | 105% | 163% | 108% | 137% | 137% | 104% | 119% | 64% | 142% | 17% | 130% | 108% | 149% | 78% | 108% | | |
| Benzotriazole | H.bckg | 109% | 118% | 102% | H.bckg | 128% | 129% | H.bckg | 109% | H.bckg | 121% | H.bckg | 78% | 95% | 94% | H.bckg | 96% | | |
| Bezafibrate | 104% | 110% | 109% | 109% | 119% | 116% | 114% | 111% | 108% | 128% | 124% | 118% | 122% | 103% | 108% | 98% | 106% | | |
| Carbamazepine | 104% | 109% | 104% | 108% | 117% | 117% | 110% | 107% | 106% | 124% | 123% | 116% | 118% | 101% | 105% | 96% | 101% | | |
| Cilastatin | 94% | 110% | 101% | 108% | 90% | 125% | 121% | 90% | 108% | 73% | 116% | 64% | 105% | 80% | 148% | 55% | 110% | | |
| Ciprofloxacin | 121% | 149% | 132% | 139% | H.bckg | 133% | 139% | 115% | 107% | 125% | 122% | 111% | 123% | 110% | 104% | 90% | 96% | | |
| Clarithromycin | 103% | 107% | 105% | 108% | 118% | 122% | 113% | 106% | 107% | 90% | 138% | 111% | 131% | 103% | 110% | 94% | 115% | | |
| Clindamycin | 242% | 169% | 228% | 151% | H.bckg | 184% | 155% | 195% | 145% | 287% | 167% | 224% | 148% | 127% | 121% | 158% | 119% | | |
| Clofibric acid | 119% | 122% | 123% | 125% | 135% | 118% | 116% | 115% | 105% | 125% | 139% | 155% | 139% | 129% | 115% | 119% | 114% | | |
| Cyclophosphamide | 113% | 111% | 113% | 112% | 122% | 121% | 118% | 110% | 110% | 134% | 126% | 128% | 123% | 106% | 109% | 104% | 103% | | |
| D617 | 125% | 127% | 127% | 129% | 131% | 119% | 121% | 121% | 121% | 146% | 147% | 107% | 115% | 120% | 105% | 108% | 106% | | |
| Dexamethasone | 113% | 108% | 109% | 105% | 103% | 107% | 107% | 80% | 97% | 103% | 124% | 95% | 137% | 97% | 111% | 98% | 97% | | |
| Diatrizoate | H.bckg | 157% | H.bckg | 157% | H.bckg | 108% | 164% | H.bckg | >300% | H.bckg | 59% | H.bckg | <10% | 123% | 125% | 110% | 125% | | |
| Diazepam | 115% | 118% | 112% | 117% | 121% | 122% | 119% | 111% | 111% | 150% | 139% | 122% | 131% | 107% | 116% | 99% | 112% | | |
| Diclofenac | 107% | 106% | 107% | 108% | 118% | 115% | 114% | 115% | 109% | 148% | 134% | 143% | 130% | 94% | 105% | 86% | 101% | | |
| Erythromycin | 105% | 111% | 105% | 112% | 125% | 124% | 114% | 110% | 117% | 139% | 220% | 164% | 206% | 106% | 116% | 99% | 119% | | |
| Erythromycin-H2O | 123% | 100% | 114% | 106% | 85% | 96% | 92% | 82% | 70% | 35% | 53% | 51% | 57% | 101% | 95% | 80% | 78% | | |
| Fluconazole | 98% | 110% | 96% | 106% | 117% | 119% | 112% | 111% | 107% | 126% | 122% | H.bckg | 116% | 100% | 106% | 96% | 104% | | |
| Fluoxetine | 140% | 121% | 145% | 110% | 121% | 117% | 113% | 121% | 107% | 115% | 115% | 119% | 111% | 113% | 116% | 103% | 98% | | |
| Furosemide | 121% | 116% | 123% | 110% | 97% | 129% | 120% | 153% | 124% | 146% | 128% | 164% | 133% | 112% | 122% | 109% | 105% | | |
| Gabapentin | 110% | 106% | 105% | 111% | 120% | 117% | 119% | 106% | 103% | 67% | 59% | 61% | 69% | 97% | 118% | 92% | 95% | | |
| Hydrochlorothiazide | 105% | 111% | 109% | 107% | 116% | 117% | 106% | 103% | 107% | 124% | 126% | 111% | 117% | 100% | 105% | 106% | 99% | | |

LEGEND: **Bold compound name** – matching isotope labeled internal standard was used for quantification
Regular compound name – other than matching isotope labeled internal standard used for quantification

H.bckg – too high background compared to spiked 1000 ng/L

table continues

Table S9. Relative recoveries determined by spiking 1000 ng/L (continued)

| | Matrix: | | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|----------------------------------|-------------------------|--------|--------|--------|--------|--------|-------------|--------|--------|--------|--------|--------|--------|--------|------|---------|------|----------|----|
| | Sample dilution factor: | | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| Ifosfamide | 101% | 122% | 103% | 120% | 109% | 120% | 111% | 104% | 107% | 128% | 129% | 152% | 130% | 107% | 106% | 105% | 104% | | |
| Indometacin | 100% | 111% | 105% | 110% | 112% | 118% | 111% | 107% | 108% | 145% | 144% | 138% | 132% | 101% | 107% | 100% | 105% | | |
| Iohexol | 98% | 121% | 116% | 114% | 141% | 114% | 134% | 96% | 90% | 98% | 162% | 99% | 126% | 113% | 93% | 85% | 97% | | |
| Iomeprol | H.bckg | 114% | H.bckg | 103% | H.bckg | H.bckg | 271% | H.bckg | H.bckg | H.bckg | 120% | H.bckg | 124% | 111% | 119% | 121% | 116% | | |
| Iopamidol | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | 136% | H.bckg | 108% | | |
| Iopromide | H.bckg | 132% | H.bckg | 139% | H.bckg | 45% | 116% | H.bckg | 133% | H.bckg | >300% | H.bckg | 176% | 126% | 121% | 125% | 130% | | |
| Ioxitalamic acid | H.bckg | 107% | H.bckg | 158% | H.bckg | H.bckg | 84% | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | H.bckg | 84% | 75% | 114% | 59% | | |
| Levetiracetam | 116% | 111% | 100% | 109% | 118% | 111% | 112% | 126% | 115% | 61% | 55% | 61% | 59% | 97% | 104% | 97% | 105% | | |
| Lidocaine | 101% | 106% | 102% | 102% | H.bckg | 132% | 127% | 99% | 102% | 142% | 127% | 132% | 123% | 100% | 105% | 91% | 103% | | |
| Mefenamic acid | 111% | 119% | 115% | 117% | 124% | 123% | 118% | 123% | 118% | 171% | 141% | 140% | 126% | 105% | 112% | 103% | 101% | | |
| Methylprednisolone | 105% | 106% | 109% | 104% | 119% | 116% | 111% | 103% | 103% | 115% | 121% | 120% | 117% | 90% | 108% | 100% | 97% | | |
| Metoprolol | 108% | 110% | 106% | 107% | 119% | 123% | 105% | 104% | 104% | 120% | 124% | 116% | 114% | 95% | 109% | 96% | 96% | | |
| Metronidazole | 42% | 74% | 43% | 69% | 36% | 63% | 80% | 35% | 70% | 37% | 67% | 18% | 56% | 31% | 79% | 25% | 58% | | |
| Morphine | 113% | 112% | 115% | 118% | 113% | 110% | 113% | <10% | 130% | 106% | 87% | 131% | 91% | 104% | 106% | 107% | 99% | | |
| N4-Acetylsulfamethoxazole | 104% | 113% | 109% | 114% | 117% | 109% | 105% | 98% | 103% | 119% | 124% | 116% | 115% | 105% | 101% | 104% | 98% | | |
| Naproxen | 49% | 43% | 45% | 42% | 28% | 77% | 61% | 31% | 69% | 27% | 56% | 35% | 55% | 49% | 67% | 64% | 75% | | |
| Norfloxacin | 110% | 152% | 104% | 139% | 183% | 120% | 143% | 113% | 108% | 98% | 125% | 95% | 130% | 108% | 121% | 81% | 106% | | |
| Oseltamivir | 231% | 165% | 223% | 147% | 242% | 180% | 152% | 193% | 146% | 265% | 166% | 199% | 150% | 136% | 123% | 142% | 119% | | |
| Oseltamivir carboxylate | 129% | 124% | 135% | 122% | 144% | 122% | 111% | 140% | 116% | 108% | 105% | 107% | 91% | 102% | 100% | 107% | 90% | | |
| Oxazepam | 106% | 108% | 106% | 103% | 106% | 106% | 114% | 100% | 101% | 119% | 117% | 114% | 114% | 96% | 96% | 93% | 95% | | |
| Paracetamol | 88% | 121% | 100% | 119% | 121% | 123% | 120% | 116% | 111% | 107% | 105% | 97% | 96% | 97% | 109% | >300% | 120% | | |
| Phenazone | 107% | 108% | 109% | 107% | 127% | 121% | 111% | 110% | 105% | 138% | 125% | 135% | 129% | 96% | 102% | 100% | 102% | | |
| Primidone | 115% | 110% | 113% | 107% | 123% | 114% | 108% | 109% | 107% | 119% | 113% | 99% | 113% | 100% | 102% | 95% | 95% | | |
| Propranolol | 116% | 125% | 116% | 125% | 138% | 126% | 128% | 132% | 124% | 144% | 140% | 124% | 123% | 112% | 108% | 100% | 107% | | |
| Ranitidine | 126% | 133% | 120% | 129% | 121% | 124% | 118% | 124% | 124% | 137% | 117% | 132% | 112% | 113% | 117% | 102% | 110% | | |
| Ritalinic acid | 113% | 124% | 119% | 127% | 132% | 116% | 116% | 106% | 105% | 112% | 117% | 110% | 108% | 116% | 113% | 109% | 105% | | |
| Ritonavir | 108% | 119% | 110% | 118% | 129% | 127% | 115% | 119% | 115% | 148% | 129% | 133% | 139% | 114% | 131% | 98% | 109% | | |
| Roxithromycin | 126% | 121% | 125% | 118% | 144% | 126% | 128% | 107% | 90% | 76% | 113% | 128% | 121% | 125% | 131% | 117% | 129% | | |
| Sotalol | 109% | 109% | 110% | 108% | 114% | 117% | 105% | 113% | 104% | 115% | 103% | 112% | 101% | 102% | 102% | 99% | 104% | | |

LEGEND: **Bold compound name** – matching isotope labeled internal standard was used for quantification
Regular compound name – other than matching isotope labeled internal standard used for quantification

H.bckg – too high background compared to spiked 1000 ng/L

table continues

Table S9. Relative recoveries determined by spiking 1000 ng/L (continued)

| | Matrix: SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|-------------------------|--------------|------|------|------|-------------|------|------|--------|------|------|------|------|------|---------|------|----------|------|
| | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| Sulfadiazine | 115% | 111% | 110% | 112% | 120% | 121% | 111% | 115% | 110% | 136% | 123% | 199% | 125% | 93% | 101% | 101% | 106% |
| Sulfamethoxazole | 104% | 107% | 107% | 106% | 107% | 114% | 109% | H.bckg | 102% | 121% | 116% | 171% | 118% | 102% | 106% | 96% | 100% |
| Sulfapyridine | 130% | 111% | 124% | 106% | 148% | 124% | 104% | 135% | 109% | 159% | 118% | 199% | 110% | 131% | 91% | 100% | 113% |
| Thiopental | 133% | 98% | 132% | 101% | 42% | 71% | 84% | 29% | 54% | 46% | 80% | 22% | 44% | 56% | 88% | 26% | 69% |
| Tramadol | 113% | 113% | 113% | 110% | 123% | 119% | 115% | 115% | 111% | 129% | 113% | 111% | 109% | 104% | 109% | 109% | 99% |
| Trimethoprim | 111% | 120% | 121% | 119% | 122% | 127% | 128% | 114% | 116% | 139% | 120% | 109% | 112% | 110% | 120% | 104% | 101% |
| Valsartan | 111% | 112% | 109% | 111% | 121% | 117% | 109% | 116% | 108% | 134% | 126% | 127% | 122% | 103% | 105% | 102% | 101% |
| Venlafaxin | 111% | 113% | 113% | 108% | 118% | 115% | 109% | 112% | 106% | 129% | 113% | 112% | 105% | 107% | 108% | 87% | 96% |
| Verapamil | 111% | 115% | 114% | 114% | 125% | 123% | 117% | 109% | 111% | 88% | 122% | 120% | 129% | 108% | 116% | 96% | 107% |

LEGEND: **Bold compound name** – matching isotope labeled internal standard was used for quantification
 Regular compound name – other than matching isotope labeled internal standard used for quantification

H.bckg – too high background compared to spiked 1000 ng/L

Table S10. Estimated limits of quantification, LOQ, in ng/L (campaign August 2009). Sample matrices are described in Table S8

| Matrix: | NANOPURE | SP-1 | | SP-2 | | SP-3 & SP-7 | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | | | |
|------------------------------------|------------|-------------------|--------------------|-------------------|--------------------|-------------|-------------------|-------|-------------------|-------------------|------|------------------|--------------------|------------------|-------------------|----------|-------------------|-------|-----|
| | water | | | | | | | | | | | | | | | | | | |
| Sample dilution factor: | - | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 | |
| 4-Acetamidoantipyrin_F1 | 1 | | 500 ^a | | 500 ^a | | 50 ^a | 220 | | 33 | 3 | 17 | 3 | 18 | 28 | 180 | 50 ^a | 19 | |
| 4-Acetamidoantipyrin_F2 | 5 | | 1000 ^a | | 1000 ^a | | 200 ^a | 1100 | | 170 | 14 | 86 | 12 | 91 | 140 | 910 | 100 ^a | 93 | |
| 4-Aminoantipyrin_F1 | 250 | | 22000 | | 18000 | | 1800 | 18000 | | 3000 ^a | 140 | 2400 | 800 ^a | | 1500 | 18000 | 1000 ^a | 6900 | |
| 4-Aminoantipyrin_F2 | 500 | | 47000 | | 34000 | | 3600 | 39000 | | 5000 ^a | 290 | 5300 | 2000 ^a | | 3000 | 39000 | 3500 ^a | 13000 | |
| 4-Dimethylaminoantipyrin_F1 | 50 | 140 | 2600 | 150 | 2200 | 7 | 200 | 2900 | 200 ^a | 2700 | 8 | 290 | 200 ^a | 2700 | 140 | 3100 | 85 | 250 | |
| 4-Dimethylaminoantipyrin_F2 | 250 | 650 | 12000 | 720 | 11000 | 35 | 1000 | 14000 | 1000 ^a | 12000 | 36 | 1500 | 1000 ^a | 23000 | 710 | 15000 | 430 | 1300 | |
| 4-Formylaminoantipyrin_F2 | 5 | | 1000 | | 1000 | | 110 | 970 | | 130 | 10 | 75 | 11 | 82 | 98 | 790 | 50 ^a | 91 | |
| 4-Formylaminoantipyrin_F3 | 1 | | 210 | | 200 | | 21 | 200 | | 27 | 2 | 15 | 2 | 16 | 20 | 160 | 20 ^a | 18 | |
| 4-Methylaminoantipyrin_F1 | 500 | | 9700 | | 5400 | | 4100 | 19000 | | 500 ^a | 240 | 2000 | 2000 ^a | 26000 | 500 ^a | 14000 | 1000 ^a | 2300 | |
| 4-Methylaminoantipyrin_F2 | 2500 | | 52000 | | 28000 | | 21000 | 90000 | | 2000 ^a | 1100 | 11000 | 10000 ^a | | 2500 ^a | | 2000 ^a | 21000 | |
| 4/5-Methyl-Benzotriazole_F1 | 5 | | 10000 ^a | | 10000 ^a | | 1000 ^a | 480 | | 76 | | 300 ^a | | 300 ^a | 69 | 590 | | 63 | |
| 4/5-Methyl-Benzotriazole_F2 | 5 | | 10000 ^a | | 10000 ^a | | 1000 ^a | 480 | | 74 | | 300 ^a | | 300 ^a | 68 | 580 | | 63 | |
| Atenolol_F1 | 10 | 44 | 700 | 49 | 680 | 3 | 58 | 770 | 3 | 76 | 2 | 64 | 2 | 66 | 56 | 800 | 3 | 66 | |
| Atenolol_F2 | 25 | 110 | 1800 | 120 | 1700 | 7 | 150 | 1900 | 8 | 190 | 5 | 160 | 5 | 170 | 140 | 1900 | 7 | 170 | |
| Atenolol-acid_F1 | 5 | 19 | 280 | 19 | 290 | | 25 | 300 | 2 | 31 | 1 | 27 | 1 | 25 | 18 | 360 | 1 | 29 | |
| Atenolol-acid_F2 | 25 | 96 | 1400 | 100 | 1500 | | 130 | 1500 | 9 | 160 | 6 | 140 | 5 | 130 | 93 | 1900 | 5 | 150 | |
| Azithromycin_F1 | 5 | 50 ^a | 2100 | 50 ^a | 2000 | 9 | 40 ^a | 1800 | 13 | 190 | 28 | 150 | 30 | 160 | 150 | 1200 | 7 | 110 | |
| Azithromycin_F2 | 5 | 50 ^a | 2100 | 50 ^a | 2100 | 9 | 40 ^a | 1800 | 13 | 210 | 29 | 160 | 29 | 160 | 150 | 1200 | 8 | 210 | |
| Benzotriazole_F1 | 50 | 1000 ^a | 7000 | 1000 ^a | 7900 | | 630 | 5800 | | 860 | | 630 | | 860 | 810 | 6800 | | 730 | |
| Benzotriazole_F2 | 50 | 1000 ^a | 7100 | 1000 ^a | 8100 | | 650 | 5600 | | 850 | | 660 | | 850 | 820 | 6600 | | 740 | |
| Bezafibrate_F1 | 1 | 16 | 130 | 14 | 140 | 2 | 12 | 120 | 1 | 13 | 1 | 13 | 2 | 15 | 12 | 98 | 2 | 11 | |
| Bezafibrate_F2 | 1 | 16 | 130 | 14 | 140 | 2 | 12 | 120 | 1 | 13 | 1 | 13 | 2 | 15 | 12 | 97 | 2 | 11 | |
| Carbamazepine_F1 | 1 | 23 | 180 | 20 | 170 | 2 | 16 | 160 | 2 | 18 | 2 | 13 | 2 | 14 | 15 | 130 | 2 | 14 | |
| Carbamazepine_F2 | 1 | 23 | 180 | 20 | 167 | 2 | 15 | 160 | 2 | 18 | 2 | 13 | 2 | 14 | 15 | 130 | 2 | 14 | |
| Cilastatin_F1 | 25 | 77 | 1100 | 81 | 1200 | 6 | 90 | 1100 | 8 | 120 | 7 | 110 | 8 | 110 | 85 | 1200 | 7 | 110 | |
| Cilastatin_F2 | 25 | 74 | 1100 | 78 | 1200 | 6 | 90 | 1100 | 8 | 120 | 7 | 110 | 7 | 110 | 83 | 1200 | 7 | 100 | |
| Ciprofloxacin_F1 | 50 | | 3500 | | 3500 | | 300 ^a | 3100 | | 18 | 220 | 16 | 150 | 22 | 150 | 150 | 1500 | 18 | 200 |
| Ciprofloxacin_F2 | 100 | | 7000 | | 6700 | | 700 ^a | 6500 | | 37 | 450 | 31 | 300 | 40 | 310 | 300 | 2900 | 35 | 380 |

LEGEND: Bold transition_F1 – quantifier
Regular transition_F2 – qualifier

100 - dilution factor used for quantification
310 - dilution factor rarely used for quantification

^a – values estimated from signal-to-noise ratio of an unspiked sample
table continues

Table S10. Estimated limits of quantification (LOQs) in ng/L (continued)

| Matrix: | NANOPURE | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|-------------------------|----------|------|-------------------|------|-------------------|-------------|-------------------|-------|------------------|-------------------|------|-------------------|------------------|-------------------|---------|-------|-------------------|------|
| | water | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| Sample dilution factor: | - | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| Clarithromycin_F1 | 1 | 29 | 300 | 29 | 300 | 2 | 24 | 280 | 2 | 33 | 3 | 26 | 2 | 27 | 23 | 180 | 2 | 21 |
| Clarithromycin_F2 | 1 | 29 | 300 | 29 | 300 | 2 | 24 | 270 | 2 | 33 | 3 | 25 | 2 | 27 | 23 | 180 | 2 | 21 |
| Clindamycin_CI | 5 | 40 | 670 | 45 | 740 | 51 | 680 | | 3 | 73 | 2 | 56 | 2 | 56 | 39 | 550 | 2 | 48 |
| Clindamycin_F1 | 5 | 40 | 670 | 44 | 730 | 51 | 690 | | 3 | 73 | 2 | 56 | 2 | 56 | 38 | 550 | 2 | 48 |
| Clofibrinsäure_CI | 5 | 71 | 480 | 65 | 480 | 8 | 46 | 440 | 8 | 54 | 16 | 50 | 12 | 55 | 57 | 430 | 9 | 49 |
| Clofibrinsäure_F1 | 5 | 65 | 470 | 57 | 480 | 8 | 46 | 450 | 8 | 56 | 14 | 49 | 10 | 53 | 51 | 420 | 9 | 47 |
| Cyclophosphamid_F1 | 5 | 110 | 1000 | 110 | 980 | 11 | 90 | 930 | 11 | 110 | 9 | 83 | 13 | 86 | 84 | 710 | 10 | 83 |
| Cyclophosphamid_F2 | 5 | 120 | 980 | 110 | 970 | 11 | 93 | 960 | 12 | 110 | 10 | 80 | 13 | 86 | 84 | 740 | 10 | 82 |
| D617_F1 | 1 | 25 | 50 ^a | 25 | 50 ^a | 2 | 27 | 340 | 2 | 33 | 2 | 24 | 2 | 26 | 16 | 220 | 1 | 21 |
| D617_F2 | 1 | 26 | 50 ^a | 26 | 50 ^a | 2 | 28 | 350 | 2 | 34 | 2 | 26 | 2 | 27 | 17 | 240 | 1 | 22 |
| Dexamethason_F1 | 5 | 130 | 890 | 120 | 920 | 17 | 86 | 840 | 15 | 95 | 13 | 84 | 17 | 109 | 92 | 640 | 14 | 75 |
| Dexamethason_F2 | 5 | 140 | 890 | 120 | 890 | 17 | 82 | 780 | 15 | 91 | 12 | 83 | 17 | 108 | 92 | 640 | 14 | 74 |
| Diatrizoate-NH4_F1 | 250 | | 5000 ^a | | 5000 ^a | | 5000 ^a | | | 3000 ^a | | 3000 ^a | | 3000 ^a | 2700 | 24000 | 1000 ^a | 2800 |
| Diatrizoate-NH4_F2 | 250 | | 5000 ^a | | 5000 ^a | | 5000 ^a | | | 3000 ^a | | 3000 ^a | | 3000 ^a | 2700 | 24000 | 1000 ^a | 2900 |
| Diazepam_F1 | 1 | 23 | 180 | 22 | 180 | 2 | 15 | 160 | 2 | 18 | 2 | 15 | 2 | 16 | 19 | 140 | 2 | 17 |
| Diazepam_F2 | 1 | 23 | 180 | 22 | 180 | 2 | 16 | 160 | 2 | 18 | 2 | 15 | 2 | 16 | 19 | 140 | 2 | 16 |
| Diclofenac_CI | 1 | 25 | 140 | 21 | 150 | 3 | 12 | 130 | 3 | 15 | 2 | 15 | 4 | 18 | 27 | 130 | 15 ^a | 15 |
| Diclofenac_F1 | 1 | 24 | 140 | 21 | 150 | 3 | 12 | 120 | 3 | 15 | 2 | 15 | 4 | 18 | 27 | 120 | 15 ^a | 15 |
| Erythromycin_F1 | 5 | 180 | 1800 | 150 | 2000 | 8 | 160 | 2000 | 12 | 210 | 8 | 91 | 6 | 96 | 140 | 1000 | 9 | 120 |
| Erythromycin_F2 | 5 | 180 | 1700 | 160 | 2000 | 10 | 170 | 1900 | 11 | 230 | 8 | 110 | 6 | 92 | 140 | 980 | 8 | 110 |
| Erythromycin-H2O_F1 | 5 | 160 | 1800 | 180 | 1700 | 28 | 140 | 3300 | 17 | 220 | 33 | 230 | 24 | 430 | 110 | 1000 | 11 | 120 |
| Erythromycin-H2O_F2 | 5 | 160 | 1900 | 180 | 1800 | 13 | 150 | 1500 | 17 | 220 | 29 | 240 | 22 | 210 | 110 | 1100 | 12 | 120 |
| Fluconazol_F1 | 5 | 68 | 530 | 67 | 550 | | 48 | 500 | 6 | 59 | | 46 | | 51 | 63 | 540 | 7 | 55 |
| Fluconazol_F2 | 5 | 68 | 530 | 67 | 540 | | 48 | 500 | 6 | 57 | | 46 | | 50 | 62 | 530 | 7 | 55 |
| Fluoxetin_F1 | 1 | 28 | 310 | 30 | 320 | 2 | 23 | 270 | 3 | 31 | 2 | 21 | 2 | 21 | 18 | 180 | 2 | 19 |
| Fluoxetin_F3 | 25 | 700 | 7500 | 700 | 8300 | 49 | 570 | 6400 | 59 | 730 | 51 | 540 | 52 | 560 | 500 | 4300 | 45 | 490 |
| Furosemid_CI | 5 | 51 | 480 | 50 | 500 | | 42 | 430 | 5 | 46 | 4 | 46 | 4 | 47 | 52 | 450 | 7 | 54 |
| Furosemid_F1 | 5 | 53 | 500 | 51 | 530 | | 43 | 450 | 4 | 48 | 4 | 47 | 4 | 45 | 54 | 470 | 8 | 53 |
| Gabapentin_F1 | 250 | 590 | 11000 | 680 | 11000 | | 950 | 11000 | 100 ^a | 1100 | | 2000 | 100 ^a | 1600 | 930 | 15000 | 42 | 1500 |
| Gabapentin_F2 | 500 | 1200 | 21000 | 1300 | 21000 | | 1900 | 23000 | 200 ^a | 2100 | | 4700 | 200 ^a | 3300 | 2000 | 33000 | 79 | 2800 |

LEGEND: Bold transition_F1 – quantifier
Regular transition_F2 – qualifier

100 - dilution factor used for quantification
310 - dilution factor rarely used for quantification

^a – values estimated from signal-to-noise ratio of an unspiked sample

table continues

Table S10. Estimated limits of quantification (LOQs) in ng/L (continued)

| Matrix: | NANOPURE | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|-----------------------|----------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|-------------------|-------|-------|------|------|---------|-------|----------|------|
| | water | - | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - |
| Hydrochlorothiazid_F1 | 5 | 69 | 410 | 49 | 420 | 45 | 400 | 12 | 50 | 13 | 53 | 18 | 51 | 81 | 410 | 9 | 60 | |
| Hydrochlorothiazid_F2 | 5 | 65 | 410 | 49 | 420 | 47 | 400 | 12 | 50 | 13 | 52 | 18 | 51 | 81 | 400 | 9 | 59 | |
| Ifosfamid_F1 | 1 | 26 | 190 | 26 | 190 | 3 | 18 | 200 | 3 | 23 | 2 | 16 | 2 | 17 | 17 | 150 | 2 | 17 |
| Ifosfamid_F2 | 1 | 25 | 188 | 26 | 190 | 3 | 18 | 200 | 3 | 23 | 2 | 16 | 2 | 16 | 17 | 150 | 2 | 16 |
| Indometacin_F1 | 1 | 28 | 150 | 21 | 160 | 3 | 13 | 130 | 3 | 15 | 3 | 17 | 5 | 20 | 23 | 120 | 3 | 17 |
| Indometacin_F2 | 1 | 28 | 148 | 21 | 160 | 2 | 13 | 130 | 3 | 15 | 2 | 16 | 5 | 20 | 23 | 130 | 3 | 17 |
| Iohexol_F1 | 100 | 1300 | 12000 | 1200 | 15000 | 170 | 980 | 10000 | 160 | 1400 | 150 | 1200 | 210 | 1300 | 1200 | 8400 | 170 | 1100 |
| Iohexol_F2 | 250 | 3200 | 30000 | 3300 | 49000 | 530 | 2800 | 26000 | 650 | 4400 | 460 | 2800 | 680 | 2700 | 3200 | 24000 | 400 | 3300 |
| Iomeprol_F1 | 100 | 1600 | 13000 ^a | 2000 | 13000 ^a | 14000 ^a | 10000 | 10000 ^a | 960 | 1000 | 1600 | 11000 | 170 | 1200 | | | | |
| Iomeprol_F2 | 250 | 2400 | 30000 ^a | 30000 ^a | 40000 ^a | 27000 | 30000 ^a | 2200 | 2000 | 4000 | 30000 | 860 | 2900 | | | | | |
| Iopamidol_F1 | 250 | 40000 ^a | 40000 ^a | 10000 ^a | 2000 ^a | 2000 ^a | 22 | 5000 ^a | 3000 ^a | | | | | | | | | |
| Iopamidol_F2 | 500 | 40000 ^a | 40000 ^a | 10000 ^a | 2000 ^a | 2000 ^a | 20 | 5000 ^a | 22000 | 3000 ^a | | | | | | | | |
| Iopromid_F1 | 100 | 50000 ^a | 50000 ^a | 7000 ^a | 4500 | 3000 ^a | 3000 ^a | 3000 ^a | 5000 ^a | 10000 | 140 | 1200 | | | | | | |
| Iopromid_F2 | 100 | 50000 ^a | 50000 ^a | 7000 ^a | 4000 | 3000 ^a | 3000 ^a | 3000 ^a | 5000 ^a | 9100 | 130 | 1100 | | | | | | |
| Ioxitalaminsäure_F1 | 250 | 20000 ^a | 20000 ^a | 5000 ^a | 3000 ^a | 3000 ^a | 130 | 2100 | 24000 | 1000 ^a | 2700 | | | | | | | |
| Ioxitalaminsäure_F2 | 500 | 20000 ^a | 20000 ^a | 5000 ^a | 3000 ^a | 3000 ^a | 200 | 3500 | 26000 | 100 ^a | 3300 | | | | | | | |
| Levetiracetam_F1 | 10 | 1000 ^a | 2000 | 1000 ^a | 1800 | 24 | 180 | 1800 | 23 | 210 | 42 | 300 | 43 | 260 | 150 | 1400 | 22 | 150 |
| Levetiracetam_F2 | 100 | 5000 ^a | 20000 | 5000 ^a | 9000 | 250 | 1900 | 18000 | 250 | 2100 | 320 | 2600 | 400 | 2600 | 1500 | 14000 | 180 | 1500 |
| Lidocaine_F1 | 5 | 48 | 780 | 55 | 800 | 64 | 760 | 5 | 82 | 3 | 64 | 3 | 59 | 31 | 750 | 3 | 52 | |
| Lidocaine_F2 | 25 | 120 | 1900 | 140 | 1900 | 150 | 1900 | 11 | 200 | 7 | 160 | 8 | 150 | 78 | 1900 | 7 | 130 | |
| Mefenaminsäure_F1 | 1 | 35 | 110 | 21 | 130 | 1 | 9 | 97 | 2 | 11 | 2 | 13 | 2 | 14 | 29 | 120 | 3 | 19 |
| Mefenaminsäure_F2 | 1 | 34 | 110 | 21 | 130 | 1 | 9 | 95 | 2 | 11 | 2 | 13 | 2 | 14 | 29 | 110 | 2 | 18 |
| Methylprednisolon_F1 | 5 | 140 | 890 | 120 | 910 | 15 | 79 | 800 | 11 | 88 | 11 | 84 | 13 | 130 | 97 | 650 | 13 | 74 |
| Methylprednisolon_F2 | 5 | 140 | 880 | 120 | 890 | 15 | 78 | 780 | 12 | 85 | 11 | 81 | 15 | 120 | 180 | 670 | 13 | 73 |
| Metoprolol_F1 | 25 | 230 | 3100 | 250 | 3300 | 15 | 260 | 3300 | 18 | 340 | 14 | 260 | 13 | 260 | 190 | 2300 | 15 | 250 |
| Metoprolol_F2 | 25 | 230 | 3200 | 250 | 3300 | 16 | 260 | 3200 | 18 | 340 | 14 | 250 | 13 | 270 | 180 | 2300 | 15 | 240 |
| Metronidazol_F1 | 25 | 220 | 2100 | 220 | 2200 | 190 | 2000 | 23 | 220 | 30 ^a | 230 | 23 | 240 | 280 | 2300 | 24 | 240 | |
| Metronidazol_F2 | 25 | 220 | 2100 | 220 | 2200 | 190 | 2000 | 22 | 220 | 30 ^a | 240 | 22 | 230 | 270 | 2300 | 24 | 240 | |
| Morphine_F1 | 25 | 100 | 1400 | 100 | 1400 | 6 | 140 | 1600 | 3000 ^a | 450 | 7 | 180 | 7 | 180 | 92 | 1900 | 4 | 140 |
| Morphine_F2 | 100 | 370 | 5400 | 400 | 5500 | 21 | 5509 | 6200 | 10000 ^a | 1900 | 28 | 710 | 26 | 710 | 340 | 7300 | 15 | 550 |

LEGEND: Bold transition_F1 – quantifier
Regular transition_F2 – qualifier

100 - dilution factor used for quantification
310 - dilution factor rarely used for quantification

^a – values estimated from signal-to-noise ratio of an unspiked sample

table continues

Table S10. Estimated limits of quantification (LOQs) in ng/L (continued)

| Matrix: | NANOPURE water | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | |
|--------------------------------------|-------------------------|--------------------|--------------------|--------------------|--------|-------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------|-------|---------|-------|----------|------|
| | Sample dilution factor: | - | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - |
| N4-Acetyl-Sulfamethoxazole_F1 | 1 | 15 | 130 | 15 | 120 | 2 | 14 | 140 | 2 | 16 | 1 | 11 | 2 | 13 | 12 | 120 | 2 | 12 |
| N4-Acetyl-Sulfamethoxazole_F2 | 1 | 15 | 130 | 15 | 120 | 2 | 14 | 130 | 2 | 16 | 1 | 11 | 2 | 13 | 12 | 110 | 2 | 13 |
| Naproxen_F1 | 100 | 5600 | 67000 | 6200 | 70000 | 680 | 3400 | 46000 | 680 | 4600 | 860 | 5800 | 490 | 5900 | 4600 | 27000 | 240 | 2900 |
| Naproxen_F2 | 250 | 50000 ^a | 210000 | 50000 ^a | 200000 | 9900 | 120000 | 5000 ^a | 10000 | 5000 ^a | 5000 ^a | 5000 ^a | 9300 | 61000 | 830 | 7600 | | |
| Norfloxacin_F1 | 500 | 1900 | 28000 | 1400 | 25000 | 1200 | 27000 | 150 | 1800 | 150 | 1200 | 190 | 1200 | 1100 | 11000 | 150 | 1300 | |
| Norfloxacin_F2 | 500 | 970 | 16000 | 720 | 16000 | 700 | 17000 | 82 | 970 | 65 | 670 | 97 | 690 | 770 | 7600 | 86 | 860 | |
| Oseltamivire_carboxylat_F1 | 25 | 32 | 160 | 34 | 170 | 1 | 15 | 200 | 1 | 18 | 1 | 19 | 1 | 20 | 11 | 290 | 1 | 20 |
| Oseltamivire_carboxylat_F2 | 50 | 44 | 790 | 47 | 840 | 3 | 73 | 980 | 4 | 89 | 4 | 93 | 4 | 100 | 52 | 1400 | 3 | 100 |
| Oseltamivire_F1 | 5 | 20 ^a | 690 | 20 ^a | 760 | 3 | 10 ^a | 710 | 3 | 73 | 3 | 57 | 2 | 56 | 36 | 540 | 2 | 49 |
| Oseltamivire_F2 | 5 | 20 ^a | 690 | 20 ^a | 740 | 3 | 10 ^a | 720 | 3 | 73 | 3 | 56 | 2 | 55 | 36 | 540 | 2 | 48 |
| Oxazepam_F1 | 1 | 12 | 110 | 12 | 120 | 1 | 10 | 95 | 1 | 11 | 1 | 10 | 1 | 10 | 13 | 110 | 1 | 12 |
| Oxazepam_F2 | 5 | 61 | 550 | 58 | 580 | 6 | 51 | 470 | 5 | 55 | 5 | 50 | 5 | 51 | 63 | 570 | 7 | 59 |
| Paracetamol_F1 | 50 | 8300 | 8000 ^a | 130 | 790 | 7100 | 220 | 1000 | 120 | 780 | 190 | 860 | 7100 | 140 | 770 | | | |
| Paracetamol_F2 | 250 | 43000 | 40000 ^a | 840 | 4700 | 40000 | 1000 ^a | 5600 | 1000 ^a | 4700 | 1000 ^a | 4400 | 33000 | 1100 | 4200 | | | |
| Phenazone_F1 | 5 | 92 | 730 | 93 | 750 | 9 | 66 | 660 | 10 | 86 | 8 | 58 | 12 | 69 | 80 | 620 | 9 | 67 |
| Phenazone_F2 | 5 | 95 | 760 | 96 | 770 | 9 | 67 | 680 | 11 | 88 | 8 | 60 | 12 | 71 | 83 | 650 | 9 | 68 |
| Primidone_F1 | 5 | 77 | 650 | 75 | 650 | 9 | 57 | 600 | 10 | 68 | 8 | 54 | 13 | 64 | 70 | 580 | 10 | 59 |
| Primidone_F2 | 10 | 160 | 1300 | 160 | 1300 | 18 | 120 | 1200 | 20 | 140 | 16 | 110 | 28 | 130 | 150 | 1100 | 21 | 120 |
| Propranolol_F1 | 5 | 14 ^a | 170 | 14 ^a | 170 | 8 | 13 ^a | 160 | 10 | 170 | 8 | 130 | 7 | 120 | 90 | 1100 | 7 | 110 |
| Propranolol_F2 | 5 | 13 ^a | 160 | 13 ^a | 170 | 8 | 13 ^a | 160 | 9 | 160 | 8 | 130 | 7 | 120 | 88 | 1100 | 7 | 110 |
| Ranitidin_F1 | 10 | 34 | 590 | 40 | 500 | 3 | 49 | 670 | 3 | 61 | 2 | 52 | 2 | 63 | 21 | 590 | 2 | 41 |
| Ranitidin_F2 | 10 | 34 | 600 | 39 | 550 | 3 | 48 | 690 | 3 | 63 | 2 | 51 | 2 | 62 | 21 | 570 | 2 | 40 |
| Ritalinic-acid_F1 | 5 | 10 | 160 | 11 | 160 | 1 | 16 | 190 | 1 | 20 | 1 | 17 | 1 | 17 | 9 | 260 | 1 | 18 |
| Ritalinic-acid_F2 | 10 | 20 | 310 | 21 | 330 | 1 | 32 | 380 | 2 | 39 | 2 | 34 | 1 | 34 | 18 | 520 | 1 | 34 |
| Ritonavir_F1 | 1 | 42 | 230 | 32 | 250 | 3 | 21 | 230 | 3 | 26 | 3 | 18 | 4 | 20 | 34 | 160 | 4 | 18 |
| Ritonavir_F2 | 1 | 41 | 230 | 31 | 250 | 3 | 20 | 210 | 3 | 27 | 3 | 18 | 3 | 18 | 34 | 150 | 4 | 18 |
| Roxithromycin_F1 | 1 | 100 ^a | 270 | 100 ^a | 280 | 1 | 60 ^a | 250 | 2 | 41 | 3 | 33 | 2 | 31 | 19 | 160 | 2 | 20 |
| Roxithromycin_F2 | 1 | 100 ^a | 290 | 100 ^a | 300 | 2 | 60 ^a | 280 | 2 | 44 | 4 | 34 | 2 | 33 | 21 | 170 | 2 | 21 |
| Sotalolol_F1 | 25 | 91 | 1600 | 98 | 1600 | 7 | 140 | 1800 | 7 | 190 | 5 | 150 | 5 | 160 | 120 | 1900 | 6 | 140 |
| Sotalolol_F2 | 10 | 36 | 640 | 40 | 610 | 3 | 56 | 700 | 3 | 71 | 2 | 62 | 2 | 63 | 48 | 730 | 2 | 56 |

LEGEND: Bold transition_F1 – quantifier
Regular transition_F2 – qualifier

100 - dilution factor used for quantification
310 - dilution factor rarely used for quantification

^a – values estimated from signal-to-noise ratio of an unspiked sample

table continues

Table S10. Estimated limits of quantification (LOQs) in ng/L (continued)

| | Matrix: NANOPURE water | | | | | | | | | | | | | | | | | |
|----------------------------|---|-----------------|------------------|-----------------|------------------------|----|-----------------|-------------|----------------|-------------|----------------|-------------|----|----------------|-----------------|-----------------|----------------|-----|
| | SP-1 | | SP-2 | | SP-3 & SP-7 | | | SP-4 | | SP-5 | | SP-6 | | WWTP-in | | WWTP-eff | | |
| Sample dilution factor: | - | 10 | 100 | 10 | 100 | - | 10 | 100 | - | 10 | - | 10 | - | 10 | 10 | 100 | - | 10 |
| Sulfadiazine_F1 | 1 | 19 | 160 | 19 | 160 | 2 | 16 | 140 | 2 | 20 | 2 | 13 | 3 | 14 | 22 | 120 | 3 | 16 |
| Sulfadiazine_F2 | 5 | 97 | 790 | 98 | 790 | 12 | 80 | 710 | 11 | 100 | 9 | 67 | 16 | 70 | 95 | 580 | 14 | 79 |
| Sulfamethoxazole_F1 | 5 | 90 | 800 | 91 | 800 | | 77 | 770 | | 100 | 8 | 60 | 15 | 76 | 86 | 680 | 12 | 78 |
| Sulfamethoxazole_F2 | 5 | 89 | 800 | 93 | 800 | | 77 | 770 | | 100 | 8 | 59 | 14 | 75 | 86 | 680 | 12 | 78 |
| Sulfapyridin_F1 | 5 | 81 | 760 | 82 | 780 | 10 | 73 | 730 | 9 | 94 | 7 | 66 | 16 | 74 | 73 | 660 | 13 | 71 |
| Sulfapyridin_F2 | 10 | 160 | 1500 | 160 | 1500 | 18 | 140 | 1400 | 17 | 190 | 14 | 130 | 30 | 140 | 140 | 1300 | 26 | 140 |
| Thiopental_F1 | 5 | 70 | 530 | 63 | 540 | 22 | 67 | 530 | 22 | 84 | 28 | 71 | 51 | 130 | 92 | 470 | 28 | 64 |
| Thiopental_F2 | only one measurable transition for Thiopental (negative ESI mode) | | | | | | | | | | | | | | | | | |
| Tramadol_F1 | 5 | 50 | 570 | 52 | 580 | 3 | 47 | 550 | 3 | 58 | 3 | 47 | 2 | 46 | 24 | 430 | 2 | 34 |
| Tramadol_F2 | 25 | 240 | 2800 | 260 | 2800 | 16 | 230 | 2800 | 16 | 290 | 14 | 230 | 11 | 230 | 130 | 2200 | 9 | 170 |
| Trimethoprim_F1 | 25 | 210 | 2500 | 200 | 2600 | 14 | 230 | 2400 | 16 | 290 | 13 | 250 | 13 | 220 | 150 | 1800 | 13 | 230 |
| Trimethoprim_F2 | 25 | 210 | 2800 | 220 | 2700 | 15 | 250 | 2400 | 16 | 300 | 13 | 260 | 13 | 220 | 170 | 1900 | 14 | 250 |
| Valsartan_F1 | 1 | 17 | 130 | 12 | 130 | 1 | 11 | 120 | 1 | 13 | 1 | 11 | 1 | 13 | 16 | 110 | 1 | 12 |
| Valsartan_F2 | 1 | 17 | 130 | 12 | 130 | 1 | 11 | 120 | 1 | 13 | 1 | 11 | 1 | 13 | 16 | 110 | 2 | 12 |
| Venlafaxin_F1 | 5 | 110 | 400 ^a | 110 | 400 ^a | 7 | 99 | 1200 | 7 | 120 | 6 | 100 | 5 | 95 | 55 | 740 | 5 | 74 |
| Venlafaxin_F2 | 5 | 110 | 400 ^a | 110 | 400 ^a | 7 | 100 | 1300 | 7 | 130 | 7 | 100 | 6 | 100 | 56 | 760 | 5 | 78 |
| Verapamil_F1 | 5 | 19 ^a | 180 | 18 ^a | 180 | 5 | 16 ^a | 180 | 5 ^a | 15 | 5 ^a | 16 | 15 | 20 | 20 ^a | 200 | 5 ^a | 20 |
| Verapamil_F2 | 5 | 19 ^a | 180 | 18 ^a | 190 | 5 | 16 ^a | 170 | 5 ^a | 15 | 5 ^a | 16 | 15 | 20 | 20 ^a | 200 | 5 ^a | 20 |

LEGEND: **Bold transition_F1** – quantifier
Regular transition_F2 – qualifier

100 - dilution factor used for quantification
310 - dilution factor rarely used for quantification

^a – values estimated from signal-to-noise ratio of an unspiked sample

Quality of the analytical method

Sensitivity. The sensitivity of the analytical method satisfies or exceeds the requirements of the study for all the analytes with exception of three: dexamethasone, methylprednisolone, and fluoxetine. The LOQs in raw hospital wastewater for the three compounds were 127, 137, and 700 ng/L respectively, which in the particular hospital requires their consumption by as many as 20, 80, and 80 patients respectively (which is 6%, 23% and 23% of all hospital patients), calculated assuming average human excretion, defined daily dose (DDD), and the hospital water flow during the sampling campaign. There were additional 8 compounds for which the removal by MBR from the hospital wastewater could not be quantified, although this was caused by very low consumption rather than by high quantification limits of the analytical method. For roxithromycin, sulfapyridine, ifosfamide, iohexol, and clofibric acid the method is capable to quantify amounts in the wastewater excreted by just one patient, while for 4-dimethylaminoantipyrine, naproxen, and diazepam the method can quantify amounts excreted by approximately 2, 3, and 5 patients respectively. Therefore non-detects were due to no or low consumption, rather than insufficient method sensitivity.

Matrix effects. The presented analytical method was developed, validated, and employed not only for raw and MBR-treated hospital wastewater, but also for other aqueous matrices (ozone treated hospital wastewater MBR effluent, activated carbon treated hospital wastewater MBR effluent, UV treated hospital wastewater MBR effluent, municipal wastewater influent/effluent, and biofilter effluent). Limits of quantification for those matrices are presented in Table S10. The matrix causing ion suppression (e.g. for benzotriazole) or ion enhancement (e.g. for atenolol) were both observed and contributed to either sensitivity loss or gain (Table S10). The influence of matrix on the accuracy of the method, as can be seen from Table S9, is minimal for compounds with matching internal standards. Employment of matching internal standards for almost all analytes is next to the high degree of the method automatization its major strength. Compounds for which other internal standards were employed were considerably influenced by the matrix and measured concentrations had to be corrected by recoveries (e.g. clindamycin or metronidazole – see Page S29 “Bias calculation”). All compounds presented in our manuscript have a method quality control label according to the overall analytical uncertainty at 95% confidence level (^a uncertainty less than 14%; ^b uncertainty 15 - 29%; ^c uncertainty 30 - 100%; ^d uncertainty above 100%), determined for all matrices after spiking, which accounts for the worst case matrix effect. The quality control labels, precision and overall uncertainty for all measured compounds are listed in Table S7.

Sample dilution. Dilution of the samples increased the quantification limits of the method, but improved the accuracy by decreasing the background noise. Some compounds, e.g. contrast media and metamizole metabolites, were present in the raw hospital wastewater at levels of hundreds of micrograms per liter. To measure such high concentrations, the samples of the raw wastewater were diluted by a factor of 100, and the calibration curve was extended to 40 µg/L.

3. Pilot-scale membrane bioreactor (MBR)

Table S11. Parameters of nutrient removal in the MBR

| | MBR influent | MBR effluent (permeate) |
|--------------------------|-----------------------------|------------------------------|
| Ammonium | 28 mg NH ₄ -N/L | 0.03 mg NH ₄ -N/L |
| Nitrite | 0.1 mg NO ₂ -N/L | 0.04 mg NO ₂ -N/L |
| Nitrate | 2 mg NO ₃ -N/L | 3.7 mg NO ₃ -N/L |
| Phosphate | 13 mg PO ₄ -P/L | 9 mg PO ₄ -P/L |
| COD _{dissolved} | 380 mg/L | 30 mg/L |
| DOC | 120-130 mg/L | 6-8 mg/L |
| pH | | 8.1-8.5 |

Hydraulic behavior of the MBR

A bromide tracer test was performed to analyze the hydraulic behavior of the pilot plant. The background concentration of bromide at the pilot plant was measured one day before at SP-2. Ammonium bromide was used as tracer, of which 100 g was dissolved in 2 L of drinking water, added into the primary clarifier and stirred. The tracer was added at 9:00 which is the time at which the sampling campaigns for the pharmaceuticals usually started. The samples were taken by automatic ISCO-Sampler at SP-2 and SP-3 and analyzed by HPLC (Agilent 1100) at a fixed wavelength of 220 nm after separation on a UltraSep ES SAX W Ion exchanger column (60 x 3 mm, Sepserv Berlin) using 10 mM H₃PO₄ (pH 3).

The pilot plant was also modeled with ASIM (Activated Sludge SIMulation Program, Holinger AG, Switzerland). The model considers all reactors as ideally mixed reactors (completely stirred reactors, CSTR).

The results of the tracer experiment and the ASIM modeling are well comparable, as shown in Figure S2.

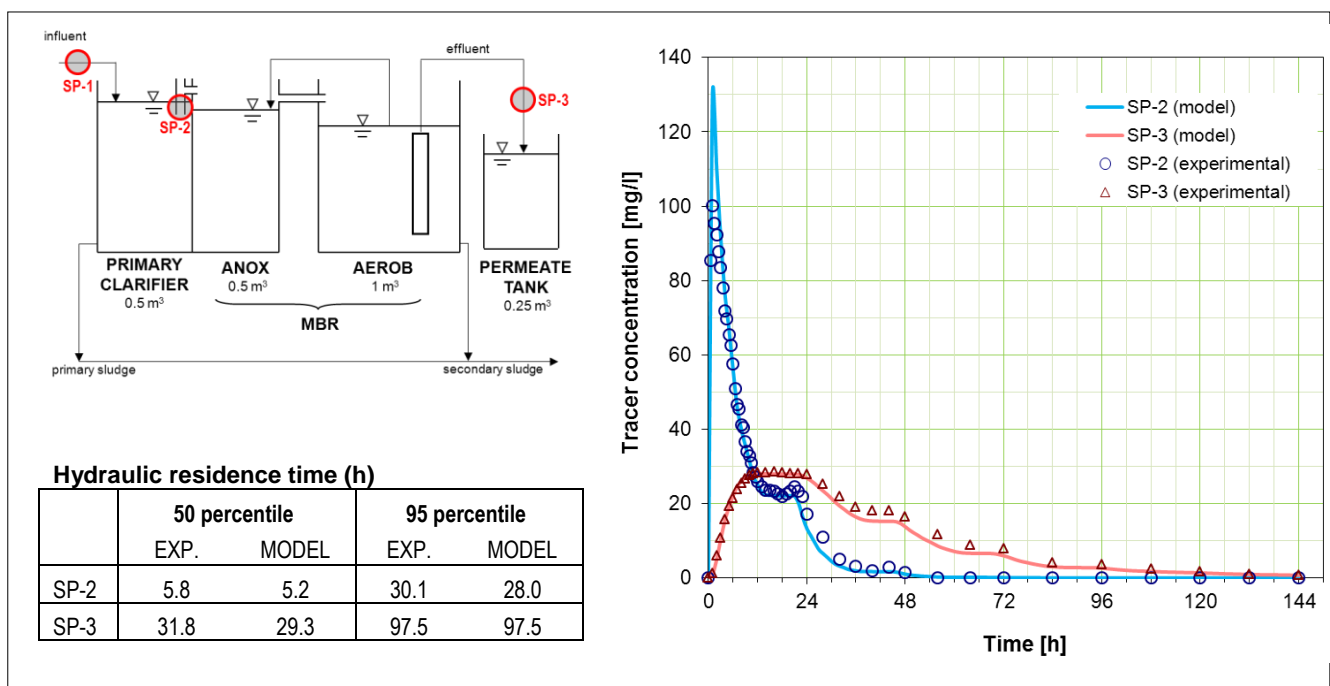


Figure S2. Hydraulic behaviour of the MBR – bromide tracer experiment

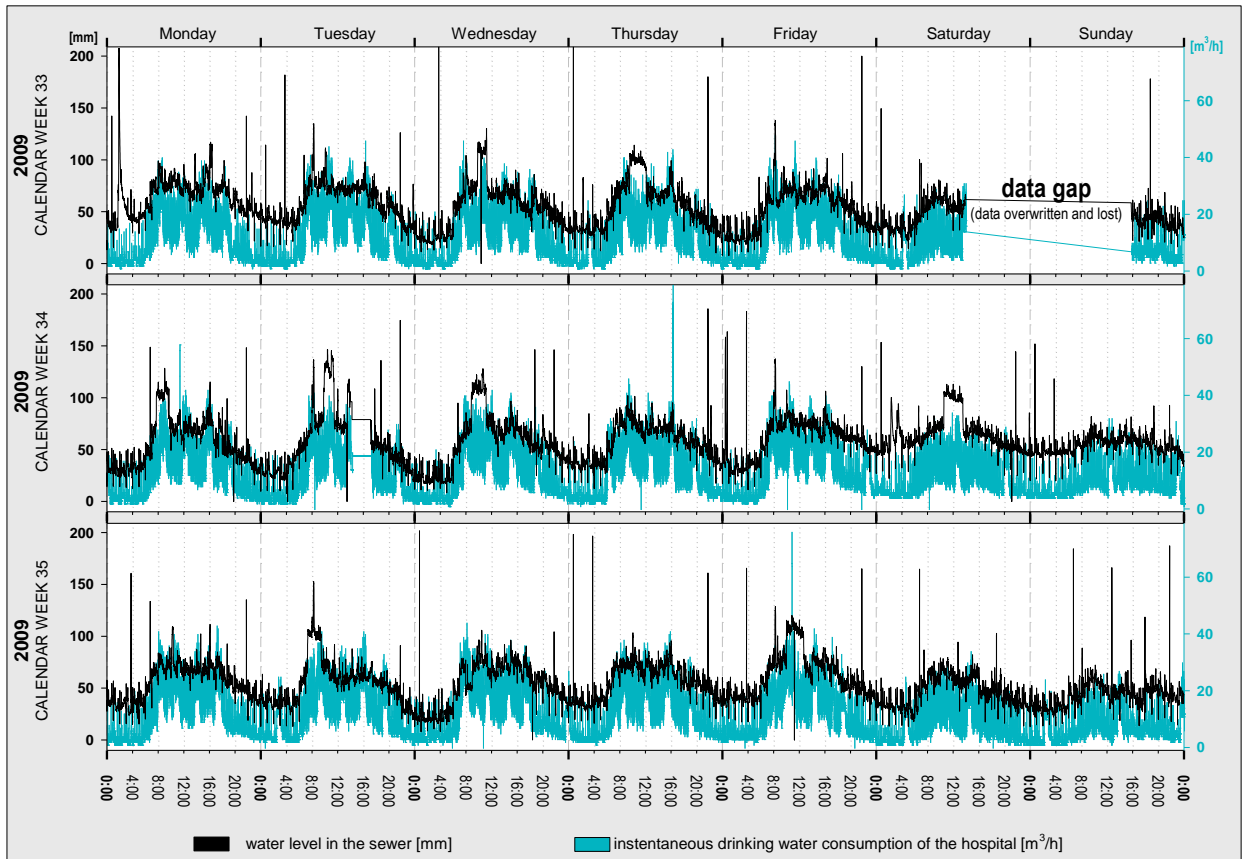


Figure S3. Comparison of the real-time drinking water consumption and the water level in the sewer during the sampling campaign August 2009.

4. Elimination in membrane bioreactor

Table S12. Comparison of elimination data with literature (this study: hospital ww, MBR, SRT 30-50 days)

| K _{biol} | K _d | Micropollutant | % elimination | | |
|--|----------------|--|---------------|---|--|
| | | | This study | Literature – municipal or synthetic waste water | |
| | | | | CAS | MBR |
| HIGH elimination in this study (12 compounds with removal >90%) | | | | | |
| | | 4-Acetamidoantipyrine ^c | 95 ± 1 | 26 ⁽⁶⁾ | |
| | | 4-Formylaminoantipyrine ^c | 90 ± 1 | none ⁽⁶⁾ | |
| | | 4-Methylaminoantipyrine ^d | 99 ± 1 | - | |
| | | Atenolol ^a | 99 ± 1 | 61±19 ⁽⁷⁾ , 59±50 ⁽⁸⁾ , 1-85 ⁽⁹⁾ , 50-60 ⁽¹⁰⁾ , 80 ⁽¹¹⁾ , 78 ⁽¹²⁾ , <0-96 ⁽¹³⁾ , <0-84 ⁽¹⁴⁾ | 57-90 _(SRT >60d) ⁽⁷⁾ , 66 ⁽¹³⁾ , 96.9±0.2 _(SRT 70d) ⁽¹⁵⁾ |
| | | Bezafibrate ^a | >91 | 81±21 ⁽⁷⁾ , 23-99 ⁽⁸⁾ , 12-75 ⁽⁹⁾ , 65 ⁽¹¹⁾ , -11-100 ⁽¹³⁾ , 50-97 ⁽¹⁴⁾ | 73-100 _(SRT >60d) ⁽⁷⁾ , 76-97 ⁽¹³⁾ |
| | | Cilastatin ^c | >90 | - | |
| | | Levetiracetam ^a | 95 ± 1 | - | |
| | | Mefenamic acid ^a | 92 ± 0 | 14-80 ⁽⁹⁾ , 2 - 92 ⁽¹³⁾ | 8-64 _(SRT >60d) ⁽⁷⁾ , 75 ⁽¹³⁾ |
| | | Morphine ^b | >96 | >90 ⁽¹⁰⁾ | |
| | | Paracetamol ^b | >99 | >99 ⁽⁷⁾ , 96-100 ⁽⁸⁾ , 100 ⁽¹¹⁾ , >99 ⁽¹³⁾ | >99 _(SRT >60d) ⁽⁷⁾ , 95±3 _(SRT 70d) ⁽¹⁵⁾ |
| | | Thiopental ^c | 91 ± 2 | - | |
| | | Trimethoprim ^c | 96 ± 1 | 40±25 ⁽⁷⁾ , 6-48 ⁽⁹⁾ , -60-31 ⁽¹⁶⁾ , 70 ⁽¹¹⁾ , -40-74 ⁽¹³⁾ , 0-69 ⁽¹⁴⁾ | 25-88 _(SRT >60d) ⁽⁷⁾ , [28, 33, 87] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ , <0 ⁽¹³⁾ , 17±4 _(SRT 70d) ⁽¹⁵⁾ |
| PARTIAL elimination in this study (20 compounds with removal 20-89%) | | | | | |
| | | 4-Aminoantipyrine ^d | 83 ± 3 | 26 ⁽⁶⁾ , 54 ⁽¹⁷⁾ | |
| | | 4/5-Methylbenzotriazole ^d | 82 ± 8 | [0-34 _{4-M} , 19-69 _{5-M}] ⁽¹⁸⁾ | |
| | | Atenolol acid ^a | 81 ± 3 | - | |
| | | Azithromycin ^b | 21 ± 95 | -34-59 ⁽¹⁶⁾ , -26-55 ⁽¹³⁾ | [-, 5, 25] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ |
| | | Benzotriazole ^b | 57 ± 6 | 29-58 ⁽¹⁸⁾ | |
| | | Ciprofloxacin ^c | 51 ± 13 | 37-99 ⁽⁸⁾ , 60-96 ⁽¹³⁾ , 78- >80 ⁽¹⁴⁾ | |
| | | Clarithromycin ^a | 50 ± 12 | 18-40 ⁽⁹⁾ , -52-26 ⁽¹⁶⁾ , -45-54 ⁽¹³⁾ , 54 ⁽¹⁴⁾ | [54, 40, 90] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ |
| | | Erythromycin + Eryt.-H ₂ O ^c | <60 | Eryt.: 50 ⁽¹¹⁾ , 35±51 ⁽⁷⁾ , -22-67 ⁽¹³⁾ , 54 ⁽¹⁴⁾ Eryt.-H ₂ O: -26-10 ⁽¹⁶⁾ | [32, 26, 90] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ , -84-134 _(SRT >60d) ⁽⁷⁾ |
| | | Gabapentin ^b | 23 ± 8 | 85 ⁽¹¹⁾ , >99 ⁽¹³⁾ | |
| | | Iopromide ^c | 31 ± 2 | 30-90 ⁽¹⁹⁾ , -862-50 ⁽¹³⁾ | [40, 68, 80] _(SRT 16, 33, 60-80d) ⁽¹⁹⁾ |
| | | Lidocaine ^a | 56 ± 13 | - | |
| | | Metoprolol ^a | 55 ± 13 | 25±45 ⁽⁷⁾ , 0-34 ⁽⁹⁾ , <0-30 ⁽¹⁰⁾ , 50 ⁽¹¹⁾ , 29 ⁽¹²⁾ , -19-65 ⁽¹³⁾ , <0-83 ⁽¹⁴⁾ | -18-74 _(SRT >60d) ⁽⁷⁾ , 59 ⁽¹³⁾ |
| | | Metronidazole ^c | 45 ± 56 | 0-17 ⁽⁹⁾ , 22 ⁽¹¹⁾ | |
| | | N4-Acetylsulfamethoxazole ^a | 81 ± 4 | 85-96 ⁽¹⁶⁾ | [>95, >95, >95] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ |
| | | Norfloxacin ^c | 47 ± 5 | 30-98 ⁽⁸⁾ , >80 ⁽¹⁴⁾ | |
| | | Ranitidine ^b | 71 ± 7 | 25±45 ⁽⁷⁾ , 50-98 ⁽⁸⁾ , 19-72 ⁽⁹⁾ , 90 ⁽¹¹⁾ , 39-84 ⁽¹³⁾ | -18-74 _(SRT >60d) ⁽⁷⁾ , 59 ⁽¹³⁾ |
| | | Ritalinic acid ^b | 28 ± 4 | -5-45 ⁽²⁰⁾ | |
| | | Ritonavir ^b | 78 ± 16 | - | |
| | | Sulfamethox. + N4-AcSMX | 36 ± 28 | -4-77 ⁽¹⁶⁾ , 0-75 ⁽¹⁹⁾ | [90, 75, 70] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ , [92, 75, 68] _(SRT 16, 33, 60-80d) ⁽¹⁹⁾ |
| | | Valsartan ^b | 85 ± 2 | 75 ⁽¹¹⁾ | |
| | | Verapamil ^a | 82 ± 3 | | 88±6 _(SRT 70d) ⁽¹⁵⁾ |
| LOW or NO elimination in this study (24 compounds with removal <20%) | | | | | |
| | | Carbamazepine ^b | -6 ± 12 | 5-24 ⁽⁹⁾ , -25 ⁽¹¹⁾ , 5 ⁽²⁰⁾ , -25-18 ⁽¹⁹⁾ , -193-53 ⁽¹³⁾ , 0-30 ⁽¹⁴⁾ | [25, -20, 0] _(SRT 16, 33, 60-80d) ⁽¹⁹⁾ , -10-13 ⁽¹³⁾ |
| | | Clindamycin ^c | -18 ± 40 | - | |
| | | Cyclophosphamide ^a | <20 | 80 ⁽²¹⁾ | |
| | | D617 ^b | 8 ± 31 | - | |
| | | Diatrizoate ^c | -5 ± 16 | 0 ⁽¹³⁾ | |
| | | Diclofenac ^b | -5 ± 3 | 22±29 ⁽⁷⁾ , 30-100 ⁽⁸⁾ , 12-52 ⁽⁹⁾ , 28-37 ⁽¹⁹⁾ , -30 ⁽¹¹⁾ , ≈40 ⁽²²⁾ , 1-80 ⁽¹³⁾ | [35, 40, 20] _(SRT >60d) ⁽⁷⁾ , 45-81 _(SRT >60d) ⁽⁷⁾ , 17±4 _(SRT 70d) ⁽¹⁵⁾ , [40, 80] _(SRT 15, 65d) ⁽²²⁾ |
| | | Fluconazole ^a | -8 ± 7 | - | |
| | | Furosemide ^b | -21 ± 11 | 20-96 ⁽⁸⁾ , 70 ⁽¹¹⁾ , 37-78 ⁽⁹⁾ | |
| | | Hydrochlorothiazide ^a | 8 ± 6 | 100 (to sludge) ⁽⁹⁾ , 24-76 ⁽¹³⁾ | 66 ⁽¹³⁾ |
| | | Indometacin ^a | 7 ± 44 | 0-40 ⁽⁹⁾ , 23-83 ⁽¹³⁾ , 75-83 ⁽¹⁴⁾ | 14-66 _(SRT >60d) ⁽⁷⁾ |
| | | lomeprol ^d | 2 ± 38 | 0-89 ⁽¹³⁾ | |
| | | Iopamidol ^d | -29 ± 218 | 17 ⁽¹³⁾ | |
| | | loxitalamic acid ^c | 0 ± 15 | 0 ⁽²³⁾ | |
| | | Oseltamivir ^c | -42 ± 149 | 0 ⁽²⁴⁾ | |
| | | Oseltamivir carboxylate ^b | 18 ± 62 | 59 ⁽²⁴⁾ | 2 - 41 _(SRT 24d) ⁽²⁵⁾ |
| | | Oxazepam ^a | 6 ± 12 | 0-18 ⁽¹⁰⁾ | |
| | | Phenazone ^c | -158 ± 99 | 33 ⁽¹³⁾ | |
| | | Primidone ^b | -57 ± 87 | 12±4 ⁽¹⁵⁾ , 20-45 ⁽¹⁰⁾ | |
| | | Propranolol ^b | -20 ± 39 | 59±25 ⁽⁷⁾ , 7-15 ⁽¹⁰⁾ , 33 ⁽¹¹⁾ , 33 ⁽¹²⁾ , 28-96 ⁽¹³⁾ , 65-96 ⁽¹⁴⁾ | 44-90 _(SRT >60d) ⁽⁷⁾ |
| | | Sotalol ^a | 18 ± 17 | 21±32 ⁽⁷⁾ , 4-52 ⁽⁹⁾ , 10-35 ⁽¹⁰⁾ , 25 ⁽¹²⁾ , 26-71 ⁽¹³⁾ , 40-80 ⁽¹⁴⁾ | 5-77 _(SRT >60d) ⁽⁷⁾ |
| | | Sulfadiazine ^a | -23 ± 235 | 43-98 ⁽⁸⁾ , -160 ⁽¹¹⁾ | |
| | | Sulfamethoxazole ^a | 7 ± 57 | 74±13 ⁽⁷⁾ , 30-92 ⁽⁸⁾ , 75 ⁽¹¹⁾ , -153-63 ⁽¹⁶⁾ , -280 - >98 ⁽¹³⁾ , <0-55 ⁽¹⁴⁾ | [38, 40, 37] _(SRT 16, 33, 60-80d) ⁽¹⁶⁾ , 64-93 _(SRT >60d) ⁽⁷⁾ , 92±1 _(SRT 70d) ⁽¹⁵⁾ |
| | | Tramadol ^a | 7 ± 17 | 35 ⁽¹¹⁾ | |
| | | Venlafaxine ^a | 16 ± 9 | ≈40 ⁽²⁶⁾ | |

LEGEND:

Biological elimination*

(K_{biol} 0.1, spec. sludge prod. 500g/m³ ≈ 20% removal)⁽²⁷⁾

- K_{biol} < 0.1 L/day.g (all literature)
- K_{biol} > 0.1 L/day.g (some literature)
- K_{biol} > 0.1 L/day.g (all literature)

Sorption to activated sludge*

(K_d 500, spec. sludge production 200g/m³ ≈ 10% removal)⁽²⁸⁾

- K_d < 500 L/kg_{ss} (all literature)
- K_d > 500 L/kg_{ss} (some literature)
- K_d > 500 L/kg_{ss} (all literature)

*see Table S13 for K_{biol} and K_d values available from literature

Table S12. Comparison of elimination data with literature (continues)

| K _{biol} | K _d | Micropollutant | % elimination | | |
|---|----------------|--|---------------|--|--|
| | | | This study | Literature – municipal or synthetic waste water | |
| | | | | CAS | MBR |
| Absence in the MBR influent (11 compounds) | | | | | |
| | | 4-Dimethylaminoantipyrine ^c | absent | 38 ⁽¹⁴⁾ | |
| | | Clofibric acid ^b | absent | 0-52 ⁽¹³⁾ , 26-52 ⁽¹⁴⁾ | 54-72 ⁽¹³⁾ |
| | | Dexamethasone ^a | absent | >98 ⁽²⁹⁾ | |
| | | Diazepam ^a | absent | 32-65 ⁽⁹⁾ , -5-25 ⁽¹³⁾ | |
| | | Fluoxetine ^b | absent | 33±29 ⁽⁷⁾ , >70 ⁽¹³⁾ , ≈40 ⁽²⁶⁾ | 96-100 _{(SRT >60d)⁽⁷⁾} |
| | | Ifosfamide ^b | absent | <3 ⁽¹³⁾ | |
| | | Iohexol ^c | absent | 0-89 ⁽¹³⁾ | |
| | | Methylprednisolone ^a | absent | - | |
| | | Naproxen ^c | absent | 72±14 ⁽⁷⁾ , 86±13 ⁽⁸⁾ , 80-97 ⁽⁹⁾ , 65-82 ⁽¹⁹⁾ , 78 ⁽¹¹⁾ , 0-95 ⁽¹³⁾ , 66-93 ⁽¹⁴⁾ | 84-100 _{(SRT >60d)⁽⁷⁾} , [28, 18, 25] _{(SRT 16, 33, 60-80d)⁽¹⁹⁾} , 40±3 _{(SRT 70d)⁽¹⁵⁾} |
| | | Roxithromycin ^b | absent | -24-43 ⁽¹⁶⁾ , -20-40 ⁽¹⁹⁾ , -80-61 ⁽¹³⁾ , 33 ⁽¹⁴⁾ | [38, 60, 57] _{(SRT 16, 33, 60-80d)⁽¹⁶⁾} , [40, 60, 55] _{(SRT 16, 33, 60-80d)⁽¹⁹⁾} |
| | | Sulfapyridine ^c | absent | 90 ⁽¹¹⁾ , -115-77 ⁽¹⁶⁾ , -107-72 ⁽¹³⁾ | [60, 48, 55] _{(SRT 16, 33, 60-80d)⁽¹⁶⁾} |

LEGEND:

| Biological elimination* | | Sorption to activated sludge* | |
|---|---|---|--|
| (K _{biol} 0.1, spec. sludge prod. 500g/m ³ ≈ 20% removal) ⁽²⁷⁾ | | (K _d 500, spec. sludge production 200g/m ³ ≈ 10% removal) ⁽²⁸⁾ | |
| K _{biol} < 0.1 L/day.g (all literature) | K _d < 500 L/kg _{ss} (all literature) | | |
| K _{biol} > 0.1 L/day.g (some literature) | K _d > 500 L/kg _{ss} (some literature) | | |
| K _{biol} > 0.1 L/day.g (all literature) | K _d > 500 L/kg _{ss} (all literature) | | |

*see Table S13 for K_{biol} and K_d values available from literature

▪ sum of AA and AAA (4-aminoantipyrine and 4-acetamidoantipyrine)

• semi-quantitative result

Analytical uncertainty: ^a less than 14%; ^b 15 - 29%; ^c 30 - 100%; ^d above 100%.

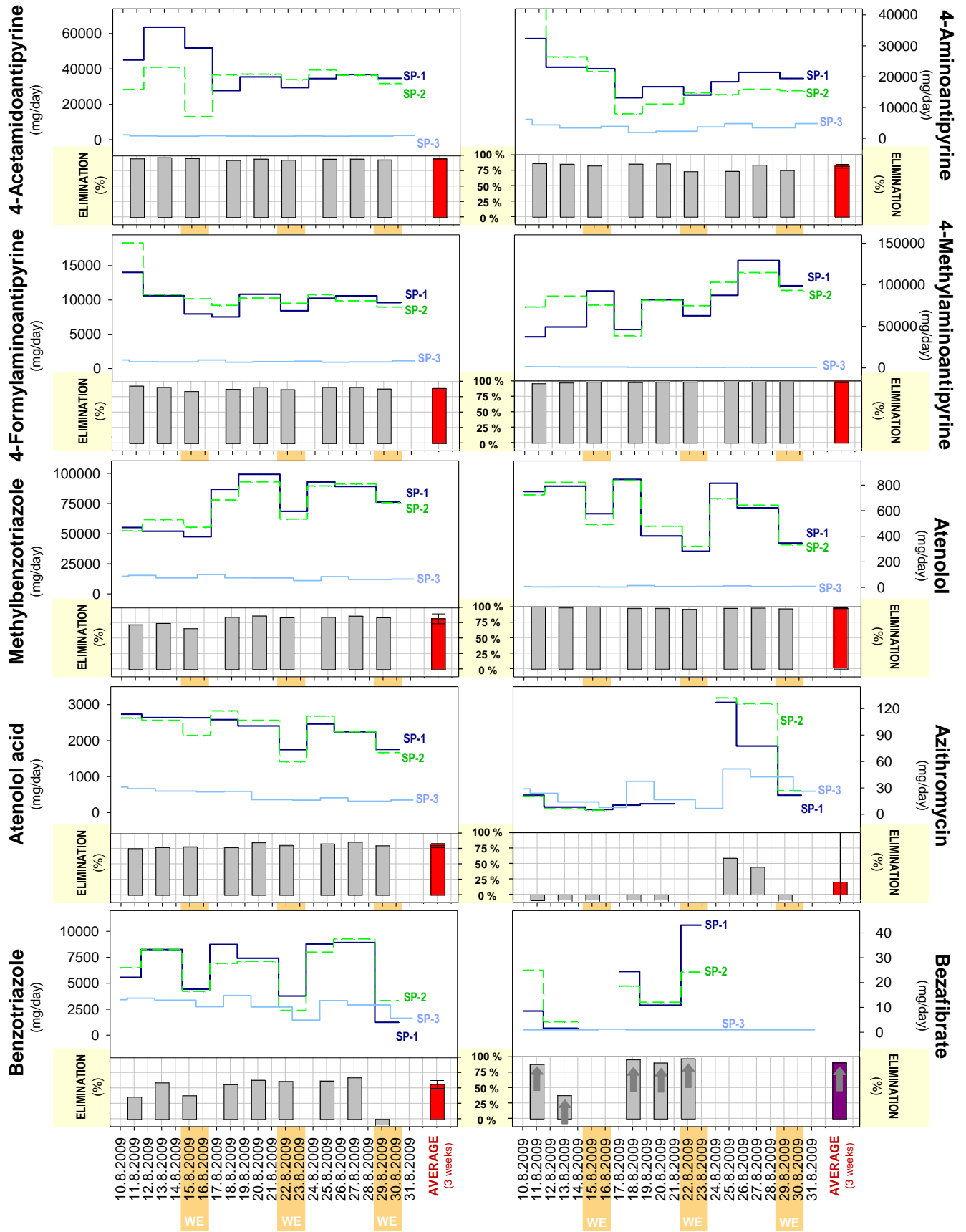
LITERATURE:

- ⁽⁶⁾ **Feldmann 2008:** one WWTP in Berlin, DE (nitrif., denitrif., HRT up to 23h), daily composite samples, 3 sampling campaigns ca. 1 week each, p 1761
- ⁽⁷⁾ **Radjenovic 2009:** one WWTP near Barcelona, ES (CAS pre-denitrif., nitrif., HRT app. 11.5h, 277 000 ei, SRT app. 10d) and two MBRs in parallel with CAS (UF 0.05 µm, MF 0.4 µm, SRT >60d), 24-h flow-proportional composite samples (1 sample/h), n=9, elimination from aqueous phase only, Tab. 3 (possible error - all data for ranitidine and metoprolol, including RSDs, are identical: CAS 24.7±44.9, FS MBR 44.2±29.6, HF MBR 29.5±47.9)
- ⁽⁸⁾ **Gros 2010:** 7 WWTPs in Erbo river basin, ES (6 CAS, 1 biofilter), 24-h time-averaged composite samples, 4 sampling campaigns, Tab.4
- ⁽⁹⁾ **Jelic 2011:** 3 WWTPs in Catalonia, ES, (CAS), 24-h time-proportional composite samples (2 samples/h), effluent taken with HRT shift, 8 sampling campaigns within 2 years, sum of removed and sorbed (overall removal rate), Fig.4
- ⁽¹⁰⁾ **Wick 2009:** one WWTP near Frankfurt, DE (CAS, SRT 18d, 1 350 000 ei), 48 and 72 h composite samples, 3 sampling campaigns ca. 1 week each, Fig.5
- ⁽¹¹⁾ **Kasprzyk-Hordern 2009:** one WWTP in UK: CAS WWPT 24-h composite samples, sampling at least twice a month for 5 months, Fig.2 (often excessive error bars, not included here)
- ⁽¹²⁾ **Alder 2010** 3 WWTPs in Glatt valley, CH, 20 000 – 37 000 ei, 1 week sampling, 24-h flow-proportional composite samples, Tab 3
- ⁽¹³⁾ **Onesios 2009:** (review paper) Tab. 2 "PPCP removal efficiencies attributed to biodegradation in addition to other removal mechanisms"
- ⁽¹⁴⁾ **Monteiro 2010:** (review paper) CAS Tab.12
- ⁽¹⁵⁾ **Tadkaew 2011:** lab MBR, synthetic waste water, SRT 70d, n=16, Tab.1 (additional comparison with literature)
- ⁽¹⁶⁾ **Gobel 2007:** 2 WWTPs in CH (CAS-K: 55 000 ei, SRT 10-12d, HRT ≈15h, MBR operating in parallel, 3 SRT tested [16d, 33d, 60-80d] Fig.4; CAS-A 52 000 ei, SRT 21-25d, HRT ≈31h) sampling campaigns of 1 week – 3 at WWTP-K and 2 at WWTP-A, 48 and 72 h composite flow-proportional samples, Tab.3
- ⁽¹⁷⁾ **Ternes 2001:** (analytical meth. paper) one WWTP near Frankfurt, DE, 24-h flow-proportional samples of 5 days, p 182 4-aminoantipyrine (semi-quant.)
- ⁽¹⁸⁾ **Reemtsma 2010:** 4 WWTPs in Berlin, DE (CAS), 24-h composite samples, p 599
- ⁽¹⁹⁾ **Joss 2005:** 2 WWTPs in CH (CAS-1: 55 000 ei, SRT 10-12d, MBR operating in parallel, 3 SRT tested [16d, 33d, 60-80d]; CAS-2: 80 000 ei, SRT 22-24d) sampling campaigns of 1 week – 3 at WWTP-1 and 2 at WWTP-2, 48 and 72 h composite flow-proportional samples, Fig. 5
- ⁽²⁰⁾ **Letzel 2010:** one WWPT at Southern Bavaria, DE (CAS, 26 000 ei, effluent taken with HRT shift, 24-h composite samples, 4 days sampling) and one continuous lab-scale sewage plant with synthetic wastewater (HRT 11.4h, SRT 11.2d) n=2
- ⁽²¹⁾ **Delgado 2009:** lab scale MBR
- ⁽²²⁾ **Kimura 2007** 1 WWPT (CAS, 200 000 ei, HRT 12h, SRT 7 days), 2 MBRs (MBR-1: SRT 15d, MBR-2: SRT 65d), grab samples were taken 11 times around 10:00 am
- ⁽²³⁾ **Ternes 2000:** one WWTP near Frankfurt, DE, (preliminary clarification followed by an aeration tank with addition of Fe(II)chloride for phosphate elimination and a final end point clarification) flow-proportional samples of ca. 1 week, Tab.4
- ⁽²⁴⁾ **Prasse 2010:** : one WWTP in Dortmund, DE (CAS: 1 350 000 ei, HRT 5h, SRT 18d), 24-h composite samples, Tab.3
- ⁽²⁵⁾ **Slater 2011:** lab scale MBR, synthetic waste water, SRT 24d
- ⁽²⁶⁾ **Metcalfe 2010:** one WWTP in southern Ontario, CA (CAS followed by UV-disinfection, HRT 11.9h, 69 000 ei, SRT 8.1 - 10.4d), a single day 24-h composite sample
- ⁽²⁷⁾ **Joss 2006:** batch, estimated from K_{biol}, Fig. 6
- ⁽²⁸⁾ **Ternes 2004:** "A rapid method to measure the solid–water distribution coefficient (Kd) for pharmaceuticals and musk fragrances in sewage sludge"
- ⁽²⁹⁾ **Chang 2007:** 7 WWTPs in Beijing, CN, 24-h composite samples, 4 weeks, Fig. 3

Table S13. Literature data on K_d and K_{biol} for municipal wastewater

| LITERATURE (municipal wastewater) | K_d (L/kg _{ss}) | K_{biol} (L/day.g) |
|--------------------------------------|---|--|
| Atenolol | 38 ⁽³⁰⁾ , 0 ⁽³¹⁾ , 0 ⁽³²⁾ , <50 ⁽³³⁾ , 10-95 ⁽⁷⁾ , 1600 ⁽³⁴⁾ | 0.69 ⁽³⁰⁾ , 1.9 ⁽¹⁰⁾ , 1.5 ⁽³⁵⁾ |
| Atenolol acid | | 1.7 ⁽³⁵⁾ |
| Azithromycin | 376 ⁽³⁶⁾ , 200 ⁽³⁷⁾ | |
| Bezafibrate | 0 ⁽³¹⁾ , 170 ⁽³⁷⁾ | 1.8 ⁽³¹⁾ , 3.3 ⁽²⁷⁾ |
| Carbamazepine | 1 ⁽²⁸⁾ , 25 ⁽³²⁾ , 17 ⁽¹⁰⁾ , 50 ⁽³⁸⁾ , 20-68 ⁽³⁹⁾ , 150 ⁽³⁷⁾ , 36-65 ⁽³³⁾ , 135-314 ⁽⁷⁾ | <0.06 ⁽⁴⁰⁾ , 0.007 ⁽²⁷⁾ |
| Ciprofloxacin | 20 000 ⁽⁴¹⁾ , 450 ⁽³⁷⁾ | |
| Clarithromycin | 262 ⁽³⁶⁾ , 280 ⁽³⁷⁾ | |
| Clofibric acid | 5 ⁽²⁸⁾ , 30 ⁽³⁸⁾ , 600 ⁽³⁷⁾ | 0.5 ⁽²⁷⁾ |
| Cyclophosphamide | 2 ⁽²⁸⁾ , 1800 ⁽³⁷⁾ | |
| Diatrizoate | | <0.1 ⁽²⁷⁾ |
| Diazepam | 21 ⁽²⁸⁾ , 120 ⁽³¹⁾ , 53 ⁽¹⁰⁾ , 240-300 ⁽³³⁾ | <0.16 ⁽¹⁰⁾ , <0.4 ⁽⁴⁰⁾ , <0.002 ⁽³¹⁾ , 0.02 ⁽²⁷⁾ |
| Diclofenac | 16 ⁽²⁸⁾ , 20 ⁽³⁸⁾ , 18-151 ⁽³⁹⁾ , 710 ⁽³⁷⁾ , <30 ⁽³³⁾ , 118-321 ⁽⁷⁾ | 1.2 ⁽⁴⁰⁾ , 0.04 ⁽²⁷⁾ |
| Erythromycin | 165 ⁽³²⁾ , 11-309 ⁽⁷⁾ | 6 ⁽⁴⁰⁾ |
| Fluoxetine | 6000 ⁽³⁴⁾ | 9 ⁽⁴⁰⁾ |
| Furosemide | 330 ⁽³⁷⁾ | |
| Hydrochlorothiazide | 20-26 ⁽⁷⁾ | |
| Ifosfamide | 1 ⁽²⁸⁾ | |
| Indomethacin | 30 ⁽³⁸⁾ , 750 ⁽³⁷⁾ | |
| Iohexol | | 1.8 ⁽²⁷⁾ |
| lomeprol | | 1 ⁽²⁷⁾ |
| Iopromide | 11 ⁽²⁸⁾ , 5-30 ⁽³⁹⁾ | 1.8 ⁽²⁷⁾ |
| Ioxitalamic acid | | 0.5 ⁽²⁷⁾ |
| Levetiracetam | 0 ⁽³¹⁾ | 1.1 ⁽³¹⁾ |
| Mefenamic acid | 18900 ⁽³²⁾ , 10100 ⁽³⁷⁾ , 294-537 ⁽⁷⁾ | |
| Metoprolol | 1 ⁽³⁰⁾ , 65 ⁽¹⁰⁾ , 515 ⁽³⁷⁾ | 0.58 ⁽³⁰⁾ , 0.4 ⁽¹⁰⁾ , 0.6 ⁽³⁵⁾ |
| Morphine | 12 ⁽¹⁰⁾ | 13.5 ⁽¹⁰⁾ |
| N4-Acetylsulfamethoxazole | | 5 ⁽²⁷⁾ |
| Naproxen | 217 ⁽³²⁾ , 20 ⁽³⁸⁾ , 11-51 ⁽³⁹⁾ , 630 ⁽³⁷⁾ , <30 ⁽³³⁾ | 9 ⁽⁴⁰⁾ , 1 ⁽²⁷⁾ |
| Norfloxacin | 15 800 ⁽⁴¹⁾ , 400 ⁽³⁷⁾ | |
| Oseltamivir | 30 ⁽³¹⁾ | 0.007 ⁽³¹⁾ |
| Oxazepam | 13 ⁽¹⁰⁾ , 1100 ⁽³⁴⁾ | <0.1 ⁽¹⁰⁾ |
| Paracetamol | 0 ⁽³²⁾ , 100 ⁽³⁷⁾ , <30 ⁽³³⁾ , 6-1160 ⁽⁷⁾ | 140 ⁽²⁷⁾ |
| Phenazone | 730 ⁽³⁷⁾ | |
| Primidone | 7 ⁽¹⁰⁾ , <50 ⁽³³⁾ | <0.1 ⁽¹⁰⁾ |
| Propranolol | 317 ⁽³⁰⁾ , 343 ⁽¹⁰⁾ , 3200 ⁽³⁷⁾ , 298-641 ⁽⁷⁾ | 0.39 ⁽³⁰⁾ |
| Ranitidine | | 1.5 ⁽³⁵⁾ |
| Roxithromycin | 14-83 ⁽³⁹⁾ , 680 ⁽³⁷⁾ | 9 ⁽⁴⁰⁾ |
| Sotalol | 37 ⁽³⁰⁾ , 18 ⁽¹⁰⁾ , 360 ⁽³⁴⁾ | 0.29 ⁽³⁰⁾ , 0.4 ⁽¹⁰⁾ |
| Sulfamethoxazole | 256 ⁽³⁶⁾ , 370 ⁽³⁴⁾ , 6-62 ⁽³⁹⁾ , 80 ⁽³⁷⁾ , 29 ⁽⁴²⁾ , <30 ⁽³³⁾ , 3-77 ⁽⁷⁾ | 0.3 ⁽⁴⁰⁾ |
| Sulfapyridine | 295 ⁽³⁶⁾ | |
| Tramadol | 47 ⁽¹⁰⁾ , 190 ⁽³⁴⁾ | <0.11 ⁽¹⁰⁾ |
| Trimethoprim | 208 ⁽³⁶⁾ , 420 ⁽³⁴⁾ , 480 ⁽³⁷⁾ , 120-250 ⁽³³⁾ , 225-427 ⁽⁷⁾ | 0.15 ⁽⁴⁰⁾ |
| Valsartan | 0 ⁽³¹⁾ | 3 ⁽³⁵⁾ , 0.7 ⁽³¹⁾ |
| Venlafaxine | 100 ⁽³⁴⁾ | |
| Verapamil | 400 ⁽³⁴⁾ , 1200-1600 ⁽³³⁾ | |

Figure S4. Profiles of micropollutant loads in the MBR over three weeks in August 2009 and elimination between the pilot plant influent (SP-1) and effluent (SP-3).

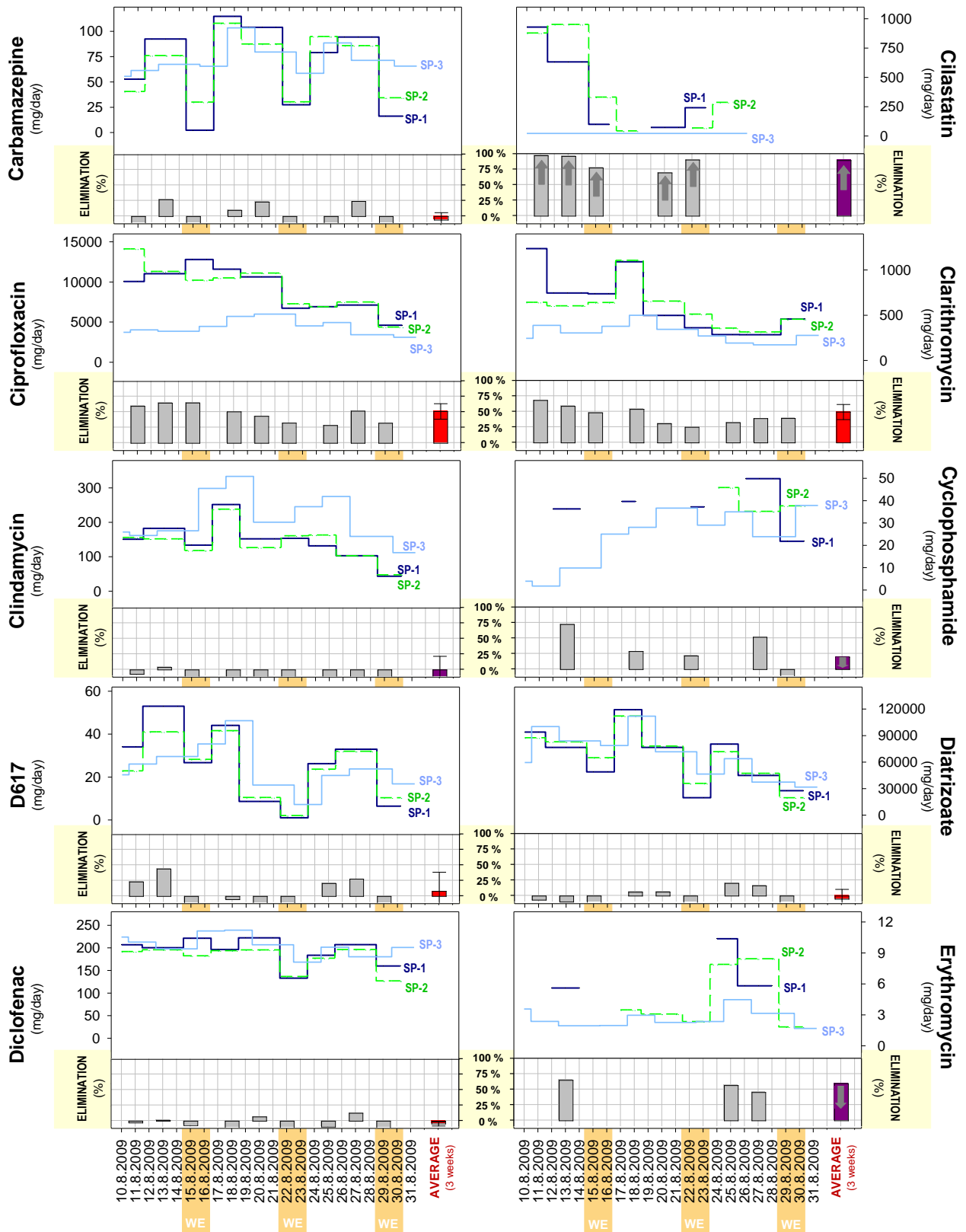


LEGEND:

- Average elimination between SP-1 and SP-3: $[1 - [(load_{eff}/load_{in})_{week1} + (load_{eff}/load_{in})_{week2} + (load_{eff}/load_{in})_{week3}] / 3] * 100\%$
- Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

figure continues

Figure S4. Profiles of micropollutant loads in the MBR. (continues)

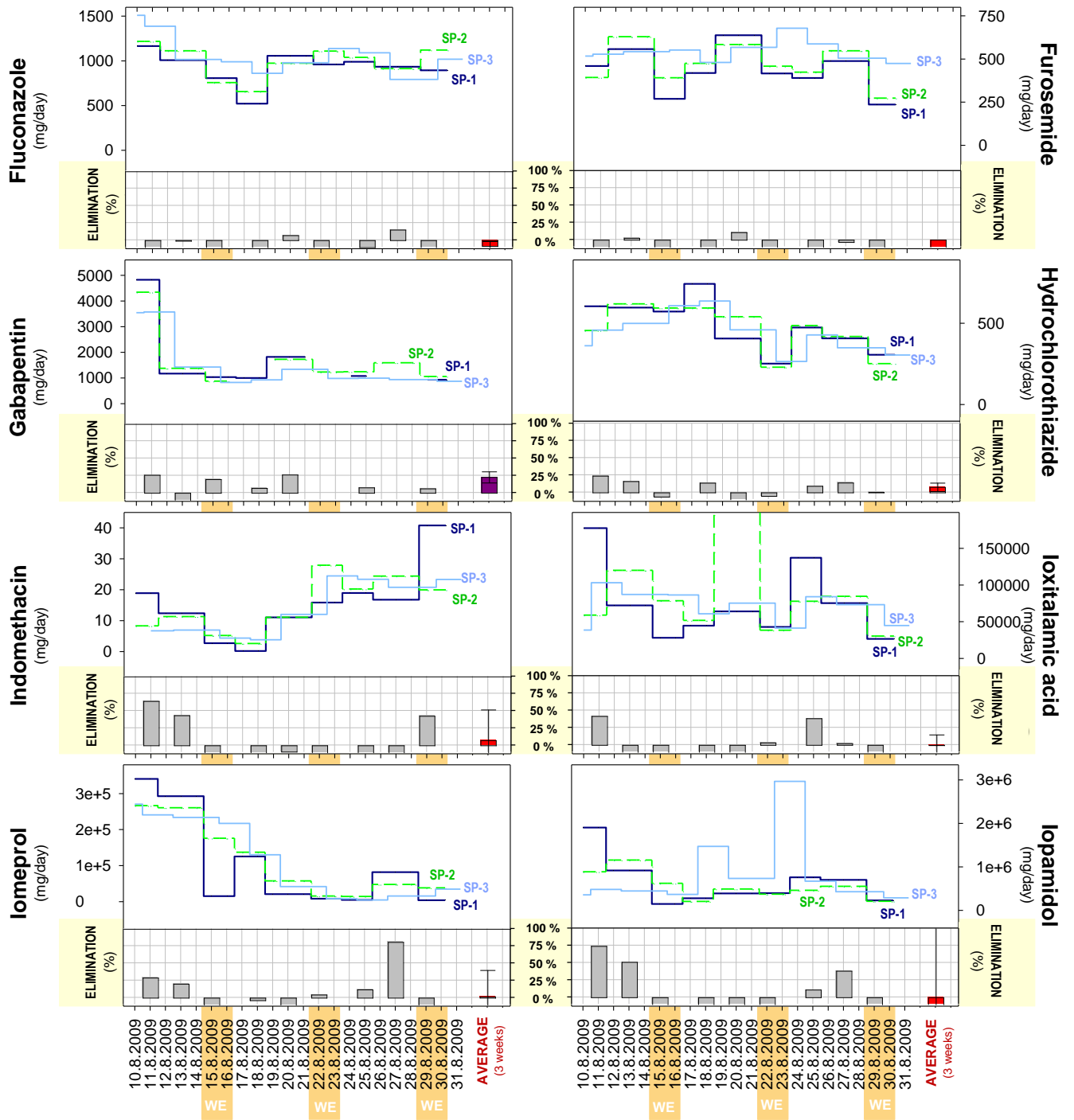


LEGEND:

- █ Average elimination between SP-1 and SP-3:
$$1 - \left[\frac{(\text{load}_{ef}/\text{load}_{in})_{\text{week1}} + (\text{load}_{ef}/\text{load}_{in})_{\text{week2}} + (\text{load}_{ef}/\text{load}_{in})_{\text{week3}}}{3} \right] * 100\%$$
- █ Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

figure continues

Figure S4. Profiles of micropollutant loads in the MBR. (continues)

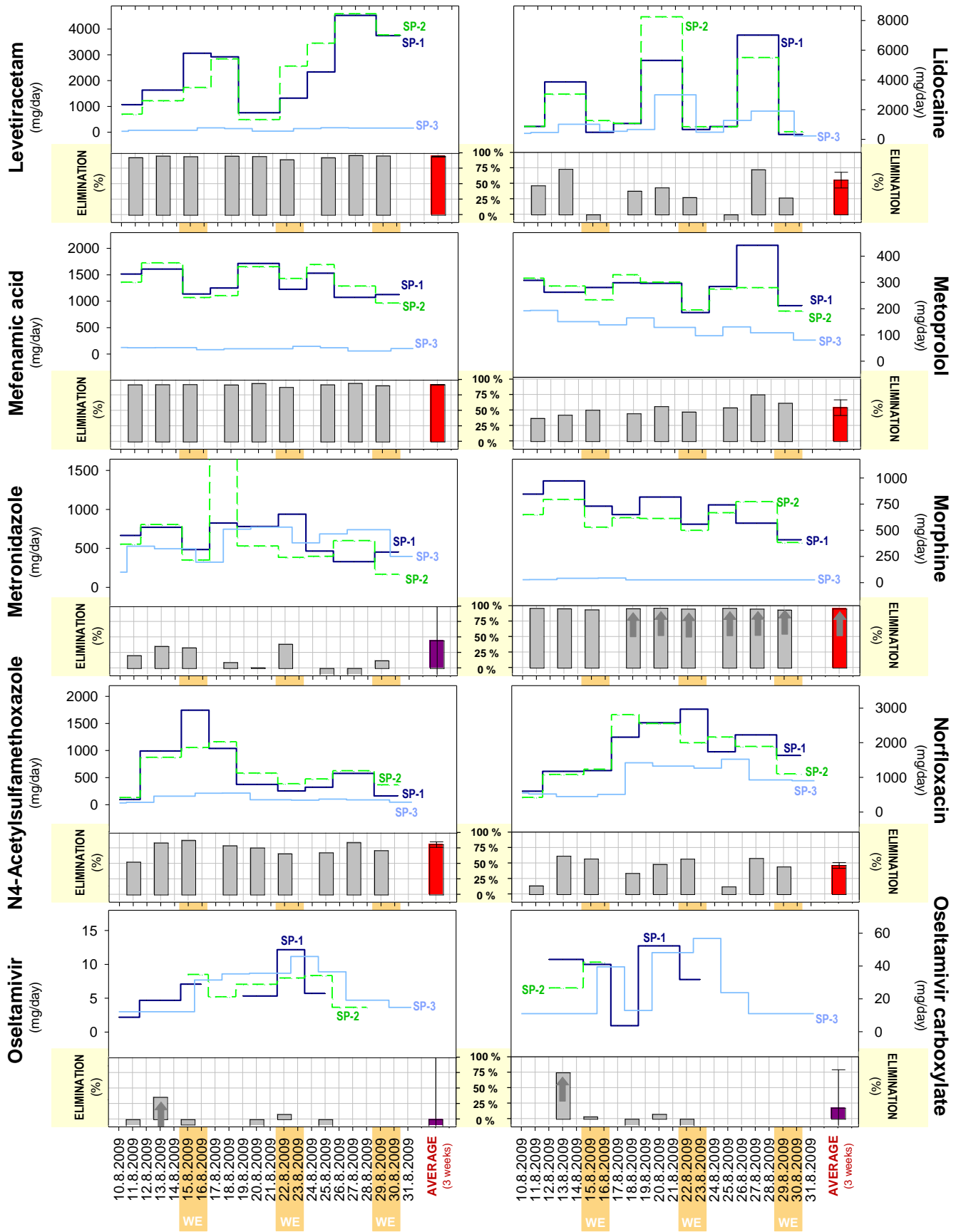


LEGEND:

- Average elimination between SP-1 and SP-3: $[1 - [(load_{ef}/load_{in})_{week1} + (load_{ef}/load_{in})_{week2} + (load_{ef}/load_{in})_{week3}] / 3] * 100\%$
- Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

figure continues

Figure S4. Profiles of micropollutant loads in the MBR. (continues)

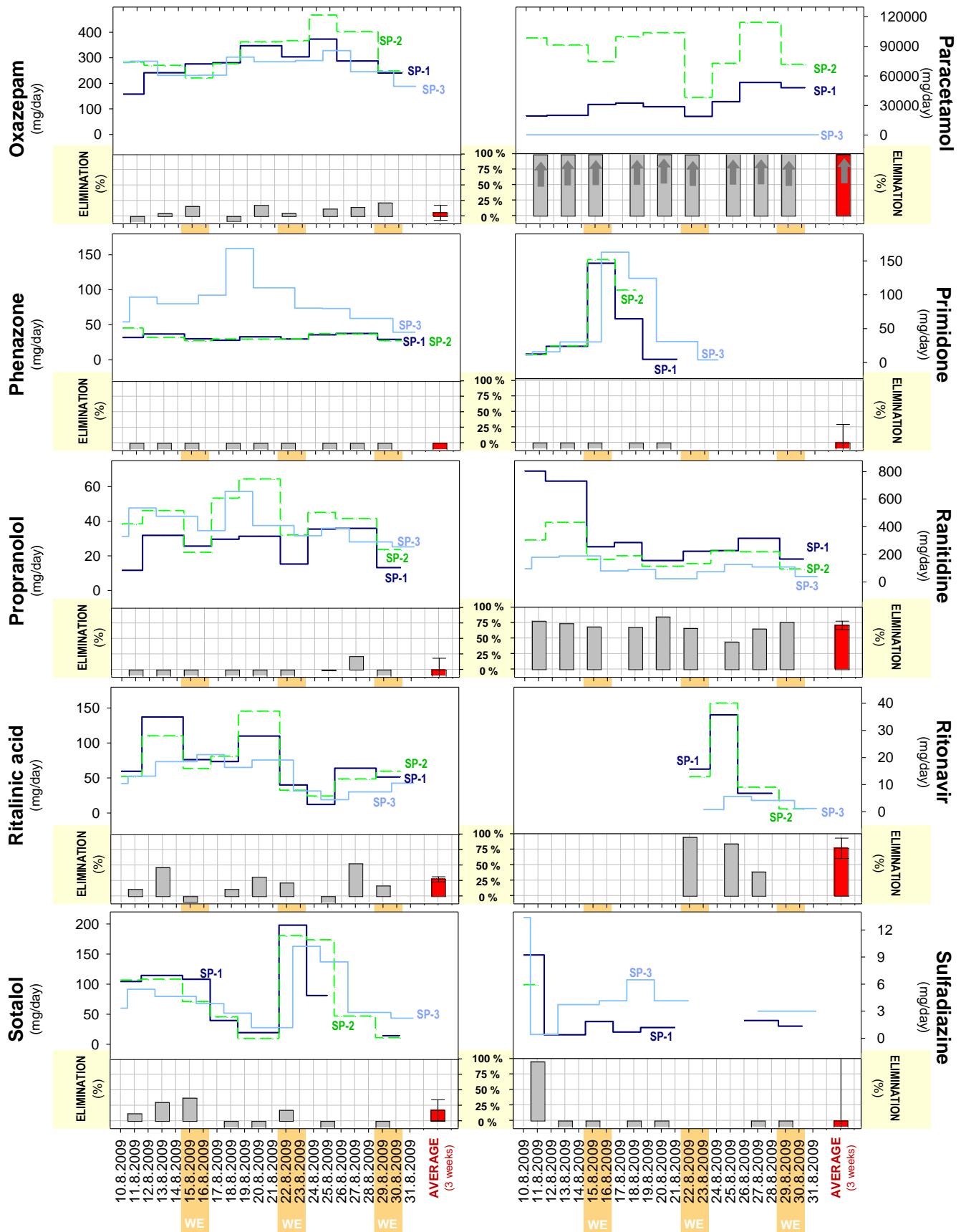


LEGEND:

- Average elimination between SP-1 and SP-3: $[1 - [(load_{ef}/load_{in})_{week1} + (load_{ef}/load_{in})_{week2} + (load_{ef}/load_{in})_{week3}] / 3] * 100\%$
- Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

figure continues

Figure S4. Profiles of micropollutant loads in the MBR. (continues)

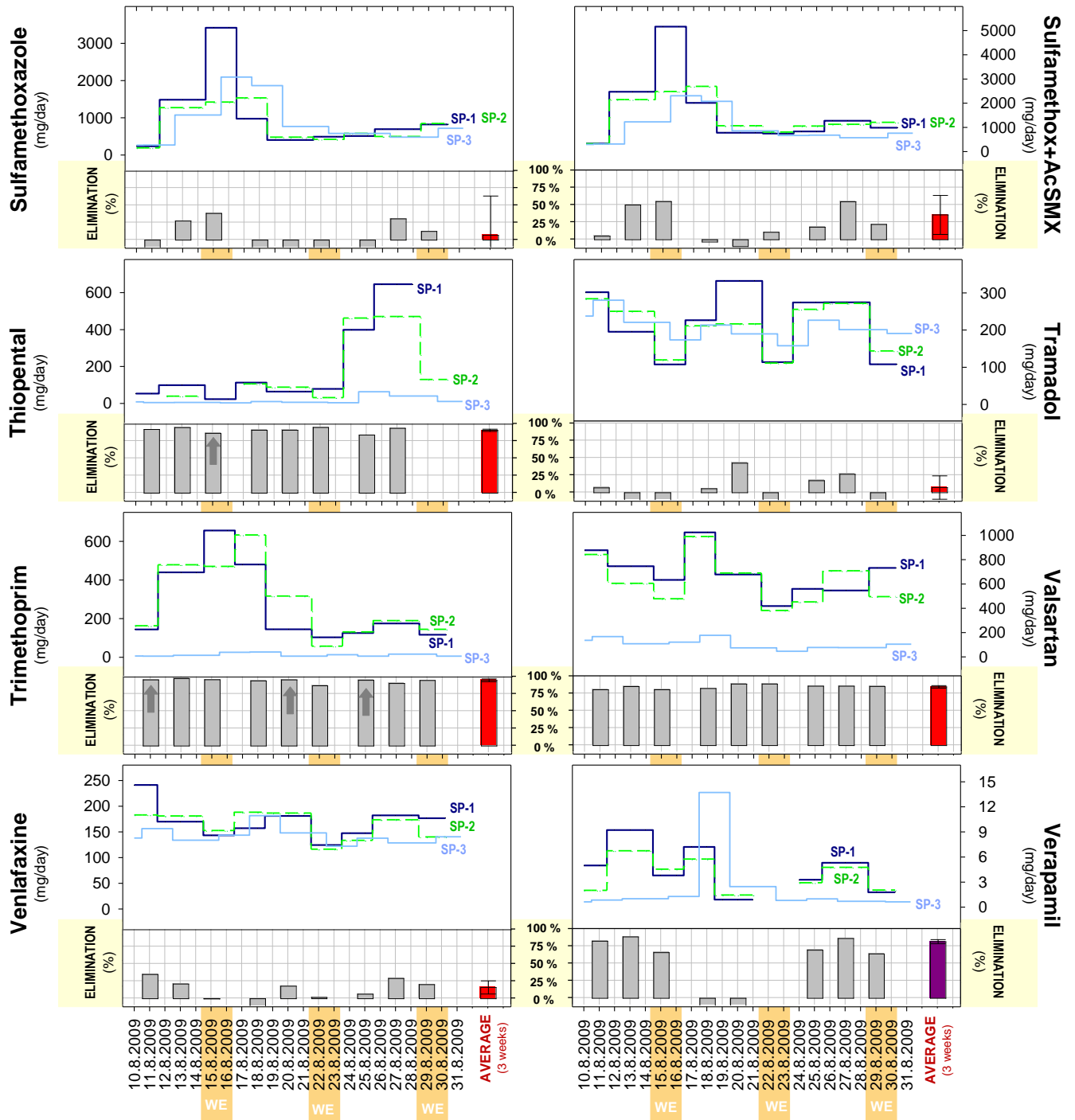


LEGEND:

- Average elimination between SP-1 and SP-3: $[1 - \frac{1}{3} \left(\frac{load_{el}}{load_{in}} \right)_{week1} + \left(\frac{load_{el}}{load_{in}} \right)_{week2} + \left(\frac{load_{el}}{load_{in}} \right)_{week3}] * 100\%$
- Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

figure continues

Figure S4. Profiles of micropollutant loads in the MBR. (continues)



LEGEND:

- Average elimination between SP-1 and SP-3: $[1 - \frac{(load_{el}/load_{in})_{week1} + (load_{el}/load_{in})_{week2} + (load_{el}/load_{in})_{week3}}{3}] * 100\%$
- Special case - average elimination between SP-1 and SP-3 calculated otherwise (e.g. with loads of 2 weeks, or loads of individual samples, or including results of June 2009 sampling campaign)

5. Human metabolism

Table S14. List of pharmaceuticals which form conjugates during human metabolism.⁽⁴³⁾

| Human metabolism | | Pilot scale membrane bioreactor |
|--------------------|---|---|
| conjugates | | increase in the MBR <i>(see Figure S4)</i> |
| Atenolol | small percentage | no |
| Bezafibrate | 20% glucuronidation | no |
| Carbamazepine | small percentage of glucuronidation | no |
| Cilastatin | 10% N4-acetylation | in SP-2 |
| Clofibric acid | glutathione conjugates | <LOQ in the influent |
| Dexamethasone | 30-40% glucuronidation and sulfation | <LOQ in the influent |
| Diazepam | 30% oxazepam glucuronidate | <LOQ in the influent |
| Diclofenac | 10% glucuronidation | (in SP-3) |
| Furosemide | 14% glucuronidation | (in SP-3) |
| Indomethacin | glucuronidation | in SP-2 and SP-3 |
| Methylprednisolone | glucuronidation, sulfation | <LOQ in the influent |
| Morphine | large percentage glucuronidation | no |
| Naproxen | large percentage | <LOQ in the influent |
| Oxazepam | large percentage glucuronidation | in SP-2 |
| Paracetamol | 60-80% glucuronidation, 20-40% sulfation | in SP-2 |
| Propranolol | glucuronidation (the only betablocker forming conjugates) | in SP-2 and SP-3 |
| Sulfadiazine | N4-acetylation | in SP-3 |
| Sulfamethoxazole | glucuronidation, N4-acetylation | no |
| Sulfapyridine | glucuronidation, N4-acetylation | <LOQ in the influent |

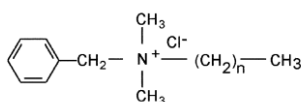
6. Disinfectants

Table S15. Loads of disinfectants used in hospitals - calculation from the consumption.

| Disinfectant | Loads of disinfectants (g.bed ⁻¹ .year ⁻¹) | |
|------------------------------------|---|---|
| | Zurich, ⁽⁴⁴⁾ Switzerland (729 beds) 2006* | Baden, ⁽⁴⁵⁾ Switzerland (346 beds) 2009 |
| Ethanol | 21061 | - |
| Propanol (1-propanol + 2-propanol) | 6361 | - |
| Methyl ethyl ketone | 1529 | - |
| Glutaraldehyde | 452 | - |
| Glucoprotamine | 394 | - |
| Glycerol | 301 | - |
| Coconut propylenediamine | 170 | - |
| BAC-C12-18 | 107 | 46 |
| DDAC | 106 | 84 |
| Povidone-iodine | 59 | - |
| Chlorhexidine gluconate | 40 | - |

(-): data not available, * additionally to the listed disinfectants, the Cantonal hospital of Zurich uses ten other disinfectants with yearly loads less than 30 g.bed⁻¹.year⁻¹ for each of them and seven other disinfectants with yearly loads less than 2 g.bed⁻¹.year⁻¹.

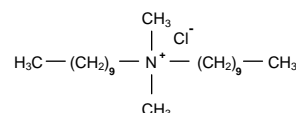
BAC-C12-18: benzalkonium chloride, DDAC-C10: -dimethyldidecylammonium chloride



BAC-C12 (n=11)

BAC-C12/14 (technical mixture, n=11, 13)

BAC-C12-18 (technical mixture, n=11, 13, 15, 17)



DDAC-C10

Table S16. Loads of disinfectants used in hospitals – measurements in hospital wastewater.

| Disinfectant | Loads of disinfectants (g.bed ⁻¹ .year ⁻¹) | | | | | |
|--------------|---|---|--|---|---|--|
| | Baden, Switzerland (346 beds) 2009 | Hospital in ⁽⁴⁶⁾ Austria (2514 beds) 1997 | Brussels, ⁽⁴⁶⁾ Belgium (174 beds) 1997 | Utrecht, ⁽⁴⁶⁾ Netherlands (857 beds) 1997 | Bologna, ⁽⁴⁶⁾ Italy (791 beds) 1997 | Freiburg, ⁽⁴⁶⁾ Germany (1 356 beds) 1997 |
| BAC-C12 | 7.9 | - | - | - | - | - |
| BAC-C12/14 | 11.3 | 362 | 15 | 8.2 | 4.5 | 21.5 |
| BAC-C12-18 | 11.5 | - | - | - | - | - |
| DDAC-C10 | 24.3 | - | - | - | - | - |

(-): data not available, BAC-C12-18: benzalkonium chloride, DDAC-C10: dimethyldidecylammonium chloride

Inhibition test with disinfectants. Activated sludge for the batch experiments was taken from the aerobic MBR compartment of the pilot plant described in Section 3. The oxygen concentration was kept between 1.8 and 2.8 mg O₂/l. Drinking water was used as matrix for all experiments except for batch 1 where hospital wastewater was used. Before the actual experiment was started the sludge was aerated for 30 to 45 minutes to eliminate remaining substrate. When the oxygen concentration was below 5 mg/l the experiment was started (usually after 1 hour). Apart from oxygen concentration and temperature that were recorded automatically, the pH was measured and samples were taken at different time steps to analyze nitrification (nitrite and nitrate were analysed with IC and ammonia with photo spectrometry). In Table S14 the experimental condition of each batch experiment is described. As disinfectant, BAC C12

(Benzyltrimethylammonium, Sigma-Aldrich, Seelze, Germany) a quaternary ammonia compound was chosen and added as BAC C12-chloride salt in different concentrations. Ammonia was always added at a concentration of 10 mg NH₄ -N/l. The time when ammonia is added marks the initiation of the experiment. The disinfectant was always added one minute before ammonia. For each batch TSS and COD_{total} (Dr. Lange) were measured (see Table S14). The measured oxygen concentration during the non-aerated time span was used to calculate the oxygen consumption rate ($r_{O_2} = \Delta C_{O_2} / \Delta t$).

Table S17. Batch experiment condition description. All batches were run with sludge from the pilot plant, and are spiked with 10 mg NH₄-N/l

| Batch Nr. | Matrix | Additive | TSS | COD _{total} |
|-----------|---------------------|-----------------|---------|----------------------|
| B1 | hospital wastewater | - | 4 g/l | 3.7 g/l |
| B2 | drinking water | - | 4 g/l | 4 g/l |
| B3 | drinking water | 1 mg BAC C12/l | 3.4 g/l | 3.4 g/l |
| B4 | drinking water | 5 mg BAC C12/l | 3.4 g/l | 3.3 g/l |
| B5 | drinking water | 10 mg BAC C12/l | 3.2 g/l | 3.0 g/l |
| B6 | drinking water | 25 mg BAC C12/l | 3.2 g/l | 3.0 g/l |
| B7 | drinking water | 50 mg BAC C12/l | 3.2 g/l | 3.2 g/l |

In Figure S5 the oxygen consumption rates (ocr) of the seven different batch experiments (B1 - B7) are shown. B1 and B2 have a higher ocr than the other ones which is due to the higher TSS (4 g/l to 3 g/l). To calculate the inhibition by the disinfectant the ocr of B3 is used as the zero inhibition value. Up to a concentration of 5 mg BAC-C12/l and a TSS of 3 g/l (1.7 mg BAC-C12/g TSS) no effect on the nitrification process is detected. A certain inhibition (10-15 %) at a concentration of 10 mg BAC-C12/l and an almost complete inhibition with 50 mg BAC-C12/l can be observed. To calculate the maximum tolerable concentration (MTC) of BAC-C12 the no effect concentration (1.7 mg BAC-C12/g TSS) and the sludge production (SP) need to be considered. In the tested hospital wastewater 380 mg/l COD_{dissolved} was measured. With the assumption of particulate COD = 50 mg/l (COD_{tot} = 430 mg/l) and a specific sludge production (sSP) of 0.2 g TSS/g COD_{tot} the MTC results in 150 mg BAC-C12/m³ hospital wastewater.

$$SP = sSP * COD_{tot} = 86 \text{ g TSS} / m^3 \text{ hospital ww}$$

$$MTC = 1.7 \frac{\text{mg BAC-C12}}{\text{g TSS}} * 86 \frac{\text{g TSS}}{m^3 \text{ hospital ww}} = 150 \frac{\text{mg BAC-C12}}{m^3 \text{ hospital ww}}$$

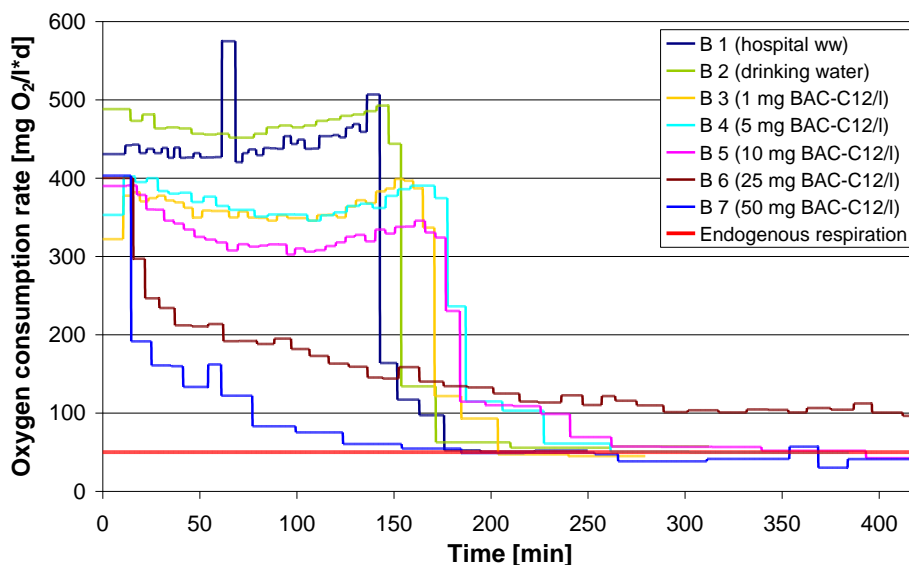


Figure S5. Oxygen consumption rates during the nitrification process in seven different batch experiments, where different amounts of BAC-C12 were added.

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