Supporting information for:

A high-resolution spatial model to predict exposure to pharmaceuticals in European surface waters – ePiE

Authors

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S1. Curation of UWWTD-Waterbase

The UWWTD-Waterbase database[1] contains spatial information on the location and characteristics of 27,695 European agglomerations, and 30,043 urban WWTPs and waste water collection systems. Agglomerations with a generated load below 2,000 p.e. (population equivalents) are not included in the database, since the directive does not require reporting on them.

The agglomeration characteristics reported in the database relevant for the ePiE model are their location (longitude and latitude coordinates), their generated load (p.e.), and the fraction connected to WWTP (-). Similarly, the UWWTD database contains for each WWTP the location (longitude and latitude coordinates), the load entering (p.e.), as well as its design capacity (p.e.). It must be noted that some WWTPs receive a combination of urban and industrial wastewater, of which the database only reports the combined load. Consequently, API loads towards such WWTPs might deviate from the estimations. In addition, each WWTP has been assigned an identification number related to the agglomeration connected to it, and the level of treatment is indicated.

Although the UWWTD-Waterbase database is extensive, it does contain some erroneous, missing, or ambiguous entries. Therefore, a curation of the database was performed. First, both agglomerations and WWTPs with missing coordinates or mixed up latitude and longitude were identified. This was the case for 1.2% of the agglomerations in the database. A few of these (16 records) had mixed up latitude and longitude, which was corrected. For another 13 agglomerations no coordinates were reported because their generated load was below 2,000 p.e. (population equivalents). These were excluded from further calculations. The remaining 292 agglomerations without correct coordinates (1.1% of the initial set) were also excluded

from further calculations. As a result, coordinates were available for 27,381 agglomerations in the database. From these, 799 were indicated in the database as 'inactive', generally due to merging of agglomerations into one record that were separately included in a previous version of the database, or because agglomerations dropped below the 2,000 p.e. size threshold for reporting. These agglomerations were also excluded from further calculations, resulting in a total of 26,582 agglomerations used in further calculations.

Of the wastewater treatment plants (WWTPs) in the database, 9.4% had missing or erroneous coordinates. Of these records, a few (11 records) had mixed up latitude and longitude, which were corrected. The exclusion of all WWTPs indicated in the database as being inactive reduced the database to 27,432 WWTPs and increased the percentage with correct coordinates to 94.2%. Of the remaining 5.8% of WWTP-records without correct coordinates (1,596 records), 784 were assigned coordinates of the agglomeration to which they were linked via the agglomeration identification number. Although this likely has led to a loss of accuracy in the estimation of the emission point for these WWTPs (location of WWTP now equals location of agglomeration linked to it), it was considered preferable over their exclusion. This resulted in a database with 26,620 WWTP-records with coordinates. The remaining 818 WWTP-records were removed from the database and excluded from further calculations. These were mainly Southern Italian, wastewater collecting systems without treatment connected to them. This resulted in 26,614 WWTP-records with coordinates in the database.

In principle, each WWTP included in the database is assigned an agglomeration identification number, ensuring that it is linked to an agglomeration in the database. In practice, however, only 12,765 of the 26,614 WWTP-records in the database (after curation for missing and

erroneous coordinates) had been assigned such an agglomeration identification number, leaving 13,849 without. In order to make a WWTP-based approach possible, the agglomerations connected to these WWTPs had to be deduced based on similarities in names, codes, coordinates, or loads generated. By doing this, we managed to increase the number of WWTPs with an agglomeration ID attached to it to 25,697. The remaining WWTPs were mainly located in Southern Italy. The 1,735 WWTP records that were excluded from the total database (818 due to missing/erroneous coordinates; 917 due to lack of agglomeration ID), represent ~3% of the total wastewater load entering all WWTPs in Europe. These WWTPs were included in the spatial distribution of the total consumption over agglomerations and WWTPs but were excluded from further concentration calculations.

After linking each WWTP to an agglomeration, 3,961 agglomerations were not yet connected to any WWTP-record. For 2,762 of these agglomerations, this is due to their 0% connectivity to wastewater collection and WWTPs. Instead, their wastewater might be (partly) addressed in independent appropriate systems (IAS), and might be (partly) discharged untreated. While the database does distinguish between these two options, we conservatively assumed direct discharge without treatment for all wastewater not directed towards a WWTP. From the remaining 1,199 of the agglomerations not connected to any WWTP, 562 could be linked to a WWTP serving multiple agglomerations (to which another agglomeration had already been linked). The final 637 agglomerations could not be linked to any WWTP. These were located in Southern Italy (428) and Croatia (209). For the Croatian records, this was due to the lack of information on their WWTP-connectivity (i.e., all Croatian agglomerations reported zero connectivity). Without knowing their WWTP-connectivity, it was not possible to determine whether they were actually connected to a WWTP. Furthermore, it should be noted that the

database does not contain any WWTPs in the vicinity of the Italian city of Napoli. Finally, a set of 26,607 unique combinations of agglomeration and WWTP was constructed.

S2. Model construction

River networks in ePiE were constructed for individual drainage basins as delineated by the global database HydroSHEDS.[2] Per basin, its borders were used to crop the river network, available as spatial line object at 30 arcseconds from the HydroSHEDS database, which were then translated into a binary 30 arcseconds raster with information on the presence or absence a river element. Next, the raster cells containing river elements were used to create a spatial point file, with each point representing a network node. All nodes were automatically classified as either:

1. junction (node where two streams meet, has two upstream nodes);
2. mouth (node where river flows into the sea);
3. start (nodes representing a river source);
4. regular node.

Via overlay of the river network with the lakes and reservoirs in the global database HydroLAKES[3], available as spatial polygons, nodes located within a lake or reservoir were identified. These nodes are skipped during model computations. Additionally, intersections between the river network and lakes and reservoirs were determined, and were added as additional nodes to the network, classified as either:

1. outlet (the one intersection per lake/reservoir closest to the river mouth);
2. inlet (all other intersections)

Properties associated to the lakes and reservoirs in HydroLAKES, i.e., depth and hydraulic retention time, were added to their corresponding outlet node.

After the curation steps described in SI1, the WWTPs and agglomerations from the UWWTD-Waterbase database[1] were snapped to the river network and incorporated as emission sources. Any WWTPs and agglomerations located within lakes or reservoirs were allocated to these as direct emission source. Direct emissions into the sea were excluded from the model. The up- and downstream node for all WWTP and agglomeration specific nodes was determined using its relative placement in the river network.

Using the flow direction raster available from HydroSHEDS, the hydrological interconnectivity of the nodes in the network was determined, including distances between them. Finally, gridded information on air temperature,[4] wind speed,[5] slope,[6] and streamflow[7] was extracted to all nodes in the network.

S3. Loss processes

Extrapolation of degradation rates

The ePiE model accounts for three degradation processes, i.e. biodegradation, photolysis and hydrolysis. It allows for the correction of individual degradation rate constants for differences between temperature under test conditions (T_{test}; K) and under field conditions (T_{field}; K), using a correction factor f_{temp} (-), based on Arrhenius' temperature dependence of reaction rates (Equation S3.1). When georeferenced water temperatures are not available, ePiE assumes a default value for T_{field} of 285 K.[8]

$$f_{temp} = 2^{\frac{\left(T_{field} - T_{test}\right)}{10}} \qquad \textit{Equation S3.1}$$

Additionally, degradation rate constants are corrected for sorption to suspended solids and dissolved organic carbon, assuming degradation processes only apply to the dissolved fraction of the API (f_{diss}; -):

$$f_{diss} = \frac{1}{1+K_{p,susp} \cdot C_{susp} + K_{p,DOC} \cdot C_{DOC}} \qquad \textit{Equation S3.2}$$

In Equation S3.2, sorption to suspended solids is characterized with the chemical's suspended solids-water partition coefficient $K_{p,susp}$ (L/kg) and the local concentration of suspended solids C_{susp} (kg/L). Similarly, sorption to dissolved organic carbon is characterized with the chemical's dissolved organic carbon-water partition coefficient $K_{p,DOC}$ (L/kg) and the local concentration of dissolved organic carbon C_{DOC} (kg/L). ePiE uses default values of $0.015*10^{-3}$ kg/L[9] and $0.005*10^{-3}$ kg/L[10] for C_{susp} and C_{DOC}, respectively, when geographical information on these parameters is not available.

Moreover, because values for $K_{p,susp}$ and $K_{p,DOC}$ are generally not available for many APIs, ePiE estimates them under the assumption that sorption is mainly driven by the organic carbon content. Values for $K_{p,DOC}$ are directly estimated from their octanol-water partition coefficient ($K_{OW,n}$; -) and acid dissociation constant (pK_a; -), according to Burkhard.[11] Values for $K_{p,susp}$ are based on a default value of 0.1 for the organic carbon content of suspended solids or ($f_{OC,susp}$)[12]. For nonionizing chemicals, the relationship derived by Sabljić et al.[13] between $K_{OW,n}$ and the organic carbon-water partitioning coefficient ($K_{OC,n}$; -) is then used to estimate $K_{p,susp}$:

$$K_{p,susp} = K_{OC,n} \cdot f_{OC,susp} = 1.26 \cdot {K_{OW,n}}^{0.81} \cdot f_{OC,susp} \qquad \textit{Equation S3.3}$$

For ionizing chemicals, estimation of $K_{p,susp}$ is more complex because their neutral and ionized forms show different sorption behaviour (Equation S3.4). Therefore, K_{OC} values are

first estimated for the individual ionization forms using quantitative structure-activity relationships (QSAR) as derived by Franco and Trapp.[14] Subsequently, these are combined based on the mass fractions of the individual forms (f_n, f_{cat}, f_{an}; -), determined via Henderson-Hasselbalch equations:

$$K_{p,susp} = \left(f_n \cdot K_{OC,n} + f_{cat} \cdot K_{OC,cat} + f_{an} \cdot K_{OC,an}\right) \cdot f_{OC,susp} \qquad \textit{Equation S3.4}$$

Because experimental photolysis rates are determined at water surface and at constant light, ePiE corrects them for reduced light intensity at local field conditions with correction factor f_{light} (-) (Equation S3.5).[15] Light intensity depends on the time fraction of light per day (f_{day}; -), for which we used a default value of 0.5, and reduces with local water depth (h_w; m) and turbidity. The latter is expressed as the ratio between the light's average path length through the water column and the water depth (D_λ; -), which we assigned a proposed default value for non-turbid waters of 1.2.[15] Finally, penetration of light through the water column differs for different wavelengths, as reflected by the wavelength-specific beam attenuation coefficient α_λ (cm^{-1}). The relationship between wavelength and α_λ as provided in Table 13.6 in Schwarzenbach et al.[15] was used to assign a value to α_λ for individual APIs based on their respective maximum absorption wavelengths λ_{max} (nm).

$$f_{light} = f_{day} \cdot \frac{1-10^{-D_\lambda \cdot \alpha_\lambda \cdot 100 \cdot h_w}}{\ln(10) \cdot D_\lambda \cdot \alpha_\lambda \cdot 100 \cdot h_w} \qquad \textit{Equation S3.5}$$

Intermedia transport rates

The ePiE model accounts for two intermedia transport processes, i.e. sedimentation and volatilization. Concentrations in sediments or air cannot be explicitly calculated with single-media models like ePiE, since they do not include separate compartments for these media.

Therefore, transport between media was directly accounted for via estimation of mass transport velocities.[16]

Sedimentation rates are derived by combining adsorption, desorption, sedimentation and resuspension velocities of suspended particulate into one equation describing the local rate of sedimentation k_{sed} (s^{-1}) (Equation S3.6). For estimation of k_{sed}, the sediment phase was treated as a homogeneous phase consisting of a water sub-phase and a solid sub-phase. Equilibrium was assumed between the pore water and solid sub-phases of the sediment phase, and the top layer of the sediment h_{sd} (m), with a default value of 0.03 m,[12] was considered to be well-mixed.

$$k_{sed} = \left(\frac{v_{ads}+v_{sed}}{h_w}\right) - \frac{\left(\frac{v_{ads}+v_{sed}}{h_w}\right)*\left(\frac{v_{res}+v_{des}}{h_{sd}}\right)}{\left(\frac{v_{res}+v_{des}+v_{sed,acc}}{h_{sd}}+k_{bio,sed}\right)} \qquad \textit{Equation S3.6}$$

in which k_{sed} is the local sedimentation rate (s^{-1}), and individual local velocities for adsorption, desorption, sedimentation, and resuspension (all expressed as m/s) are represented by v_{ads} (Equation S3.8), v_{des} (Equation S3.9), v_{sed} (Equation S3.10), and v_{res}, respectively (Equation S3.11). Additionally, k_{sed} depends on the net sediment accumulation rate in water $v_{sed,acc}$ (m/s), for which ePiE applies a default value $8.6*10^{-11}$ m/s, the same value that is used in the USEtox 2.0 model under default conditions. Moreover, k_{sed} is inversely related to the biodegradation of the chemical that might take place in the sediment layer ($k_{bio,sed}$; s^{-1}), since reduction of chemical in the sediment layer due to degradation will increase the mass flux towards the sediment layer to restore the equilibrium between water and sediment. In the absence of an experimental value for $k_{bio,sed}$, it is estimated from the biodegradation rate constant in surface water ($k_{bio,w}$; s^{-1}), with an extrapolation factor of 0.1,[17] a correction factor

for temperature (f_{temp}; Equation S3.1), and a correction factor for sorption ($f_{sed,diss}$; -) as proposed by Honti et al.[18]:

$$f_{sed,diss} = \frac{1}{1+Kp_{tot,sed}\cdot\rho_{s,sed}\cdot\frac{(1-\theta_{sed})}{\theta_{sed}}} \qquad \textit{Equation S3.7}$$

in which $Kp_{tot,sed}$ is the partitioning coefficient between water and sediment solids (L_{water}/kg_{solids}); $\rho_{s,sed}$ is the local mineral density of the sediment solids (kg_{solids}/L_{solids}); and θ_{sed} is the local porosity of the sediment ($L_{water}/L_{sediment}$). For $\rho_{s,sed}$ and θ_{sed}, ePiE applies default values of 2.33 kg_{solids}/L_{solids}[12, 18] and 0.8 $L_{water}/L_{sediment}$[19], respectively.

$$v_{ads} = \frac{v_{m,w,w|sd}\cdot v_{m,sd,w|sd}}{v_{m,w,w|sd}+v_{m,sd,w|sd}} \cdot f_{diss} \qquad \textit{Equation S3.8}$$

$$v_{des} = \frac{v_{m,w,w|sd}\cdot v_{m,sd,w|sd}}{v_{m,w,w|sd}+v_{m,sd,w|sd}} \cdot \frac{1}{K_{sd|w}} \qquad \textit{Equation S3.9}$$

Adsorption velocities v_{ads} and desorption velocities $v_{des,}$ are both estimated via partial mass transfer coefficients at the water/sediment interface, with $v_{m,w,w|sd}$ (m/s) representing the coefficient at the water side and $v_{m,sd,w|sd}$ (m/s) the coefficient at the sediment side. As proposed by Mackay [20], $v_{m,w,w|sd}$ and $v_{m,sd,w|sd}$ were assigned default values of $2.778*10^{-6}$ m/s and $2.778*10^{-8}$ m/s. The affinity of the chemical for sorption to the sediment is reflected in Equation S3.9 by the dimensionless sediment/water partition coefficient $K_{sd|w}$ (-).

$$v_{sed} = f_{V_{solid,sd}} \cdot v_{sed,gross} \cdot \rho_{sd} \cdot K_{p,susp} \cdot f_{diss} \qquad \textit{Equation S3.10}$$

$$v_{res} = v_{sed,gross} - v_{sed,acc} \qquad \textit{Equation S3.11}$$

Local sedimentation velocities v_{sed} and resuspension velocities v_{res} both depend on the gross local sedimentation rate from water $v_{sed,gross}$ (m/s), which is derived as follows:

If $v_{sed,susp} \cdot \frac{C_{susp}}{\rho_{sd,bulk}} > v_{sed,acc}$ then:

$v_{sed,gross} = v_{sed,susp} \cdot \frac{C_{susp}}{\rho_{sd,bulk}}$ else: *Equation S3.12*

$v_{sed,gross} = v_{sed,acc}$

in which $\rho_{sd,bulk}$ is the local bulk density of the sediment (kg/L; see Equation S3.13), and $v_{sed,susp}$ is the settling velocity of suspended particles (m/s), for which we applied a default value of 2.89*10^{-5} m/s.[21] Moreover, $v_{sed,acc}$ is the aforementioned net sediment accumulation rate in water (see Equation S3.6). Equations S3.10 through S3.12 imply that, if the sedimentation of particles from the water column is greater than the resuspension (i.e., there is a net sedimentation), the top layer is continuously refreshed. The older sediment layer, and with it the chemicals that are associated with the sediment, then gets buried under the freshly deposited material.

$\rho_{sd,bulk} = 1 - f_{V_{solid,sd}} + f_{V_{solid,sd}} \cdot \rho_{sd}$ *Equation S3.13*

In which the volume fraction solids in sediment is represented by $f_{V_{solid,sd}}$ (-), and the mineral density of the sediment by ρ_{sd} (kg/L). These were assigned default values of 0.2[19] and 2.1633 kg/L[12], respectively.

Same as for sediments, concentrations in air are not explicitly calculated by ePiE, since it does not include a separate air compartment. Therefore, the intermedia volatilization rate between water and air k_{vol} (s^{-1}) was directly accounted for in Equation S3.14 via estimation of the volatilization velocity (Equation S3.15):

$k_{vol} = \frac{v_{vol}}{h_w}$ *Equation S3.14*

$v_{vol} = \frac{v_{m,a,a|w} \cdot v_{m,w,a|w}}{v_{m,a,a|w} \cdot K_{a|w} + v_{m,w,a|w}} \cdot K_{a|w} \cdot f_{diss}$ *Equation S3.15*

The volatilization velocity v_{vol} (m/s) was estimated via local partial mass transfer coefficients at the air/water interface, with $v_{m,a,a|w}$ (m/s) representing the coefficient at the air side (Equation S3.16) and $v_{m,a,a|w}$ (m/s) the coefficient at the water side (Equation S3.17). Moreover, $K_{a|w}$ represents the dimensionless chemical-specific air/water partition coefficient, estimated via Equation S3.18.

$$v_{m,a,a|w} = 0.01 \cdot (0.3 + 0.2 \cdot v_{wind}) \cdot \frac{18}{MW}^{(0.67 \cdot 0.5)} \qquad \textit{Equation S3.16}$$

$$v_{m,w,a|w} = 0.01 \cdot (0.0004 + 0.00004 \cdot {v_{wind}}^2) \cdot \frac{32}{MW}^{(0.5 \cdot 0.5)} \qquad \textit{Equation S3.17}$$

$$K_{a|w} = \frac{P_v \cdot MW}{S_w \cdot R \cdot T_{air}} \qquad \textit{Equation S3.18}$$

In these equations, environmental parameters v_{wind} and T_{air} represent the local wind speed (m/s) and air temperature (K), respectively. Physicochemical properties required are molecular weight MW (g/mol), vapour pressure P_v (Pa), and water solubility S_w (mg/L). R is the universal gas constant (8.314 Pa/m^3/mol/K).

S4. Chemical model parameterization

Table S4.1. Physicochemical parameterisation of APIs.

API	CAS RN	MW (g/mol)	Ref	Pv (Pa)	Ref	S (mg/L)	Ref	Class [a]	pK_a (-)	Ref	$K_{OW,n}$ (-)	Ref
Acetaminophen	103–90–2	151.16	[22]	$2.59*10^{-4}$	[23]	$1.40*10^{4}$	[22]	acid	9.46	[22]	1.86	[23]
Amitriptyline	28981–97–7	277.40	[22]	$4.83*10^{-5}$	[23]	9.71	[22]	base	9.76	[22]	$8.89*10^{4}$	[23]
Atenolol	29122–68–7	266.34	[22]	$1.03*10^{-7}$	[23]	$1.33*10^{4}$	[22]	base	9.60	[22]	$9.42*10^{-1}$	[23]
Bezafibrate	41859–67–0	361.82	[22]	$8.15*10^{-9}$	[23]	1.22	[23]	acid	3.83	[22]	$1.78*10^{4}$	[23]
Carbamazepine	298–46–4	236.27	[22]	$1.17*10^{-5}$	[23]	$1.77*10^{1}$	[22]	neutral	NA	[22]	$1.77*10^{2}$	[23]
Cimetidine	51481–61–9	252.34	[22]	$1.85*10^{-7}$	[23]	$9.38*10^{3}$	[22]	base	6.80	[22]	3.75	[23]
Citalopram	59729–33–8	324.39	[22]	$1.51*10^{-5}$	[23]	$3.11*10^{1}$	[23]	base	9.78	[22]	$5.52*10^{3}$	[23]
Codeine	76-57-3	299.36	[22]	$2.55*10^{-8}$	[23]	$9.00*10^{3}$	[23]	base	9.19	[22]	$1.89*10^{1}$	[23]
Desvenlafaxine	93413–62–8	263.38	[22]	$9.13*10^{-6}$	[23]	$3.67*10^{3}$	[23]	base	8.87	[22]	$5.25*10^{2}$	[23]
Diazepam	439–14–5	284.74	[22]	$1.36*10^{-5}$	[23]	$5.00*10^{1}$	[22]	base	3.40	[22]	$5.01*10^{2}$	[23]
Diclofenac	15307–86–5	296.15	[22]	$8.19*10^{-6}$	[23]	2.37	[22]	acid	4.15	[22]	$3.24*10^{4}$	[23]
Diltiazem	42399–41–7	414.52	[22]	$3.97*10^{-9}$	[23]	$4.65*10^{2}$	[22]	base	8.18	[22]	$6.23*10^{2}$	[23]
Erythromycin	114–07–8	733.93	[22]	$2.83*10^{-23}$	[23]	$2.00*10^{3}$	[22]	base	8.38	[22]	$3.01*10^{2}$	[23]
Gabapentin	60142-96-3	171.24	[22]	$3.92*10^{-8}$	[23]	$4.49*10^{3}$	[22]	acid	4.63	[22]	$4.27*10^{-2}$	[23]
Hydrocodone	125–29–1	299.36	[22]	$1.61*10^{-5}$	[23]	$1.79*10^{3}$	[23]	base	8.61	[22]	$1.46*10^{2}$	[23]
Ibuprofen	15687–27–1	206.28	[22]	$2.48*10^{-2}$	[23]	$2.10*10^{1}$	[22]	acid	4.85	[22]	$9.33*10^{3}$	[23]
Indomethacin	53–86–1	357.79	[22]	$6.82*10^{-8}$	[23]	$9.37*10^{-1}$	[22]	acid	3.8	[22]	$1.86*10^{4}$	[23]
Lidocaine	137–58–6	234.34	[22]	$9.01*10^{-4}$	[23]	$7.97*10^{-1}$	[22]	base	7.75	[22]	$4.56*10^{1}$	[23]
Loratadine	79794–75–5	382.88	[22]	$1.21*10^{-6}$	[23]	$4.10*10^{3}$	[22]	neutral	NA	[22]	$4.54*10^{5}$	[23]
Metformin	657–24–9	129.16	[22]	$1.01*10^{-2}$	[23]	$1.00*10^{6}$	[23]	base	12.4	[22]	$2.29*10^{-3}$	[23]
Naproxen	22204–53–1	230.26	[22]	$1.70*10^{-4}$	[23]	$1.59*10^{1}$	[22]	acid	4.15	[22]	$1.51*10^{3}$	[23]
Norethindrone	68–22–4	298.42	[22]	$3.15*10^{-7}$	[23]	7.04	[22]	neutral	NA	[22]	$9.74*10^{2}$	[23]
Oseltamivir	196618-13-0	312.40	[22]	$1.75*10^{-6}$	[23]	$6.86*10^{-1}$	[22]	acid	7.7	[22]	8.91	[23]
Oxazepam	604-75-1	286.71	[22]	$8.04*10^{-10}$	[23]	$1.79*10^{2}$	[22]	neutral	NA	[22]	$2.10*10^{2}$	[23]
Propranolol	525–66–6	259.34	[22]	$1.26*10^{-5}$	[23]	$6.17*10^{1}$	[22]	base	9.67	[22]	$3.96*10^{2}$	[23]

Ranitidine	66357–35–5	314.40	[22]	$1.86*10^{-4}$	[23]	$2.47*10^{1}$	[22]	base	8.08	[22]	1.97	[23]
Sertraline	79617–96–2	306.23	[22]	$1.56*10^{-4}$	[23]	3.50	[22]	base	9.85	[22]	$1.93*10^{5}$	[23]
Sitagliptin	486460–32–6	407.31	[22]	$3.88*10^{-6}$	[23]	$3.40*10^{-2}$	[22]	base	8.78	[22]	$2.45*10^{1}$	[23]
Sulfamethoxazole	723–46–6	253.28	[22]	$1.73*10^{-5}$	[23]	$6.10*10^{2}$	[22]	acid	6.16	[22]	3.05	[23]
Temazepam	846–50–4	300.74	[22]	$2.27*10^{-8}$	[23]	$1.64*10^{2}$	[22]	neutral	NA	[22]	$1.41*10^{2}$	[23]
Tramadol	27203–92–5	263.38	[22]	$6.09*10^{-5}$	[23]	$1.15*10^{3}$	[23]	base	9.23	[22]	$1.03*10^{3}$	[23]
Triamterene	396–01–0	253.26	[22]	$1.45*10^{-9}$	[23]	$4.82*10^{1}$	[22]	neutral	NA	[22]	6.29	[23]
Trimethoprim	738–70–5	290.32	[22]	$1.00*10^{-6}$	[23]	$4.00*10^{2}$	[22]	base	7.12	[22]	5.36	[23]
Venlafaxine	93413–69–5	277.40	[22]	$3.28*10^{-5}$	[23]	$5.72*10^{5}$	[22]	base	8.91	[22]	$1.91*10^{3}$	[23]
Verapamil	52–53–9	454.60	[22]	$5.57*10^{-7}$	[23]	4.47	[22]	base	9.68	[22]	$6.26*10^{4}$	[23]

MW: molecular weight; Pv: vapour pressure; S: water solubility; pK_a: acid dissociation constant; $K_{OW,n}$: octanol-water partition coefficient of the neutral form. [a] Classification as neutral/acid/base was based on ionization states at pH 7 of strongest acid and strongest base pKa values.

Table S4.2. Environmental fate parameterisation of APIs.

API	CAS RN	f_{pc} (-)	Ref	f_{met} (-)	Ref	$K_{p,ps}$ (L/kg)	n	Ref	$K_{p,as}$ (L/kg)	n	Ref	$K_{p,sed}$ (L/kg)	n	Ref
Acetaminophen	103–90–2	0.52	[24]	NA	-	$5.11*10^1$	6	[25-28]	$3.15*10^2$	5	[25, 27-30]	3.27	7	[31-34]
Amitriptyline	28981–97–7	0.03	[35]	NA	-	$1.19*10^4$	3	[28, 36, 37]	$3.46*10^3$	15	[28, 36-39]	NA	0	-
Atenolol	29122–68–7	0.86	[24]	NA	-	$2.00*10^2$	3	[27, 28, 36]	$4.13*10^2$	9	[27, 28, 36, 38, 40-43]	7.82	11	[31, 33, 34, 44-46]
Bezafibrate	41859–67–0	0.63	[24]	NA	-	$1.79*10^1$	2	[25]	$8.70*10^1$	1	[47]	$3.18*10^1$	3	[48]
Carbamazepine	298–46–4	0.15	[24]	NA	-	$1.16*10^2$	13	[25-28, 37, 49-51]	$5.89*10^2$	29	[25-30, 37, 39-41, 47, 49, 51-54]	$1.24*10^1$	14	[31-34, 55-58]
Cimetidine	51481–61–9	0.48	[59]	NA	-	NA	0	-	$3.60*10^2$	6	[39]	$1.43*10^2$	6	[33, 58]
Citalopram	59729–33–8	0.97	[24]	NA	-	$1.28*10^4$	2	[36, 37]	$2.56*10^3$	7	[36-38, 41]	$1.37*10^4$	2	[60]
Codeine	76-57-3	0.40	[61]	NA	-	NA	0	-	$1.40*10^1$	2	[30, 40]	8.10	2	[62]
Desvenlafaxine	93413–62–8	0.65	[63]	0.55	[64]	$1.40*10^2$	1	[37]	$1.01*10^2$	4	[37]	NA	0	-
Diazepam	439–14–5	0.11	[24]	NA	-	$1.68*10^2$	2	[28, 51]	$1.42*10^2$	11	[28, 39, 40, 51]	7.43	4	[45, 55, 62]
Diclofenac	15307–86–5	0.06	[24]	NA	-	$2.42*10^2$	8	[25, 27, 50, 51, 65, 66]	$2.16*10^2$	13	[27, 29, 36, 38, 39, 51-53, 65-69]	$2.94*10^1$	9	[48, 58]
Diltiazem	42399–41–7	0.03	[35]	NA	-	$2.19*10^2$	1	[26]	$1.96*10^2$	6	[26, 30, 36, 41]	$4.33*10^2$	3	[33, 70]
Erythromycin	114–07–8	0.98	[24]	NA	-	$1.74*10^2$	4	[25, 27, 71]	$9.49*10^1$	5	[25, 27, 38, 71]	$5.32*10^2$	3	[72-74]
Gabapentin	60142-96-3	1.00	[35]	NA	-	NA	0	-	NA	0	-	NA	0	-
Hydrocodone	125–29–1	0.12	[35]	0.11	[75]	NA	0	-	$1.19*10^2$	5	[39]	NA	0	-
Ibuprofen	15687–27–1	0.20	[24]	NA	-	$1.08*10^1$	3	[25, 27]	$2.00*10^2$	9	[36, 39, 51-53, 68, 69]	$1.50*10^1$	15	[34, 48, 57, 58]
Indomethacin	53–86–1	0.20	[76]	NA	-	NA	0	-	$1.26*10^2$	2	[38, 52]	2.81	3	[34]
Lidocaine	137–58–6	0.08	[24]	NA	-	NA	0	-	$3.30*10^1$	1	[43]	NA	0	-
Loratadine	79794–75–5	0.20	[77]	NA	-	$2.34*10^3$	1	[27]	$3.32*10^3$	1	[27]	NA	0	-
Metformin	657–24–9	1.00	[63]	NA	-	NA	0	-	$1.62*10^1$	2	[29, 30]	NA	0	-
Naproxen	22204–53–1	0.70	[63]	NA	-	$1.26*10^1$	1	[66]	$6.03*10^1$	7	[38, 39, 52, 53, 66, 68, 69]	1.73	7	[31, 45, 57, 58]
Norethindrone	68–22–4	0.05	[35]	NA	-	$5.15*10^1$	2	[50]	NA	0	-	$1.28*10^2$	1	[78]
Oseltamivir	196618-13-0	0.25	[24]	NA	-	NA	0	-	9.96	2	[79]	NA	0	-
Oxazepam	604-75-1	1.00	[24]	0.03	[63]	$7.90*10^2$	1	[36]	$9.91*10^2$	4	[36, 40, 41]	9.23	3	[55, 62]

Propranolol	525–66–6	0.26	24	NA	-	$3.92*10^3$	4	26, 27	$6.11*10^2$	14	26, 27, 38, 40-43, 49, 80	$1.78*10^2$	10	33, 34, 44, 56, 70, 81
Ranitidine	66357–35–5	0.38	24	NA	-	NA	0	-	$4.25*10^2$	2	30, 82	NA	0	-
Sertraline	79617–96–2	0.14	63	NA	-	$3.00*10^4$	2	36, 37	$1.97*10^4$	7	36-38, 41	$1.71*10^2$	2	60
Sitagliptin	486460–32–6	0.79	35	NA	-	NA	0	-	NA	0	-	NA	0	-
Sulfamethoxazole	723–46–6	0.35	24	NA	-	$5.82*10^1$	7	25, 27, 28, 36, 50, 71	$1.74*10^2$	21	25-28, 30, 36, 38, 39, 47, 53, 71, 82, 83	$5.06*10^1$	10	31, 62, 72, 74, 84, 85
Temazepam	846–50–4	0.05	35	0.07	86	NA	0	-	NA	0	-	$1.66*10^1$	2	62
Tramadol	27203–92–5	0.27	61	NA	-	$1.10*10^2$	1	36	$1.19*10^2$	2	36, 40	5.05	2	62
Triamterene	396–01–0	0.21	35	NA	-	NA	0	-	NA	0	-	NA	0	-
Trimethoprim	738–70–5	0.50	63	NA	-	$2.42*10^2$	6	25, 27, 28, 36, 71	$2.09*10^2$	22	25-28, 30, 36, 38, 39, 47, 71, 83, 87	$1.21*10^3$	8	45, 58, 70, 74, 88
Venlafaxine	93413–69–5	0.05	35	NA	-	$1.50*10^3$	1	37	$2.42*10^2$	7	36, 37, 41, 43	NA	0	-
Verapamil	52–53–9	0.04	35	NA	-	$1.72*10^3$	2	28, 36	$3.15*10^3$	5	28, 36, 41	$1.70*10^2$	1	58

API	**$k_{bio,wwtp}$ (s^{-1})**	**n**	**Ref**	**$k_{bio,sw}$ (s^{-1})**	**n**	**Ref**	**k_{photo} (s^{-1})**	**n**	**Ref**	**λ_{max} (nm)**	**Ref**	**$k_{hyd,sw}$ (s^{-1})**	**n**	**Ref**
Acetaminophen	$5.01*10^{-4}$	4	30, 89-91	$8.36*10^{-6}$	3	34, 92, 93	$4.55*10^{-6}$	5	34, 92-94	250	94	0.00	3	92-94
Amitriptyline	NA	0	-	0.00	1	93	0.00	1	93	270	95	$2.35*10^{-7}$	2	93, 95
Atenolol	$5.37*10^{-5}$	5	40, 42, 43, 96, 97	$5.42*10^{-7}$	2	34, 93	$3.33*10^{-6}$	14	34, 93, 98-106	275	95, 100, 101, 107	$7.25*10^{-7}$	7	93, 95, 101-103, 106
Bezafibrate	$5.95*10^{-5}$	2	47, 90	NA	0	-	NA	0	-	NA	-	NA	0	-
Carbamazepine	$1.75*10^{-6}$	11	30, 40, 52, 54, 68, 82, 89, 108-110	$2.31*10^{-8}$	5	34, 92, 93, 111, 112	$9.48*10^{-6}$	20	34, 92, 93, 99, 111, 113-120	285	95, 114, 115, 118	$1.67*10^{-9}$	5	92, 93, 95, 111, 114
Cimetidine	NA	0	-	0.00	2	121	$1.74*10^{-4}$	2	105, 122	218	122	0.00	1	122
Citalopram	$5.56*10^{-5}$	1	110	NA	0	-	$3.88*10^{-7}$	2	60	285	95	$8.59*10^{-8}$	2	60, 95
Codeine	$2.28*10^{-5}$	2	30, 40	$2.38*10^{-7}$	1	123	$6.83*10^{-5}$	2	105, 123	300	124	0.00	1	123
Desvenlafaxine	NA	0	-	$1.57*10^{-8}$	3	112, 125, 126	$8.96*10^{-6}$	1	126	275	126	$4.06*10^{-7}$	1	126
Diazepam	$1.85*10^{-5}$	1	68	$3.85*10^{-11}$	1	127	$4.67*10^{-6}$	3	128-130	315	128, 130	$4.06*10^{-7}$	3	127, 128, 130
Diclofenac	$1.41*10^{-5}$	9	47, 52, 59, 68, 89, 90, 109, 110	$8.28*10^{-8}$	6	70, 93, 131-134	$4.84*10^{-4}$	7	70, 93, 113, 132, 133, 135-137	275	133, 137-139	$1.16*10^{-8}$	4	70, 133, 134, 140
Diltiazem	$8.15*10^{-6}$	3	30	$1.08*10^{-6}$	2	121	$2.06*10^{-5}$	1	98	280	98	$1.43*10^{-6}$	1	141

Erythromycin	$4.63*10^{-5}$	4	54, 68, 90, 110, 142	$8.02*10^{-8}$	1	143	$4.51*10^{-6}$	2	105, 144	214	144	NA	0	-
Gabapentin	$1.15*10^{-6}$	1	91	$8.02*10^{-8}$	1	145	$2.00*10^{-5}$	1	106	276	146	$1.33*10^{-5}$	1	106
Hydrocodone	NA	0	-	$4.34*10^{-7}$	2	121	NA	0	-	NA	-	NA	0	-
Ibuprofen	$1.97*10^{-4}$	8	47, 52, 59, 68, 90, 109, 110, 147	$8.27*10^{-7}$	4	34, 93, 134, 147	$3.85*10^{-6}$	6	34, 93, 119, 120, 148, 149	265	119, 150	$2.31*10^{-7}$	2	134, 148
Indomethacin	$4.73*10^{-5}$	2	52, 90	$2.69*10^{-7}$	3	34, 93, 94	$2.46*10^{-5}$	3	34, 93, 94	265	94	0.00	1	94
Lidocaine	$1.62*10^{-7}$	1	43	$7.22*10^{-8}$	1	126	$4.36*10^{-6}$	1	126	260	126	$4.06*10^{-7}$	1	126
Loratadine	NA	0	-	NA	0	-	NA	0	-	NA	-	NA	0	-
Metformin	$1.05*10^{-4}$	2	30, 151	$8.02*10^{-8}$	1	152	$3.33*10^{-7}$	1	106	232	153	$1.50*10^{-5}$	1	106
Naproxen	$1.63*10^{-5}$	9	47, 52, 59, 68, 90, 108	$7.72*10^{-7}$	2	93, 134	$1.15*10^{-4}$	3	93, 148, 149	260	149	$5.02*10^{-8}$	3	134, 148
Norethindrone	NA	0	-	$2.55*10^{-7}$	1	131	NA	0	-	NA	-	0.00	1	131
Oseltamivir	0.00	1	79	$5.02*10^{-8}$	3	79, 154	$8.08*10^{-6}$	2	155, 156	225	156	$6.19*10^{-8}$	3	95, 155, 156
Oxazepam	0.00	1	40	NA	0	-	$7.82*10^{-6}$	2	128, 130	315	95, 128, 130	0.00	3	95, 128, 130
Propranolol	$1.83*10^{-5}$	4	40, 42, 43, 80	$1.24*10^{-5}$	3	34, 93, 111	$3.91*10^{-5}$	14	34, 70, 93, 99-101, 103, 105, 111, 113, 149, 157	288	100, 101	0.00	3	93, 111, 121
Ranitidine	$2.55*10^{-5}$	3	30, 82, 97	$6.80*10^{-8}$	2	121	$4.55*10^{-5}$	1	122	315	122, 158	0.00	1	122
Sertraline	NA	0	-	0.00	1	92	$1.23*10^{-6}$	2	92, 129	205	159	0.00	1	92
Sitagliptin	NA	0	-	NA	0	-	NA	0	-	NA	-	NA	0	-
Sulfamethoxazole	$2.63*10^{-5}$	10	30, 68, 82, 89, 90, 110, 142, 160, 161	$8.90*10^{-6}$	6	85, 92, 93, 111, 132, 162	$1.11*10^{-4}$	15	92, 99, 108, 111, 113, 115, 144, 163-166	274	115, 144, 165	$4.95*10^{-8}$	5	85, 92, 95, 111, 131
Temazepam	NA	0	-	NA	0	-	$5.39*10^{-6}$	1	130	315	130	0.00	1	130
Tramadol	0.00	1	40	NA	0	-	$4.33*10^{-4}$	2	126, 167	271	126, 167	$1.47*10^{-7}$	3	95, 126, 167
Triamterene	NA	0	-	NA	0	-	NA	0	-	NA	-	NA	0	-
Trimethoprim	$2.53*10^{-6}$	7	54, 68, 87, 110, 142, 161	0.00	2	92, 93	$7.85*10^{-6}$	5	92, 105, 108, 166, 168	283	95	$2.70*10^{-8}$	4	92, 93, 95, 169
Venlafaxine	$8.09*10^{-8}$	2	43, 147	$1.94*10^{-8}$	3	125, 126, 147	$3.41*10^{-6}$	1	126	275	95, 126	$2.10*10^{-7}$	2	95, 126
Verapamil	NA	0	-	NA	0	-	NA	0	-	NA	-	NA	0	-

f_{pc}: fraction of administered parent compound excreted/egested unchanged or as reversible conjugates via urine and feces; f_{met}: fraction of prodrug metabolized to the API of interest and excreted/egested via urine and feces; $K_{p,ps}$: sorption coefficient to primary sewage; $K_{p,as}$: sorption coefficient to activated sludge; $K_{p,sed}$: sorption coefficient to sediment; $k_{bio,wwtp}$: (pseudo-)first order biodegradation rate in WWTP; $k_{bio,sw}$: (pseudo-)first order biodegradation rate in surface water; k_{photo}: first order photolysis rate in surface water; λ_{max}: maximum absorption wavelength; $k_{hyd,sw}$: first order hydrolysis rate in surface water.

S5. Consumption data

Table S5.1. Consumption data per API for each country and year as included in the model evaluation (kg/yr).

	Austria				Belgium				France			
API	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**
Acetaminophen	$1.58*10^{5}$ [a]	-	-	-	$2.08*10^{5}$ [a]	-	-	-	$3.45*10^{6}$ [b]	-	-	[170]
Amitriptyline	$7.00*10^{2}$ [a]	-	-	-	$9.20*10^{2}$ [a]	-	-	-	$5.43*10^{3}$ [a]	-	-	-
Atenolol	$1.39*10^{3}$ [a]	$1.41*10^{3}$ [a]	$1.42*10^{3}$ [a]	-	$1.83*10^{3}$ [a]	$1.85*10^{3}$ [a]	$1.86*10^{3}$ [a]	-	$1.91*10^{4}$ [b]	$1.93*10^{4}$ [b]	$1.94*10^{4}$ [b]	[170]
Bezafibrate	$1.28*10^{3}$ [a]	-	-	-	$1.68*10^{3}$ [a]	-	-	-	$2.18*10^{4}$ [b]	-	-	[170]
Carbamazepine	$4.40*10^{3}$ [a]	$4.39*10^{3}$ [a]	$4.39*10^{3}$ [a]	-	$5.78*10^{3}$ [a]	$5.78*10^{3}$ [a]	$5.77*10^{3}$ [a]	-	$3.50*10^{4}$ [b]	$3.53*10^{4}$ [b]	$3.55*10^{4}$ [b]	[170]
Cimetidine	-	-	-	-	-	-	-	-	-	-	-	-
Citalopram	$5.52*10^{2}$ [a]	$5.62*10^{2}$ [a]	$5.69*10^{2}$ [a]	-	$7.25*10^{2}$ [a]	$7.40*10^{2}$ [a]	$7.47*10^{2}$ [a]	-	$3.64*10^{3}$ [b]	$3.67*10^{3}$ [b]	$3.69*10^{3}$ [b]	[170]
Codeine	-	-	-	-	-	-	-	-	-	-	-	-
Desvenlafaxine	-	-	-	-	-	-	-	-	-	-	-	-
Diazepam	$4.91*10^{1}$ [a]	-	-	-	$6.45*10^{1}$ [a]	-	-	-	$5.49*10^{2}$ [b]	-	-	[170]
Diclofenac	$4.67*10^{3}$ [a]	-	-	-	$6.14*10^{3}$ [a]	-	-	-	$1.03*10^{4}$ [b]	-	-	[170]
Diltiazem	-	$1.64*10^{3}$ [a]	$1.56*10^{3}$ [a]	-	-	$2.16*10^{3}$ [a]	$2.05*10^{3}$ [a]	-	-	$1.27*10^{4}$ [a]	$1.21*10^{4}$ [a]	-
Erythromycin	$4.31*10^{2}$ [a]	$4.26*10^{2}$ [a]	$4.21*10^{2}$ [a]	-	$5.66*10^{2}$ [a]	$5.61*10^{2}$ [a]	$5.53*10^{2}$ [a]	-	$3.34*10^{3}$ [a]	$3.30*10^{3}$ [a]	$3.26*10^{3}$ [a]	-
Gabapentin	$4.39*10^{3}$ [a]	$4.47*10^{3}$ [a]	$4.53*10^{3}$ [a]	-	$5.76*10^{3}$ [a]	$5.89*10^{3}$ [a]	$5.96*10^{3}$ [a]	-	$3.40*10^{4}$ [a]	$3.47*10^{4}$ [a]	$3.51*10^{4}$ [a]	-
Hydrocodone	-	-	-	-	-	-	-	-	-	-	-	-
Ibuprofen	$3.32*10^{4}$ [a]	-	-	-	$4.36*10^{4}$ [a]	-	-	-	$2.50*10^{5}$ [b]	-	-	[170]
Indomethacin	$1.05*10^{2}$ [a]	-	-	-	$1.38*10^{2}$ [a]	-	-	-	$1.04*10^{3}$ [b]	-	-	[170]
Lidocaine	$4.54*10^{3}$ [a]	-	-	-	$5.96*10^{3}$ [a]	-	-	-	$3.52*10^{4}$ [a]	-	-	-
Loratadine	-	-	-	-	-	-	-	-	-	-	-	-
Metformin	$1.05*10^{5}$ [a]	-	-	-	$1.38*10^{5}$ [a]	-	-	-	$7.48*10^{5}$ [b]	-	-	[170]
Naproxen	$3.36*10^{3}$ [a]	-	-	-	$4.41*10^{3}$ [a]	-	-	-	$3.89*10^{4}$ [b]	-	-	[170]
Norethindrone	-	-	-	-	-	-	-	-	-	-	-	-

Oseltamivir	-	-	-	-	-	-	-	-	-	-	-	-
Oxazepam	-	-	-	-	-	-	-	-	-	-	-	-
Propranolol	$8.60*10^{2\,a}$	$8.69*10^{2\,a}$	$8.71*10^{2\,a}$	-	$1.13*10^{3\,a}$	$1.14*10^{3\,a}$	$1.14*10^{3\,a}$	-	$1.30*10^{4\,b}$	$1.32*10^{4\,b}$	$1.32*10^{4\,b}$	[170]
Ranitidine	$2.04*10^{3\,a}$	-	-	-	$2.68*10^{3\,a}$	-	-	-	$1.22*10^{4\,b}$	-	-	[170]
Sertraline	-	-	-	-	-	-	-	-	-	-	-	-
Sitagliptin	$3.66*10^{2\,a}$	$4.19*10^{2\,a}$	$4.10*10^{2\,a}$	-	$4.81*10^{2\,a}$	$5.52*10^{2\,a}$	$5.39*10^{2\,a}$	-	$2.84*10^{3\,a}$	$3.25*10^{3\,a}$	$3.18*10^{3\,a}$	-
Sulfamethoxazole	$2.28*10^{3\,a}$	$2.18*10^{3\,a}$	$2.17*10^{3\,a}$	-	$3.00*10^{3\,a}$	$2.88*10^{3\,a}$	$2.85*10^{3\,a}$	-	$1.75*10^{4\,b}$	$1.76*10^{4\,b}$	$1.77*10^{4\,b}$	[170]
Temazepam	-	-	-	-	-	-	-	-	-	-	-	-
Tramadol	$2.43*10^{3\,a}$	-	-	-	$3.19*10^{3\,a}$	-	-	-	$2.70*10^{4\,b}$	-	-	[170]
Triamterene	-	-	-	-	-	-	-	-	-	-	-	-
Trimethoprim	$4.26*10^{2\,a}$	$4.24*10^{2\,a}$	$4.22*10^{2\,a}$	-	$5.60*10^{2\,a}$	$5.59*10^{2\,a}$	$5.55*10^{2\,a}$	-	$3.49*10^{3\,b}$	$3.52*10^{3\,b}$	$3.54*10^{3\,b}$	[170]
Venlafaxine	$1.32*10^{3\,a}$	$1.35*10^{3\,a}$	$1.37*10^{3\,a}$	-	$1.73*10^{3\,a}$	$1.79*10^{3\,a}$	$1.80*10^{3\,a}$	-	$1.02*10^{4\,b}$	$1.05*10^{4\,b}$	$1.06*10^{4\,b}$	[170]
Verapamil	$1.74*10^{3\,a}$	-	-	-	$2.28*10^{3\,a}$	-	-	-	$1.35*10^{4\,a}$	-	-	-
	Germany				**Luxembourg**				**Netherlands**			
API	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**
Acetaminophen	$5.52*10^{5\,c}$	-	-	[170]	$9.68*10^{3\,a}$	-	-	-	$5.52*10^{5}$	-	-	[171]
Amitriptyline	$7.34*10^{3\,c}$	-	-	[170]	$4.28*10^{1\,a}$	-	-	-	$1.26*10^{3}$	-	-	[171]
Atenolol	$7.32*10^{3\,c}$	$7.35*10^{3\,c}$	$7.37*10^{3\,c}$	[170]	$8.52*10^{1\,a}$	$9.11*10^{1\,a}$	$9.33*10^{1\,a}$	-	$2.50*10^{3}$	$2.20*10^{3}$	$2.05*10^{3}$	[171]
Bezafibrate	$1.51*10^{4\,c}$	-	-	[170]	$7.83*10^{1\,a}$	-	-	-	$3.96*10^{2}$	-	-	[171]
Carbamazepine	$6.29*10^{4\,c}$	$6.31*10^{4\,c}$	$6.33*10^{4\,c}$	[170]	$2.69*10^{2\,a}$	$2.79*10^{2\,a}$	$2.83*10^{2\,a}$	-	$7.56*10^{3}$	$7.23*10^{3}$	$7.01*10^{3}$	[171]
Cimetidine	-	-	-	-	-	-	-	-	-	-	-	-
Citalopram	$4.89*10^{3\,c}$	$4.91*10^{3\,c}$	$4.92*10^{3\,c}$	[170]	$3.37*10^{1\,a}$	$3.57*10^{1\,a}$	$3.67*10^{1\,a}$	-	$8.20*10^{2}$	$8.64*10^{2}$	$8.90*10^{2}$	[171]
Codeine	-	-	-	-	-	-	-	-	-	-	-	-
Desvenlafaxine	-	-	-	-	-	-	-	-	-	-	-	-
Diazepam	$4.89*10^{2\,c}$	-	-	[170]	$3.00^{\,a}$	-	-	-	$9.44*10^{1}$	-	-	[171]
Diclofenac	$8.96*10^{4\,c}$	-	-	[170]	$2.86*10^{2\,a}$	-	-	-	$5.13*10^{3}$	-	-	[171]

Diltiazem	-	$4.91*10^{3}$ [c]	$4.92*10^{3}$ [c]	-	-	$1.04*10^{2}$ [a]	$1.01*10^{2}$ [a]	-	-	$3.25*10^{3}$	$3.08*10^{3}$	[171]
Erythromycin	$9.23*10^{3}$ [c]	$9.26*10^{3}$ [c]	$9.29*10^{3}$ [c]	[170]	$2.63*10^{1}$ [a]	$2.71*10^{1}$ [a]	$2.72*10^{1}$ [a]	-	$4.38*10^{2}$	$3.87*10^{2}$	$3.41*10^{2}$	[171]
Gabapentin	$6.85*10^{4}$ [c]	$6.88*10^{4}$ [c]	$6.90*10^{4}$ [c]	[170]	$2.68*10^{2}$ [a]	$2.84*10^{2}$ [a]	$2.93*10^{2}$ [a]	-	$6.55*10^{3}$	$6.83*10^{3}$	$7.05*10^{3}$	[171]
Hydrocodone	-	-	-	-	-	-	-	-	-	-	-	-
Ibuprofen	$6.08*10^{5}$ [c]	-	-	[170]	$2.03*10^{3}$ [a]	-	-	-	$1.97*10^{4}$	-	-	[171]
Indomethacin	$9.78*10^{2}$ [c]	-	-	[170]	6.44 [a]	-	-	-	$1.44*10^{2}$	-	-	[171]
Lidocaine	$7.34*10^{3}$ [c]	-	-	[170]	$2.77*10^{2}$ [a]	-	-	-	$2.33*10^{4}$	-	-	[171]
Loratadine	-	-	-	-	-	-	-	-	-	-	-	-
Metformin	$9.78*10^{5}$ [c]	-	-	[170]	$6.43*10^{3}$ [a]	-	-	-	$2.80*10^{5}$	-	-	[171]
Naproxen	$1.44*10^{4}$ [c]	-	-	[170]	$2.05*10^{2}$ [a]	-	-	-	$1.16*10^{4}$	-	-	[171]
Norethindrone	-	-	-	-	-	-	-	-	-	-	-	-
Oseltamivir	-	-	-	-	-	-	-	-	-	-	-	-
Oxazepam	-	-	-	-	-	-	-	-	-	-	-	-
Propranolol	$2.45*10^{3}$ [c]	$2.45*10^{3}$ [c]	$2.46*10^{3}$ [c]	[170]	$5.26*10^{1}$ [a]	$5.52*10^{1}$ [a]	$5.63*10^{1}$ [a]	-	$1.38*10^{3}$	$1.39*10^{3}$	$1.37*10^{3}$	[171]
Ranitidine	$2.45*10^{4}$ [c]	-	-	[170]	$1.25*10^{2}$ [a]	-	-	-	$5.87*10^{3}$	-	-	[171]
Sertraline	-	-	-	-	-	-	-	-	-	-	-	-
Sitagliptin	$4.89*10^{3}$ [c]	$4.91*10^{3}$ [c]	$4.92*10^{3}$ [c]	[170]	$2.24*10^{1}$ [a]	$2.66*10^{1}$ [a]	$2.65*10^{1}$ [a]	-	$4.41*10^{2}$	$6.40*10^{2}$	$5.95*10^{2}$	[171]
Sulfamethoxazole	$3.42*10^{4}$ [c]	$3.43*10^{4}$ [c]	$3.44*10^{4}$ [c]	[170]	$1.39*10^{2}$ [a]	$1.39*10^{2}$ [a]	$1.40*10^{2}$ [a]	-	$4.42*10^{3}$	$3.49*10^{3}$	$3.26*10^{3}$	[171]
Temazepam	-	-	-	-	-	-	-	-	-	-	-	-
Tramadol	$3.28*10^{4}$ [c]	-	-	[170]	$1.48*10^{2}$ [a]	-	-	-	$3.40*10^{3}$	-	-	[171]
Triamterene	-	-	-	-	-	-	-	-	-	-	-	-
Trimethoprim	$7.31*10^{3}$ [c]	$7.34*10^{3}$ [c]	$7.36*10^{3}$ [c]	[170]	$2.60*10^{1}$ [a]	$2.70*10^{1}$ [a]	$2.73*10^{1}$ [a]	-	$4.37*10^{2}$	$3.95*10^{2}$	$3.58*10^{2}$	[171]
Venlafaxine	$1.17*10^{4}$ [c]	$1.17*10^{4}$ [c]	$1.17*10^{4}$ [c]	[170]	$8.04*10^{1}$ [a]	$8.61*10^{1}$ [a]	$8.84*10^{1}$ [a]	-	$3.27*10^{3}$	$3.45*10^{3}$	$3.49*10^{3}$	[171]
Verapamil	$2.45*10^{4}$ [c]	-	-	[170]	$1.06*10^{2}$ [a]	-	-	-	$3.12*10^{3}$	-	-	[171]

	Switzerland				**United Kingdom**	
API	**2011**	**2013**	**2014**	**Ref**	**2016**	**Ref**

Acetaminophen	$1.02*10^{5}$ [c]	-	-	[170]	$2.52*10^{6}$ [d]	[172]
Amitriptyline	$6.58*10^{2}$ [a]	-	-	[170]	$1.28*10^{4}$ [d]	[172]
Atenolol	$1.02*10^{3}$ [c]	$1.05*10^{3}$ [c]	$1.06*10^{3}$ [c]	[170]	$1.63*10^{4}$ [d]	[172]
Bezafibrate	$5.11*10^{2}$ [c]	-	-	[170]	-	-
Carbamazepine	$2.55*10^{3}$ [c]	$2.62*10^{3}$ [c]	$2.64*10^{3}$ [c]	[170]	$3.65*10^{4}$ [d]	[172]
Cimetidine	-	-	-	-	$1.11*10^{3}$ [d]	[172]
Citalopram	$7.66*10^{2}$ [c]	$7.85*10^{2}$ [c]	$7.93*10^{2}$ [c]	[170]	$1.04*10^{4}$ [d]	[172]
Codeine	-	-	-	-	$5.62*10^{4}$ [d]	[172]
Desvenlafaxine	-	-	-	-	0.00	[172]
Diazepam	$2.55*10^{1}$ [c]	-	-	[170]	$6.38*10^{2}$ [d]	[172]
Diclofenac	$5.11*10^{3}$ [c]	-	-	[170]	-	-
Diltiazem	-	$1.56*10^{3}$ [a]	$1.49*10^{3}$ [a]	-	$2.06*10^{4}$ [d]	[172]
Erythromycin	$1.02*10^{2}$ [c]	$1.05*10^{2}$ [c]	$1.06*10^{2}$ [c]	[170]	$1.88*10^{4}$ [d]	[172]
Gabapentin	$2.55*10^{3}$ [c]	$2.62*10^{3}$ [c]	$2.64*10^{3}$ [c]	[170]	$1.60*10^{5}$ [d]	[172]
Hydrocodone	-	-	-	-	$9.42*10^{3}$ [d]	[172]
Ibuprofen	$2.55*10^{4}$ [c]	-	-	[170]	-	-
Indomethacin	$1.02*10^{2}$ [c]	-	-	[170]	-	-
Lidocaine	$1.02*10^{3}$ [c]	-	-	[170]	$8.15*10^{3}$ [d]	[172]
Loratadine	-	-	-	-	$8.58*10^{2}$ [d]	[172]
Metformin	$7.66*10^{4}$ [c]	-	-	[170]	$1.15*10^{6}$ [d]	[172]
Naproxen	$1.02*10^{3}$ [c]	-	-	[170]	-	-
Norethindrone	-	-	-	-	$1.66*10^{2}$ [d]	[172]
Oseltamivir	-	-	-	-	$6.66*10^{1}$ [d]	[172]
Oxazepam	-	-	-	-	8.04 [d]	[172]
Propranolol	$7.66*10^{2}$ [c]	$7.85*10^{2}$ [c]	$7.93*10^{2}$ [c]	[170]	$1.24*10^{4}$ [d]	[172]
Ranitidine	$1.02*10^{3}$ [c]	-	-	[170]	$4.63*10^{4}$ [d]	[172]
Sertraline	-	-	-	-	$2.88*10^{4}$ [d]	[172]

Sitagliptin	$3.44*10^{2}$ [a]	$3.99*10^{2}$ [a]	$3.92*10^{2}$ [a]	-	$1.91*10^{4}$ [d]	[172]
Sulfamethoxazole	$1.02*10^{3}$ [c]	$1.05*10^{3}$ [c]	$1.06*10^{3}$ [c]	[170]	$2.17*10^{3}$ [d]	[172]
Temazepam	-	-	-	-	$4.81*10^{2}$ [d]	[172]
Tramadol	$1.02*10^{3}$ [c]	-	-	[170]	$4.55*10^{4}$ [d]	[172]
Triamterene	-	-	-	-	$1.65*10^{1}$ [d]	[172]
Trimethoprim	$2.55*10^{2}$ [c]	$2.61*10^{2}$ [c]	$2.64*10^{2}$ [c]	[170]	$7.34*10^{3}$ [d]	[172]
Venlafaxine	$1.02*10^{3}$ [c]	$1.05*10^{3}$ [c]	$1.06*10^{3}$ [c]	[170]	$1.56*10^{4}$ [d]	[172]
Verapamil	$1.02*10^{3}$ [c]	-	-	[170]	$5.80*10^{3}$ [d]	[172]

[a]: average per capita consumption from other countries in basin, for which consumption data were available, extrapolated to country and year of interest based on demographics from Eurostat [173]; [b]: per capita consumption in 2004 [170] extrapolated to year of interest based on demographics from Eurostat [173]; [c]: per capita consumption in 2009 [170] extrapolated to year of interest based on demographics from Eurostat [173]; [d]: per capita consumption in England [172] extrapolated to whole of United Kingdom based on demographics from Office for National Statistics [174].

Table S5.2. Consumption data per API for each country and year as included in the model evaluation (g/capita).

	Austria				Belgium				France			
API	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**
Acetaminophen	$1.89*10^{1\,a}$	-	-	-	$1.89*10^{1\,a}$	-	-	-	$5.30*10^{1\,b}$	-	-	[170]
Amitriptyline	$8.36*10^{-2\,a}$	-	-	-	$8.36*10^{-2\,a}$	-	-	-	$8.36*10^{-2\,a}$	-	-	-
Atenolol	$1.66*10^{-1\,a}$	$1.67*10^{-1\,a}$	$1.67*10^{-1\,a}$	-	$1.66*10^{-1\,a}$	$1.66*10^{-1\,a}$	$1.66*10^{-1\,a}$	-	$2.94*10^{-1\,b}$	$2.94*10^{-1\,b}$	$2.94*10^{-1\,b}$	[170]
Bezafibrate	$1.53*10^{-1\,a}$	-	-	-	$1.53*10^{-1\,a}$	-	-	-	$3.35*10^{-1\,b}$	-	-	[170]
Carbamazepine	$5.25*10^{-1\,a}$	$5.19*10^{-1\,a}$	$5.16*10^{-1\,a}$	-	$5.25*10^{-1\,a}$	$5.19*10^{-1\,a}$	$5.16*10^{-1\,a}$	-	$5.38*10^{-1\,b}$	$5.38*10^{-1\,b}$	$5.38*10^{-1\,b}$	[170]
Cimetidine	-	-	-	-	-	-	-	-	-	-	-	-
Citalopram	$6.59*10^{-2\,a}$	$6.65*10^{-2\,a}$	$6.68*10^{-2\,a}$	-	$6.59*10^{-2\,a}$	$6.65*10^{-2\,a}$	$6.68*10^{-2\,a}$	-	$5.60*10^{-2\,b}$	$5.60*10^{-2\,b}$	$5.60*10^{-2\,b}$	[170]
Codeine	-	-	-	-	-	-	-	-	-	-	-	-
Desvenlafaxine	-	-	-	-	-	-	-	-	-	-	-	-
Diazepam	$5.86*10^{-3\,a}$	-	-	-	$5.86*10^{-3\,a}$	-	-	-	$8.44*10^{-3\,b}$	-	-	[170]
Diclofenac	$5.58*10^{-1\,a}$	-	-	-	$5.58*10^{-1\,a}$	-	-	-	$1.59*10^{-1\,b}$	-	-	[170]
Diltiazem	-	$1.94*10^{-1\,a}$	$1.83*10^{-1\,a}$	-	-	$1.94*10^{-1\,a}$	$1.83*10^{-1\,a}$	-	-	$1.94*10^{-1\,a}$	$1.83*10^{-1\,a}$	-
Erythromycin	$5.15*10^{-2\,a}$	$5.04*10^{-2\,a}$	$4.94*10^{-2\,a}$	-	$5.15*10^{-2\,a}$	$5.04*10^{-2\,a}$	$4.94*10^{-2\,a}$	-	$5.15*10^{-2\,a}$	$5.04*10^{-2\,a}$	$4.94*10^{-2\,a}$	-
Gabapentin	$5.24*10^{-1\,a}$	$5.29*10^{-1\,a}$	$5.33*10^{-1\,a}$	-	$5.24*10^{-1\,a}$	$5.29*10^{-1\,a}$	$5.33*10^{-1\,a}$	-	$5.24*10^{-1\,a}$	$5.29*10^{-1\,a}$	$5.33*10^{-1\,a}$	-
Hydrocodone	-	-	-	-	-	-	-	-	-	-	-	-
Ibuprofen	$3.96*10^{0\,a}$	-	-	-	$3.96*10^{0\,a}$	-	-	-	$3.85*10^{0\,b}$	-	-	[170]
Indomethacin	$1.26*10^{-2\,a}$	-	-	-	$1.26*10^{-2\,a}$	-	-	-	$1.61*10^{-2\,b}$	-	-	[170]
Lidocaine	$5.42*10^{-1\,a}$	-	-	-	$5.42*10^{-1\,a}$	-	-	-	$5.42*10^{-1\,a}$	-	-	-
Loratadine	-	-	-	-	-	-	-	-	-	-	-	-
Metformin	$1.26*10^{1\,a}$	-	-	-	$1.26*10^{1\,a}$	-	-	-	$1.15*10^{1\,b}$	-	-	[170]
Naproxen	$4.01*10^{-1\,a}$	-	-	-	$4.01*10^{-1\,a}$	-	-	-	$5.99*10^{-1\,b}$	-	-	[170]
Norethindrone	-	-	-	-	-	-	-	-	-	-	-	-
Oseltamivir	-	-	-	-	-	-	-	-	-	-	-	-

Oxazepam	-	-	-	-	-	-	-	-	-	-	-	-
Propranolol	$1.03*10^{-1\,a}$	$1.03*10^{-1\,a}$	$1.02*10^{-1\,a}$	-	$1.03*10^{-1\,a}$	$1.03*10^{-1\,a}$	$1.02*10^{-1\,a}$	-	$2.00*10^{-1\,b}$	$2.00*10^{-1\,b}$	$2.00*10^{-1\,b}$	170
Ranitidine	$2.44*10^{-1\,a}$	-	-	-	$2.44*10^{-1\,a}$	-	-	-	$1.87*10^{-1\,b}$	-	-	170
Sertraline	-	-	-	-	-	-	-	-	-	-	-	-
Sitagliptin	$4.37*10^{-2\,a}$	$4.96*10^{-2\,a}$	$4.82*10^{-2\,a}$	-	$4.37*10^{-2\,a}$	$4.96*10^{-2\,a}$	$4.82*10^{-2\,a}$	-	$4.37*10^{-2\,a}$	$4.96*10^{-2\,a}$	4.82*10-2 a	-
Sulfamethoxazole	$2.72*10^{-1\,a}$	$2.58*10^{-1\,a}$	$2.55*10^{-1\,a}$	-	$2.72*10^{-1\,a}$	$2.58*10^{-1\,a}$	$2.55*10^{-1\,a}$	-	$2.69*10^{-1\,b}$	$2.69*10^{-1\,b}$	$2.69*10^{-1\,b}$	170
Temazepam	-	-	-	-	-	-	-	-	-	-	-	-
Tramadol	$2.90*10^{-1\,a}$	-	-	-	$2.90*10^{-1\,a}$	-	-	-	$4.16*10^{-1\,b}$	-	-	170
Triamterene	-	-	-	-	-	-	-	-	-	-	-	-
Trimethoprim	$5.09*10^{-2\,a}$	$5.02*10^{-2\,a}$	$4.97*10^{-2\,a}$	-	$5.09*10^{-2\,a}$	$5.02*10^{-2\,a}$	$4.97*10^{-2\,a}$	-	$5.37*10^{-2\,b}$	$5.37*10^{-2\,b}$	$5.37*10^{-2\,b}$	170
Venlafaxine	$1.57*10^{-1\,a}$	$1.60*10^{-1\,a}$	$1.61*10^{-1\,a}$	-	$1.57*10^{-1\,a}$	$1.60*10^{-1\,a}$	$1.61*10^{-1\,a}$	-	$1.57*10^{-1\,b}$	$1.60*10^{-1\,b}$	$1.61*10^{-1\,b}$	170
Verapamil	$2.07*10^{-1\,a}$	-	-	-	$2.07*10^{-1\,a}$	-	-	-	$2.07*10^{-1\,a}$	-	-	-
	Germany				**Luxembourg**				**Netherlands**			
API	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**	**2011**	**2013**	**2014**	**Ref**
Acetaminophen	$6.89*10^{0\,c}$	-	-	170	$1.89*10^{1\,a}$	-	-	-	$2.73*10^{0}$	-	-	171
Amitriptyline	$9.15*10^{-2\,c}$	-	-	170	$8.36*10^{-2\,a}$	-	-	-	$7.58*10^{-2}$	-	-	171
Atenolol	$9.12*10^{-2\,c}$	$9.12*10^{-2\,c}$	$9.12*10^{-2\,c}$	170	$1.66*10^{-1\,a}$	$1.70*10^{-1\,a}$	$1.70*10^{-1\,a}$	-	$1.50*10^{-1}$	$1.31*10^{-1}$	$1.22*10^{-1}$	171
Bezafibrate	$1.88*10^{-1\,c}$	-	-	170	$1.53*10^{-1\,a}$	-	-	-	$2.37*10^{-2}$	-	-	171
Carbamazepine	$7.84*10^{-1\,c}$	$7.84*10^{-1\,c}$	$7.84*10^{-1\,c}$	170	$5.25*10^{-1\,a}$	$5.19*10^{-1\,a}$	$5.16*10^{-1\,a}$	-	$4.54*10^{-1}$	$4.31*10^{-1}$	$4.16*10^{-1}$	171
Cimetidine	-	-	-	-	-	-	-	-	-	-	-	-
Citalopram	$6.10*10^{-2\,c}$	$6.10*10^{-2\,c}$	$6.10*10^{-2\,c}$	170	$6.59*10^{-2\,a}$	$6.65*10^{-2\,a}$	$6.68*10^{-2\,a}$	-	$4.92*10^{-2}$	$5.15*10^{-2}$	$5.29*10^{-2}$	171
Codeine	-	-	-	-	-	-	-	-	-	-	-	-
Desvenlafaxine	-	-	-	-	-	-	-	-	-	-	-	-
Diazepam	$6.10*10^{-3\,c}$	-	-	170	$5.86*10^{-3\,a}$	-	-	-	$5.67*10^{-3}$	-	-	171
Diclofenac	$1.12*10^{0\,c}$	-	-	170	$5.58*10^{-1\,a}$	-	-	-	$3.08*10^{-1}$	-	-	171
Diltiazem	-	$6.10*10^{-2\,c}$	$6.10*10^{-2\,c}$	-	-	$1.94*10^{-1\,a}$	$1.83*10^{-1\,a}$	-	-	$1.94*10^{-1}$	$1.83*10^{-1}$	171

Erythromycin	$1.15*10^{-1}$ [c]	$1.15*10^{-1}$ [c]	$1.15*10^{-1}$ [c]	[170]	$5.15*10^{-2}$ [a]	$5.04*10^{-2}$ [a]	$4.94*10^{-2}$ [a]	-	$2.63*10^{-2}$	$2.31*10^{-2}$	$2.03*10^{-2}$	[171]
Gabapentin	$8.54*10^{-1}$ [c]	$8.54*10^{-1}$ [c]	$8.54*10^{-1}$ [c]	[170]	$5.24*10^{-1}$ [a]	$5.29*10^{-1}$ [a]	$5.33*10^{-1}$ [a]	-	$3.93*10^{-1}$	$4.07*10^{-1}$	$4.19*10^{-1}$	[171]
Hydrocodone	-	-	-	-	-	-	-	-	-	-	-	-
Ibuprofen	$7.58*10^{0}$ [c]	-	-	[170]	$3.96*10^{0}$ [a]	-	-	-	$1.18*10^{0}$	-	-	[171]
Indomethacin	$1.22*10^{-2}$ [c]	-	-	[170]	$1.26*10^{-2}$ [a]	-	-	-	$8.66*10^{-3}$	-	-	[171]
Lidocaine	$9.15*10^{-2}$ [c]	-	-	[170]	$5.42*10^{-1}$ [a]	-	-	-	$1.40*10^{0}$	-	-	[171]
Loratadine	-	-	-	-	-	-	-	-	-	-	-	-
Metformin	$1.22*10^{1}$ [c]	-	-	[170]	$1.26*10^{1}$ [a]	-	-	-	$1.68*10^{1}$	-	-	[171]
Naproxen	$1.80*10^{-1}$ [c]	-	-	[170]	$4.01*10^{-1}$ [a]	-	-	-	$6.95*10^{-1}$	-	-	[171]
Norethindrone	-	-	-	-	-	-	-	-	-	-	-	-
Oseltamivir	-	-	-	-	-	-	-	-	-	-	-	-
Oxazepam	-	-	-	-	-	-	-	-	-	-	-	-
Propranolol	$3.05*10^{-2}$ [c]	$3.05*10^{-2}$ [c]	$3.05*10^{-2}$ [c]	[170]	$1.03*10^{-1}$ [a]	$1.03*10^{-1}$ [a]	$1.02*10^{-1}$ [a]	-	$8.26*10^{-2}$	$8.29*10^{-2}$	$8.12*10^{-2}$	[171]
Ranitidine	$3.05*10^{-1}$ [c]	-	-	[170]	$2.44*10^{-1}$ [a]	-	-	-	$3.52*10^{-1}$	-	-	[171]
Sertraline	-	-	-	-	-	-	-	-	-	-	-	-
Sitagliptin	$6.10*10^{-2}$ [c]	$6.10*10^{-2}$ [c]	$6.10*10^{-2}$ [c]	[170]	$4.37*10^{-2}$ [a]	$4.96*10^{-2}$ [a]	$4.82*10^{-2}$ [a]	-	$2.65*10^{-2}$	$3.81*10^{-2}$	$3.54*10^{-2}$	[171]
Sulfamethoxazole	$4.26*10^{-1}$ [c]	$4.26*10^{-1}$ [c]	$4.26*10^{-1}$ [c]	[170]	$2.72*10^{-1}$ [a]	$2.58*10^{-1}$ [a]	$2.55*10^{-1}$ [a]	-	$2.65*10^{-1}$	$2.08*10^{-1}$	$1.94*10^{-1}$	[171]
Temazepam	-	-	-	-	-	-	-	-	-	-	-	-
Tramadol	$4.08*10^{-1}$ [c]	-	-	[170]	$2.90*10^{-1}$ [a]	-	-	-	$2.04*10^{-1}$	-	-	[171]
Triamterene	-	-	-	-	-	-	-	-	-	-	-	-
Trimethoprim	$9.12*10^{-2}$ [c]	$9.12*10^{-2}$ [c]	$9.12*10^{-2}$ [c]	[170]	$5.09*10^{-2}$ [a]	$5.02*10^{-2}$ [a]	$4.97*10^{-2}$ [a]	-	$2.62*10^{-2}$	$2.35*10^{-2}$	$2.13*10^{-2}$	[171]
Venlafaxine	$1.45*10^{-1}$ [c]	$1.45*10^{-1}$ [c]	$1.45*10^{-1}$ [c]	[170]	$1.57*10^{-1}$ [a]	$1.60*10^{-1}$ [a]	$1.61*10^{-1}$ [a]	-	$1.96*10^{-1}$	$2.06*10^{-1}$	$2.07*10^{-1}$	[171]
Verapamil	$3.05*10^{-1}$ [c]	-	-	[170]	$2.07*10^{-1}$ [a]	-	-	-	$1.87*10^{-1}$	-	-	[171]

	Switzerland				**United Kingdom**	
API	**2011**	**2013**	**2014**	**Ref**	**2016**	**Ref**
Acetaminophen	$1.30*10^{1}$ [c]	-	-	[170]	$3.86*10^{1}$ [d]	[172]

Amitriptyline	$8.36*10^{-2}$ [a]	-	-	[170]	$1.96*10^{-1}$ [d]	[172]
Atenolol	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	[170]	$2.50*10^{-1}$ [d]	[172]
Bezafibrate	$6.49*10^{-2}$ [c]	-	-	[170]	-	-
Carbamazepine	$3.25*10^{-1}$ [c]	$3.25*10^{-1}$ [c]	$3.25*10^{-1}$ [c]	[170]	$5.58*10^{-1}$ [d]	[172]
Cimetidine	-	-	-	-	$1.70*10^{-2}$ [d]	[172]
Citalopram	$9.74*10^{-2}$ [c]	$9.76*10^{-2}$ [c]	$9.74*10^{-2}$ [c]	[170]	$1.59*10^{-1}$ [d]	[172]
Codeine	-	-	-	-	$8.59*10^{-1}$ [d]	[172]
Desvenlafaxine	-	-	-	-	$0.00*10^{0}$ [d]	[172]
Diazepam	$3.25*10^{-3}$ [c]	-	-	[170]	$9.76*10^{-3}$ [d]	[172]
Diclofenac	$6.49*10^{-1}$ [c]	-	-	[170]	-	-
Diltiazem	-	$1.94*10^{-1}$ [a]	$1.83*10^{-1}$ [a]	-	$3.15*10^{-1}$ [d]	[172]
Erythromycin	$1.30*10^{-2}$ [c]	$1.30*10^{-2}$ [c]	$1.30*10^{-2}$ [c]	[170]	$2.87*10^{-1}$ [d]	[172]
Gabapentin	$3.25*10^{-1}$ [c]	$3.25*10^{-1}$ [c]	$3.25*10^{-1}$ [c]	[170]	$2.45*10^{0}$ [d]	[172]
Hydrocodone	-	-	-	-	$1.44*10^{-1}$ [d]	[172]
Ibuprofen	$3.25*10^{0}$ [c]	-	-	[170]	-	-
Indomethacin	$1.30*10^{-2}$ [c]	-	-	[170]	-	-
Lidocaine	$1.30*10^{-1}$ [c]	-	-	[170]	$1.25*10^{-1}$ [d]	[172]
Loratadine	-	-	-	-	$1.31*10^{-2}$ [d]	[172]
Metformin	$9.74*10^{0}$ [c]	-	-	[170]	$1.76*10^{1}$ [d]	[172]
Naproxen	$1.30*10^{-1}$ [c]	-	-	[170]	-	-
Norethindrone	-	-	-	-	$2.54*10^{-3}$ [d]	[172]
Oseltamivir	-	-	-	-	$1.02*10^{-3}$ [d]	[172]
Oxazepam	-	-	-	-	$1.23*10^{-4}$ [d]	[172]
Propranolol	$9.74*10^{-2}$ [c]	$9.76*10^{-2}$ [c]	$9.74*10^{-2}$ [c]	[170]	$1.89*10^{-1}$ [d]	[172]
Ranitidine	$1.30*10^{-1}$ [c]	-	-	[170]	$7.07*10^{-1}$ [d]	[172]
Sertraline	-	-	-	-	$4.40*10^{-1}$ [d]	[172]
Sitagliptin	$4.37*10^{-2}$ [a]	$4.97*10^{-2}$ [a]	$4.82*10^{-2}$ [a]	-	$2.92*10^{-1}$ [d]	[172]

Sulfamethoxazole	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	[170]	$3.32*10^{-2}$ [d]	[172]
Temazepam	-	-	-	-	$7.36*10^{-3}$ [d]	[172]
Tramadol	$1.30*10^{-1}$ [c]	-	-	[170]	$6.95*10^{-1}$ [d]	[172]
Triamterene	-	-	-	-	$2.52*10^{-4}$ [d]	[172]
Trimethoprim	$3.25*10^{-2}$ [c]	$3.25*10^{-2}$ [c]	$3.25*10^{-2}$ [c]	[170]	$1.12*10^{-1}$ [d]	[172]
Venlafaxine	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	$1.30*10^{-1}$ [c]	[170]	$2.38*10^{-1}$ [d]	[172]
Verapamil	$1.30*10^{-1}$ [c]	-	-	[170]	$8.87*10^{-2}$ [d]	[172]

[a]: average per capita consumption from other countries in basin, for which consumption data were available, extrapolated to country and year of interest based on demographics from Eurostat [173]; [b]: per capita consumption in 2004 [170] extrapolated to year of interest based on demographics from Eurostat [173]; [c]: per capita consumption in 2009 [170] extrapolated to year of interest based on demographics from Eurostat [173]; [d]: per capita consumption in England [172] extrapolated to whole of United Kingdom based on demographics from Office for National Statistics [174].

S6. Additional model results

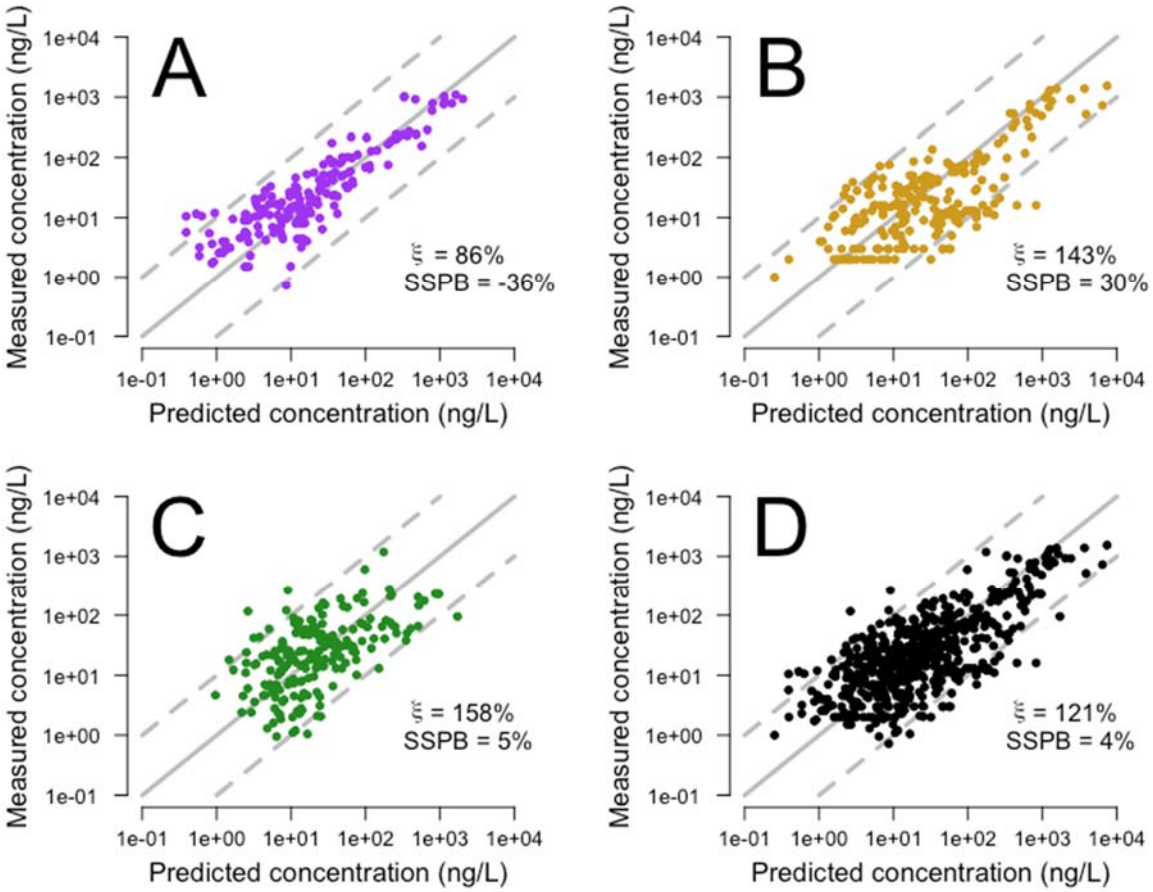

Figure S6.1 Predicted concentrations (i.e., > 0) versus detects (i.e., <40% of the measurements above below LOD) and non-detects if predicted concentration > LOD. Measured data originate from Burns et al.[41] (purple; A), Ruff et al.[42] (golden; B), Munz et al.[43] (green; C), and for all studies combined (black; D). Concentrations predicted under annual mean flow conditions (A) or lowest monthly mean flow conditions (B and C). Solid line represents 1:1 relationship; dashed lines represent 1:10 and 10:1 relationships. ξ: median symmetric accuracy; SSPB: symmetric signed percentage bias.

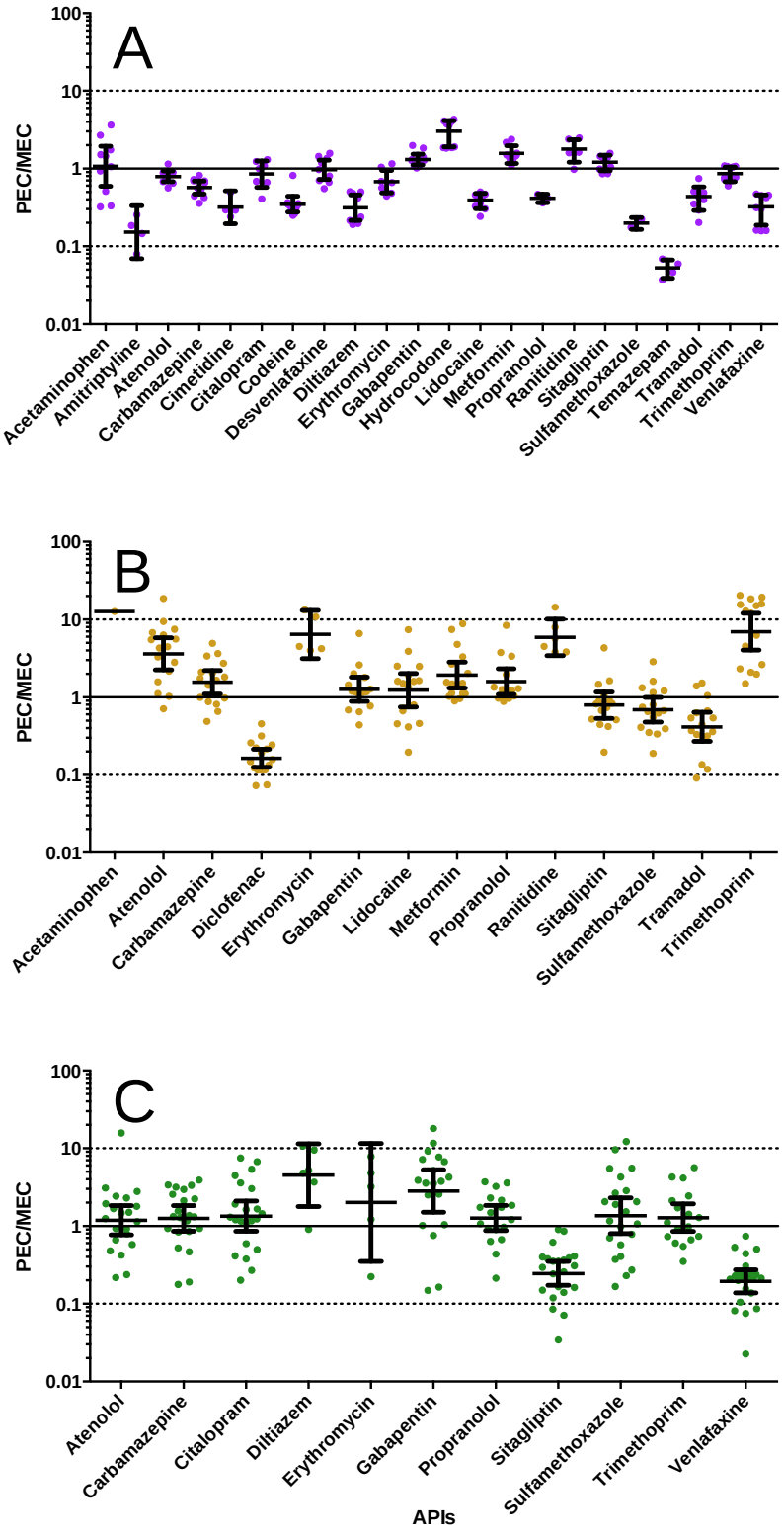

Figure S6.2 Ratios of predicted over measured concentrations (PEC/MEC), reported by Burns et al.,[175] (A), Ruff et al.,[176] (B) and Munz et al.[177] (C). Coloured dots are individual combinations of API and location, measured above LOD; black bars represent 95th percentile and median over all locations per API measured. Concentrations predicted under annual mean flow conditions (A) or lowest monthly mean flow conditions (B and C).

Table S6.1. Predicted and measured mean annual flow (in $m^3 s^{-1}$) at two gauging stations in the rivers Ouse and Foss, respectively.

	River Ouse	River Foss
Measured (2016)	51.83	0.990
Predicted (based on 2015 data)	52.00	1.145

S7. Interactive html-maps

Interactive html-maps with concentrations and risks per API resulting from the model application exercise can be found as online supplementary file, accessible via the file "*Supporting Information S7.html*".

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