RiSKWa

TransRisk

Transformation products: new emerging contaminants in the water cycle

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GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

Which are the new emerging compounds?

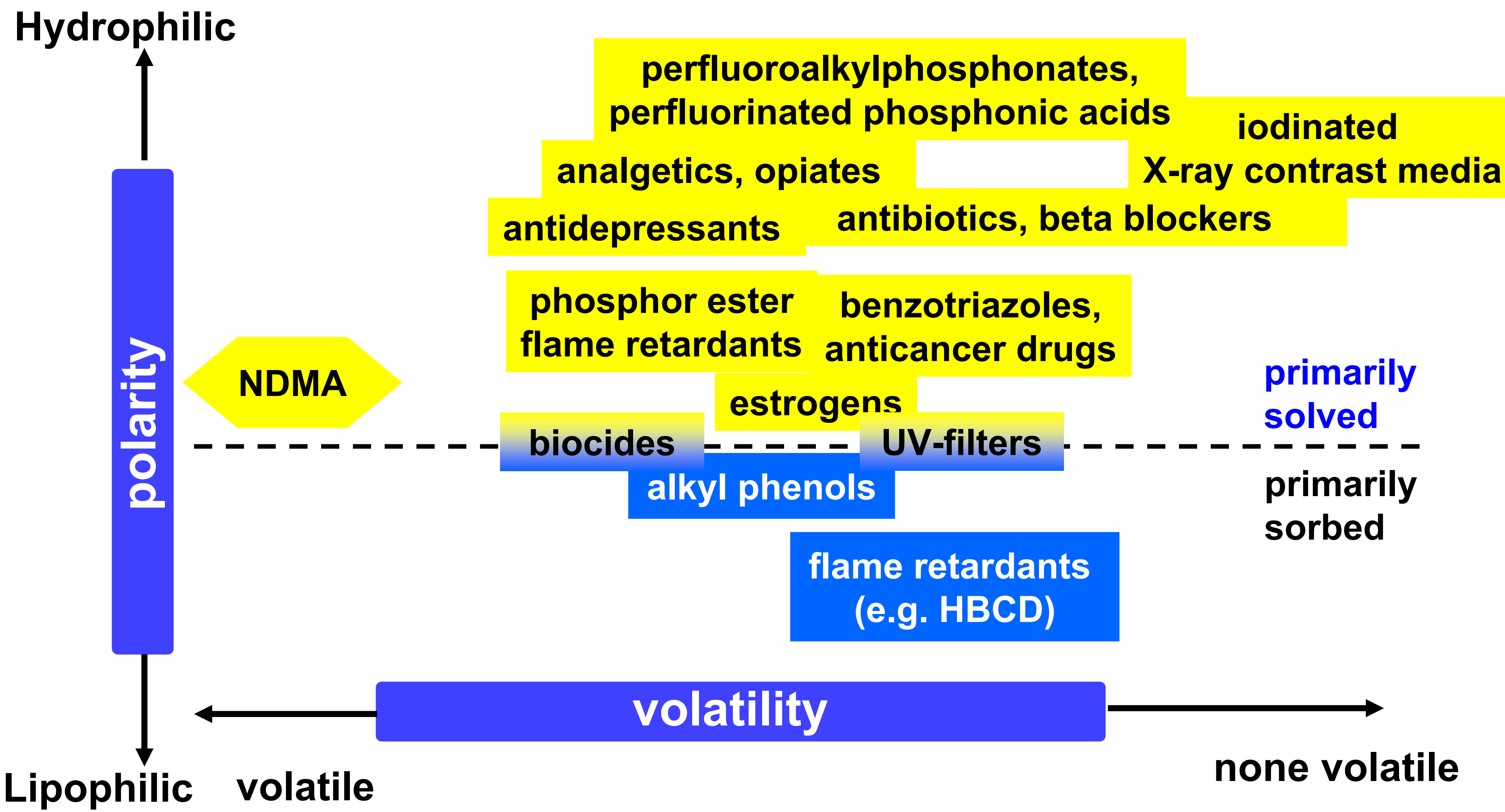
Bundesanstalt für Gewässerkunde

Estimated number of chemicals used in the EU

- 100000 "old chemicals" until 1981
- > 4000 "new chemicals" since 1981

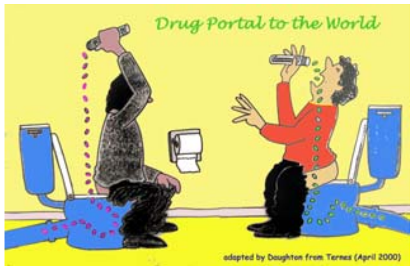
- 30000 chemicals > 1 t yr^{-1}
- 2900 chemicals > 100 t yr^{-1}
- 2600 chemicals > 1000 t yr^{-1}

„Emerging“ compounds (selection)

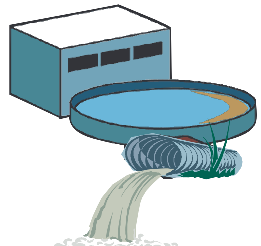


Transformation products (TPs): new emerging compounds ?

Pharma-
ceutical →



Metabolites
TP1 →

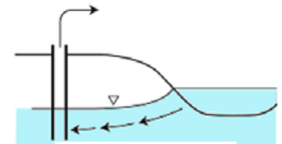


TP2 →

UV-photolysis
sunlight

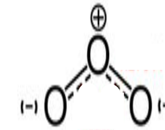
TP3 →

bank
filtration



TP4 →

ozonation,
chlorination



TP5

Identification of TPs: **how to identify the relevant TPs (toxic, persistent) formed?**

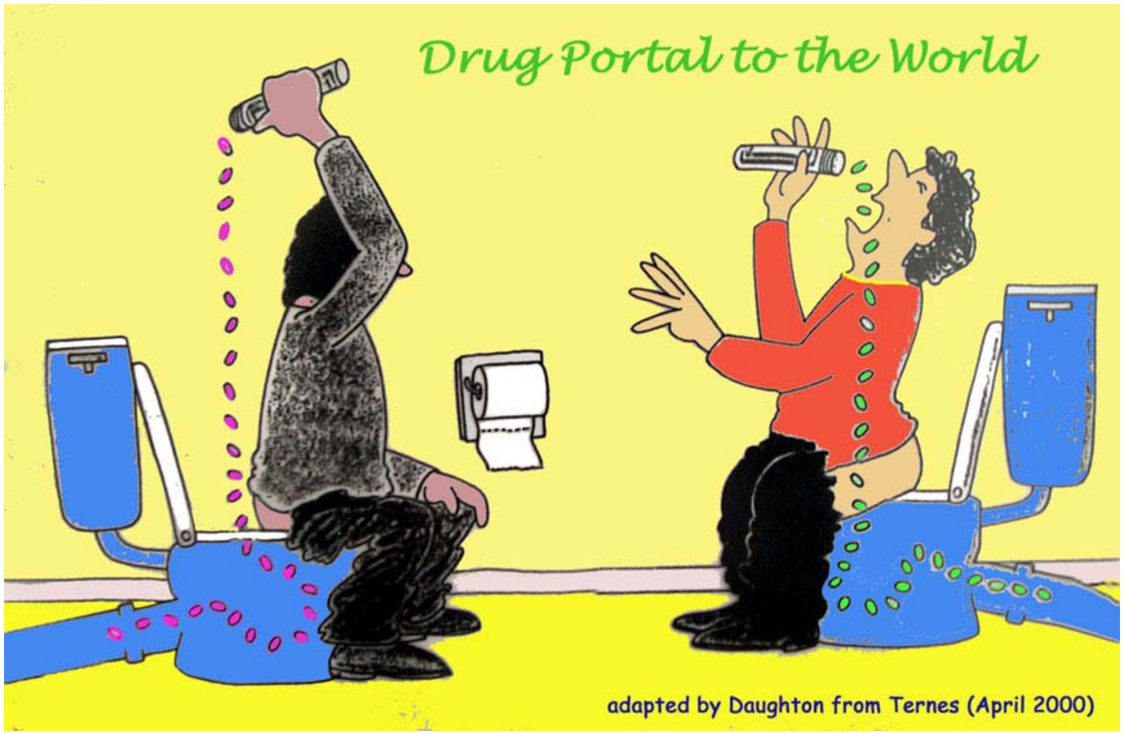
a) analytical approaches
b) modelling approaches
c) ecotoxicological approaches

Technical challenges

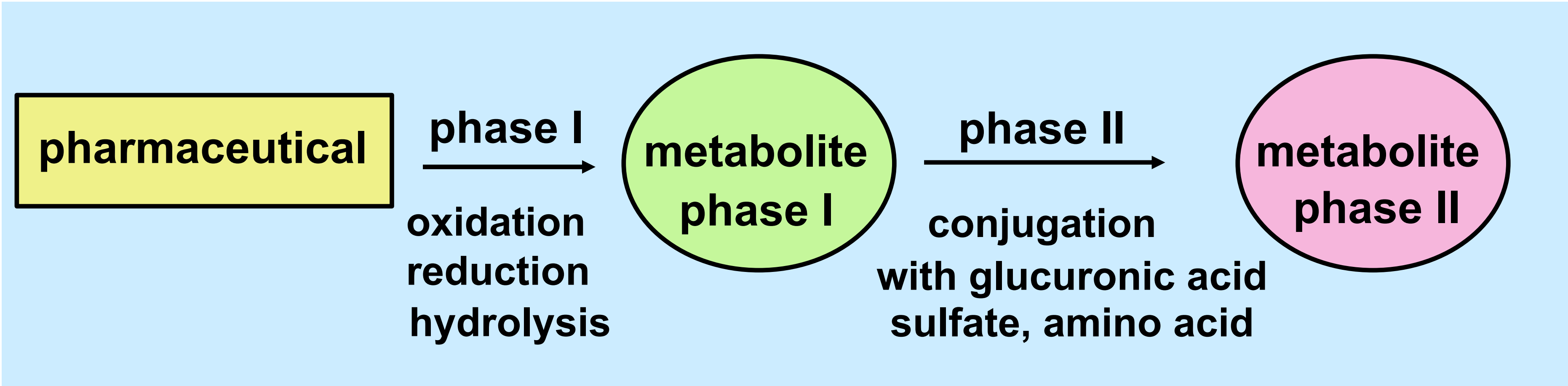
a) how to avoid the formation of (toxic) TPs?

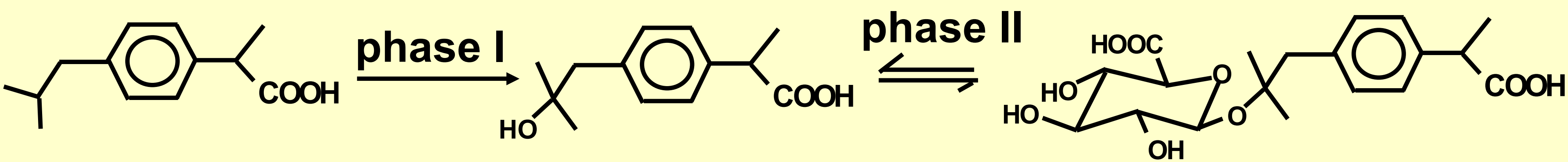
b) how to remove TPs?

Pharmacokinetic: human metabolism?



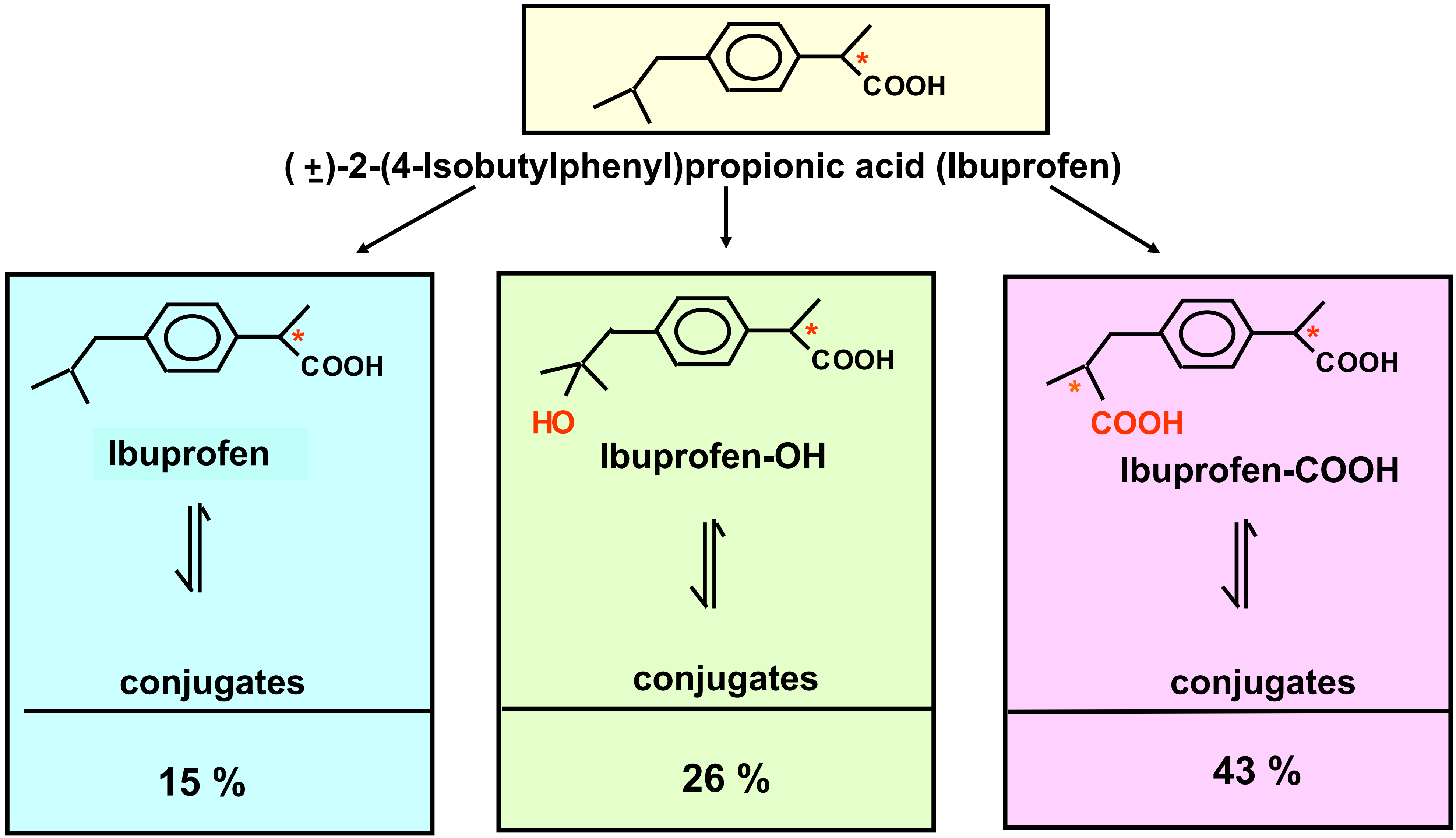
Metabolism of pharmaceuticals





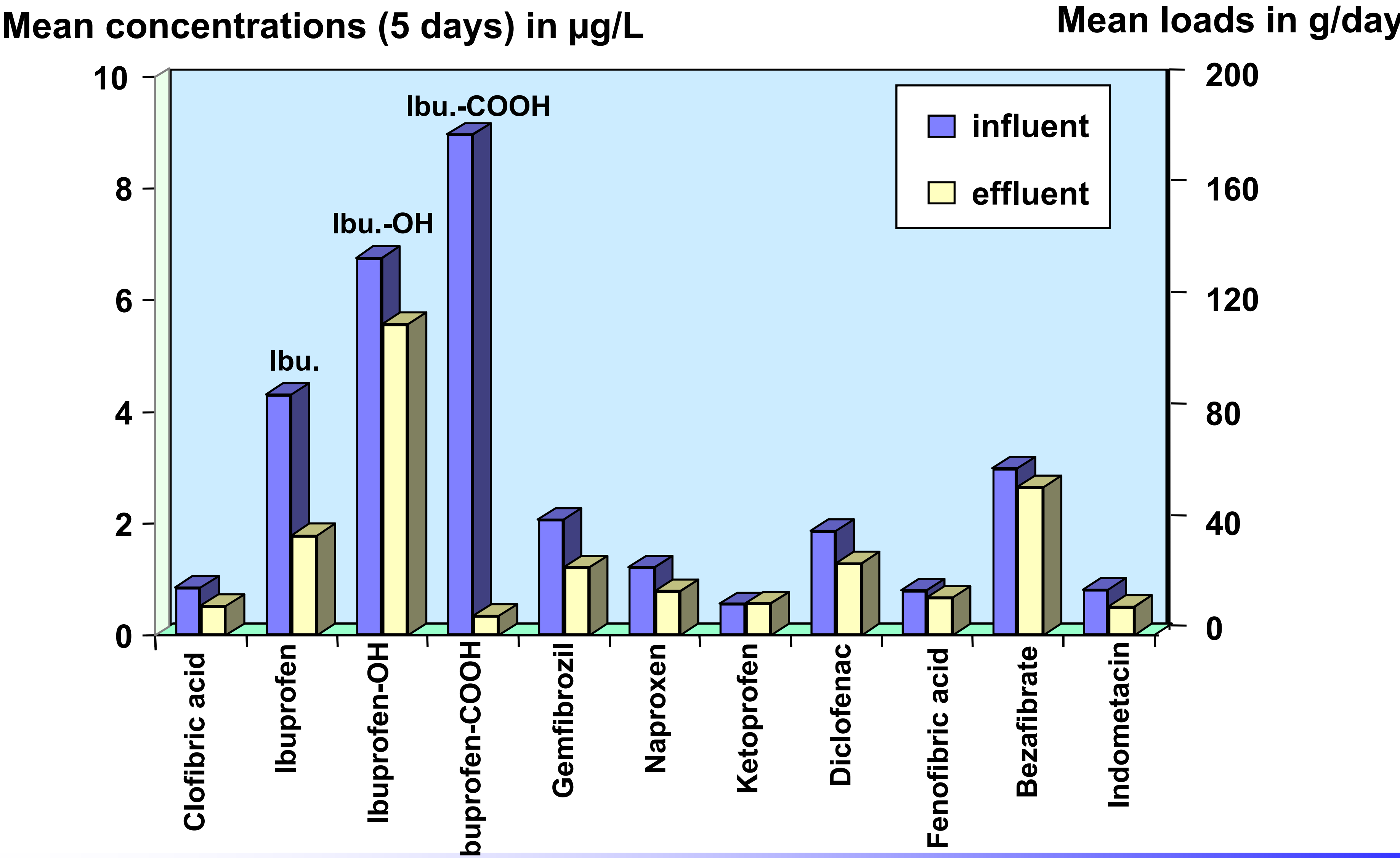
Ibuprofen | Ibuprofen-OH (9 %) | conjugate (17 %)

Metabolism and excretion of Ibuprofen

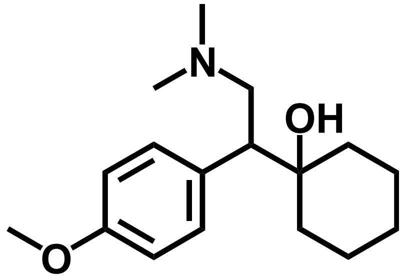


Metabolites of Ibuprofen in a municipal WWTP

WWTP Wiesbaden, sampling 1996, nitrification, sludge age: 4-5 days



The antidepressant venlafaxine

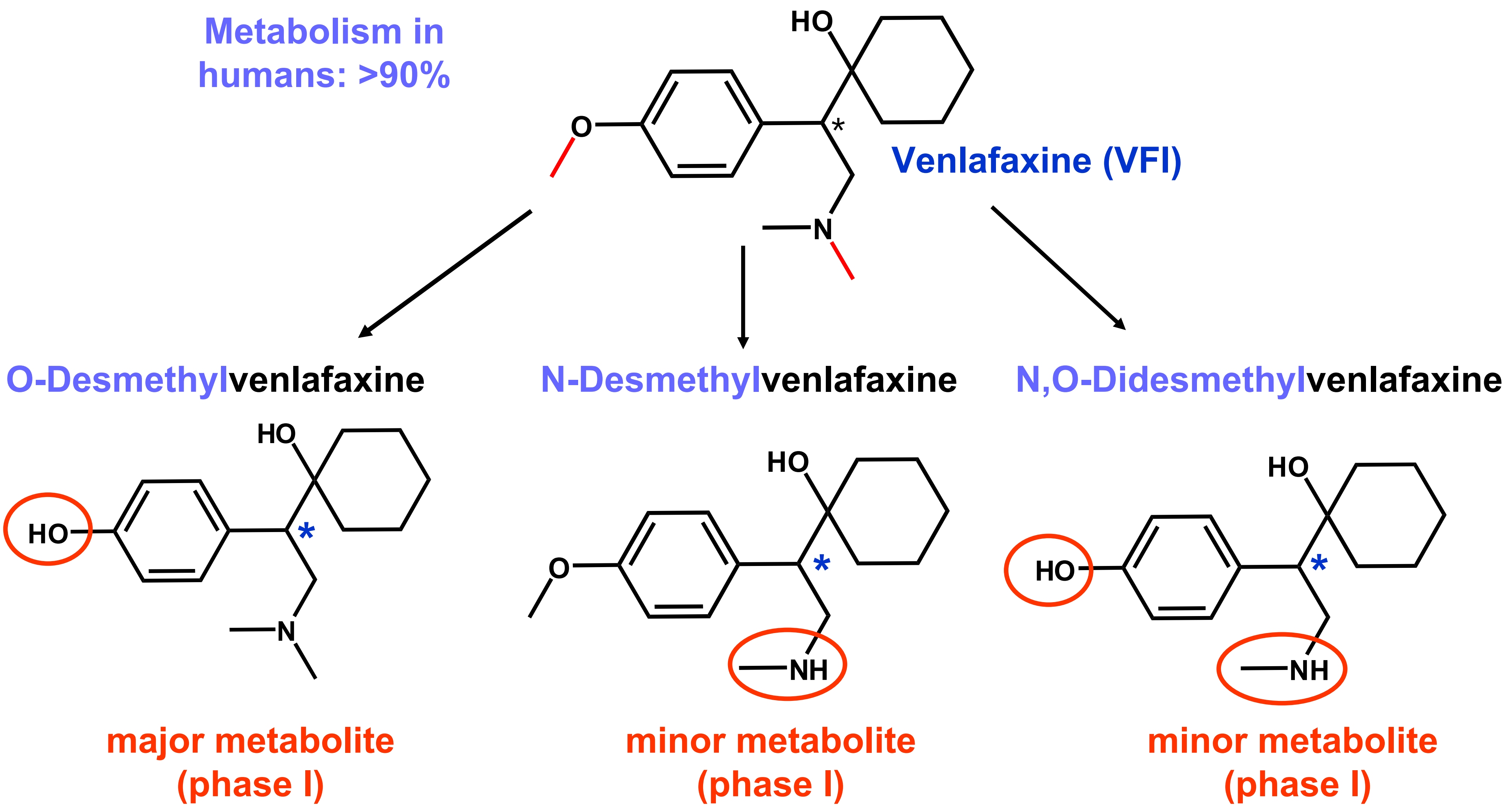


	Germany	Canada
Consumption [mg $cap^{-1}a^{-1}$]	170	680
Consumption [t a^{-1}]	7.5	22.2
Concentrations [ng L^{-1}]	73 (Rhine)	690 (Grand river)

15% increase of venlafaxine concentrations expected the next years due to

- **Increasing consumption per capita of venlafaxine as seen from 2006-2008 in Germany (1. demographic changes; 2. changing of life style)**
- **Climate change: increasing number of draughts due to extreme weather conditions**

Metabolism and excretion of venlaflaxine



Occurrence and „removal“ of venlaflaxine in two German WWTPs

	Venlafaxine [ng/L]	O-Desmethyl-venlafaxine [ng/L]	N,O-Dides-methylvenlafaxine [ng/L]	Sum [ng/L]
WWTP I influent	**200**	**510**	**130**	**840**
WWTP I effluent	220	600	160	960
WWTP II influent	**250**	**780**	**200**	**1230**
WWTP II effluent	290	720	150	1160

Conclusion: no removal at all in a WWTP!

Biological transformation in WWTPs?

Enzyme-catalyzed reactions during nitrification (1)

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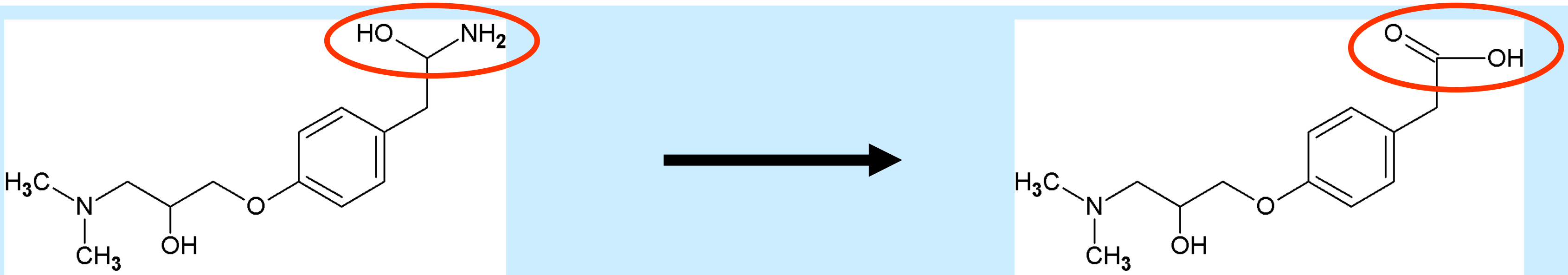
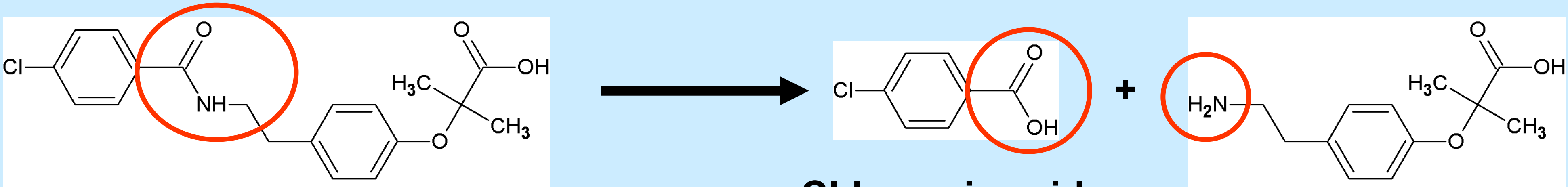
Amide hydrolysis (Radjenovic et al., 2008; Quintana et al., 2005)

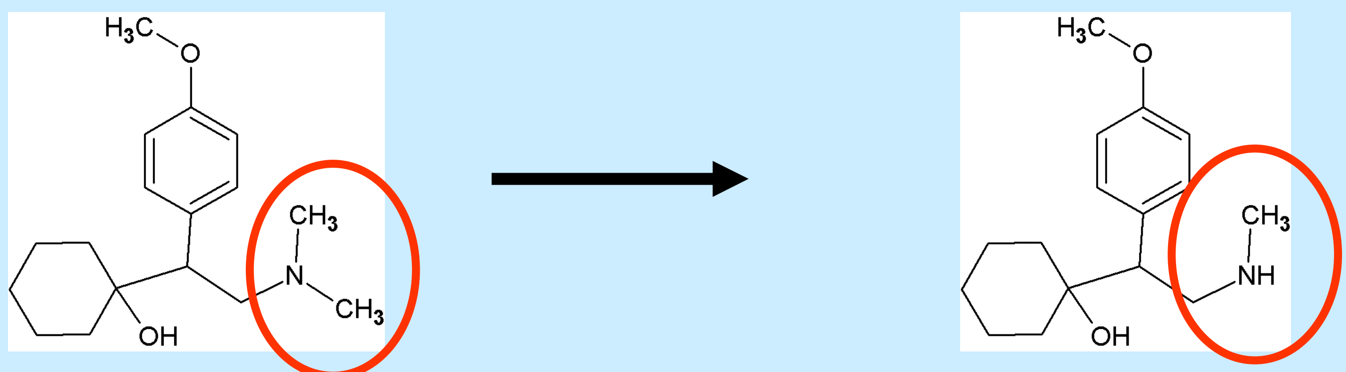


Atenolol → **Atenololic acid**



Bezafibrate → **p-Cl-benzoic acid** + **Bezafibrate-TP**

N-dealkylation (Kern et al., 2009)



Venlaflaxin → **N-Demethyl-Venlaflaxin**

Enzyme-catalyzed reactions during nitrification (2)

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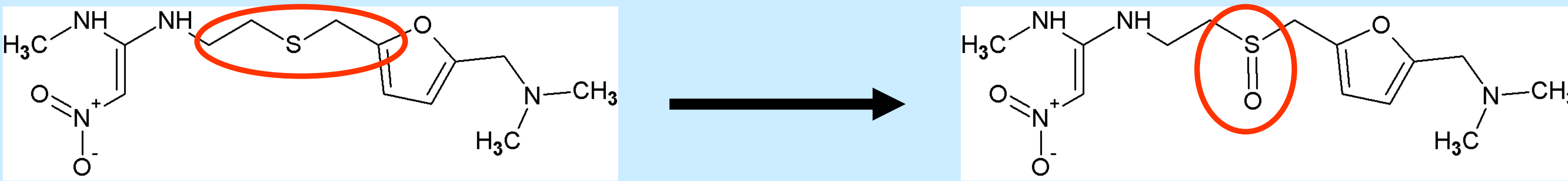
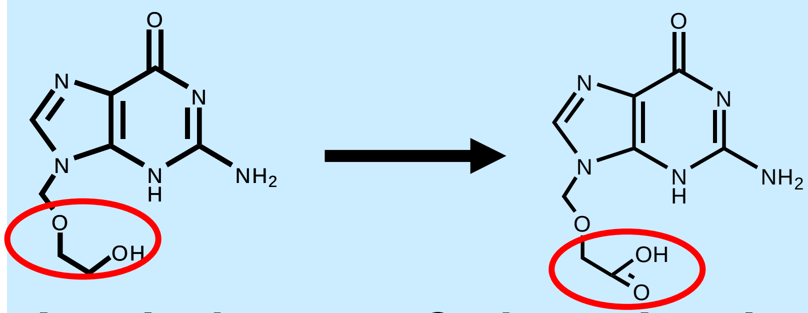
Thiol ether oxidation (Kern et al., 2009)



Ranitidin

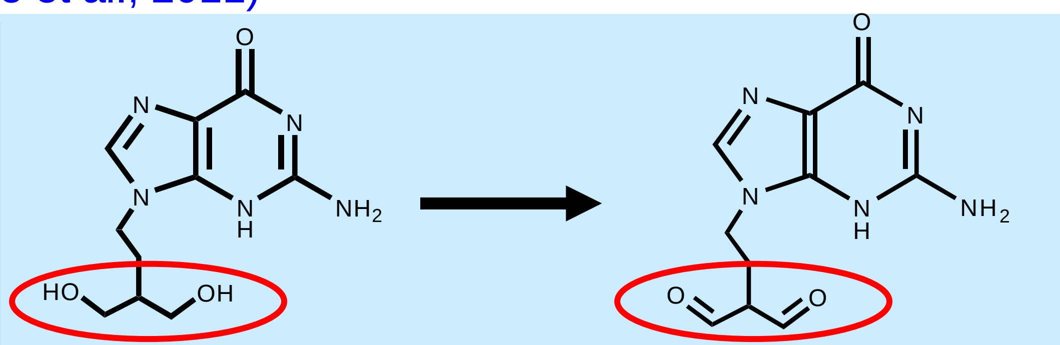
Ranitidin-sulfoxid

Alcohol and aldehyde oxidation (Prasse et al., 2011)



Acyclovir

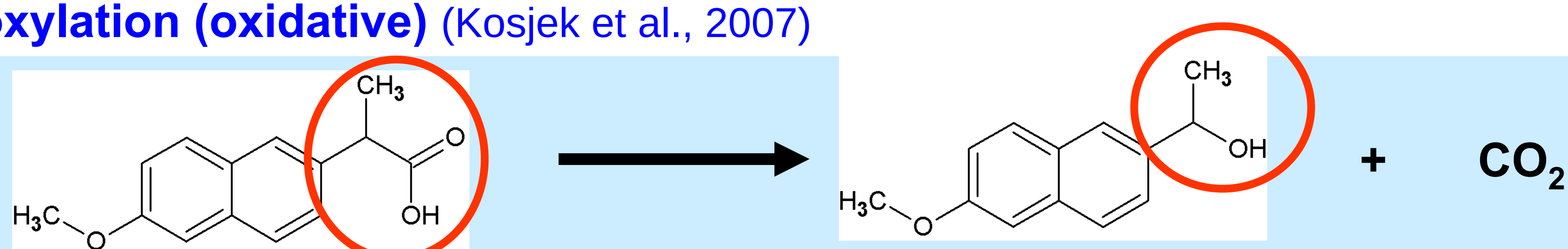
Carboxy-Acyclovir



Penciclovir

Bialdehyde-Penciclovir

Decarboxylation (oxidative) (Kosjek et al., 2007)



Naproxen

Decarboxyhydroxy-Naproxen

BfG approach to identify TPs

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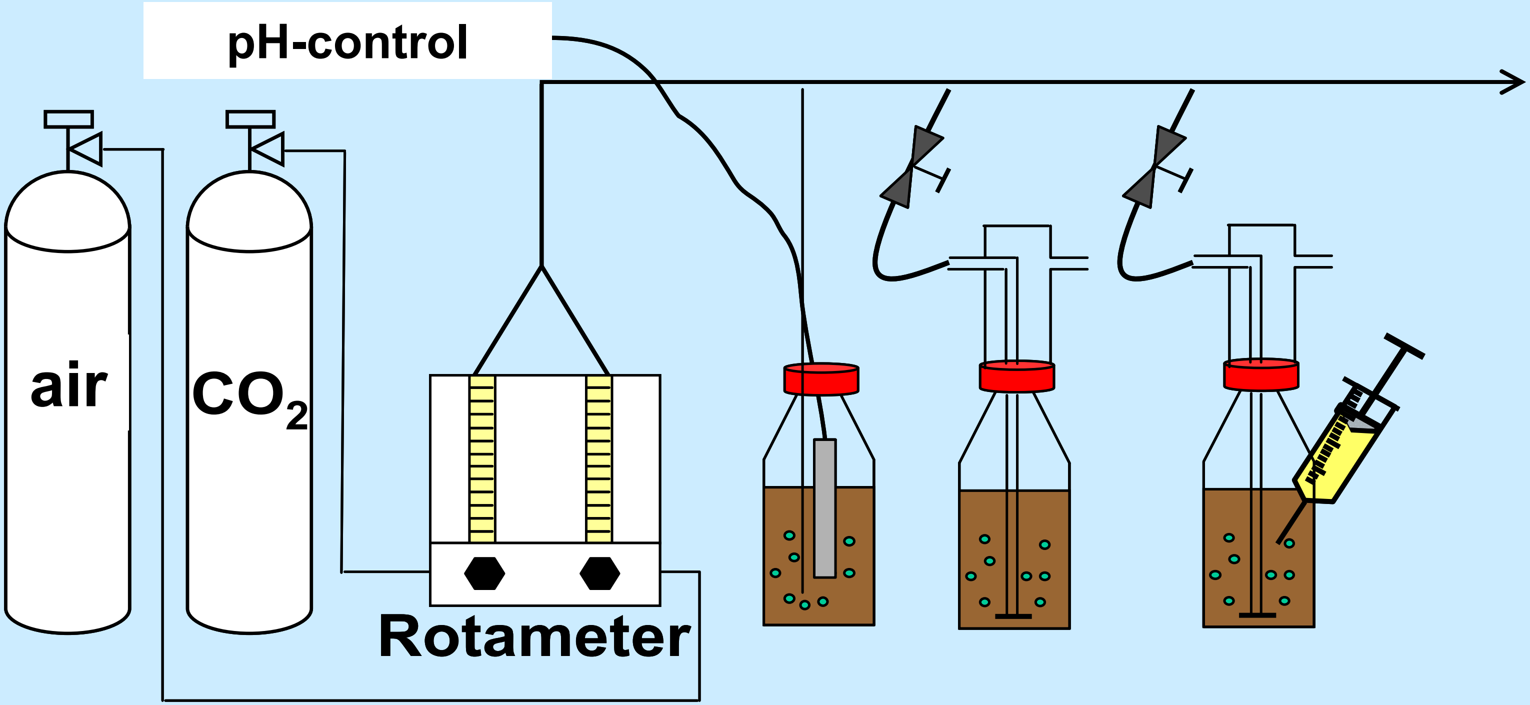
1. Transformation in lab systems: relevance for WWTPs/environment?
2. TP-Screening via HR-MS: "exact" masses → elemental composition
3. MS^n-fragmentation via HR-MS, Q-MS
   → functional moieties,
   → *first proposal of chemical structure*
4. Chemical synthesis of TPs or isolation of TPs from lab systems
   → standards and NMR
5. NMR → a) confirmation of the chemical structure proposed,
   b) revised proposal of the chemical structure
6. Mass balance → indication if the predominant TPs have been identified
7. Detection of TPs in wastewater, rivers, ground water, drinking water

Forming TPs in aerobic batch experiments

Simulation of WWTP nitrification

Taking activated sludge from a full-scale WWTP, diluting 1:10 to minimize sorption) and bubbling a definite ratio of air/CO_2 to adjust a stable pH.



UV-filters – Sulisobenzone – benzophenone 4

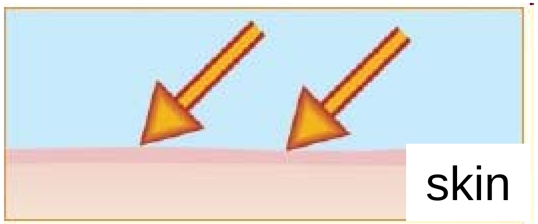
suntan cream, suntan lotion, sunscreen spray…
cosmetics: shampoo, lipsticks, mascara…

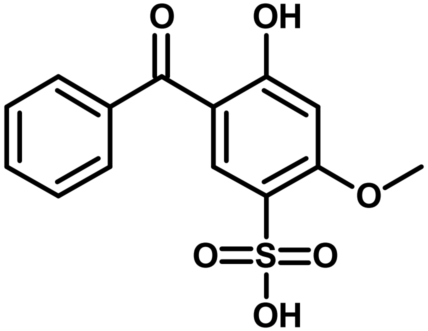
absorbs UV-A & UV-B radiation

approved in cosmetics:
< 10% US, < 5% Europe

recommended for products in transparent packagings

product protection: paints & textiles

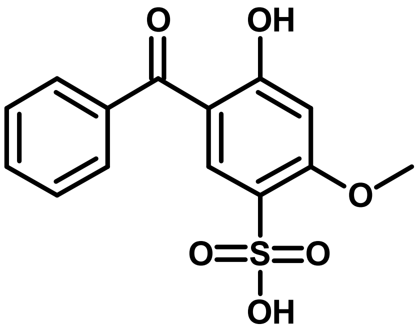




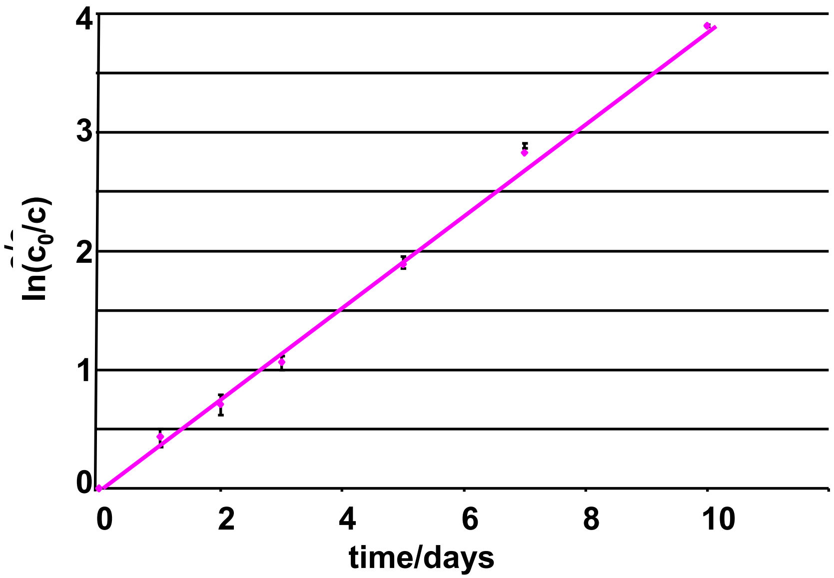
Ph.D. thesis Rita Beel

BP-4 degradation

WWTP influent:	**2.1 - 5.1 µg/L**
WWTP effluent:	**0.11 - 0.57 µg/L**
	→ 73-98% elimination
surface waters:	**0.05 - 2.0 µg/L**



- Sulisobenzone



pseudo 1st order:

$$\ln(c_0/c) = k_{biol} * SS * t$$

$$k_{biol} = 0.92 \pm 0.10\ L/(g_{SS}*d)$$

$$t_{1/2} = \ln 2/(k_{biol}*SS)$$
$$= 1.76 \pm 0.04\ d$$

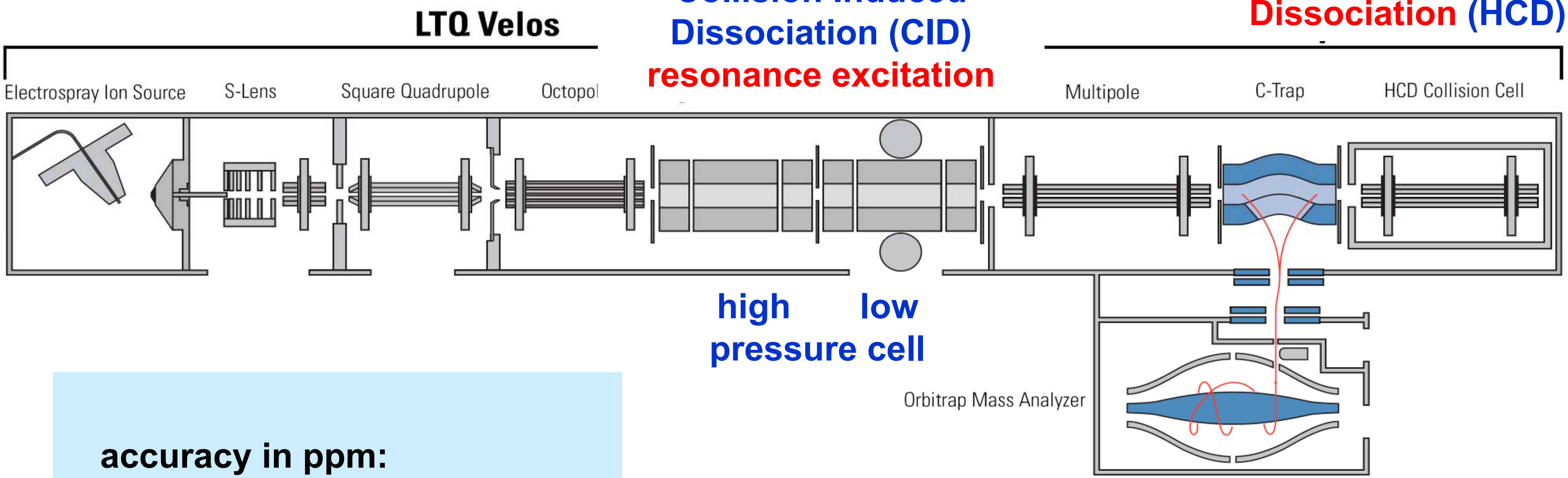
LC-LTQ-Orbitrap Velos

MS^n (n_{max} = 10)

Linear ion trap

Collision Induced Dissociation (CID)
resonance excitation

Higher energy Collision Dissociation (HCD)

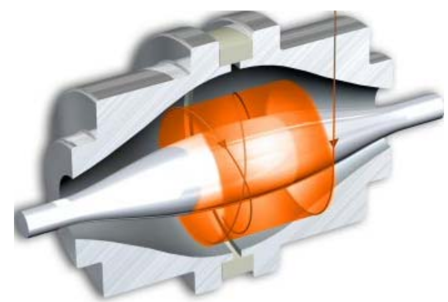


high low
pressure cell

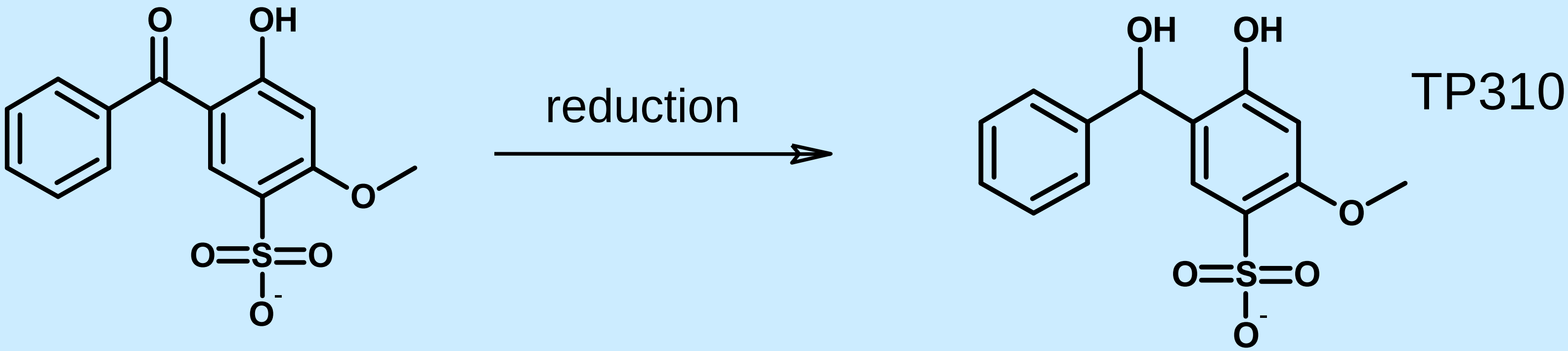
accuracy in ppm:
1 ppm: 700.0000 ± 0.0007 Da
100 ppm: 700.00 ± 0.07 Da

=> Exact molecular mass

Orbitrap Mass Analyser

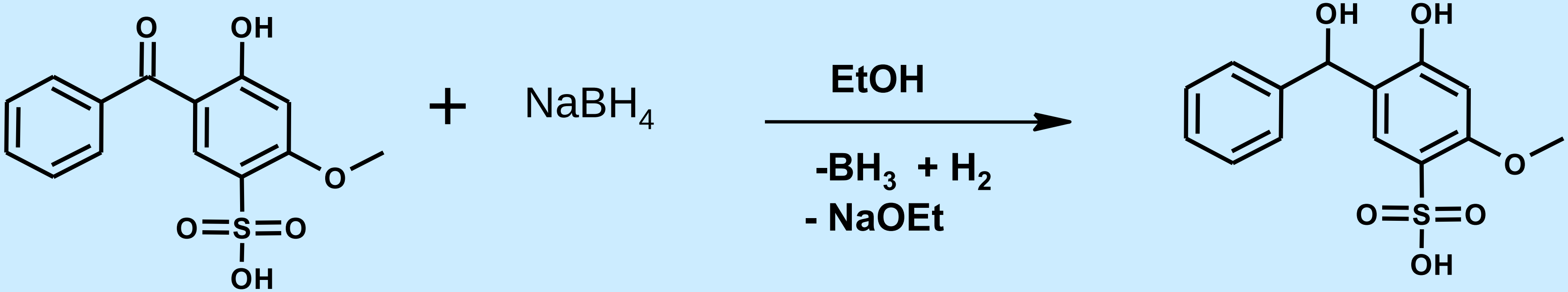


BP-4: First transformation product TP310

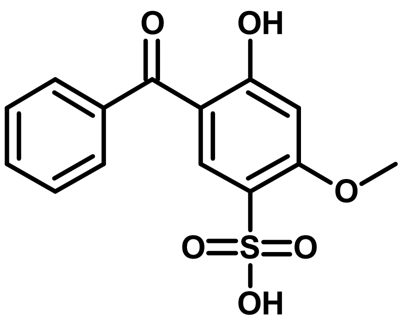


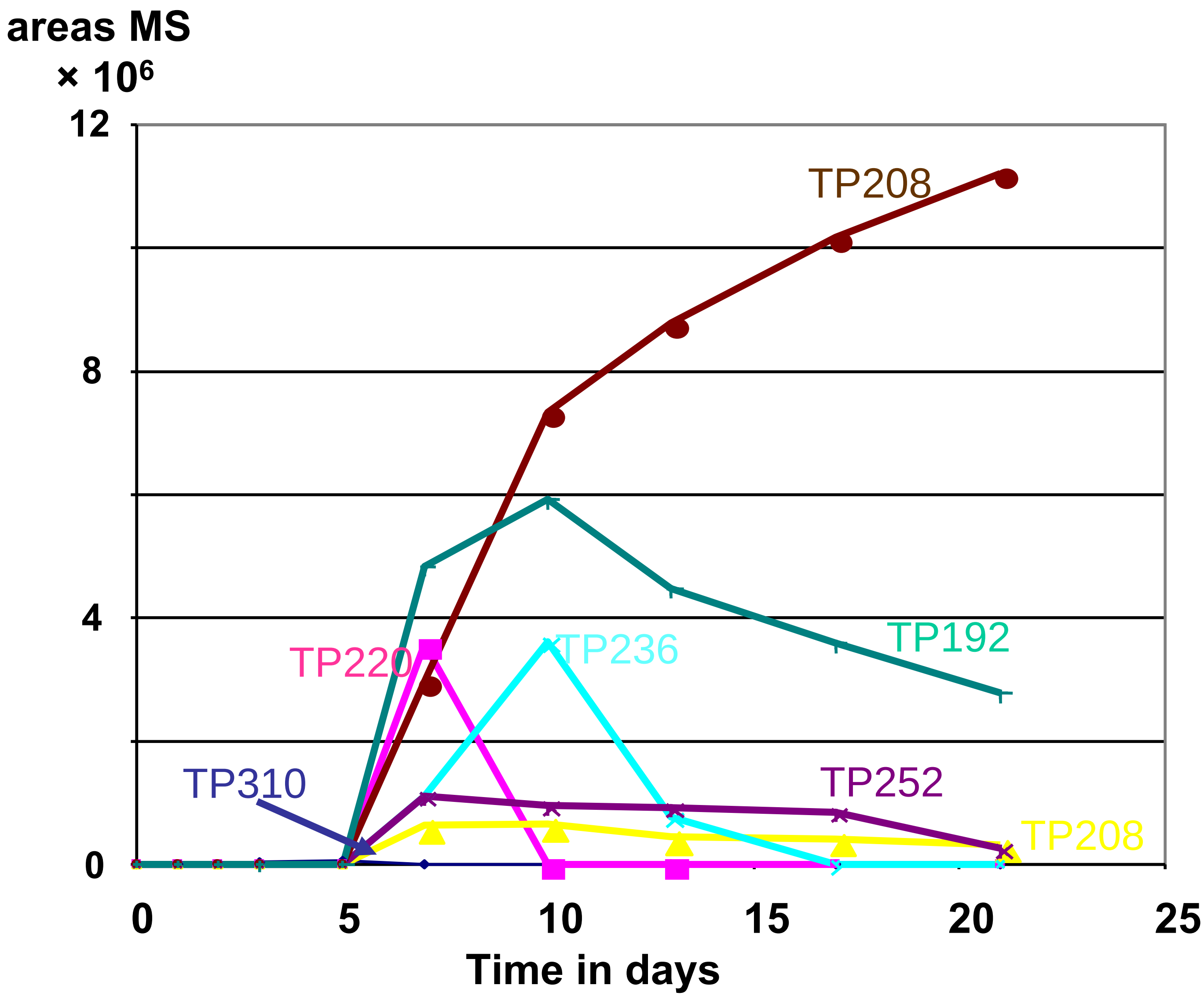
m/z = 307.02829
$C_{14}H_{11}O_6S$

m/z = 309.04330
$C_{14}H_{13}O_6S$

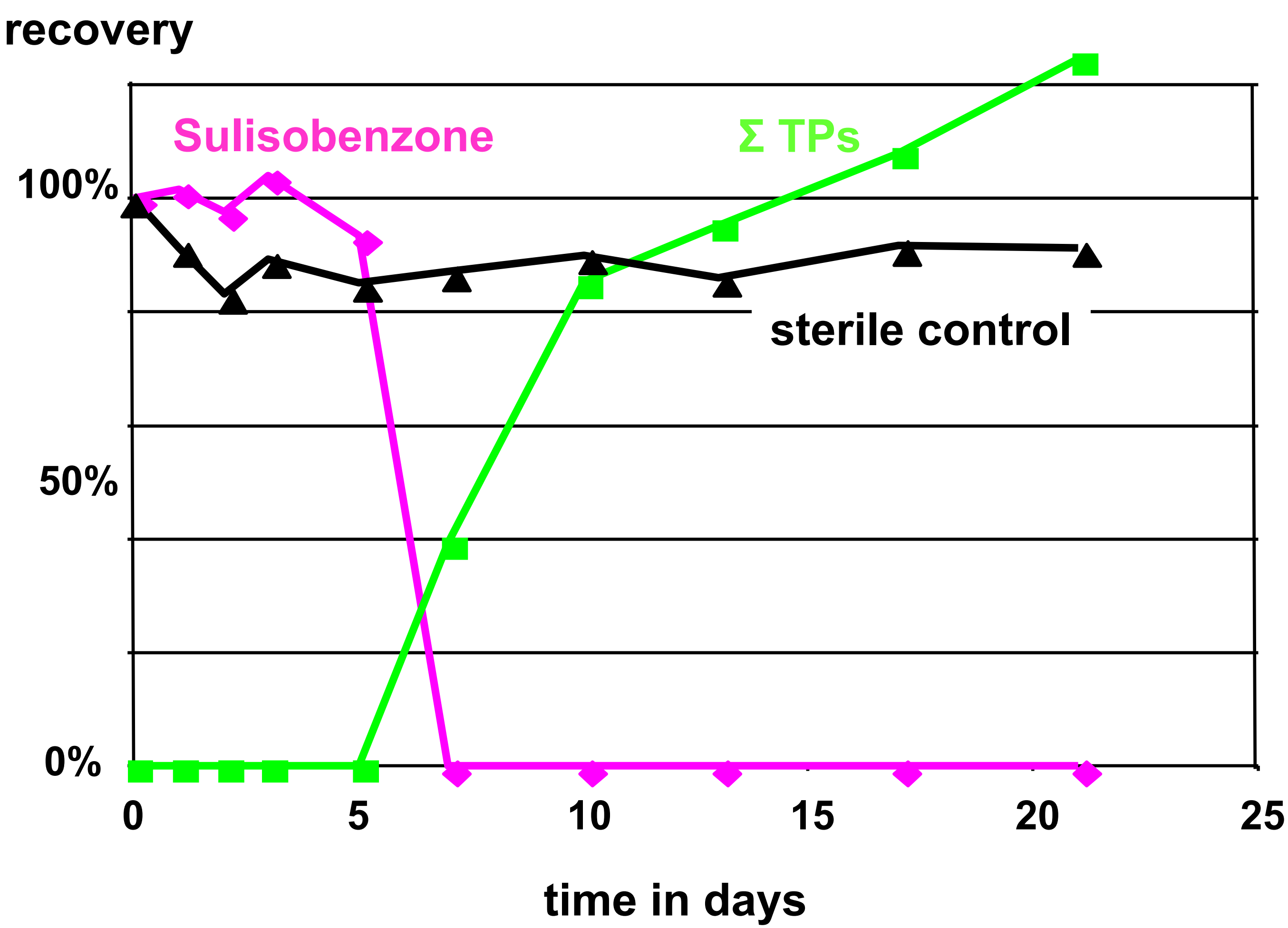


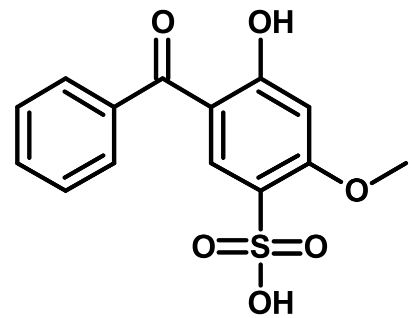
Formation of TPs in batch experiments





Mass balance (recovery) in the batch experiments





Sulisobenzone

Biological transformation and ozonation?

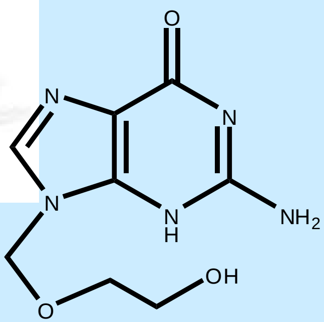
Carsten Prasse, Michael Schlüsener, Ralf Schulz, Thomas Ternes
ES&T 44(5), 1728–1735, 2010

Carsten Prasse, Manfred Wagner, Ralf Schulz, Thomas Ternes
ES&T 45, 2761–2769, 2011

Carsten Prasse, Manfred Wagner, Ralf Schulz, Thomas Ternes
ES&T in press, 2012

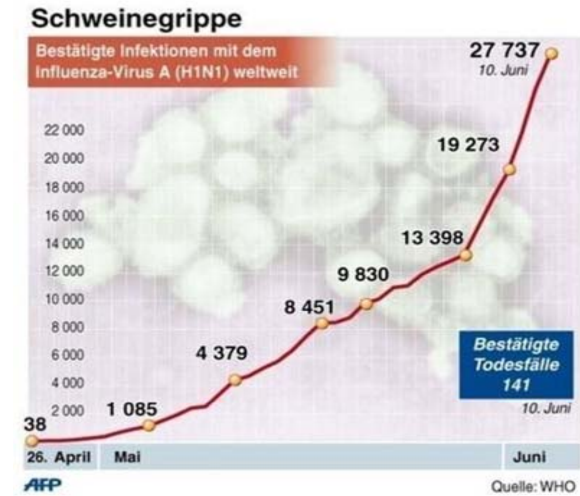
Antivirus drugs – therapeutic use

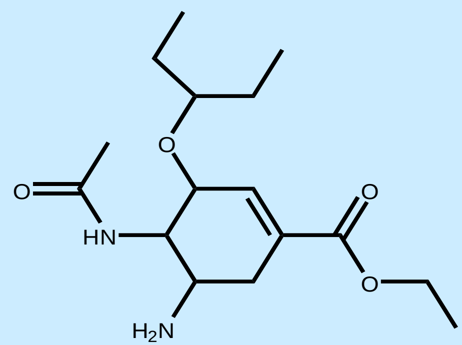
Herpes Virus



Acyclovir

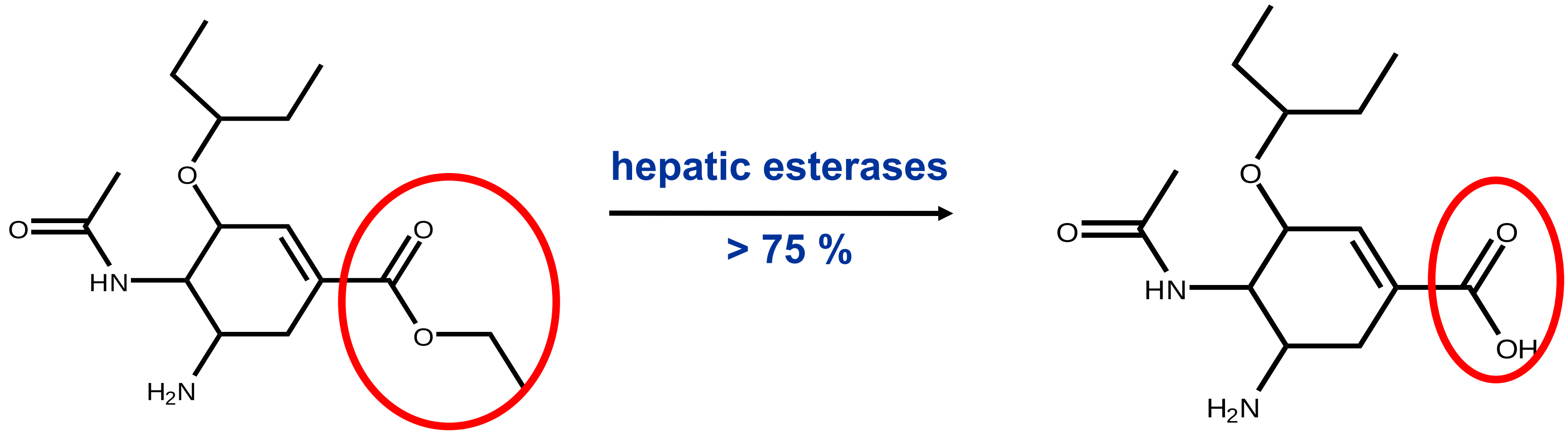
Influenza Virus





Oseltamivir

Metabolism of Oseltamivir in patients



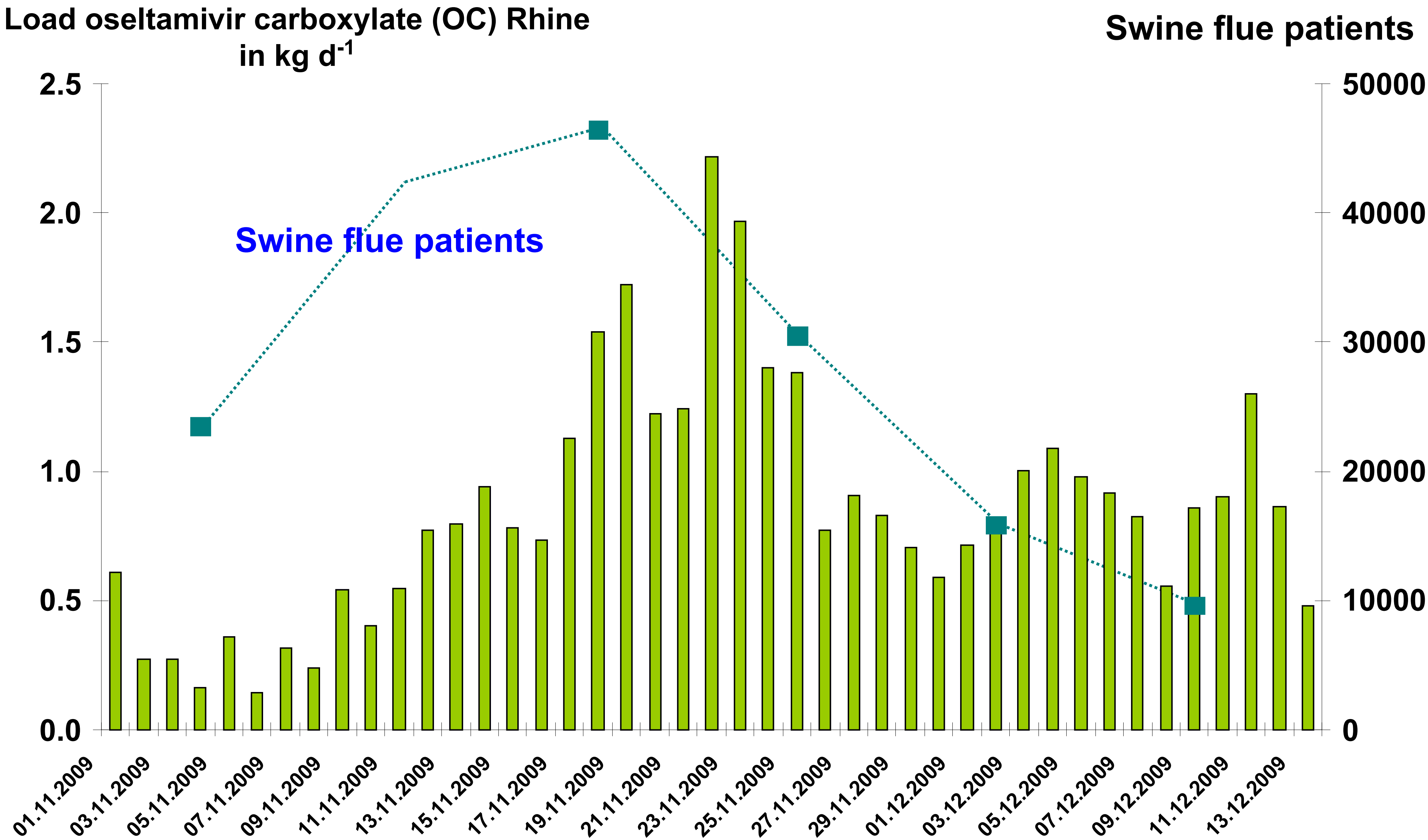
Oseltamivir (OP)
(pro-drug)

Oseltamivir carboxylate (OC)

→ active metabolite!

→ urine: ratio OP/OC = 0.2-0.3

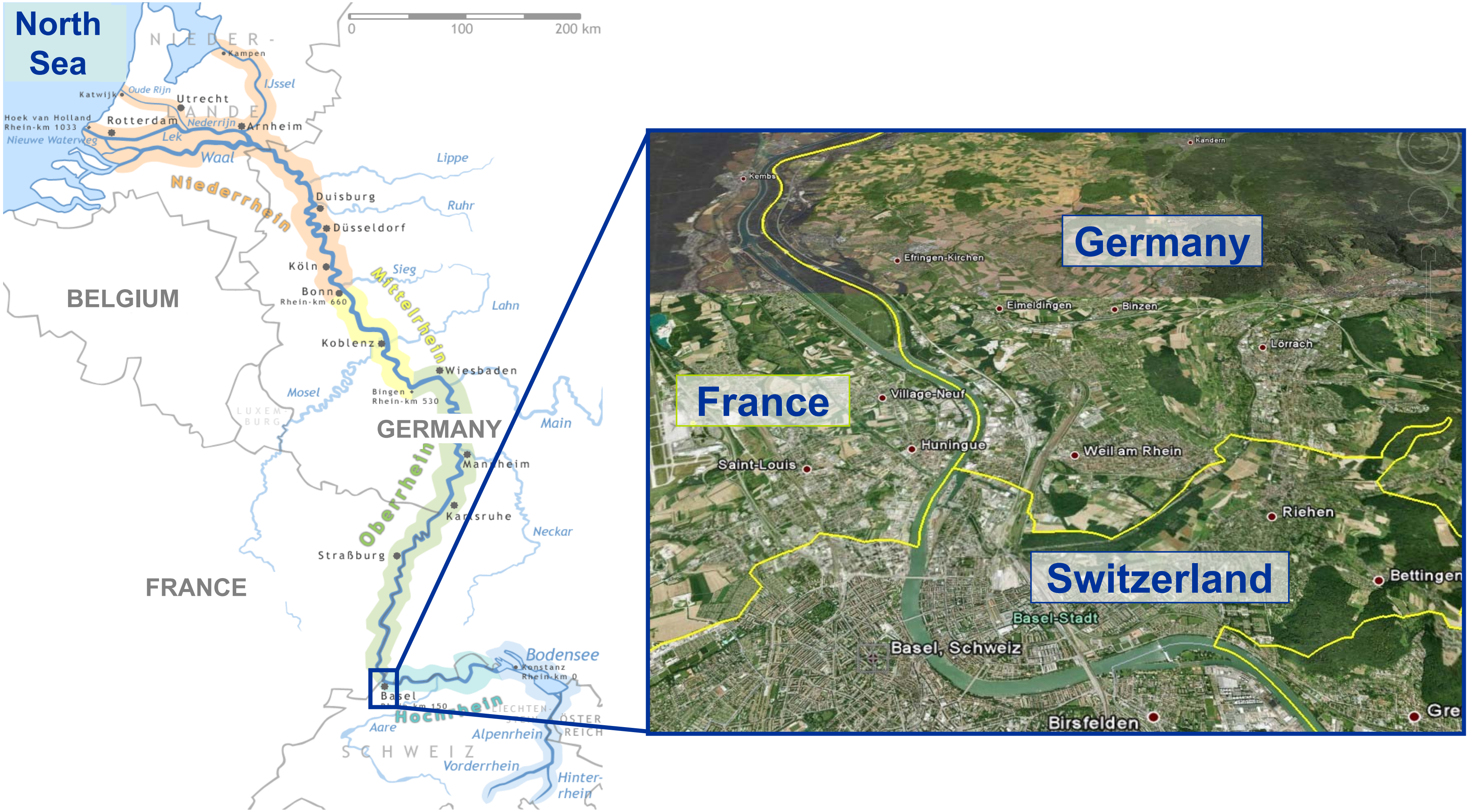
Oseltamivir carboxylate in the Rhine: Nov./Dec. 2009



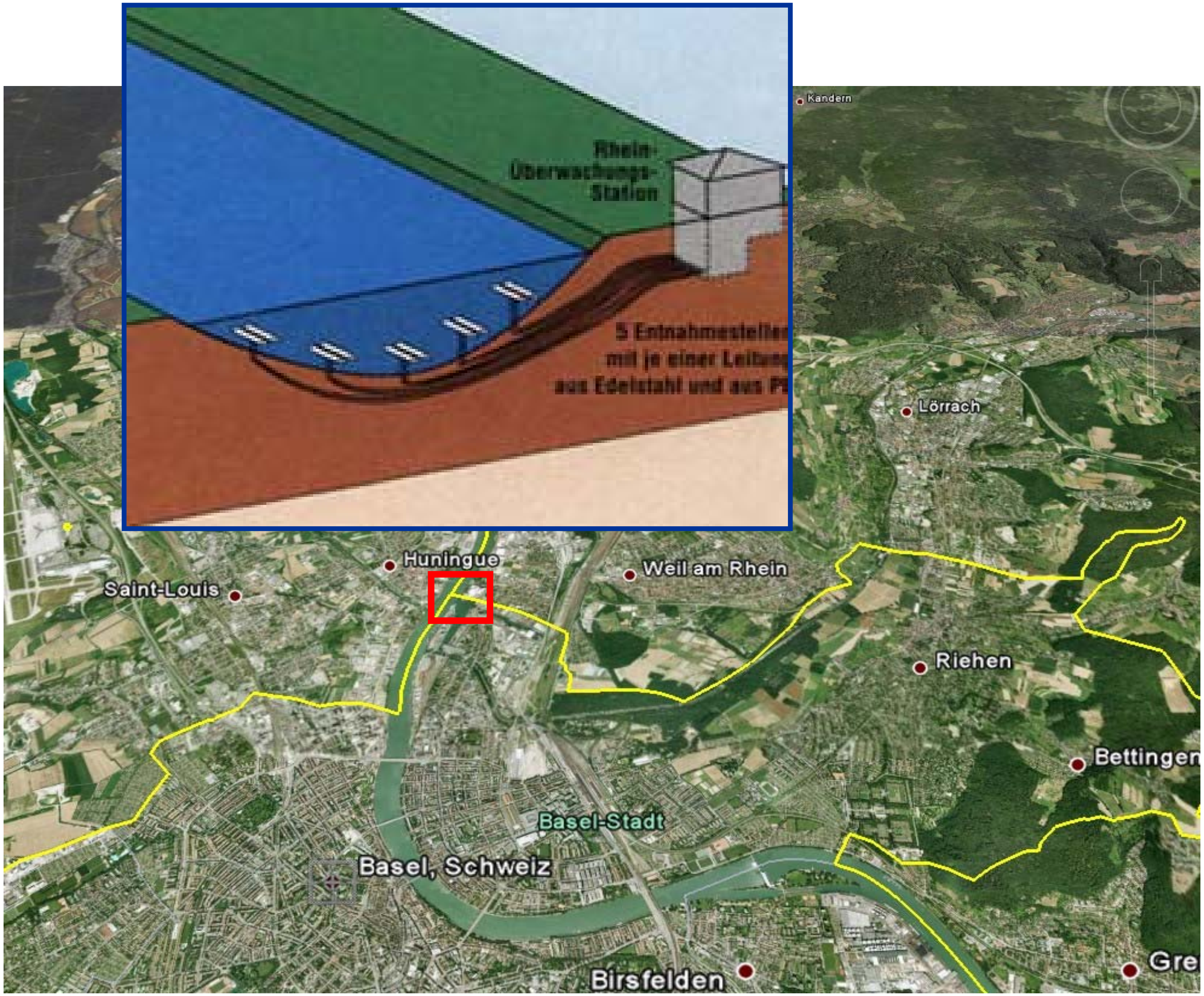
Ratio of oseltamivir (OP)/oseltamivir carboxylate (OC)

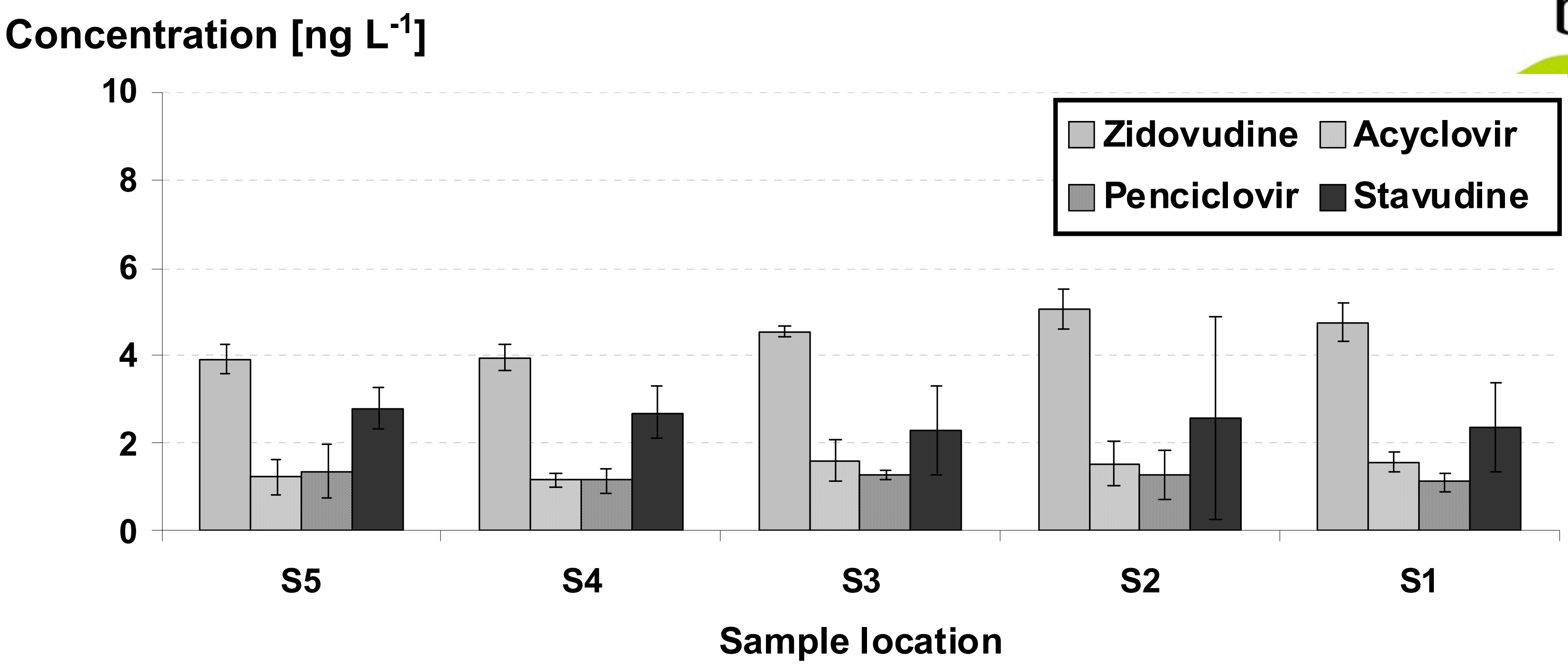
	OP/OC
Urine	0.2 - 0.3
Raw wastewater	0.3
WWTP effluent	0.7
Ruhr	0.3 - 1.8
Emscher	1.2
Hessian Ried	0.6 - 3.1
Rhine	**12.4-13.8**

Source for Oseltamivir in the Rhine



Monitoring station at Weil (Germany)

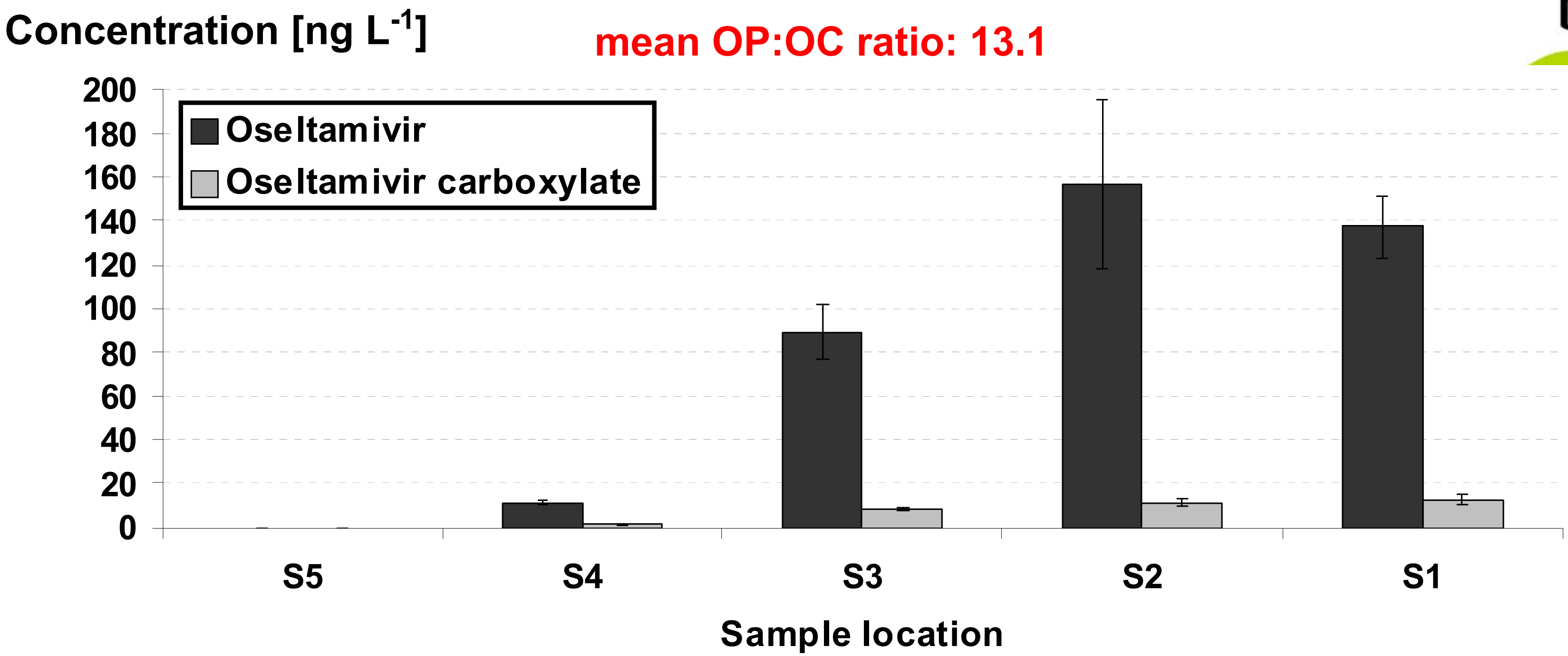




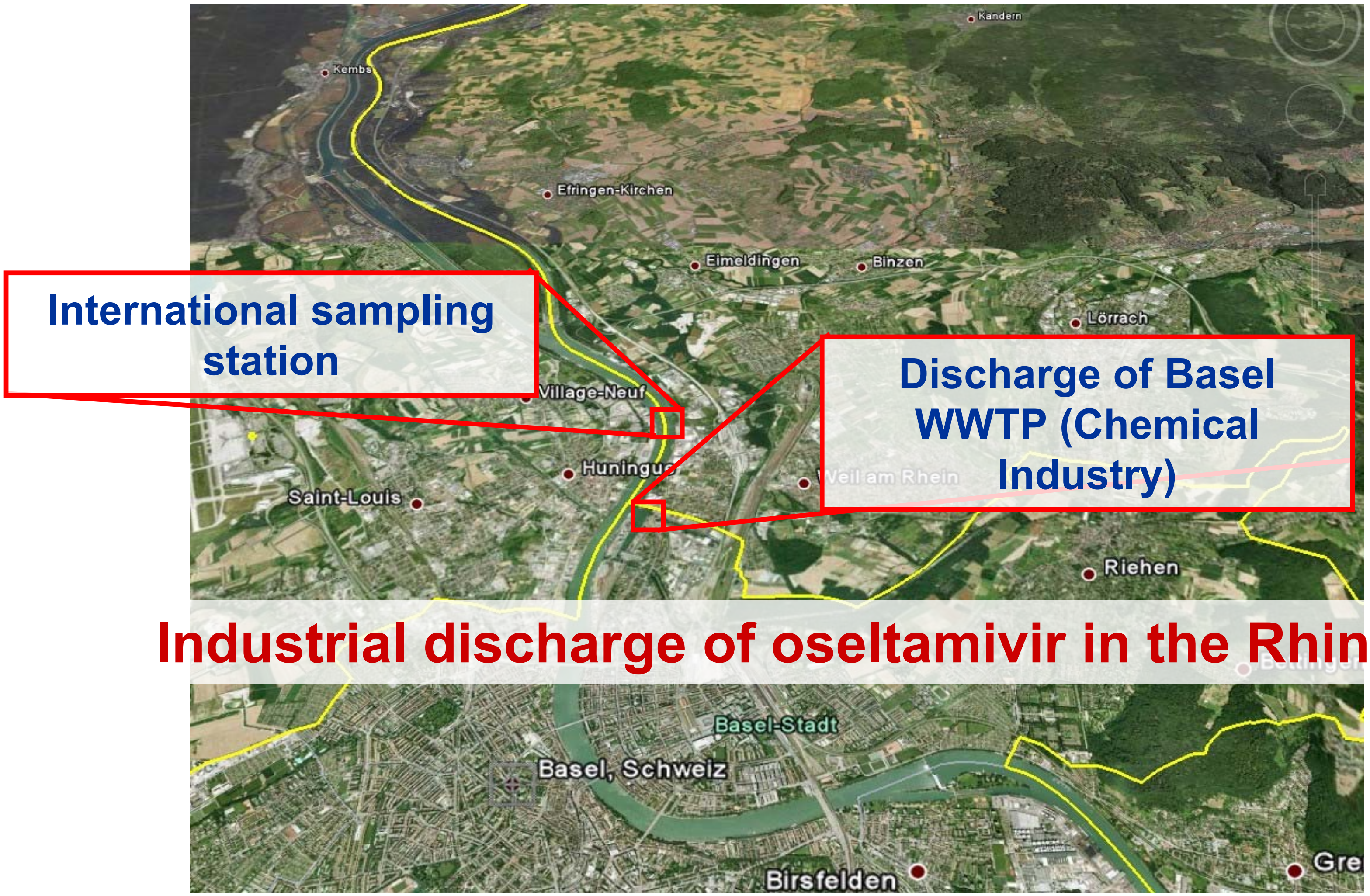
Concentration [ng L-1]
10
8
6
4
2
0
Zidovudine
Acyclovir
Penciclovir
Stavudine
S5
S4
S3
S2
S1
Sample location

Village-Neuf
Huningue
Saint-Louis
Weil am Rhein
Riehen
Bettingen
Basel-Stadt
Basel, Schweiz
Birsfelden

mean OP:OC ratio: 13.1



Source for Oseltamivir in the Rhine



Industrial discharge of oseltamivir in the Rhine

Source for Oseltamivir in the Rhine

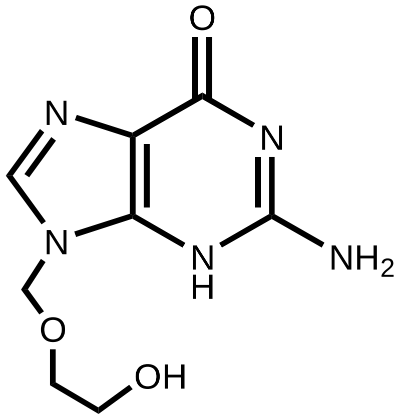
Calculated load: 1.8 kg d^{-1} oseltamivir in the Rhine!

→ equivalent to 12,000 treated individuals!!

(Sampling date: 07.10.2009)

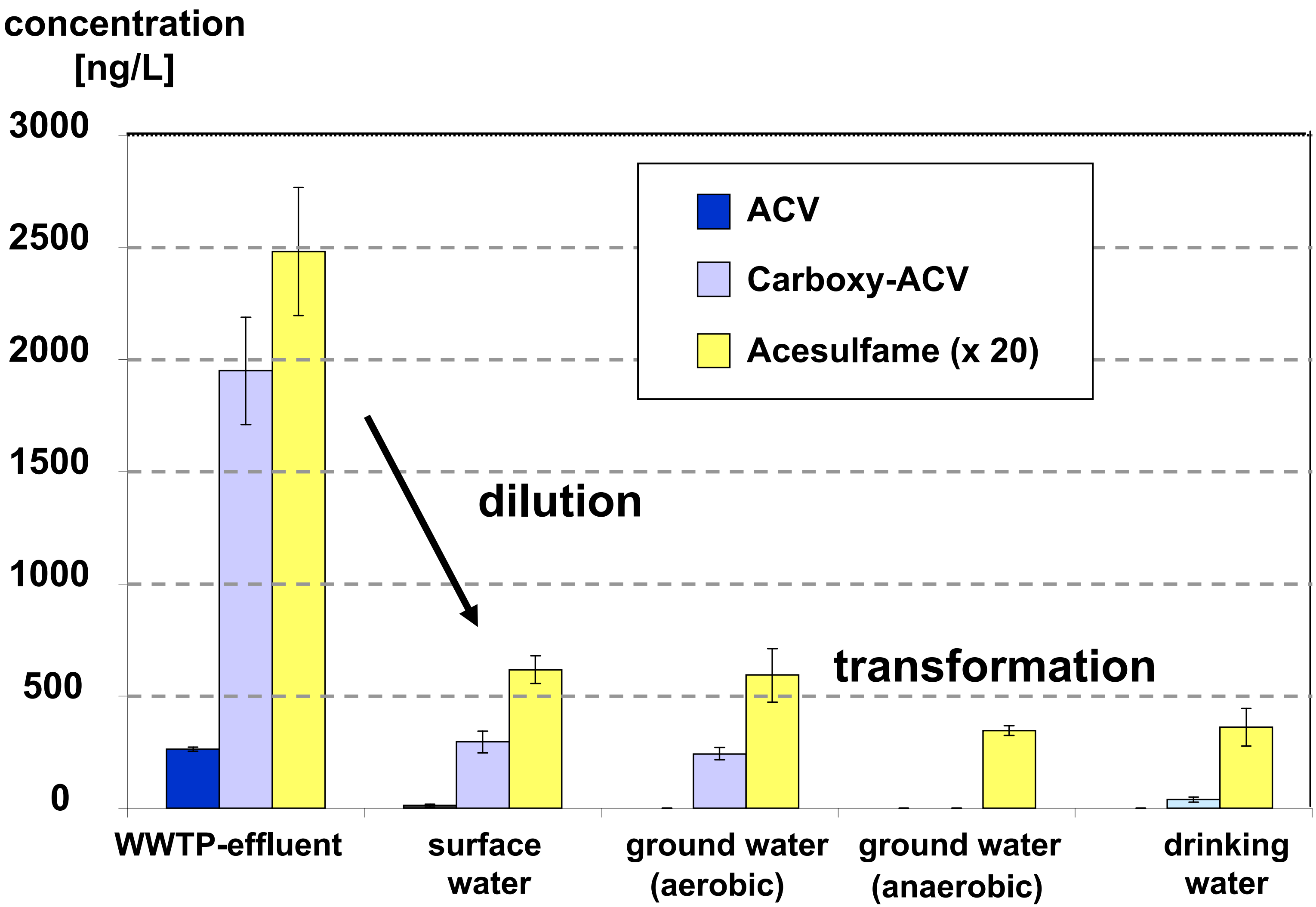
Transformation of acyclovir in a municipal WWTP

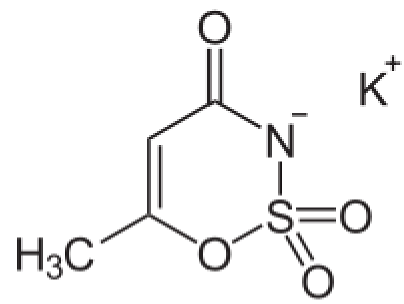
Acyclovir
(ACV)



ng/L	ACV
Influent	1990
effluent	140
elimination	**93 %**

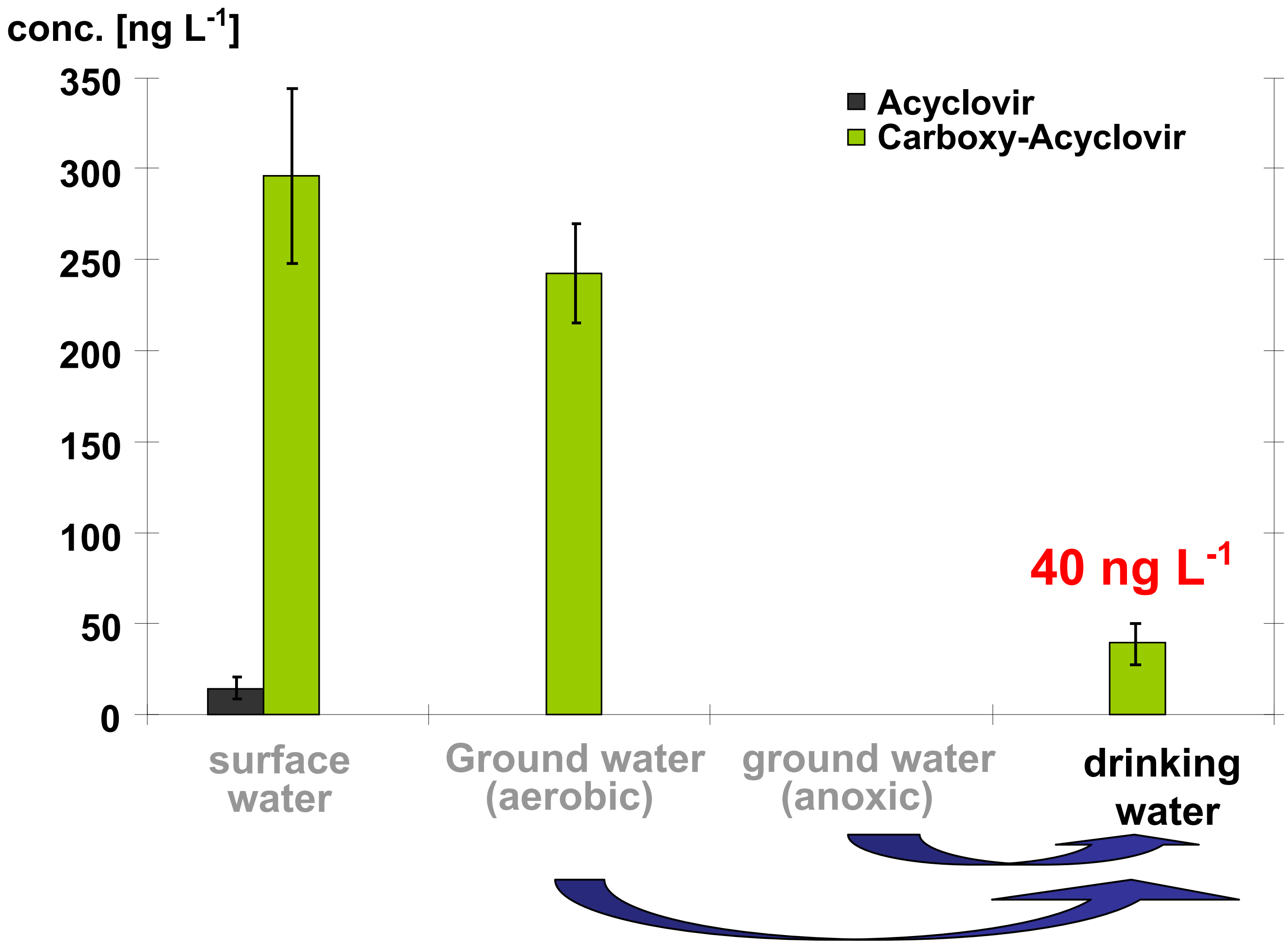
Detection of Carboxy-Acyclovir from WWTP effluent to drinking water



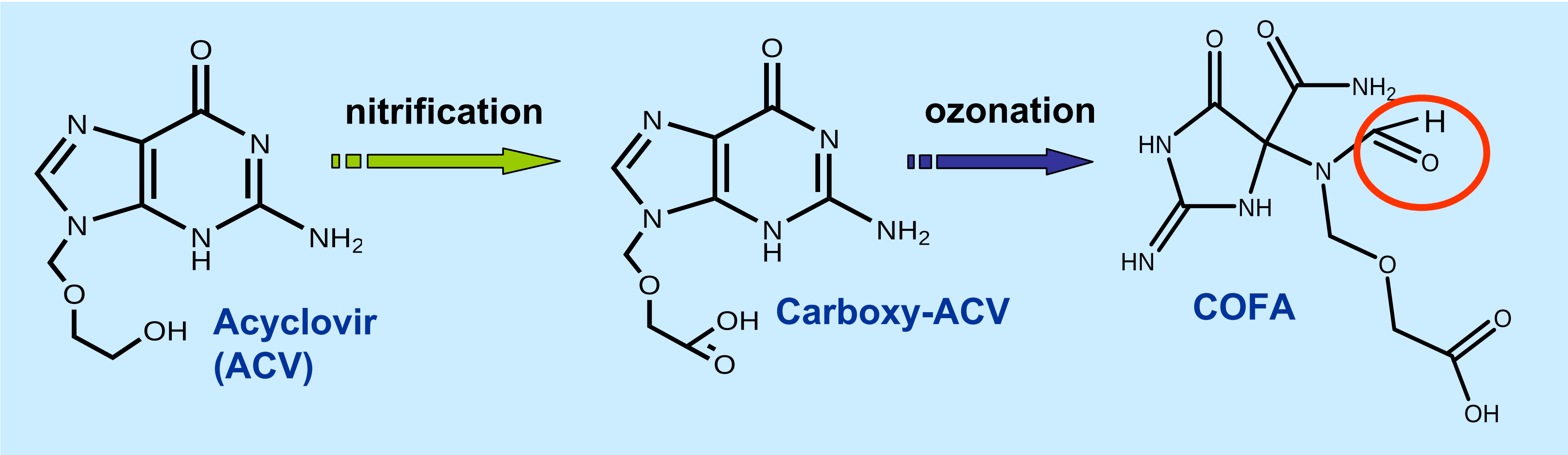


Acesulfame

Detection of Carboxy-Acyclovir from WWTP effluent to drinking water



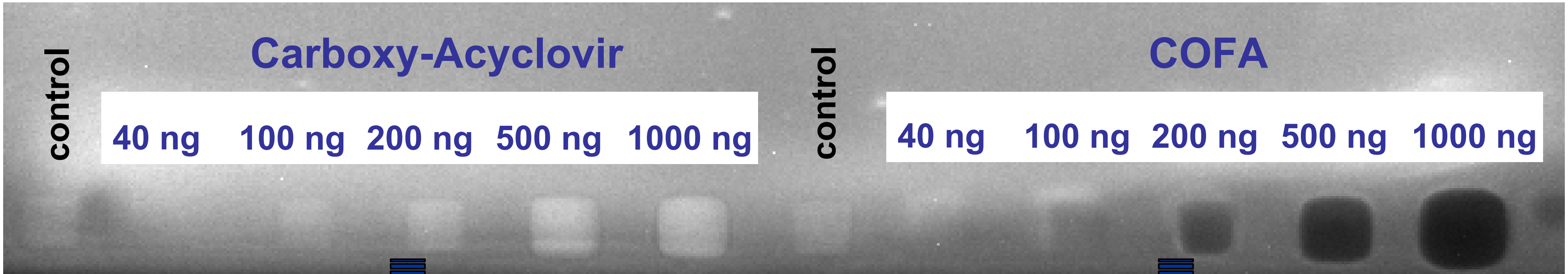
Transformation of Acyclovir (ACV)



COFA:

N-(4-Carbamoyl-2-imino-5-oxoimidazolidin)formamido-N-methoxyacetic acid

Inhibition of bioluminescent bacteria *Vibrio fischeri*



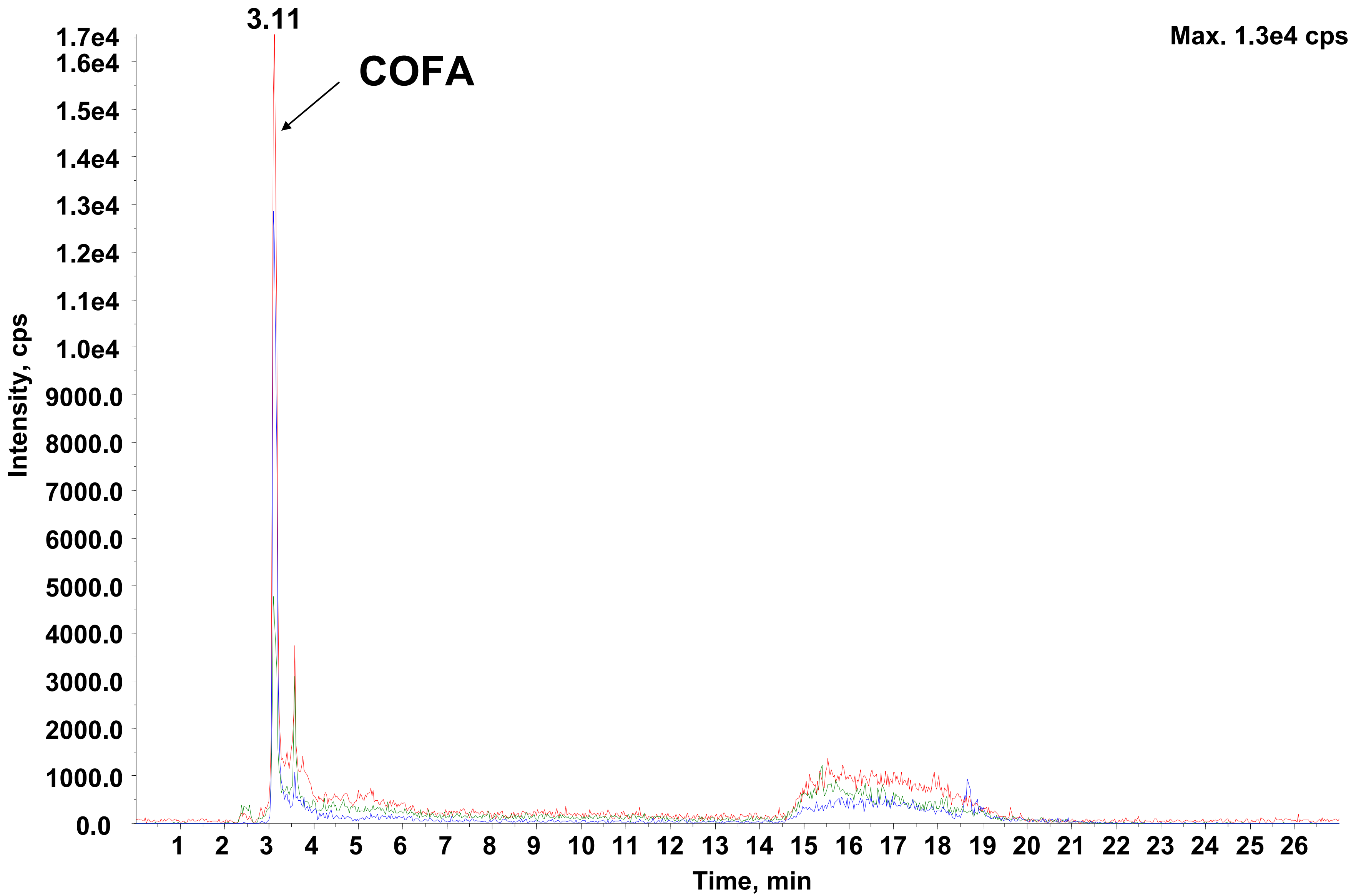
non toxic for *Vibrio fischeri*

toxic for *Vibrio fischeri!*

Conclusion:

Ozonation can transfer an untoxic compound into a toxic TP!

Detection of COFA in a waterworks after GAC filtration



Conclusions

It needs a) a lot of time and b) independent techniques to elucidate and confirm the complete chemical structure of a unknown molecule including its stereochemistry.

But we should have a dream!

Currently biological wastewater treatment **does not** lead to a removal of emerging pollutants, it causes the formation of a multitude of **polar biological** and **chemical** TPs. Some TPs even reach drinking water.

A challenge for the future!

Strong oxidants used for disinfection are prone to form (halogenated) TPs (disinfection by-products). Nontoxic TPs can be transformed into toxic TPs.

Can only be avoided if the emerging pollutants have been removed before.

=> TPs are new emerging frequently unknown contaminants

bfg Bundesanstalt für Gewässerkunde

Financial Support

EU for funding Neptune and Athene

from the Sixth Framework Programme and ERC

and

the German BMBF for funding TransRisk

Thank you for your attention