Fate of pharmaceuticals (PhCs) in sewage sludge and proposal of indicator substances for monitoring

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in Dessau, Germany

Workshop „Pharmaceuticals in Soil, Sludge and Slurry" 18th of June 2013, Dessau, Germany

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Overview

Aim of the talk

Provoke Discussion on

How to

classify and predict

fate and effects of PhCs

in sludge and soil

based on literature data?

How are human PhCs distributed in the environment?

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faeces, urine

sewage

Disposal into toilett

sewage treatment plant (STP)

sewage sludge as fertilizer for agriculture

surface water

soil

groundwater

drinking water

plants

mikro-organisms

insects

worms

Why addressing PhCs in sewage sludge?

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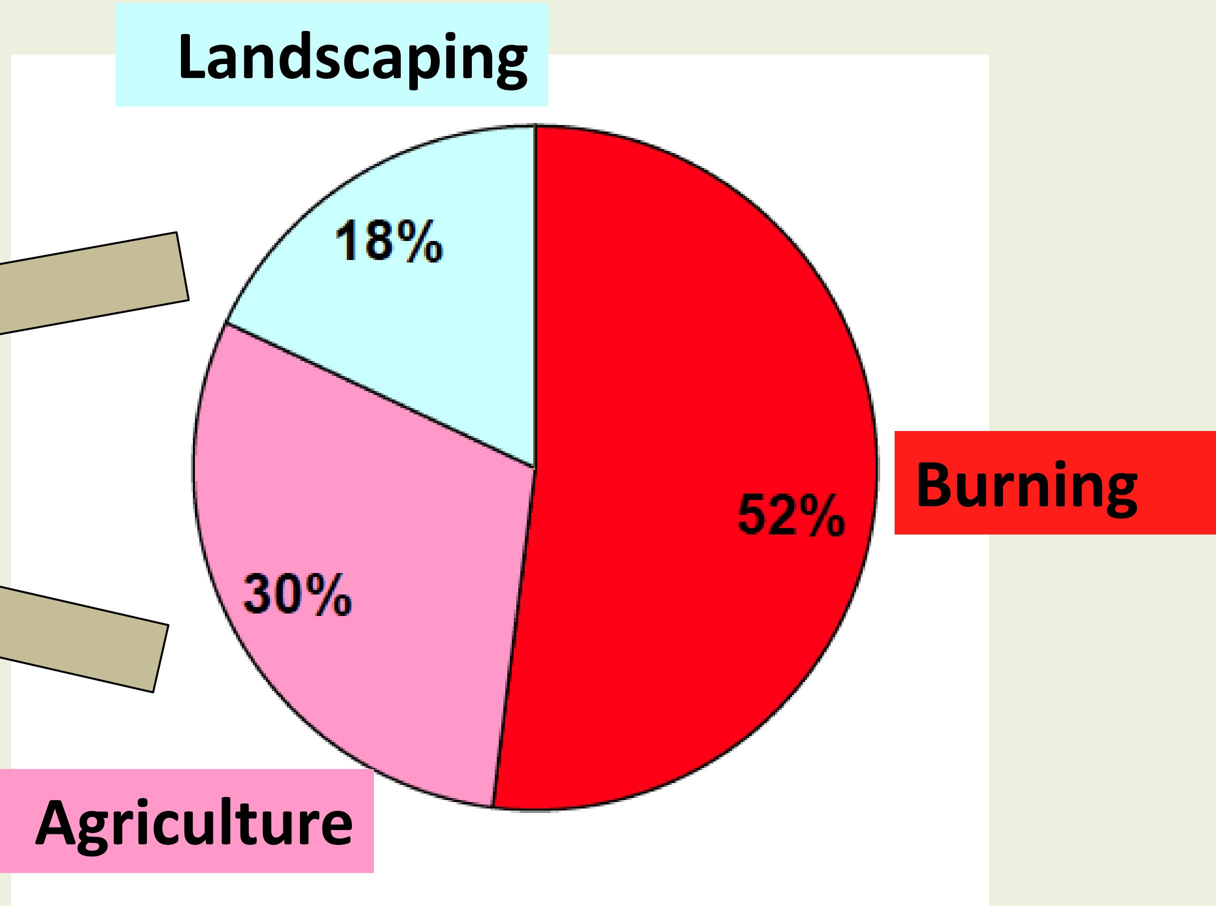
Disposal of 2.100.000 tons Ts/year sewage sludge in Germany

~ 1Mio t/a of sewage sludge disposed on soil



No regulation for PhCs

(Statist. Bundesamt 2009) adopted from Prof. Ulf Theilen , Kompetenzzentrum ZEuUS, Presentation: Zukunft Klärschlammverwertung und -entsorgung

Good news: German sewage sludge usage ordinance In agriculture is under revision

Draft of German "Abfallklärschlamm Verordnung" AbfklärV

Regulation on oganic pollutants

Category1: Previously regulated pollutants
- Ø Dioxines / Furane
- Ø PCB

lower threshold values

Category2: Pollutants currently at high environ. concentrations
- Ø PAH Polyaromatic Hydrocarbons
- Ø PFT perfluorated tensides

New legal limit values

Category4: pollutants that are readily degradable,
No limit values, no Monitoring

Category3: pollutants of concern that are not regulated
Ø Phtalates, Ø Triclosan
No threshold values but Monitoring

New concept of sewage sludge quality certificates
Monitoring via certified organisations

NEW: Hygiene Standards for sewage sludge to kill pathogenes

Bad news: no regulation, monitoring planned for PhCs

adopted from a Presentation of Prof. Ulf Theilen, Kompetenzzentrum ZEuUS, TH Mittelhessen

HOWEVER:

Since Draft is still under debate

Overview

1. Regulation sewage sludge usage in agriculture

2. Fate of PhCs during sewage treatment

3. Priorization strategy

4. Fate of PhCs in sludge/soil

5. Terrestrial Ecotoxicity PhCs

6. List of indicator substances

7. Conclusion and future Research

We aim to provide **scientific evidence** for **PhCs of concern** in sludge and soil to suggest for regulatory monitoring (category 3)

Identify indicator PhCs of high concern

- high occurrence in sludge and soil
- high sorption potential
- low degradation
- toxic to terrestric organisms

What fate of PhCs in sewage treatment plant STP?

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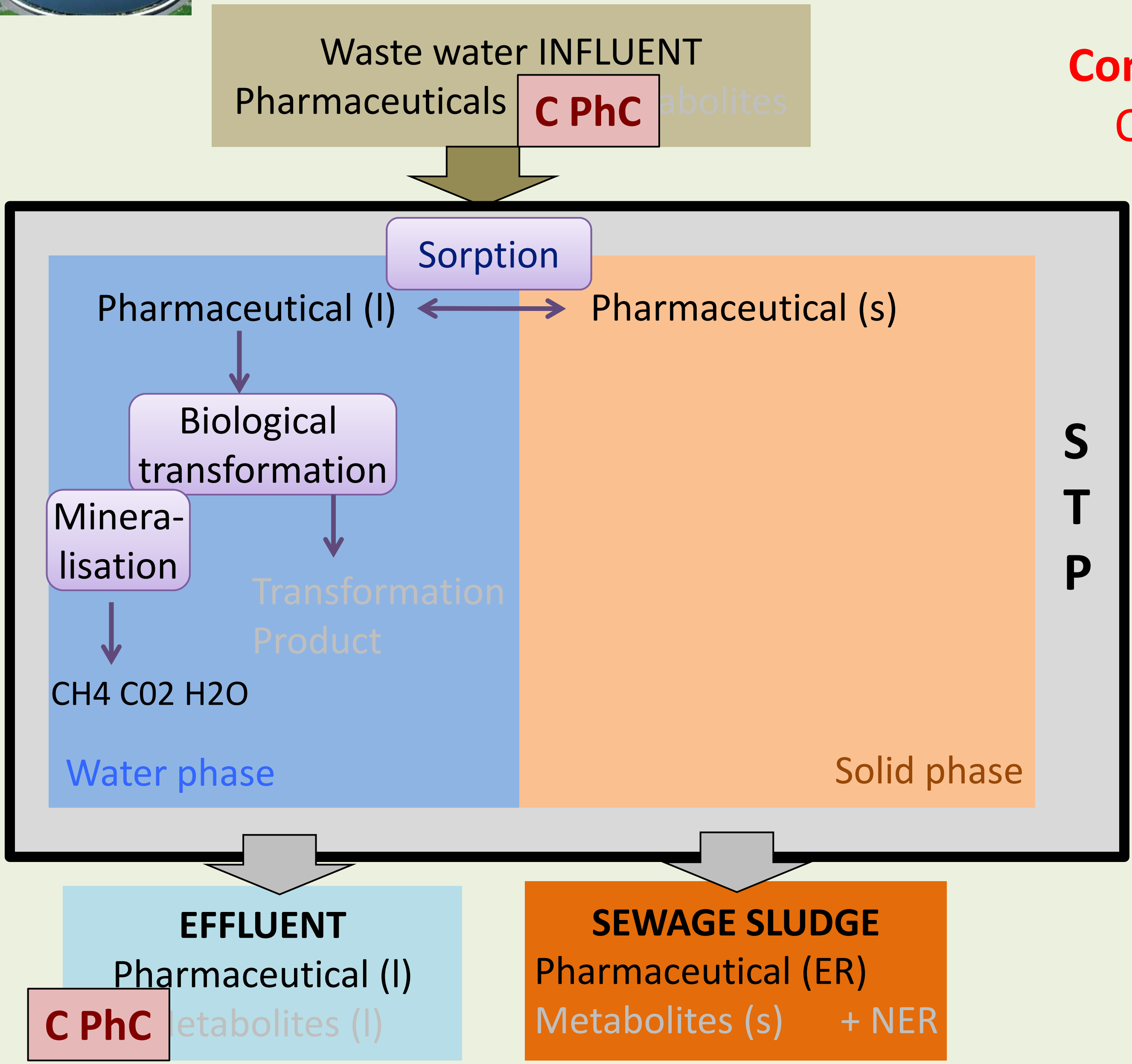


Conventional Monitoring

Only Concentrations:

Influent, Effluent

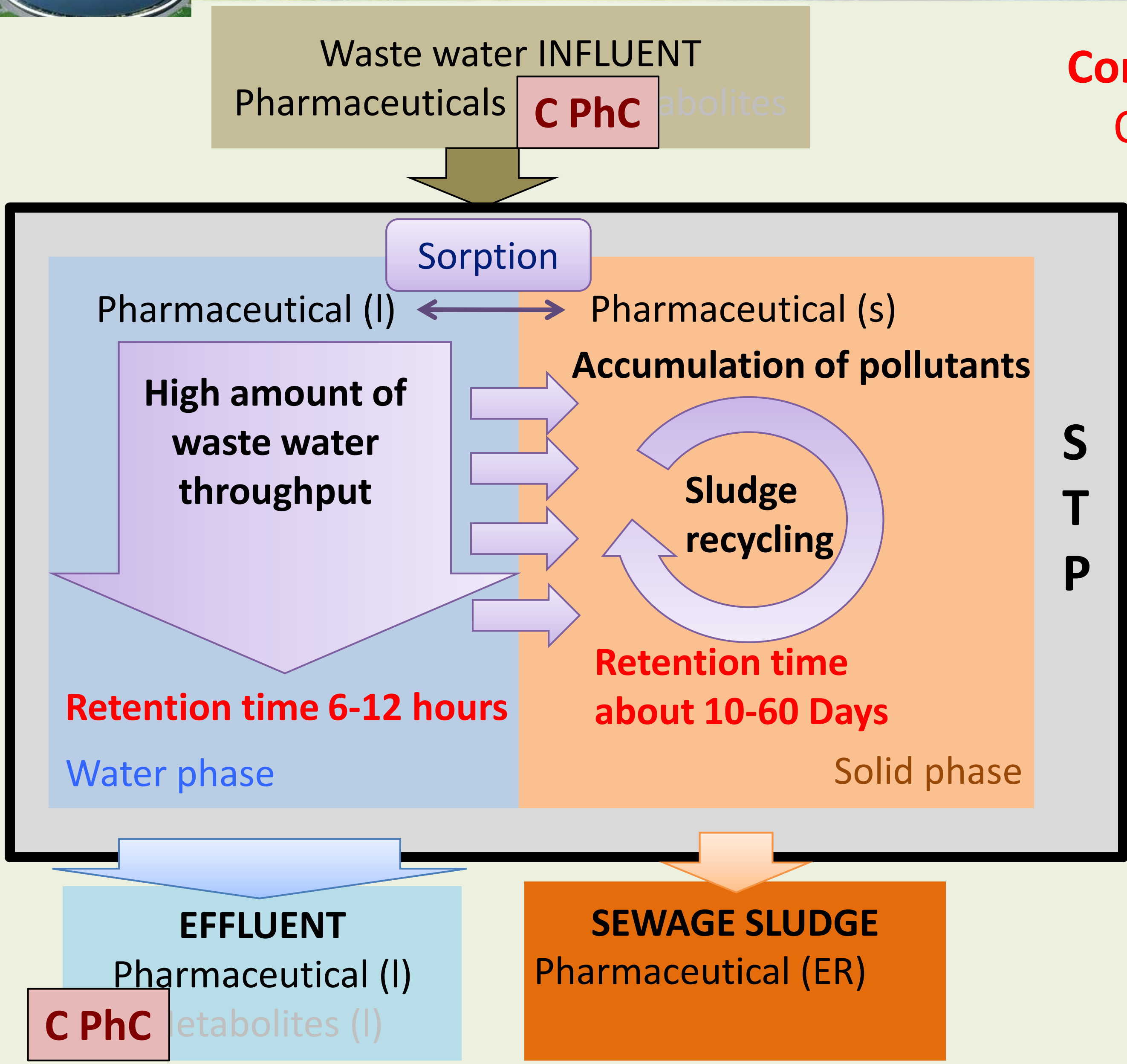
Too simple view

Conventional clearance

C influent - Ceffluent = removal from water phase

Sorption to sludge metabolites and NER are not considered

Sewage Sludge is a sink for pollutants



Conventional Monitoring

Only Concentrations:
Influent, Effluent

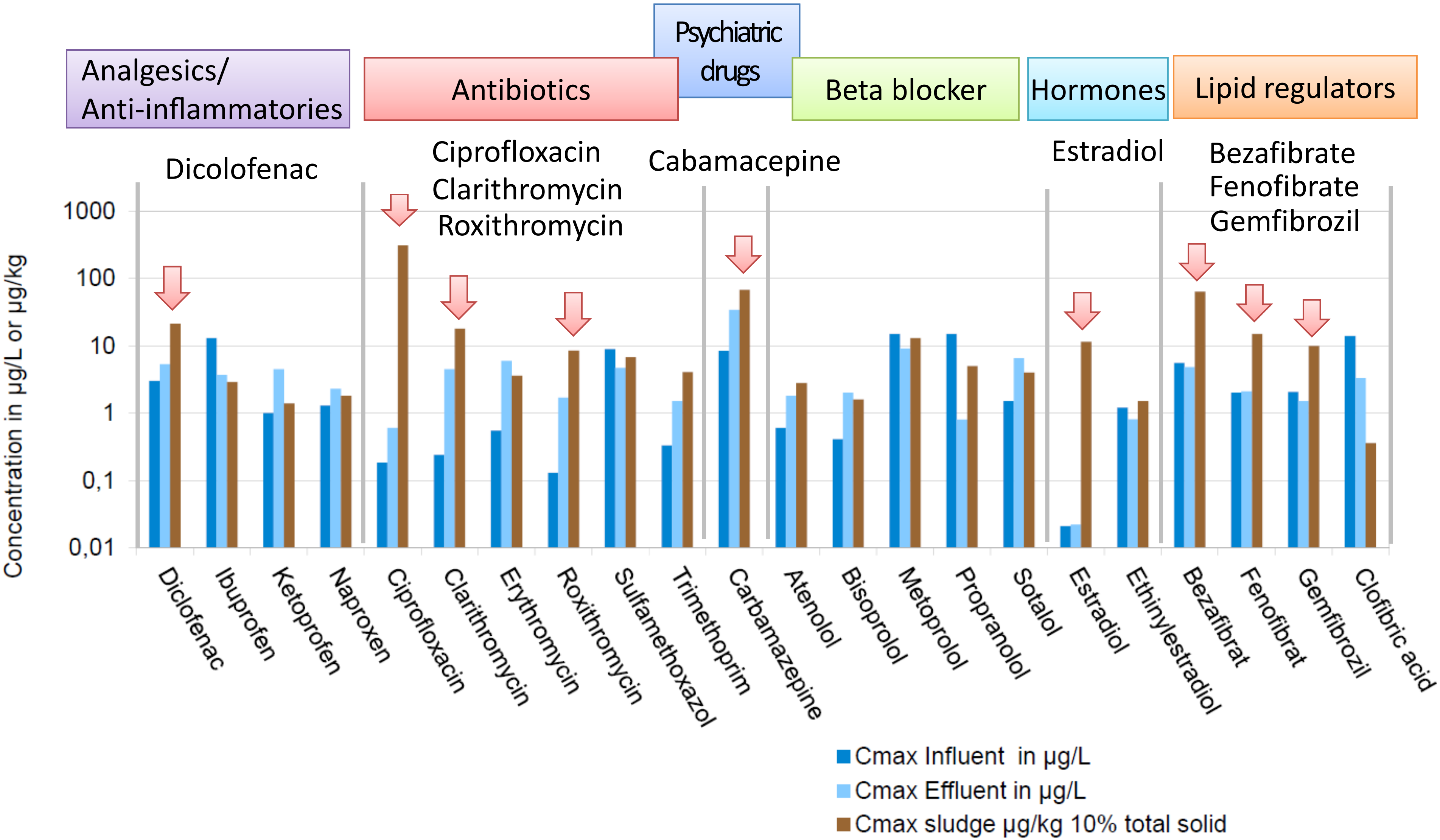
HOWEVER

Pollutants can accumulate in sludge because of

- ➔ **sludge recycling**
- ➔ **long retention time**

➔ Sludge is a sink for pollutants

Occurrence of PhCs in sewage and sludge



Bergmann A. Monitoring Data on environment concentration of Pharmaceuticals, UBA-FB 001525
Zusammenstellung von Monitoring Daten zu Umweltkonzentrationen von Arzneimitteln

Consumption of human antibiotics ~ 450-600t/year in Germany

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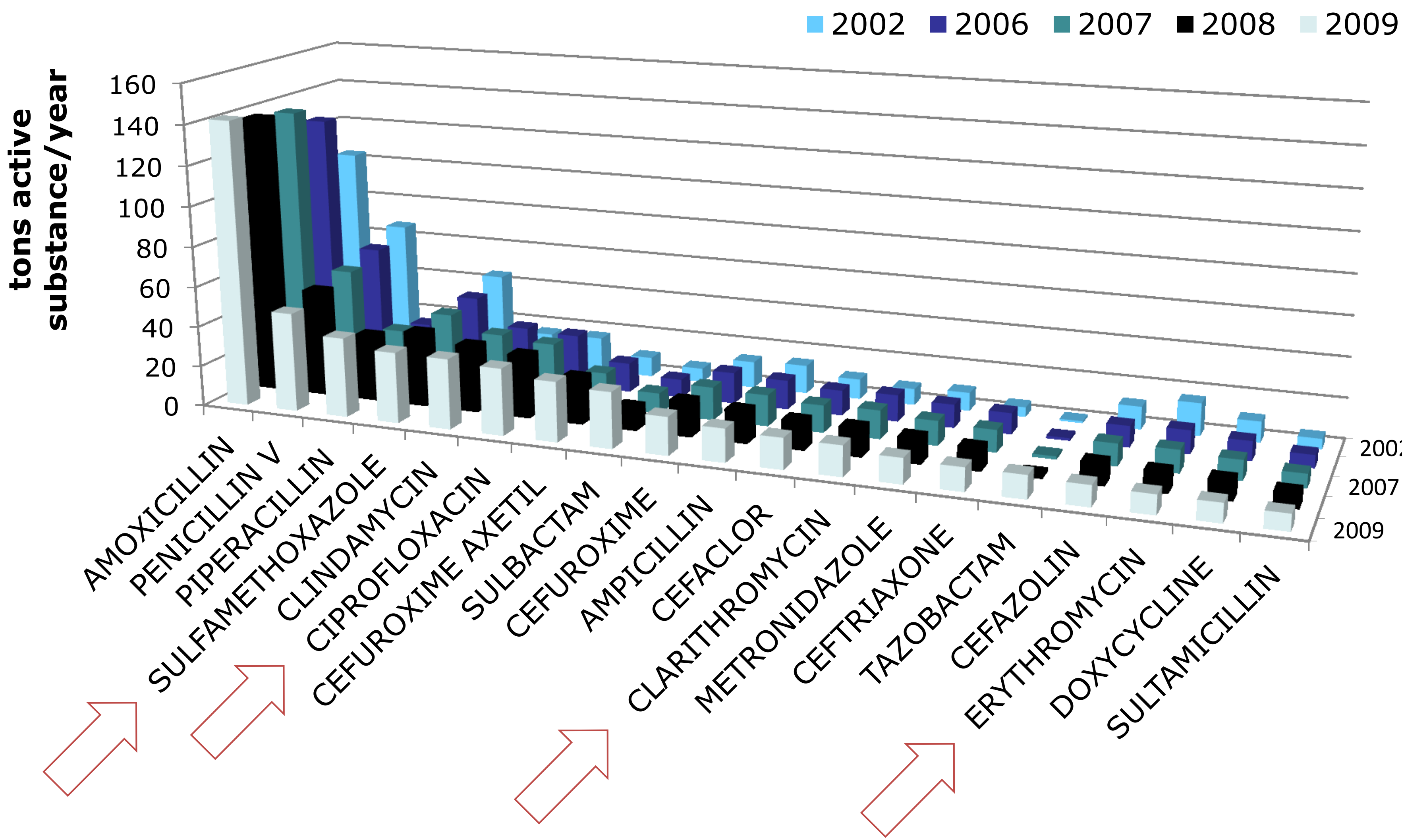

Increased consumption of antibiotics in the last few years

Fate of PhCs in sewage treatment plant (STP)

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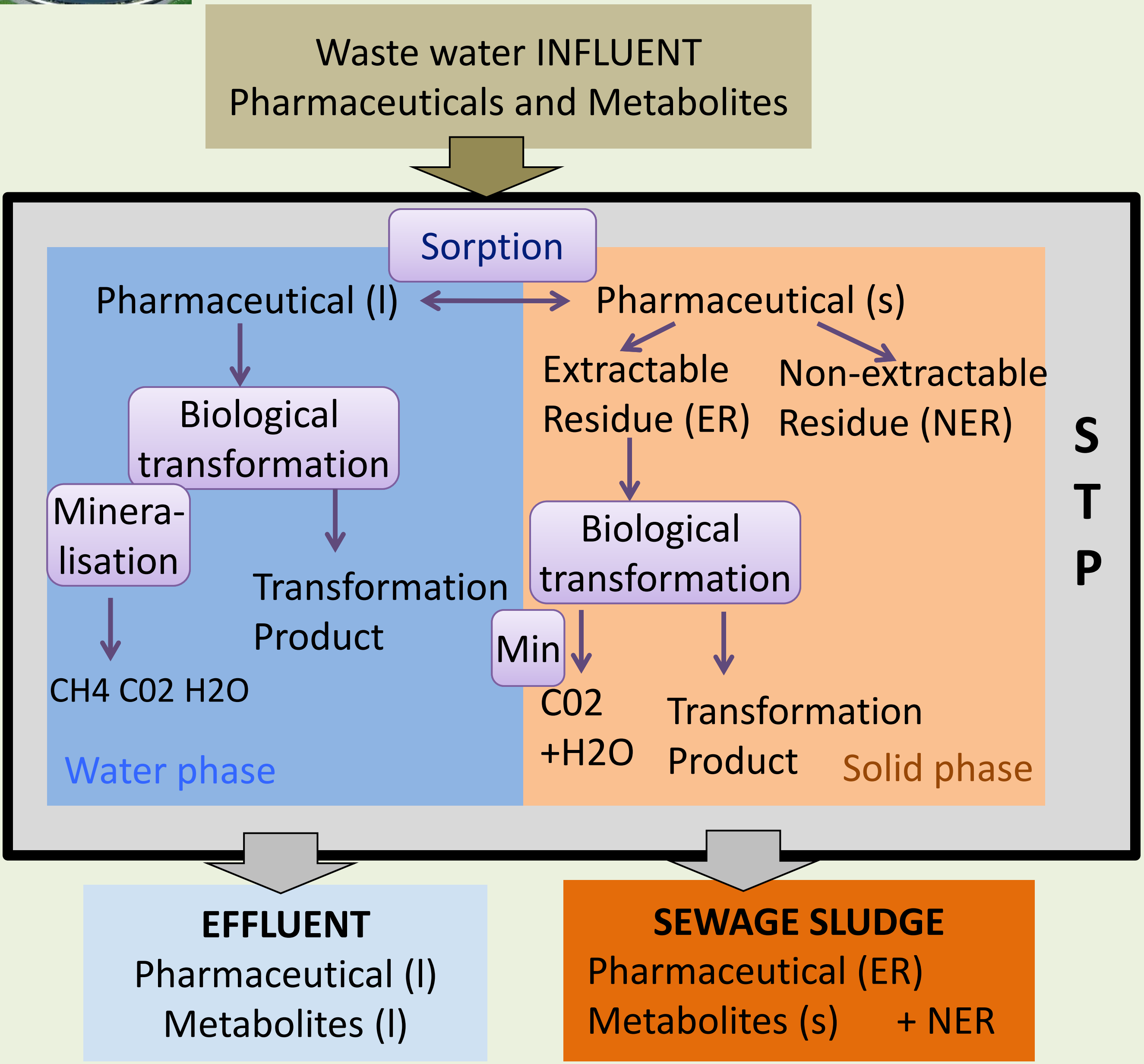
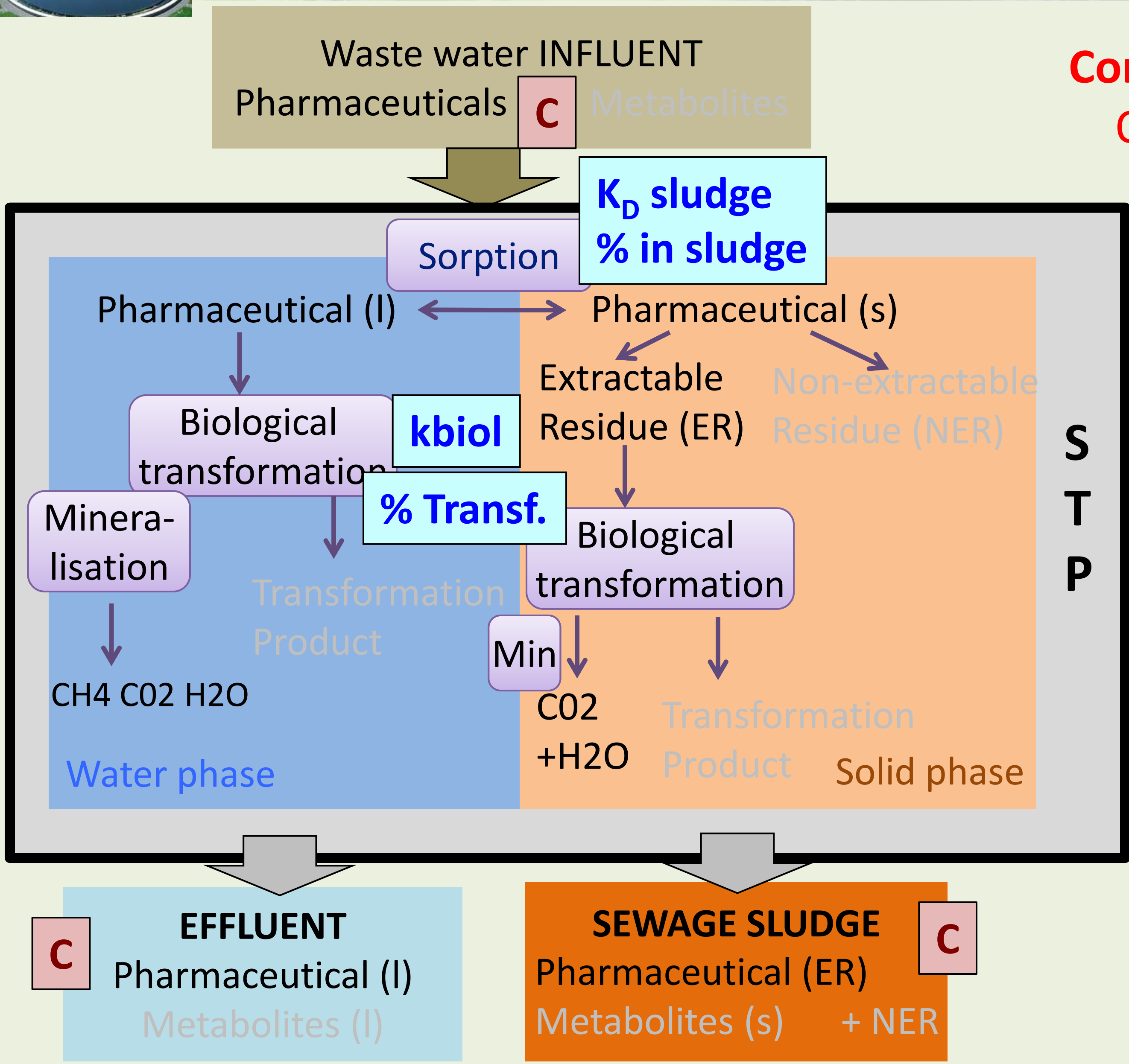


Fate of PhCs in sewage treatment plant (STP)



Conventional Monitoring

Only Concentrations:

Influent, Effluent

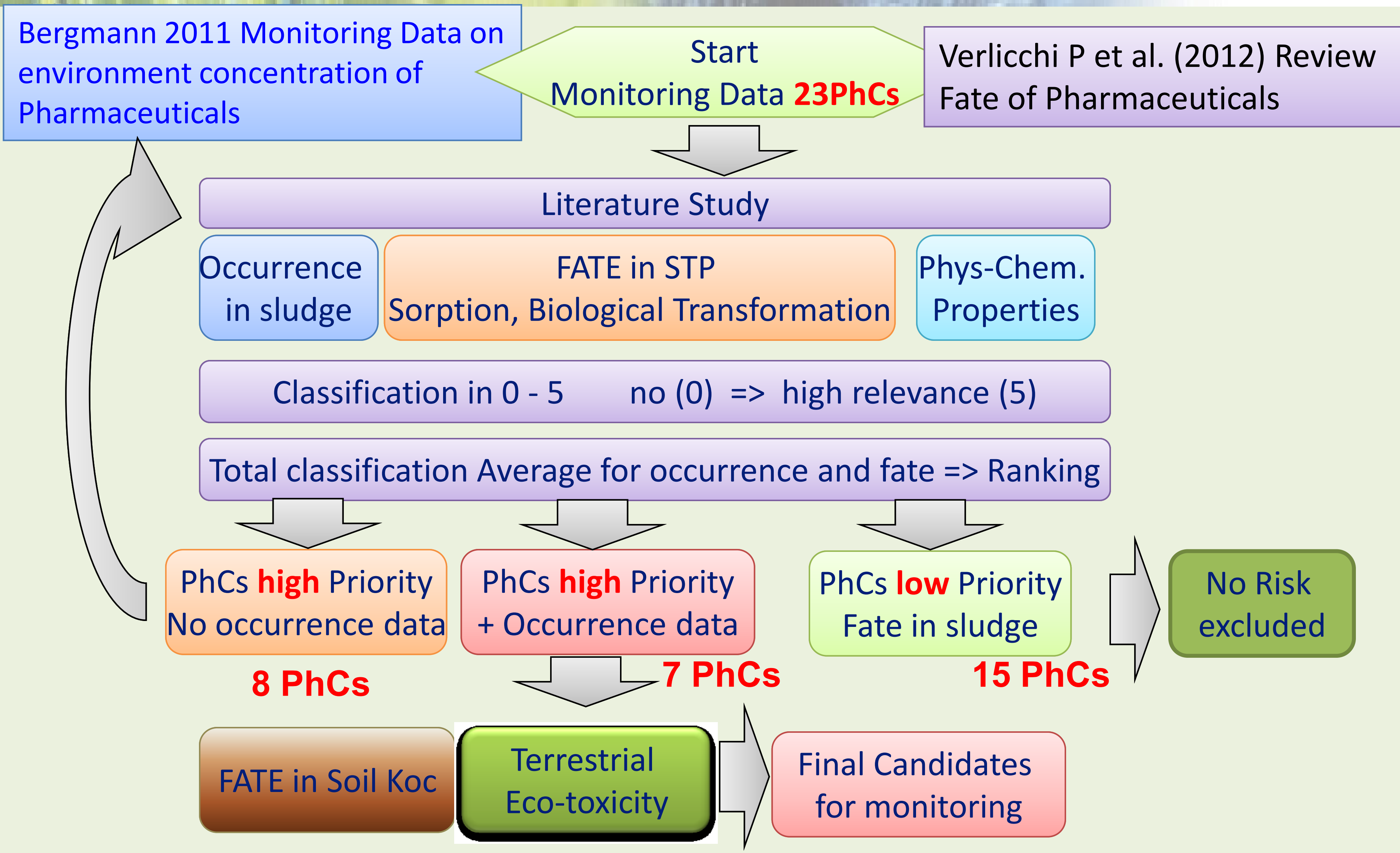
Research Experiments

Fate/Dissipation of PhCs

- **Sorption** K_D, % sludge
- **Biolog. Transformation**

- Transformation rate kbiol.
- % transformation efficiency

Flow chart of classification strategy



Verlicchi P et al. 2012 Occurrence of Pharmaceutical Compounds in Urban Wastewater: Removal, Mass Load and Environmental Risk after a Secondary Treatment - A Review

Classification of Occurrence Data

- Classification according to range of monitoring data
- Maximum concentration observed in STP in Germany were selected
- Concentration in sludge in µg/kg normalized to 100% Total solids
- concentration in sludge not directly comparable to influent conc. estimated 10% TS

Class	Concentration Influent µg/L	Concentration sludge 10%TS µg/kg	Concentration sludge 100%TS µg/kg	concentration
0	< 0.1	< 0.1	< 1	Very low
1	0.1—1	0.1—1	1—10	low
2	1—5	1—5	10—50	moderate
3	5—10	5—10	50—100	intermediate
4	10—50	10—50	100—500	high
5	>50	>50	>500	very high

Classification of physico-chemical properties of PhCs

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Water Solubility S_w in mg/L

"…maximum amount of the chemical that will dissolve in pure water Lyman 1990

Classification modified after (Mensink 1995)

n-Octanol/Water Partition coefficient K_{ow}

" … ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system " Lyman 1990

Classification modified after (Jones 2005)

Class	Solubility Sw in mg/L	water Solubility	$\log K_{ow}$	Ratio conc. n-octanol: H_20	sorption potential
0	>1000	readily	<1	<10:1	no sorption potential
1	100—1000	Medium	1-2	10-100:1	low sorption potential
2	10—100	moderate	2-3	100-1000:1	medium sorption potential
3	10—1	low	3-4	$1000\text{-}10^4$:1	moderate sorption potential
4	0.1—1	slightly	4-5	$10^4\text{-}10^5$:1	high sorption potential
5	<0.1	very slightly	>5	>100.000:1	very high sorption potential

Lyman, W.J. (1990), Handbook of chemical property estimation methods--Environmental behavior of organic compounds,
Mensink (1995), Manual of summarizing and evaluating the environmental aspects of pesticides Report no 679101022
National Institute of public Health and environmental protection Bilthoven, Netherlands
Jones, O. A. H. (2005). "Human pharmaceuticals in wastewater treatment process." Critical reviews in Environmental Science and Technology 35: 401-427.

Classification of fate parameters in sewage treatment plant

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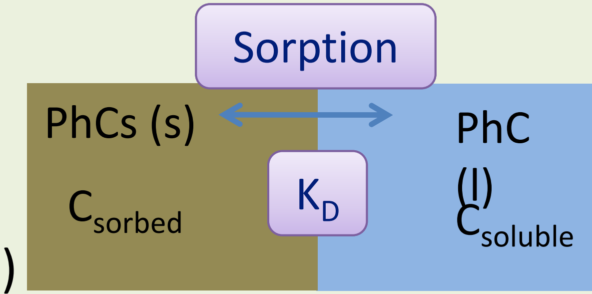
Sorption solid-liquid partition coefficient K_D



– sorption constant describing the overall sorption affinity of a substance to solid phase

- K_D sludge <500 ~10% sorption to sewage (Ternes 2005)

$$K_D = \frac{C_{sorbed}\ mg/kg)}{(C_{soluble}\ mg/L)}$$

Class	KD sludge in L/kg	% sorbed to sludge	sorption
0	<100	<5%	No
1	100--500	5-10%	Very low sorpt.
2	500--1000	10-30%	Sorption
3	1000--4000	30-50%	Medium sorpt.
4	4000--10000	50-80%	high sorption
5	>10000	80-100%	very high

Ternes, T., Joss, A., Kreuzinger, N., Miksch, K., Lema, J.M., and U. von Gunten, McArdell, Ch.S., Siegrist, H. (2005). Removal of pharmaceuticals and personal care products: results of Poseidon project. WEFTEC.

Classification of biotransformation

Biological transformation rate kbiol (L gSS^{-1} d^{-1})

Rate of dissipation = concentration change over time

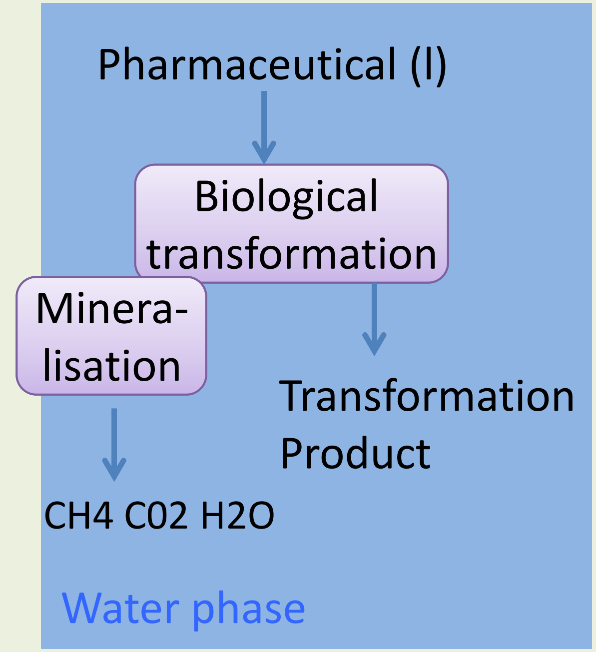
$dc/dt = kbiol. * SS * C\ total$ SS suspended solids

Biodegradation shows kinetics pseudo 1st order (Ternes 2006)

k< 0.1 no transformation ~ less than 20% transformation

- complete transformation => mineralization C02 +H20
- partial transformation => Transformation products

- total dissipation efficiency of PhC depends on
  - concentration of PhCs,
  - sorption properties,
  - type of sewage treatment, pH, biomass,
  - sewage sludge retention time
  - temperature (fermentation, winter/summer)



Classification of biotransformation modified after Joss 2006

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Biological transformation rate kbiol (L gSS^{-1} d^{-1})

Rate of transformation = concentration change over time dc/dt = kbiol. * SS *Ctotal

Data for 16-20d sludge retention time selected from review Verlicchi 2012

Class	Biolog. Trans-formation rate kbiol (L gSS^{-1} d^{-1})	% of Transformation	Biological transformation
0	>10	>95%	good
1	5--10	75-95%	medium
2	1--5	75-50%	not sufficient
3	0.1-1	20--50%	low
4	0.01--0.1	10-20%	poor
5	<0.01	10%	no

Verlicchi P et al. 2012 Occurrence of Pharmaceutical Compounds in Urban Wastewater: Removal, Mass Load and Environmental Risk after a Secondary Treatment - A Review

Pharmaceuticals with low priority excluded from selection

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Therapeutic Group	Pharmaceutical	PC-S	Data Kow		Occurrence STP: C influent	Occurrence STP: C sldge		FATE STP: Sorption	FATE STP: Dissipat.		Fate Class
Antibiotics	Clarithromycin										2,5
Antibiotics	Roxithromycin										2,3
Antibiotics	Erythromycin										1,8
Analgesics	Naproxen										1,8
Antibiotics	Trimethoprim										1,3
Lipid regulators	Clofibric acid										2,8
Lipid regulators	Benzafibrate										2,4
Beta-blockers	Propranolol										2,8
Beta-blockers	Atenolol										1,5
Beta-blockers	Bisoprolol										1,3
Beta-blockers	Sotalol										2,0
Analgesics	Ibuprofen										2,0
Analgesics	Ketoprofen										1,0

Pharmaceuticals with high priority but excluded because No data for occurrence in sludge and soil

Therapeutic Group	Pharmaceutical	PC-	Data		Occurrence STP			FATE STP			Fate Class
		S	Kow		C inf-luent	C sldge		Sorp-tion	Dissi-pat.		
Antibiotics	Ofloxacin										4,8
Antibiotics	Lomefloxacin										4,8
Antibiotics	Enrofloxacin										4,3
Antibiotics	Norfloxacin										3,5
Antibiotics	Sulfamethazine										3,0
Antidiabetics	Glibenclamide										3,8
Antihypertensives	Hydrochlorothiazide										3,8
Psychiatric drugs	Diazepam										3,3

Pharmaceuticals with high priority but excluded because no data for occurrence in sludge in Germany

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Therapeutic Group	Pharmaceutical	PC-S	Data Kow		Occurrence STP C inf-luent	Occurrence STP C sldge		FATE STP Sorp-tion	FATE STP Dissi-pat.		Fate Class
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Antibiotics	Lomefloxacin										4,8
Antibiotics	Enrofloxacin										4,3
Antibiotics	Norfloxacin										3,5
Antibiotics	Sulfamethazine										3,0
Antidiabetics	Glibenclamide										3,8
Antihypertensives	Hydrochlorothiazide										3,8
Psychiatric drugs	Diazepam										3,3

further literature search for concentration in sludge

Pharmaceuticals with high priority selected for effect analysis

Therapeutic Group	Pharmaceutical	PC-S	Data Kow		Occurrence STP: C influent	Occurrence STP: C sldge		FATE STP: Sorption	FATE STP: Dissipat.		Fate Class
Antibiotics	Ciprofloxacin										3,9
Antibiotics	Sulfamethoxazole										3,6
Lipid regulators	Fenofibrate										3,3
Lipid regulators	Gemfibrozil										3,0
Psychiatric drugs	Carbamazepine										3,3
Beta-blockers	Metoprolol										3,1
Analgesics	Diclofenac										2,9
Hormones included because of very toxic to aquatic organisms (ng/L)											
Hormones	Ethinylestradiol										1,9
Hormones	Estradiol										1,4

Pharmaceuticals with high priority selected for effect analysis

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Therapeutic Group	Pharmaceutical	PC-S	Data Kow		Occurrence STP C inf-luent	Occurrence STP C sldge		FATE STP Sorp-tion	FATE STP Dissi-pat.		Fate Class
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Antibiotics	Sulfamethoxazole										3,6
Lipid regulators	Fenofibrate										3,3
Lipid regulators	Gemfibrozil										3,0
Psychiatric drugs	Carbamazepine										3,3
Beta-blockers	Metoprolol										3,1
Analgesics	Diclofenac										2,9
Hormones	Ethinylestradiol										1,9
Hormones	Estradiol										1,4

High concentration

Low/no Dissipation

Conclusion from fate analysis

Many PhCs low correlation between Kow and sorption to sludge might be dependent on complex structure of pharmaceuticals

→ Solubility/ Kow excluded from priorisation

→ Antibiotics are dominant in sludge because of specific properties

- low degradation and high sorption to sludge

Therapeutic group	Pharmaceutical
Antibiotics	Ciprofloxacin, Sulfamethoxazole
Lipid regulator	Fenofibrate
Lipid regulator	Gemfibrozil
Psychiatric drugs	Carbamazepine
Beta-blocker	Metoprolol
Analgesics	Diclofenac
Hormones	Ethinylestradiol Estradiol

→ **Selected for further literature study on**

- **Fate in soil**
- **Terrestrial toxicity**

Classification of fate parameters in soil – mobility, dissipation

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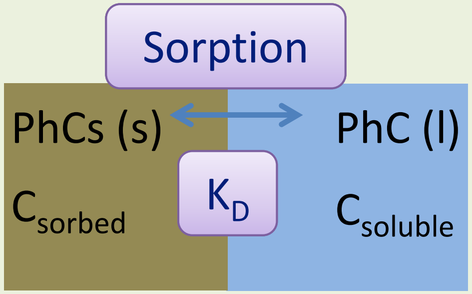
solid-liquid partition coefficient
Koc = Kd for 100% organic carbon
- sorption constant that is normalized to 100% organic carbon content of soil
- **Describes the mobility of a substance**

Degadability/Dissipation in soil
- DT50 measure for the time where 50% of substance dissipated
- measured with radioactive labeling
- describes the persistence in soil



Class	Koc L/kg	Mobility in soil	DT50 n days Half life in soil	Dissipation in Soil	criteria
0	0to50	very highly mobile	<10	fast degradable	
1	50-150	highly mobile	10—40	readily degradable	
2	150-500	moderate mobile	40—60	fairly degradable	
3	500-2000	low mobility	60—120	slightly degradable	
4	2000-5000	Slightly mobile	120-180	persistent in Soil	P criteria
5	>5000	immobile	> 180	Very Persistent very slightly degradable	vP criteria

McCall, P.J. et al. (1981): Measurement of Sorption Coeffi-cients of organic Chemicals and their use in Environ-mental Fate Analysis; Test protocols for Environmental Fate & Movement of Toxicants (1981); Proceedings of Symposium AOAC, 21.-22.10.1980, Washington, DC

Fate of selected PhCs in soil mobility and dissipation

- Persistence of PhCs in soil strongly depends on soil type analysed, high variability

Therapeutic Group	Pharmaceutical	PC-	Data	Occur-rence STP		FATE STP		Fate Soil		Fate Class
		S	Kow	C inf-luent	C sldge	Sorp-tion	Dissi-pat.	Koc	DT50 soil	
Antibiotics	Ciprofloxacin									4,3
Antibiotics	Sulfamethoxazole									3,1
Lipid regulators	Fenofibrate									3,6
Lipid regulators	Gemfibrozil									3,2
Psychiatric drug	Carbamazepine									3,7
Beta-blockers	Metoprolol									3,3
Analgesics	Diclofenac									2,8
Hormones	Ethinylestradiol									2,6
Hormones	Estradiol									2,2

Summary of Fate of PhCs in sludge and soil

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- Dissipation rates of PhCs in sludge during STP are higher than in soil, because sludge treatment conditions promote dissipation of pollutants
  - → higher temperature
  - → higher microbial activity
  - → higher content of organic matter

- Evidence that PhCs in biosolid matrices(Faeces, sludge from STP) show higher persistence when applied to soil than pure PhCs (Walters et al. 2010)
  - → Nofloxacin $DT50_{biosolids}$ 1155 days to $DT50_{alone}$ 300 days
  - → Gemfibrozil $DT50_{biosolids}$ 231 days to $DT50_{alone}$ 20 days

- Dissipation rates of PhCs in soil are highly variable because of high variability between soil types
  - → organic content
  - → microbial content and activity

Walters, E., et al. (2010) "Occurrence and loss over three years of 72 pharmaceuticals and personal care products from biosolids-soil mixtures in outdoor mesocosms." Water Research 44(20): 6011-6020.

Ecotoxicity of PhCs on terrestrial organisms

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Hazard Classification for terrestrial organisms, microbes, plants and earthworms Proposed by Fabrice Renaud , Alistair B.A. Boxall (2004)

Class	EC50 1mg/kg soil	Toxicity	Uptake in Plants
0	>10000	not toxic	No uptake described
1	>1000	Very slightly toxic	
2	100-1000	slightly toxic	
3	10—100	harmful	Uptake but no accumulation above initial soil concentration
4	1—10	Toxic	
5	< 1	Very toxic	Uptake and accumulation above initial soil concentration

Renaud FG, Boxall ABA, **et al. 2004** **“**Evaluation of approaches for terrestrial hazard classification”; Chemosphere 57 1697–1706

Ecotoxicity of PhCs on terrestrial organisms

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Therapeutic Group	Pharmaceutical	Ecotoxicity				up-take in plant		Tox Class		Fate Class
		Micro-orga-nism	Myco-rhizza fungi	Earth-worm	Plants					
Antibiotics	Ciprofloxacin							4,0		4,3
Antibiotics	Sulfamethoxazole							4,0		3,1
Psychiatric drug	Carbamazepine	*						4,3		3,6
Beta-blockers	Metoprolol	*			*			3.5*		3,2
Analgesics	Diclofenac	*			*			4.0*		3,7
Lipid regulators	Fenofibrate	*						2.0*		3,3
Lipid regulators	Gemfibrozil	*						3.0*		2,8
Hormones	Ethinylestradiol							3,8		2,6
Hormones	Estradiol							2,0		2,2

*Data for aquatic organisms used because no data for terrestrial organisms

Ecotoxicity of PhCs on terrestrial organisms

Therapeutic Group	Pharmaceutical	Ecotoxicity				up-take in plant		Tox Class		Fate Class
		Micro-orga-nism	Myco-rhizza fungi	Earth-worm	Plants					
Antibiotics	Ciprofloxacin							4,0		4,3
Antibiotics	Sulfamethoxazole							4,0		3,1
Psychiatric drug	Carbamazepine	*						4,3		3,6
Beta-blockers	Metoprolol	*			*			3.5*		3,2
Analgesics	Diclofenac	*			*			4.0*		3,7
Lipid regulators	Fenofibrate	*						2.0*		3,3
Lipid regulators	Gemfibrozil	*						3.0*		2,8
Hormones	Ethinylestradiol							3,8		2,6
Hormones	Estradiol							2,0		2,2

*Data for aquatic organisms used because no data for terrestrial organisms

Big gaps for effects on terrestrial microorganisms, plants, earthworms and uptake in plants → Research needed

Summary Ecotoxicity of PhCs on terrestrial organisms

Antibiotics Ciprofloxcacine, Sulfamethornizadole show very high toxicity on terrestrial organisms → uptake and toxic to terrestrial plants (Carrots, Rice)

→ toxic to soil microbs (Pseudomonas putida, Enterococcus faecales)

→very toxic to mycorrhizza fungi associated with roots of carrots (Hillis 2008)

Ethinylestradiol act as endocrine disruptors - extremely toxic to fish (0.000001mg/L) and also toxic for terrestric organisms (0.1-50mg/kg soil)

- Plants 10.000x less sensitive than fish, fungi more sensitive than plants

→ Ethinlylestradiol selected as indicator substance, because

→ very toxic to plants and mycorrhizza fungi (Hillis 2008)

→ uptake and accumulation in plants

No Data on terrestrial toxicity of Metroprolol, Fenofibrate and Diclofenac

→ **more research needed** addressing terrestrial ecotoxicity of PhCs in soil

→ mycorrhizza fungi and soil microbs seem most sensitive species

→ plant toxicity and uptake into plants

→ accumulation in food chain??

Hillis, D. G., et al. 2008 "Structural responses of Daucus carota root-organ cultures and the arbuscular mycorrhizal fungus, Glomus intraradices, to 12 pharmaceuticals." Chemosphere 73(3): 344-352.

List of indicator substances for monitoring in sludge

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Therapeutic group	Compounds	Occurrence in sludge	Fate in Sewage treatment plant and soil	Toxicity to terrestrial organisms
Antibiotics	**Ciprofloxacin, Sulfamethoxazole**	>500µg/kg TS in sludge	**Very high sorption very low dissipation Immobile**	Very toxic EC50 >1mg/kg
Psychiatric drugs	**Carbamazepine**	>500µg/kg TS in sludge	**Very Low sorption no dissipation Very slightly mobile**	Very toxic EC50 >1mg/kg
Analgesics	**Diclofenac**	100—500 µg/kg TS in sludge	**Low sorption no dissipation Very slightly mobile**	No data
Hormone	**Ethinylestradiol**	10-50µg/kg TS in sludge	**moderate sorption Slight dissipation immobile**	Very-toxic-toxic EC50 0.1- 10mg/kg
Beta-blocker	**Metoprolol**	50—100 µg/kg TS in sludge	**Very Low sorption no dissipation Very slightly mobile**	No data
Lipid regulator	**Fenofibrate Gemfibrozil**	100—500 µg/kg TS in sludge	**High sorption very low dissipation low mobility**	No data

General conclusion and discussion

Antibiotics are pre-dominant PhCs in sludge, due to high sorption and Low degradation => predicted to be immobile and may persistent in soil

Cirpofloxacin **Sulfamethoxazole**

Ofloxacin **Clarithromycin**

Selection pressure on Microorganism communities

Shift of Microorg. Populations
soil formation/nitrification
organic material digestion
Growth of unwanted pathogens

Cocktail of Antibotics in soil

Potential risks:

- spreading Antibiotics resistance
- Shift of microorganism populations

Multi-resistant pathogens

Food

Animals

Questions for future research

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1. **Scientific proof of increase of antibiotics resistance spread**

2. **What is the fate of PhCs (antibiotics) in soil?**
   Accumulation? Long term persistence in active form?

3. **Understanding balance of microorganism communities in soil**
   What are the effects of antibiotics?

4. **Uptake and accumulation** of **PhCs in plants and other terrestrial organisms** – Enter the food chain?

5. **What are the hot spots for PhCs on terrestrial toxicity?**
   - sensitive species? Which PhCs - high toxicity potential?

6. **Which PhCs are present in soil? Concentrations? Monitoring?**

7. **Techniques to eliminate PhCs from sludge in STP?**

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THANK YOU FOR DISCUSSION