
Water Framework Directive and Emerging Pollutants

Measures to Minimize River Contamination by WWTP Discharges

Evaluation of Quality Standards (EQS) and Predicted No Effect Concentrations (PNEC)

Thomas Knacker

ECT Oekotoxikologie GmbH, Flörsheim/Main

Outline

- **Introduction**
- **Conceptual approach for determining EQS**
- **Effects assessment in water**
- **Trigger values for sediment**
- **Examples for pro- and retrospective ERA**
- **Conclusions**

Introduction - Definitions

EQS - Retrospective level of environmental safety

Concentration below which the ecological functions and the community structure of the water body are not changed (WFD 2000, Lepper 2006)

PNEC - Prospective level of environmental safety

Concentration below which adverse effects are not expected to occur (TGD 2003)

Specified Task

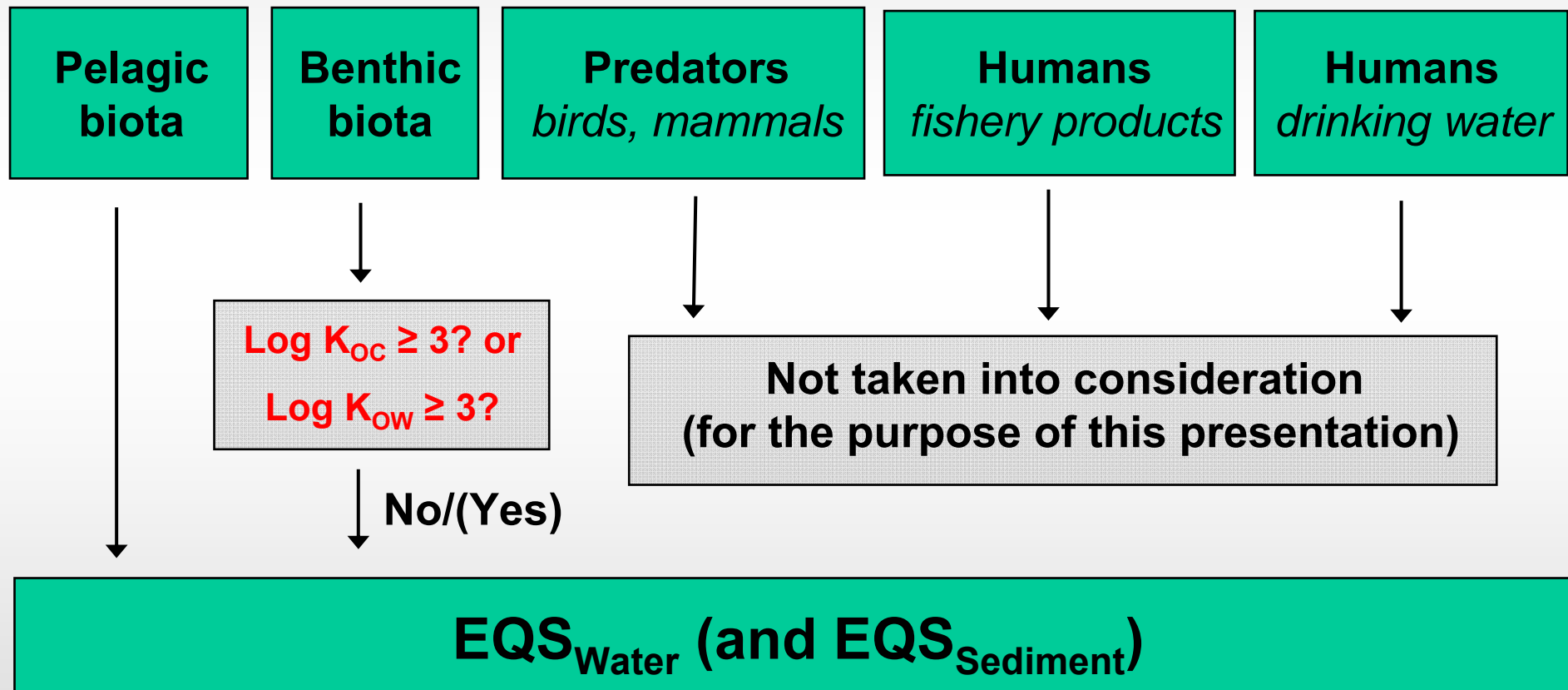
**The following statement is tested for
human pharmaceuticals**

For chemicals

**the process of deriving environmental standards (EQS)
is the same as that used in the effects assessment when
marketing authorisation is requested (PNEC) (Lepper 2006)**

Conceptual Approach for Determining EQS

Receptors at risk (Lepper 2006)



Determination of PNEC_{water}

The main route of entry of pharmaceuticals into the surface water is the sewage system (EMEA 2006)

Effects assessment	Assessment factor
Phase I: ➤ Action Limit: 10 ng/L If exposure concentration below 10 ng/L, effects assessment not required; however, ...	-
Phase II: ➤ 3 long-term toxicity tests at 3 trophic levels (algae, <i>Daphnia</i> , fish)	10

Determination of EQS_{water}

Effects assessment (Lepper 2006)	Assessment factor
At least <u>3 short-term</u> toxicity tests at 3 trophic levels (algae, <i>Daphnia</i> , fish)	1000
<u>1 long-term</u> toxicity test (<i>Daphnia</i> or fish)	100
<u>2 long-term</u> toxicity tests at 2 trophic levels (<i>Daphnia</i> and/or fish and/or algae)	50
At least <u>3 long-term</u> toxicity tests at 3 trophic levels (algae, <i>Daphnia</i> , fish)	10

Comparison of EQS and PNEC in water

For determining the PNEC and EQS the same procedure and the same OECD test guidelines are recommended

- **For new pharmaceuticals PNEC and EQS concentrations should be the same**

For 3 out of 11 substances the assessment factor of 1000 applied to acute toxicity would not be protective (Schmitt et al. 2009, submitted)

- **For existing pharmaceuticals the EQS should be based on long-term toxicity data**

Effects assessment in sediment

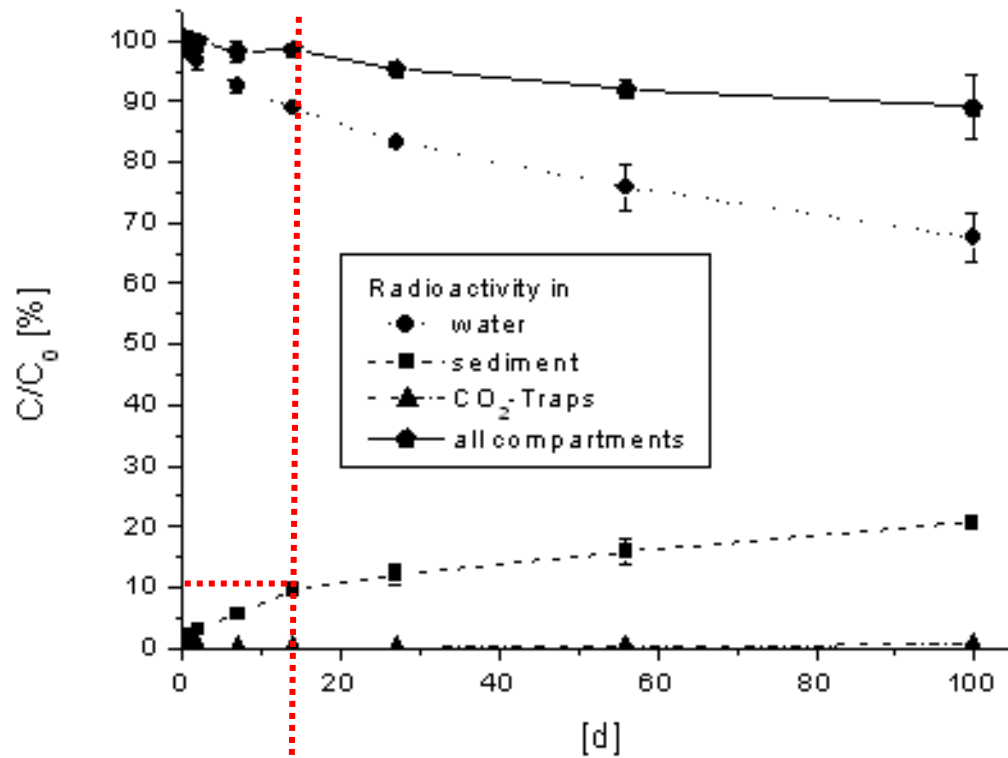
	Pharmaceuticals (EMEA 2006)	WFD (Lepper 2006)
Trigger	≥ 10% of the substance present in sediment after 14 days	Log K _{OC} ≥ 3 or Log K _{OW} ≥ 3
Test requirement	1 long-term study	1 long-term study 2 long-term studies* 3 long-term studies*
Assessment factor	Not specified	100 50 10

* Studies with organisms representing different living and feeding conditions

Determination of trigger values

For $PNEC_{\text{Sediment}}$:

Aerobic and Anaerobic Transformation in Aquatic Sediment Systems (OECD Guideline 308)



Partitioning of parent compound needs to be determined

Guideline requires also the determination of transformation products

Partitioning of radioactivity after 14 d \geq 10%

Determination of trigger values

For EQS_{Sediment}:

K_{oc} (organic carbon-water partition coefficient)

is the K_d value normalised to the carbon content of the sorbent; K_d is the ratio of a dissolved substance in water and soil or sewage sludge at equilibrium

(OECD Guideline 106 or 121)

K_{ow} (n-octanol-water partition coefficient)

is the ratio of a dissolved substance in water and n-octanol at equilibrium

(OECD Guideline 107 or 117 or 123)

Comparison of trigger value determination

For $PNEC_{\text{Sediment}}$:

Matrices not standardised; hence, high uncertainty when comparing data from different laboratories

OECD Guideline 308 not focused on trigger values

(Schlüsener et al. 2009, in prep.)

For EQS_{Sediment} :

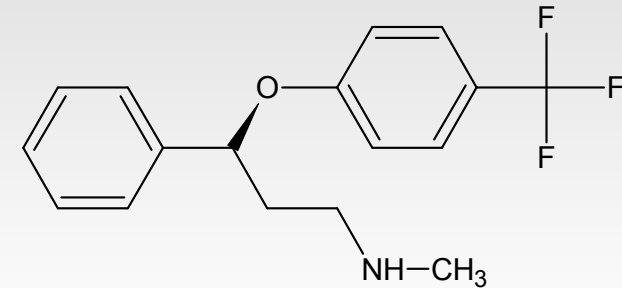
60% of pharmaceuticals are charged; therefore, the selection of methods to determine K_{oc} or K_{ow} should be taken with care

(ECHA 2008, Tarazona et al. 2009, submitted)

Example Fluoxetine

Anti-depressant (SSRI)

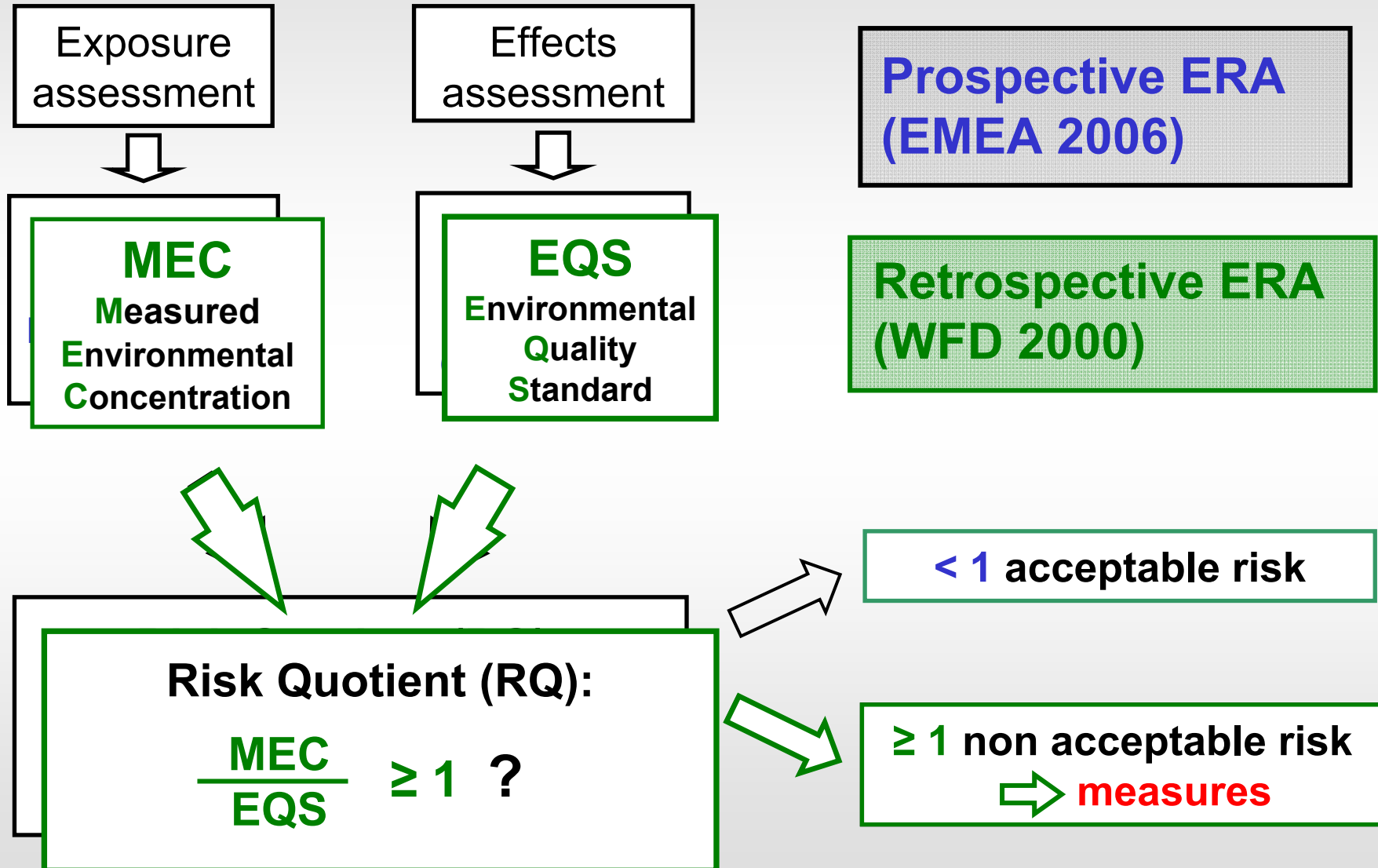
(Cationic form at environmental pHs)



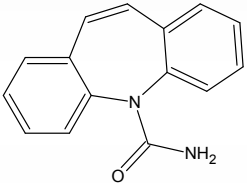
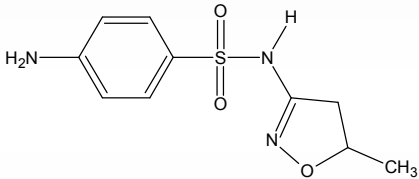
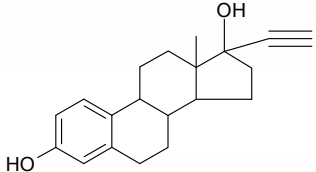
Log K_{oc} (measured)	Soil Sediment Sludge	3.44 - 4.87 3.91 - 5.18 2.73 - 4.13
Log K_{ow} (measured and calculated)	(per definition: K _{ow} refers to neutral species)	1.22 - 4.67
OECD 308	Sediment	After 14 d 100% in sed.

Oakes et al.
2009 (subm.)

Simplified scheme for ERA



Examples for Pro- and Retrospective ERA

	Carbamazepine (CBZ)	Sulfamethoxazole (SMX)	17 α -Ethinylestradiol (EE2)
Pharmaceutical group	Antiepileptic	Antibiotic	Oral contraceptive
Chemical group	Tricyclic dibenzazepin derivative	Sulfonamide	Synthetic steroid
			
log K _{OW}	2.45	0.89	4.2
log K _{oc}	2.42	n.a.	3.0
Significant shifting of the substance into the sediment	14 d: ca. 28%	n.a.	n.a.

n.a.: data not available

Prospective ERA (Knacker et al. 2008)

	Species	NOEC [µg/L]	AF	PNEC [µg/L]	PEC [µg/L]	$\frac{PEC}{PNEC}$
CBZ	Crustacean (water)	25	10	2.5	0.234	0.09
	Insect (sediment) ^a	< 140 ng/g	50 ^c	< 2.8 ng/g	42 ng/g	> 15
SMX	Plant ^b	10	100 ^d	0.1	0.088	0.88
EE2	Fish ^b	0.0003	10	0.00003	0.00076	25.3

^a) Assessment of sediment toxicity required since trigger value for “transfer into sediment” is met

^b) No data on “transfer into sediment” available

^c) AF = 50 since data for 2 sediment dwelling organisms available

^d) AF = 100 since data for 3 trophic level are not available

Retrospective ERA (Knacker et al. 2008)

	Species	NOEC [µg/L]	AF	EQS [µg/L]	MEC [µg/L]	$\frac{MEC}{EQS}$
CBZ	Crustacean ^a	25	10	2.5	0.454	0.18
SMX	Plant	10	100	0.1	0.126	1.26
EE2	Fish (water)	0.0003	10	0.00003	0.00058	19.3
	Worm ^b (sediment)	31.6 µg/g	100	316 ng/g	0.9 ng/g	0.003

^{a)} Assessment of sediment is not required since trigger value is not met

^{b)} Assessment of sediment required since trigger value of $\log K_{oc} \geq 3$ is met

Summary ERAs

	Prospective ERA	Retrospective ERA using	
		all available data	only acute data
CBZ	No Risk (water)	No Risk	No Risk
	Risk (sediment)		
SMX	No Risk	Risk	No Risk
EE2	Risk	Risk (water)	No Risk
		No Risk (sediment)	

Conclusions

- **Results from long-term studies should be used to derive EQS since the AF applied to results from short-term studies might not be appropriate**
- **The trigger values for assessing effects in sediments are different for EQS and PNEC**
- **For HP the process of deriving environmental standards is **not** the same as that used in the effects assessment when marketing authorisation is requested**

Evaluation of Quality Standards (EQS) and Predicted No Effect Concentrations (PNEC)

**Thank you
for your attention!**

Financial support was provided by
(1) European Commission, project POSEIDON
(2) European Commission, project ERAPharm
(3) UBA, project FKZ 20524205