EFFECT-BASED MONITORING AND EVALUATION OF WATER TREATMENT USING BIOASSAYS

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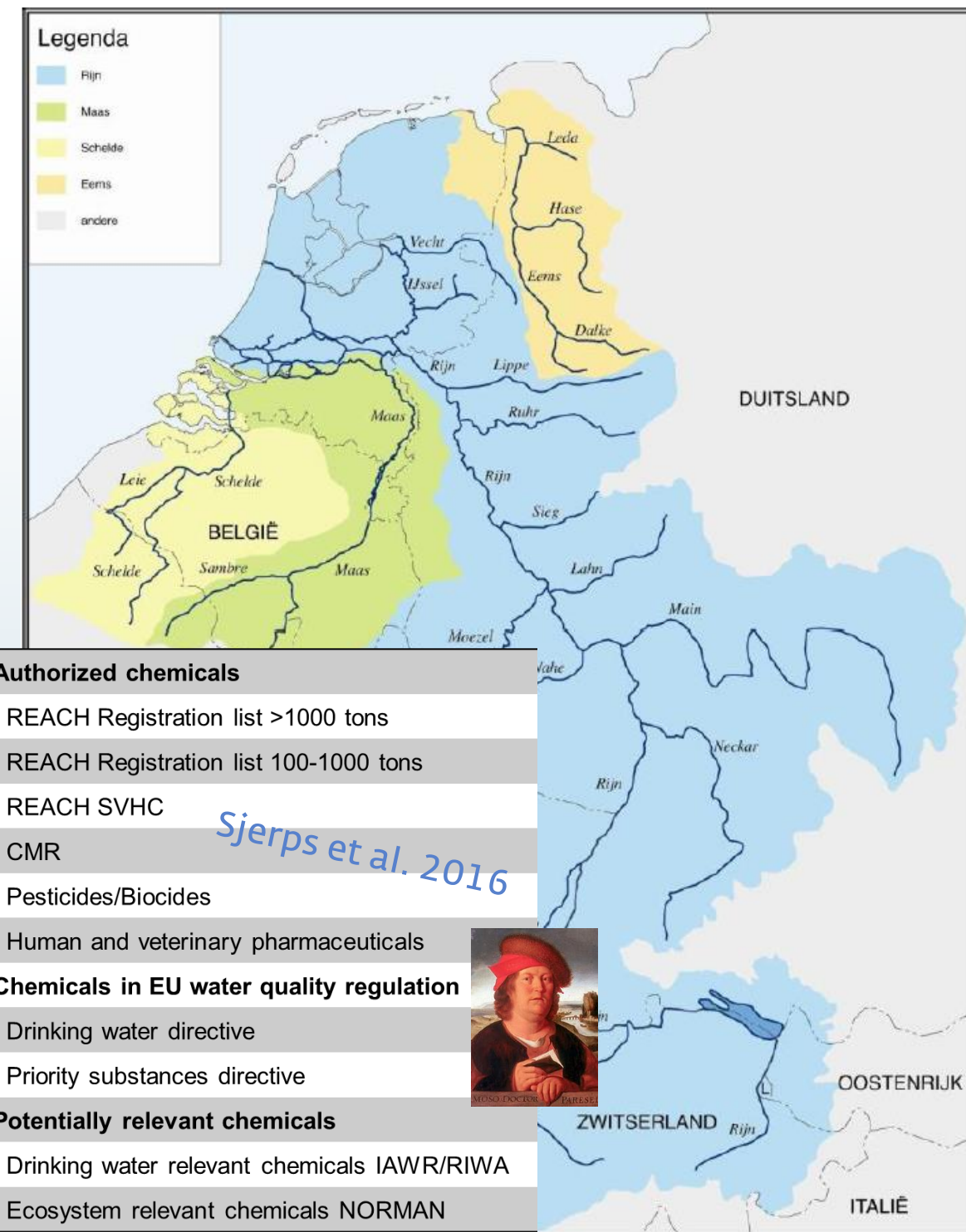
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Chemical water quality
Let's work together

Many chemicals (potentially)

reach the water system

Assess risks of chemicals

(exposure * hazardous properties)

pGLV / TTC (Baken et al. 2018)

Different responsibilities at

different parties

Authorized chemicals
REACH Registration list >1000 tons
REACH Registration list 100-1000 tons
REACH SVHC
CMR
Pesticides/Biocides
Human and veterinary pharmaceuticals
Chemicals in EU water quality regulation
Drinking water directive
Priority substances directive
Potentially relevant chemicals
Drinking water relevant chemicals IAWR/RIWA
Ecosystem relevant chemicals NORMAN

Sjerps et al. 2016

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Bioanalytical tools for effect-based monitoring
bioassays

- insight in potential risks for environmental and human health

- (unknown) complex low-level mixtures of micropollutants

- risk-based approach (revision of EU Drinking Water Directive) > implementation ongoing

Main challenges:

selection and interpretation of bioassays.

Toxicity endpoints relevant for drinking water monitoring	Specific pathway	Most promising bioassay(s)
Xenobiotic metabolism	PXR receptor agonists	HG5LN PXR assay, PXR HepG2 assay
	AhR receptor agonists	DR CALUX, AhR geneblazer
Hormone-mediated mode of action	(anti)estrogenic activity	ERα CALUX, YES assay
	(anti)androgenic activity	AR CALUX, AR-MDA-kb2
	(anti)glucocorticoid activity	GR CALUX, GR-MDA-kb2
Reactive mode of action	Gene mutations	Ames fluctuation assay, ToxTracker
	Chromosomal mutations	Micronucleus assay, ToxTracker
	DNA damage response	UMUc assay, Vitotox, p53 CALUX, BlueScreen
		Nrf2 CALUX, AREc32 assay
Developmental toxicity	Focus point ... distrup...on	Various nuclear receptor activation assays, H295R assay)

2015 (what happens in 3 years?)
1- assay scores may be different now
2- new relevant endpoints (pharmaceuticals, antibiotic resistance, neurotoxicity)

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reviewed in Dingemans et al. 2018

Bioassays at work
Guidelines, frameworks and other applications

Australian Guidelines for Water Recycling (2008)

Potable reuse: Guidance for producing safe drinking-water (WHO 2017)

Bioassays mentioned as promising innovative method

no guidelines for implementation

Proposed EU minimum quality requirements for water reuse in agricultural irrigation and aquifer recharge (2018)

SCHEER opinion: current proposed regulation not sufficient, include novel methods such as bioassays < EU proces ongoing

Water quality monitoring

- RIWA (river water)
- SIMONI framework (surface water)

Evaluation of water treatment processes

- formation of transformation products
- reduction in emissions (e.g. crop protection products)
- resilience analysis of treatment trains

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U.S. EPA ToxCast database
New candidate bioassays for chemical drinking water quality

EPA United States Environmental Protection Agency

Vitens

high throughput *in vitro* toxicity information

(> 8000 environmentally relevant chemicals; >1500 *in vitro* bioassays endpoints)

- selection of new candidate bioassays as bioanalytical tools to detect polycyclic aromatic hydrocarbons and (chloro)phenols

- criteria for sensitivity and specificity

- molecular or cellular effects identified that are not covered by currently applied bioassays (Louisse et al. 2018).

Name	CAS	A	B	C	D	E	F	G	H	I	J
Anthracene	120-12-7	8.3						11			
Benz(a)anthracene	56-55-3	13	1.7	1.9	0.77	0.22	10	4.5	5.9	1.5	1.5
Benzo(a)pyrene	50-32-8	0.23			0.14	0.21	0.54	11	6.1		
Benzo(b)fluoranthene	205-99-2	3.5	1.9		0.11	0.049	7.8	13	7.3		
Benzo(g,h,i)perylene	191-24-2	0.40			1.0						
Benzo(k)fluoranthene	207-08-9	0.040			0.035	0.0014	0.081				
Chrysene	218-01-9				2.4	0.71					
Fluoranthene	206-44-0	10	2.6	4.7			11	4.9	14	5.1	6.1
Indeno(1,2,3-cd)pyrene	193-39-5			0.73							
Phenanthrene	85-01-8		6.8	9.8						8.5	11
Pyrene	129-00-0		3.4	1.7					14	7.0	8.1

A. TOX21_ESRE_BLA_ratio
B. CEETOX_H295R_OHPROG_dn
C. ATG_PXRE_CIS_up
D. TOX21_ARE_BLA_agonist_ratio
E. TOX21_AhR_LUC_Agonist
F. TOX21_ERa_BLA_Agonist_ratio
G. TOX21_ERa_LUC_BG1_Agonist
H. TOX21_MMP_ratio_down
I. CEETOX_H295R_TESTO_dn
J. CEETOX_H295R_ANDR_dn

no effect
not tested

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U.S. EPA ToxCast database
Prioritization for risk-based monitoring

Risk-based monitoring: Include the most relevant

chemicals

1) Prioritize target chemical data

2) Prioritize HRMS non-target data for further

    confirmation

high resolution mass spectrometry
pos/neg ionization modes
features: combinations of
retention time + accurate mass

7000 features detected in 151 Dutch
water samples taken during 2007–2014

Brunner et al. submitted

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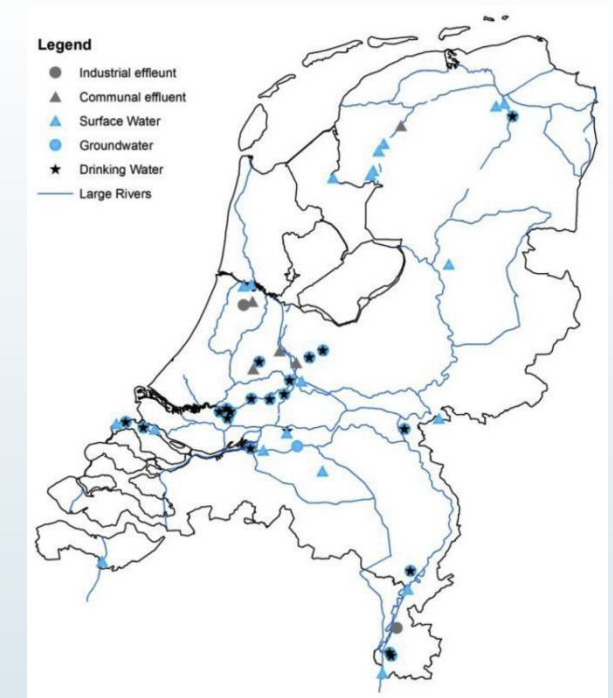
New trigger values (EBT)
Interpretation of bioassay responses

- bioassay responses can occur (far) below exposure concentrations that are relevant for potential effects on human health
- EBT can be used to distinguish whether a response may be linked to a potential adverse health outcome

Different methods are available

Health-based EBT (Brand et al. 2013)

Environmental EBT (Van der Oost et al. 2017)

Guideline read-across EBT (Escher et al. 2018)

New EBT method

(joint research of Dutch drinking water companies)

- pGLV of relevant chemicals in assay
- internal exposure at safe intake levels
- differentiating for low, acceptable and increased risks

Applied to CALUX assays

Performance testing planned

(experimental evaluation and comparison with monitoring data)

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Bioassays in AquaNES
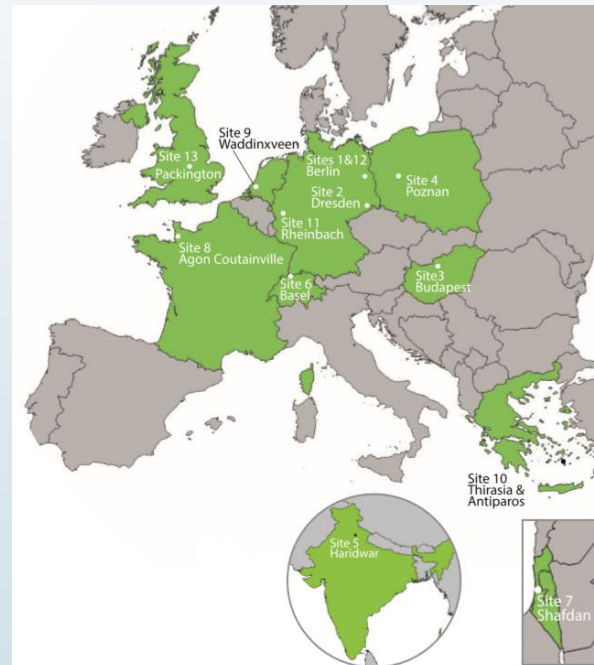## natural and engineered treatment systems

Bioassay responses at different treatment steps

18 different CALUX assays / 13 demonstration sites

Europe, India and Israel

river bank filtration sites
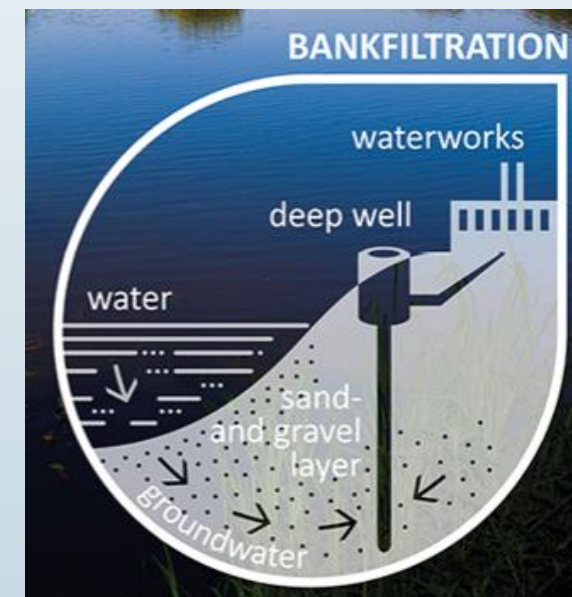aquifer recharge sites
constructed wetlands

2nd tier
selected CALUX assays and demonstration sites
(ongoing research)

Evaluate efficiency and robustness of combined natural and engineered treatment systems

Correlation between bioassay and chemical target / non-target data

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Dutch bioassay implementation support
Implementation guidance and research

Intentieverklaring Delta-aanpak Waterkwaliteit en Zoetwater
Intent for Delta-approach on Water Quality and Freshwater
Dutch government, civil-social organisations and research institutes

Contaminants of emerging concern (CEC) partnership
www.cec-partnership.nl
Projects on bioassays: EMERCHE, RoutinEDA

Kennis Impuls Waterkwaliteit
Knowledge impuls for water quality
Project KIW ESFT2 on Effect-based monitoring

Ketenaanpak Medicijnresten uit Water
Chain approach medicine residues out of the water
Aim to use effect-based monitoring

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NORMAN Collaborative Trial
Bioassays for genotoxicity testing

Explore the performance of different bioassays for genotoxicity and related mechanisms

- communication, discussion and inspiration within the NORMAN network

Participants blindly test water-relevant micropollutants mixtures using their own methods

Sample constituents will be revealed in the report

Time schedule

- Deadline for registration - June 15th 2018

24 participants ☺

- Preparation and distribution of samples - July 2018

2 water samples, 2 DMSO samples + solvent control

- Test results reported to KWR - November 2018

- Dissemination of results - from December 2018

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Thank you!

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