

Results of the FP7 project PHARMAS – Ecological and human health risk assessments of antibiotics and anti-cancer drugs found in the environment.

Summary of the presentation at Science-Policy Event on Pharmaceuticals in the Environment (21.11.2013, Brussels, Belgium) by Ad Ragas, Radboud University Nijmegen.

(Please scroll down in this document for presentation slides.)

The main aim of the PHARMAS project (www.pharmas-eu.org) was to answer the question: “Does environmental exposure to human pharmaceuticals cause (un)acceptable risks for humans and/or the environment?” This question was addressed by a combination of experimental research and modeling studies. The project focused on two particular classes of pharmaceuticals, i.e., antibiotics and anti-cancer drugs. Examples of modeling studies included the prediction of cyclophosphamide concentrations in European surface waters, simulation of the fate of ionizable compounds in the environment, and the prediction of mixture effects. Examples of experimental studies included an interlaboratory comparison of detection techniques for pharmaceuticals, identification of transformation products in sewage treatment plants (STPs), the development of novel (eco)toxicity tests and a large measurement campaign in European surface waters. PHARMAS furthermore developed a spatially explicit prioritization tool for human pharmaceuticals in Europe. The main conclusion of the project was that human health effects are highly unlikely, but adverse effects cannot be excluded for the aquatic environment. The potential of adverse effect can be further minimized by developing pharmaceuticals that have a minimal impact on the environment (“Benign by design”), wise use policies (Sustainable Pharmacy) and more efficient removal techniques in sewage treatment plants (STPs). To improve future risk assessments, research should focus on transformation products, the fate of ionizable substances, the collection of (eco)toxicity data, the development, dispersal and transfer of antibiotic resistance in the environment, and effects of low dose exposures to complex mixtures.



PHARMAS: Human and Ecological Risk Assessment of Human Pharmaceuticals

21 November 2013, DG Research and Innovation, Brussels

Radboud University Nijmegen



Human and Ecological Risk Assessment of Human Pharmaceuticals



“Ecological and human health risk assessment of antibiotics and anti-cancer drugs found in the environment”

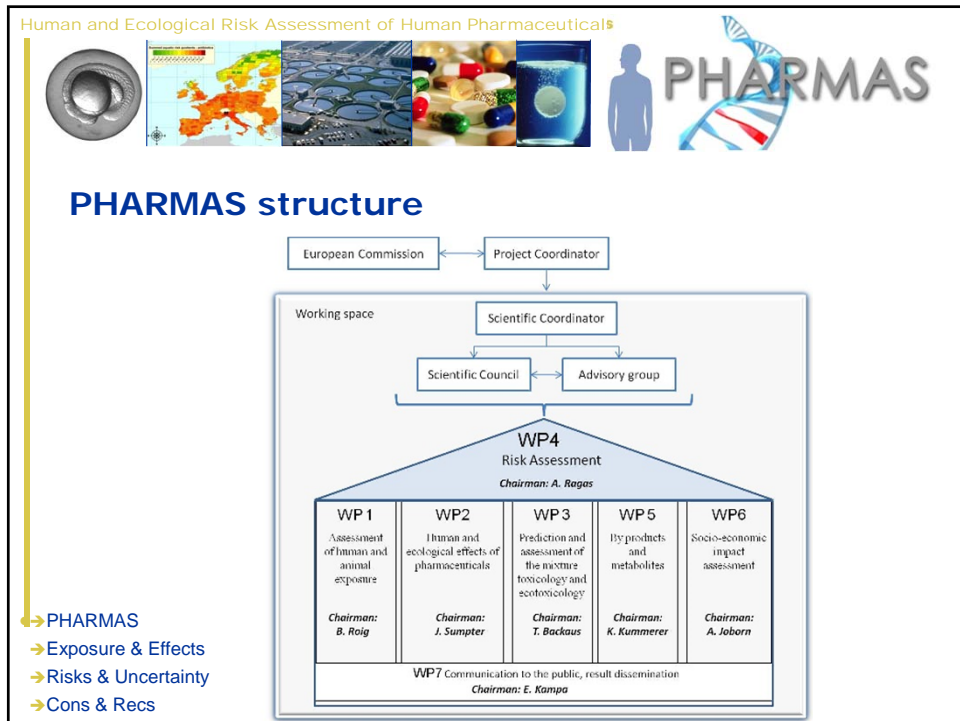
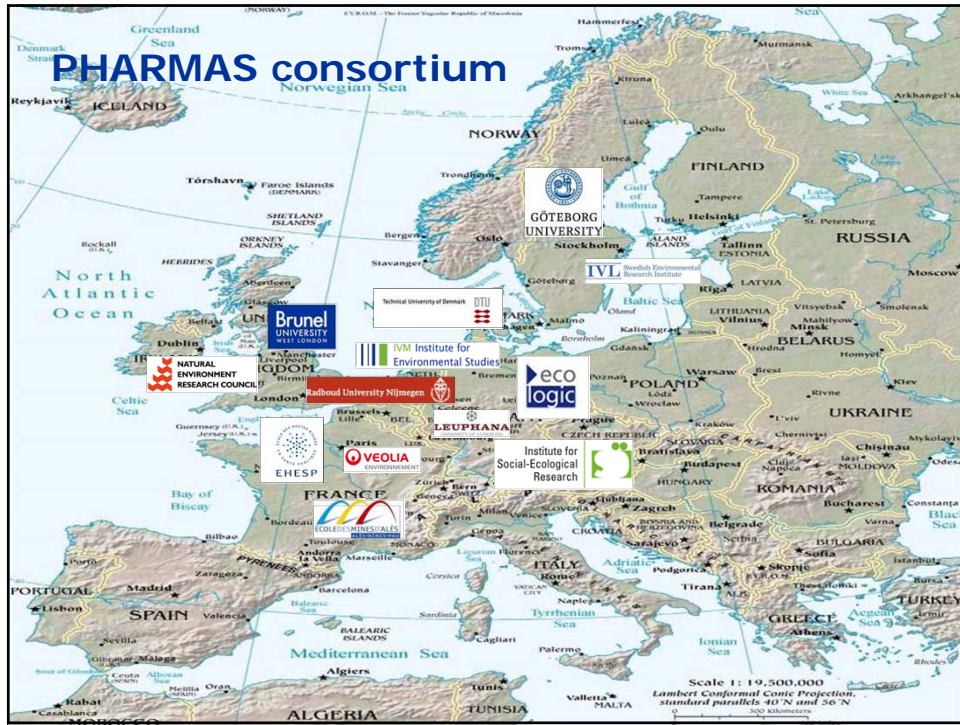


John Sumpter
Project Coordinator



Benoit Roig
Scientific Coordinator

- PHARMAS
- Exposure & Effects
- Risks & Uncertainty
- Cons & Recs





Problem definition

- We are using large quantities of hundreds of different pharmaceuticals on a daily basis
- Part of these pharmaceuticals end up – either directly or indirectly – in the environment
- This results in *chronic* exposure to *low* levels of *complex mixtures*, for humans as well as ecosystems
- **Main question:** Does this exposure result in (un)acceptable risks for human health and/or the environment?

Strategies:

Measurements
Modelling

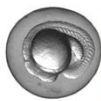
Benign by Design
Clever Risk Assessment

→ PHARMAS

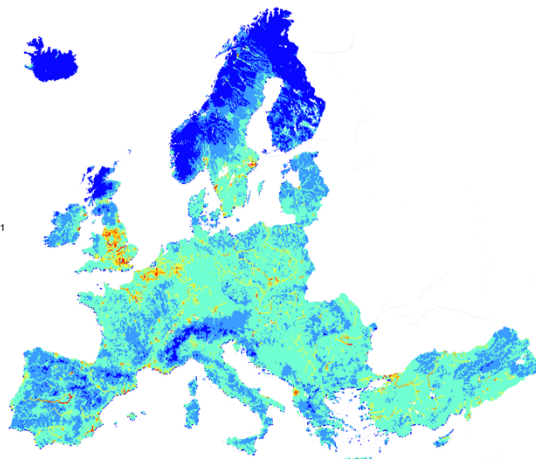
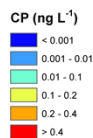
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Modelling



Predicted cyclophosphamide (CP) concentrations in surface water

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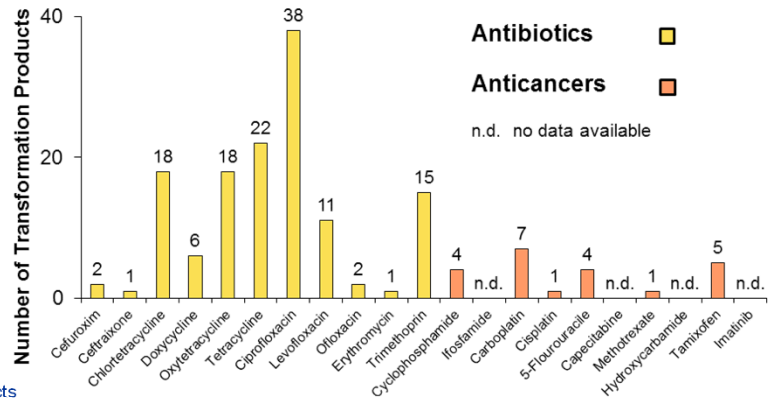
→ Exposure & Effects

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→ Cons & Recs



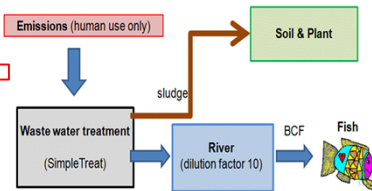
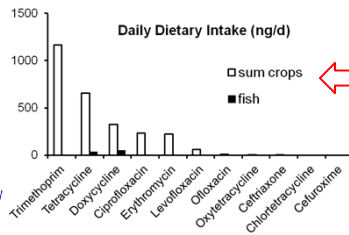
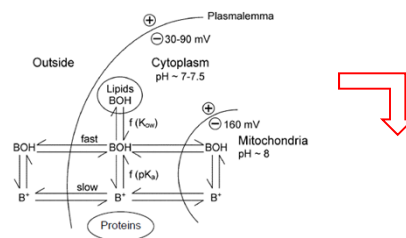
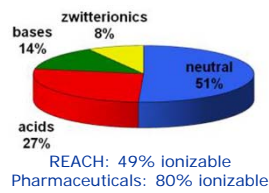
Transformation products



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Accumulation of ionizable compounds



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- Risks & Uncertainty
- Cons & Recs

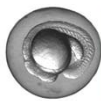


Chemical detection: interlaboratory exercise

	ERY		CIP.	OFL		TMP		SMX	
	TW	SW	SW	TW	SW	TW	SW	TW	SW
Lab 1	0	1	0	0	1	0	0	0	0
Lab 2	0	0				0	0	0	0
Lab 3			0	0	0	0	0		
Lab 4						0	0	2	0
Lab 5		0	0	0	0	0	0	1	0
Lab 6	0	0	0	0	0	0	2	2	0
Lab 7	0	0	0	0	0	0	0	0	0
Lab 8	0	0	0	0	1	1	2	2	1
Lab 9	0	0	0	0	0	0	0	0	0
Lab 10			1	1	0	0	0		
Lab 11	0	0				0	0	1	1
Lab 12	0	0				0	0	1	0
Lab 13	0		0			0	0	0	0
Lab 14	0	0	0	0	0	0	0	0	0

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$D \geq 3.0\sigma$ indicating an "action signal" (2)
 $2.0\sigma \leq D < 3.0\sigma$ considered as "warming signal" (1)
 $D < 2.0\sigma$ indicating "acceptable value" (0).



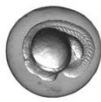
Chemical detection

C (ng/L)	06/2010		09/2010		03/2011		04/2012		10/2012	
	U	D	U	D	U	D	U	D	U	D
Flumequine µg/L	-	-	-	-	-	-	-	-	-	-
Sulfamethoxazole	-	-	10	-	10	-	20	-	-	-
Ofloxacin	-	-	-	-	-	-	-	-	-	-
Trimetoprim	-	-	-	-	-	-	-	-	-	-
Cyclophosphamid	-	-	-	-	-	-	-	-	-	-
Oxazepam	44	-	40	-	-	-	130	-	50	-
Iopromide	35	-	70	-	-	-	80	35	-	-
Caféine	96	-	160	20	60	-	70	-	40	-
Atenolol	-	-	-	-	-	-	-	-	-	-
Codeïne	-	-	-	-	-	-	-	-	-	-
Carbamazepine	28	-	44	-	-	-	40	-	-	-
Morphine	-	-	-	-	-	-	-	-	-	-

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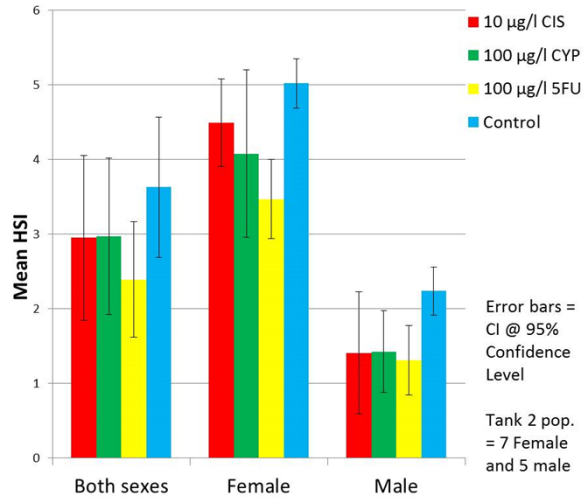
Campaign in France

Sampling in a Brittany river between 2010 -2012
 DWTP : 500 000 inhabitants Eq

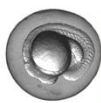


Effect detection

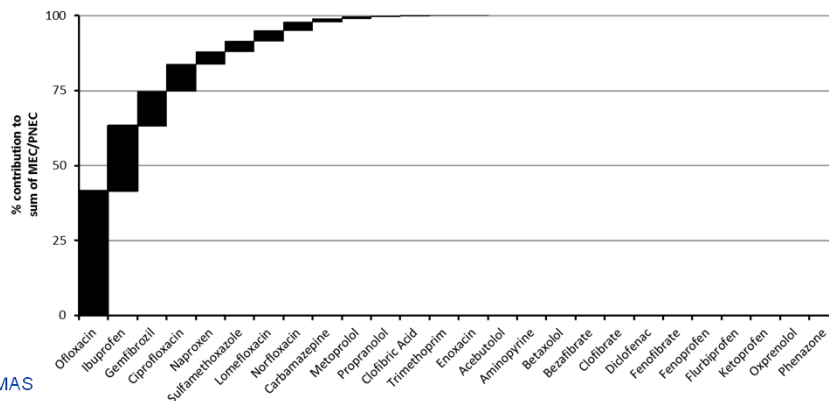
Mean Hepatic Somatic Index (HSI) per treatment



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Mixtures

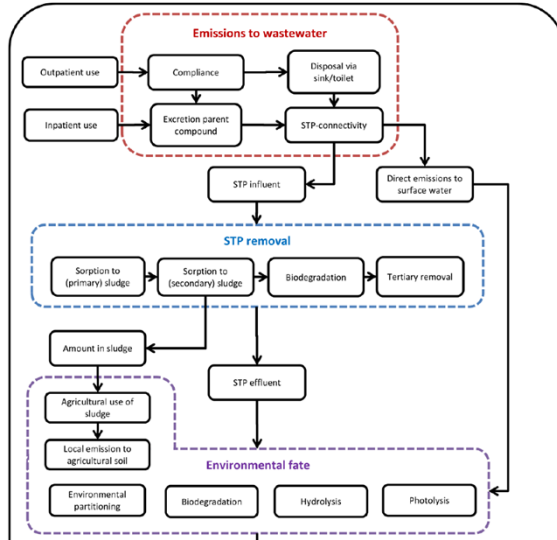


Contribution of individual substances to the overall environmental risk of a pharmaceutical mixture in STP effluent

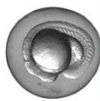
- PHARMAS
- Exposure & Effects
- Risks & Uncertainty
- Cons & Recs



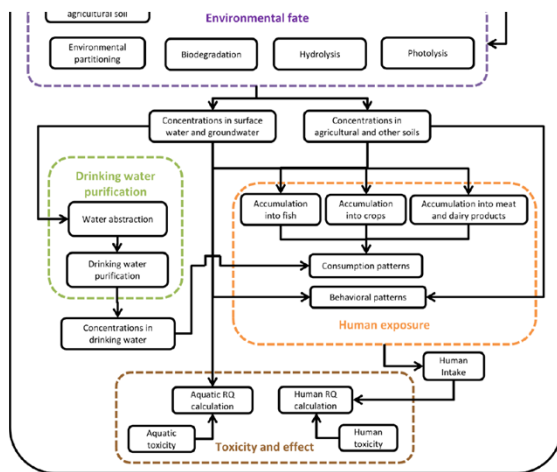
Prioritization tool



- PHARMAS
- Exposure & Effects
- Risks & Uncertainty
- Cons & Recs



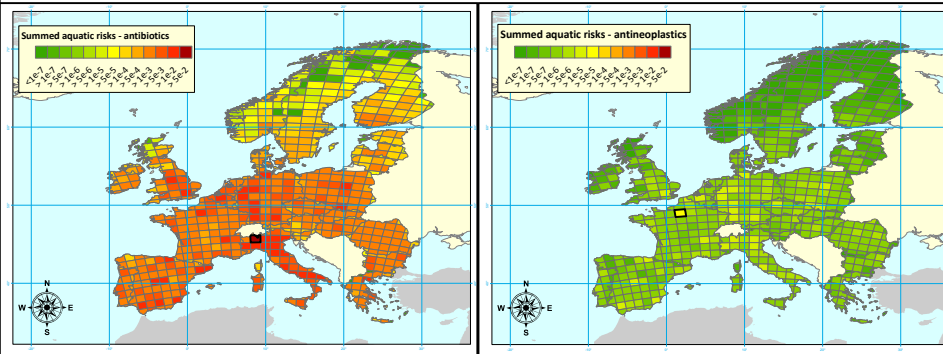
Prioritization tool



- PHARMAS
- Exposure & Effects
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- Cons & Recs



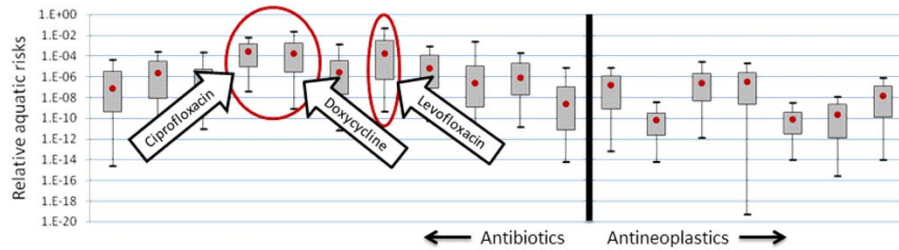
Aquatic risk maps



- PHARMAS
- Exposure & Effects
- Risks & Uncertainty
- Cons & Recs



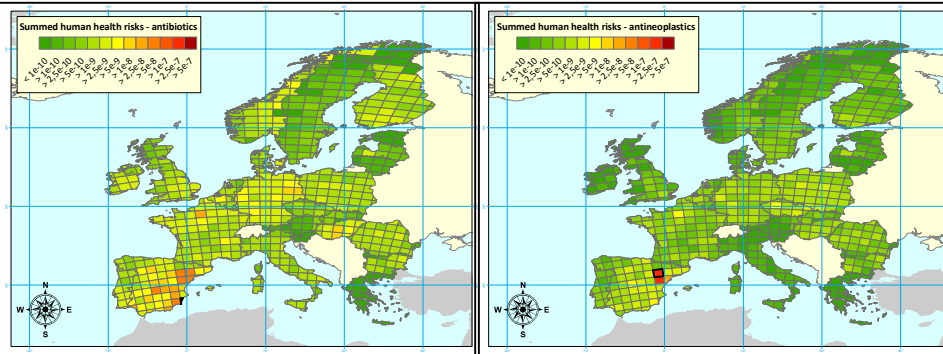
Relative aquatic risks



- PHARMAS
- Exposure & Effects
- Risks & Uncertainty
- Cons & Recs



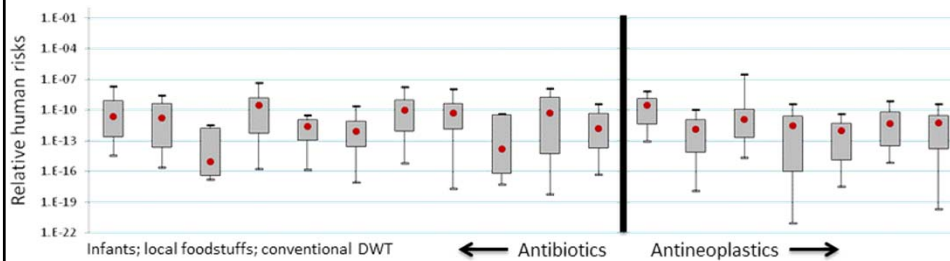
Human risk maps



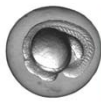
- PHARMAS
- Exposure & Effects
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Relative human risks



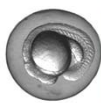
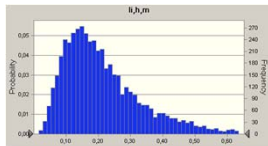
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Uncertainties...

- Uncertainty in input data and parameters
- Estimates where consumption data were lacking
- Sewage treatment processes
- Lacking data on transformation products
- Absorption and accumulation of ionizable compounds
- Drinking water treatment techniques
- Lacking toxicity data & extrapolation of toxicity data
- Antibiotic resistance
- Mixture toxicity

- PHARMAS
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Conclusions

- There are currently no scientific indications that environmental exposure to human pharmaceuticals, i.e. antibiotics and anti-cancer drugs, results in significant direct human health effects
- Model predictions show that some human pharmaceuticals (i.e., ciprofloxacin and levofloxacin) in some European water bodies may approach concentration levels that could trigger *ecological effects*
- Life is uncertain

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Recommendations

Measures:

- Benign by Design
- Wise Use Policy (Sustainable Pharmacy)
- Improved SWTPs (i.e., for protection of aquatic ecosystems)

Research:

- Transformation products / "Benign by Design"
- Accumulation of ionizable substances
- (Eco)toxicity data
- Antibiotic resistance
- Effects of chronic low dose (mixture) exposures => Threshold?

- PHARMAS
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Acknowledgements



- John Sumpter
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