Global Water Research Coalition

Pharmaceuticals and Personal Care Products in the Water Cycle

Report of the GWRC Research Strategy Workshop

PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN THE WATER CYCLE

REPORT OF THE GWRC RESEARCH STRATEGY WORKSHOP

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GLOBAL WATER RESEARCH COALITION:

GLOBAL COOPERATION FOR THE GENERATION OF WATER

Knowledge GWRC is a non-profit organization that serves as the collaborative mechanism for water research. The product the GWRC offers its members is water research information and knowledge. The Coalition will focus on water supply and wastewater issues and renewable water resources: the urban water cycle.

The founder members of the GWRC are: the Awwa Research Foundation (US), CRC Water Quality and Treatment (Australia), Kiwa (Netherlands), Sues Environment- CIRSEE (France), Stowa - Foundation for Applied Water Research (Netherlands), DVGW - TZW Water Technology Center (Germany), UK Water Industry Research (UK), Veolia- Anjou Recherché (France), Water Environment Research Foundation (US), Water Research Commission (South Africa), WaterReuse Foundation and the Water Services Association of Australia.

These organizations are all in charge of a national research program addressing the different parts of the water cycle. They have provided the impetus, credibility, and initial funding for the GWRC. Each brings a unique set of skills and knowledge to the Coalition. Through its member organisations GWRC represents the interests and needs of 500 million consumers.

The Global Water Research Coalition is affiliated with the International Water Association (IWA). The GWRC was officially formed in April 2002 with the signing of the partnership agreement at the International Water Association 3rd World Water Congress in Melbourne. With the US Environmental Protection Agency a partnership agreement was signed in July 2003.

DISCLAIMER

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ACKNOWLEDGEMENTS

The project team wishes to express their gratitude to all members of the GWRC, to the program steering group and to participants who made a contribution to this project.

PROJECT TEAM

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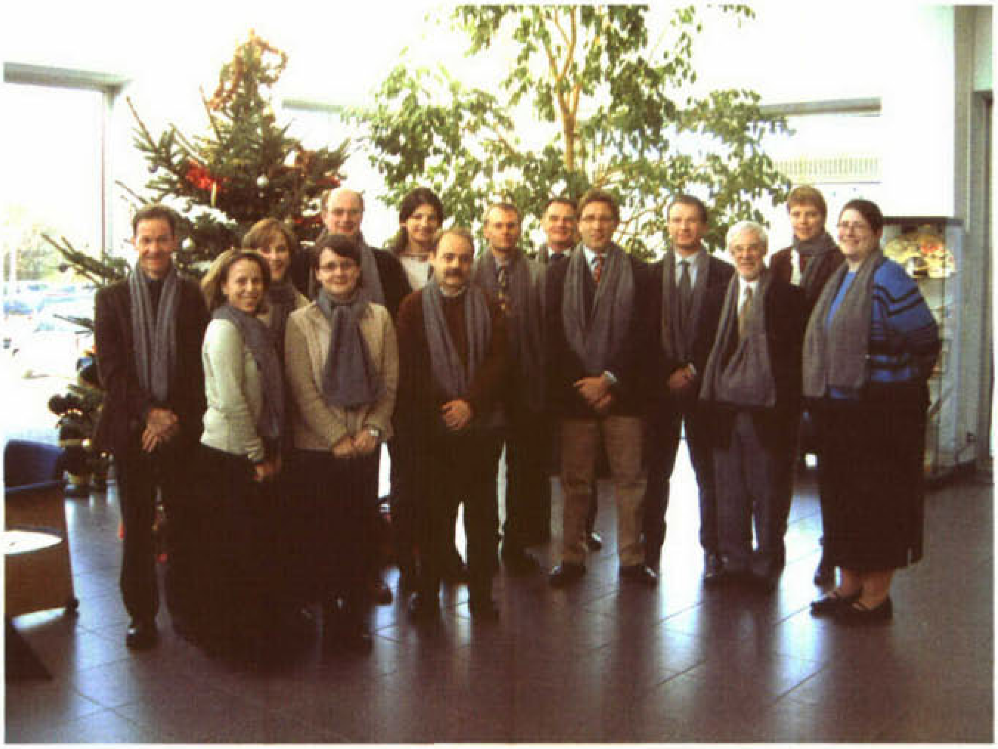


EXECUTIVE SUMMARY

Recent studies in Europe and the United States have documented the presence of a wide variety of pharmaceuticals and substances contained in personal care products in the environment. Information on the effects of the presence of PPCPs on aquatic life or human health is largely lacking. A workshop was held in Nieuwegein at December 15/16 2003 in order to define a GWRC research strategy on pharmaceuticals and personal care products.

It was concluded that the first step to be taken was to develop a *priority list of pharmaceuticals* to identify those on which research should be focussed. Secondly, the implementation of a limited number of *validated analytical methods* is required. A large number of analytical methods are used worldwide but the number of validated methods is limited. This is a prerequisite for conducting further research (occurrence, fate, treatment) in order to ensure harmonization of measurement methods and reliability and comparability of future data collected within the coalition. When robust and reliable analytical methods are available, studies on *removal during wastewater treatment and drinking water treatment* can be conducted.
The potential risk of pharmaceuticals in the (water) environment is not clear but wastewater treatment plants are one of the main point sources. Information is, therefore, needed to play an active role in understanding sources, processes and relative contributions.

Although human health effects are unlikely, the public can still be concerned about the presence of pharmaceuticals in (drinking) water. This makes the subject also an issue of perception. It is therefore of importance to avoid negative media attention on this topic and develop a *communication and risk perception strategy*. This can be done in a multi-stakeholder workshop.

Considering personal care products it was concluded that data are lacking. Furthermore, it would be hard to determine which personal care products should be included in the research and which not. Most of the personal care products are bulk chemicals used in paint, food and cleaning agents as well. Further research should focus on pharmaceuticals and mention personal care products only when relevant. Personal care products were identified as a relevant issue for further research within GWRC.

Based on the research strategy , five project themes were defined:

1. Priority list of pharmaceuticals
2a. Procedures & exchange of knowledge for analytical techniques
2b. Occurrence & removal efficiency of pharmaceuticals in wastewater treatment
2c. Occurrence & removal efficiency of pharmaceuticals in drinking water treatment
3. A multi-stakeholder workshop.

1

INTRODUCTION

1.1 BACKGROUND

Recent studies in Europe and the United States have documented the presence of a wide variety of pharmaceuticals and substances contained in personal care products in the environment. Pharmaceuticals and Personal Care Products (PPCPs) can enter the water system via several routes, but municipal sewage effluent is considered to be one of the most important routes. Pharmaceuticals have been detected in sewage influent and effluent, in surface water and groundwater and occasionally also in drinking water.
Information on the effects of the presence of PPCPs on aquatic life or human health is largely lacking.

In the light of this concern, the board of the Global Water Research Coalition determined this subject to be of priority for collaborative research and decided to conduct a project with the aim of to

- Review the present knowledge on occurrence, fate and effects of PPCPs in the urban water cycle
- Develop a research strategy and accompanying suite of project proposals

This workshop report summarises the presentations and findings of the Workshop on Pharmaceuticals and Personal Care Products in the Water Cycle that was held in Nieuwegein at December 15/16 2003. The GWRC research strategy on pharmaceuticals and personal care products that was defined during this workshop is also published separately.

1.2 OBJECTIVE AND APPROACH OF THE WORKSHOP

OBJECTIVE

The *objective* of the workshop was to present the current state of knowledge on PPCPs and to identify knowledge gaps and research needs. Based on the overview on the current knowledge and the missing links a research strategy was developed.

APPROACH

As a first step information on occurrence, fate and effects of pharmaceuticals and personal care products was collected via a literature survey. Additional information was obtained from the GWRC-partners. This information was summarised in the State of the Science report *Pharmaceuticals and Personal Care Products in the Water Cycle: an International Review*.
A workshop was organised to discuss the report and to develop a research strategy within GWRC on pharmaceuticals and personal care products within the water cycle. This Research Strategy Workshop was held on December 15 and 16 2003 at Kiwa Water Research in Nieuwegein, The Netherlands (the workshop program and presentations is given in annex II).

1.3 THE WORKSHOP

The first day of the workshop was attributed to the current state of knowledge. GWRC-members had been invited to give presentations on the different aspects of the subject. These formed, together with the State of the Art report, a view on the information currently available on the issue of PPCPs in the water cycle.

The second day started with the presentation by Leo Puijker of the 'State of the Art' report. Based on the presentations of Day 1 and the 'State of the Art' report a list of knowledge gaps and research needs was set up.

During the workshop all participants actively contributed to the design of the draft project proposals, resulting in an enthusiastic and co-operative atmosphere with many lively and interesting discussions. Participants were content with the outline and organisation of the different aspects of the workshop.

2

KNOWLEDGE ON PPCP IN THE WATER SYSTEM

2.1 PRESENT KNOWLEDGE, GAPS AND NEEDS

For the different stages in the route of PPCP from production , use and emissions to occurrence in water systems and impact on the environment and public health, presentations were given by the participants. Together with the review study, the presentations were the cornerstones of the map of knowledge regarding PPCP in the water system. The information was discussed by the participants and for each of the stages the knowledge gaps and needs were identified. The results are summarised in the next paragraphs.

2.2 USE & EMISSIONS

(presented by Marie-Laure Janex-Habibi)

Data on presription and use are important as a basis for selection of priority pharmaceuticals to be monitored. However, differences exist between countries on the availability of such data. For Europe in general there is a fairly good view on use and production, but for individual countries it differs per the country whether these data are easily accessible. For the US not many data are available yet. The EPA indicated that they probably have access to the prescription data, but patterns of use are likely to differ between Europe and the US. It was concluded that trying to acquire detail information about the prescription data, especially for over-the-counter drugs will cost a lot of effort and money.

It was felt that overall there is enough information on pharmaceuticals available to give focus to the future activities and research.Based on this information the development within the framework of the GWRC of a priority list of pharmaceuticals is needed.

Regarding Personal Care products very limited data are available.

> Sufficient data on pharmaceuticals but, limited data on PCP are present
> Need of a priority list of Pharmaceuticals

2.3 OCCURRENCE

(presented by Djanette Khiari, Susan Glassmeyer and Frank Sacher)

Pharmaceuticals are ubiquitous present in the water environment. Upstream of waste water treatment plants background levels of pharmaceuticals in surface water are low, downstream concentrations are higher, but decrease with increasing distance from the wastewater treatment plant. Microbiological parameters are not a good indicator for pollution with pharmaceuticals. Seasonal effects should be included in monitoring campaigns.

Also in groundwater pharmaceuticals have been detected. The compounds identified where the same as in surface water. Mostly the occurrence in groundwater is due to wastewater impact and leakage of sewage systems. Influence of agricultural activity has not been noted yet.

On the occurrence of pharmaceuticals in drinking water only limited data exist.

Although some monitoring data are available for the different types of water, these data are mostly from grab samples. Frequent monitoring has hardly been conducted yet. Main questions in monitoring are: "When, where and what to measure?" "How much can we live with?" "Are we able to detect all pharmaceuticals that are important?" "How sensitive do we want analytical techniques to be?" "Should we include seasonal effects in monitoring?"

Again the need for a priority list for pharmaceuticals was urged.

> Pharmaceuticals are widely present in surface water, wastewater influent and effluent and to a lesser extend in ground water
>
> The development of adequate monitoring schemes based on the PhAC priority list is needed

2.4 ANALYSIS

(presented by Johanne Beausse, Auguste Bruchet and Frank Sacher)

At this moment many work has already been done on analytical techniques. Most of the pharmaceuticals that are considered to be relevant can be analysed within GWRC- membership.

There is however a lack in exchange of knowledge between countries/laboratories. In addition there is a need for round robin tests for further validation of the analytical techniques.

New pharmaceuticals and metabolites can enter the water cycle. To detect these pharmaceuticals broad-spectrum analysis might be useful.

Matrix effects and poor recoveries are an important difficulty in analysis of pharmaceuticals. X-ray contrast media and sulphonamide antibiotics still have low recoveries.

When developing harmonised analytical techniques within GWRC a rationale for selection of the pharmaceuticals to be studied should be created first.

> A number of adequate analytical methods is available
>
> Exchange of information about available methods and round robin tests are needed

2.5 REMOVAL

(presented by Gordon Wheale, Francis Luck and Marie-Laure Janex-Habibi)

At this moment not much information is available on the removal of pharmaceuticals in wastewater treatment plants (WWTPs). Removal depends on the type of pharmaceutical.

Low sludge retention times (e.g. caused by rainfall) results in poor removal. Membrane reactors have an influence on the removal of pharmaceuticals in wastewater treatment plants, but removal is not complete.

For identifying necessary measures in wastewater treatment mass balances could be very helpful.

First results on the removal of pharmaceuticals during drinking water treatment have been generated within the POSEIDON project. Several (polar) pharmaceuticals are relevant for bank filtration near urban areas. Many pharmaceuticals react very quickly with ozone and substantial removal can be achieved via AOPs (Advanced Oxidation Procedures).

(Powder) Activated carbon is also a good candidate for removal of pharmaceuticals but acidic compounds do not absorb very well. Natural organic matter (NOM) has a major influence on the removal.

Membrane filtration has obtained good results in the removal of pharmaceuticals during drinking water treatment.

Conclusion was that treatment processes are available to avoid a drinking water contamination (multiple-barrier treatment), but to which costs? Iodinated X-ray contrast media could be the exception as they are very stable and polar and are difficult to remove during drinking water treatment.

> Wastewater treatment systems only remove pharmaceuticals partly
> Advanced drinking water treatment systems are effective to remove most of the pharmaceuticals

2.6 EFFECTS

(presented by Jami Montgomery and John Fawell)

Considering ecotoxicity there are not much effect data at this moment. The majority of acute effects of pharmaceuticals occur at concentrations > 1 mg/l, but chronic effects can occur at the μg/l-level. DNA techniques might be the way forward for detecting ecotoxicity effects.

For human health effects the opposite is true. Many human toxicological data are available. Therapeutic doses of pharmaceuticals present in drinking water are much higher than the concentration detected. It is very unlikely that the concentrations detected in drinking water pose a risk to human health. The presence of pharmaceuticals is an issue of perception, but therefore not less important. Communication is essential to keep consumers' confidence in drinking water quality.

Questions have been raised on the development of antibiotic resistance. However, antibiotics that can result in resistance (like Penicillin) have not been detected in the water cycle yet.

> The presence of pharmaceuticals in water is no risk to public health; communication about this issue is important.
> The impact of pharmaceuticals in water on the ecological system is likely, but sound data are not available yet

3

RESEARCH STRATEGY

3.1 RESEARCH SUBJECTS OF MAIN CONCERN

During the workshop an outline for prioritisation of the different research subjects was developed.

It was concluded that the first step to be taken was to develop a *priority list of pharmaceuticals* to identify those on which research should be focussed. Secondly, the implementation of a limited number of *validated analytical methods* is required. A large number of analytical methods are used worldwide but the number of validated methods is limited. This is a prerequisite for conducting further research (occurrence, fate, treatment) in order to ensure harmonization of measurement methods and reliability and comparability of future data collected within the coalition. When robust and reliable analytical methods are available, studies on *removal during wastewater treatment and drinking water treatment* can be conducted.

The potential risk of pharmaceuticals in the (water) environment is not clear but wastewater treatment plants are one of the main point sources. Information is, therefore, needed to play an active role in understanding sources, processes and relative contributions.

Limited data are available on removal of pharmaceuticals during drinking water treatment, but it has been demonstrated that drinking water is not always completely free from pharmaceuticals. For optimisation of drinking water treatment and to safeguard drinking water quality and to demonstrate the effectiveness of available technology, information on the removal efficiency of drinking water treatment processes is needed.

Considering human health, it was concluded that effects of the presence of pharmaceuticals in drinking water are unlikely. It was estimated that the lifetime exposure via drinking water is less then 20% of one daily therapeutic dose. Further research seems therefore not necessary at this moment.

Information on the potential ecotoxic effects of pharmaceuticals is largely lacking. However, it seems that more fundamental research is needed to obtain a good understanding of this issue, which is beyond the scope of the GWRC.

Although human health effects are unlikely, the public can still be concerned about the presence of pharmaceuticals in (drinking) water. This makes the subject also an issue of perception. It is therefore of importance to avoid negative media attention on this topic and develop a *communication and risk perception strategy*. This can be done in a multi-stakeholder workshop.

Considering personal care products it was concluded that data are lacking. Furthermore, it would be hard to determine which personal care products should be included in the research and which not. Most of the personal care products are bulk chemicals used in paint, food and cleaning agents as well. Further research should focus on pharmaceuticals and mention personal care products only when relevant. Personal care products were identified as a relevant issue for further research within GWRC.

3.2 PROJECTS PROPOSED

Based on the research strategy , five project themes were defined:

1. PRIORITY LIST OF PHARMACEUTICALS

Prior to any other research a GWRC consensus list of representative priority PhAC has to be developed. This priority list is indispensable for any further joint GWRC studies on analytical methods, occurrence, water treatment, and potential risks associated with exposure to PhAC in the water supply.

2A. PROCEDURES & EXCHANGE OF KNOWLEDGE FOR ANALYTICAL TECHNIQUES

Development of a limited set of validated analytical methods for priority pharmaceuticals to be use in monitoring studies.

2B. OCCURRENCE & REMOVAL EFFICIENCY OF PHARMACEUTICALS IN WASTEWATER TREATMENT

Fate and transport of PhAC through the wastewater treatment train (i.e. from influent to effluent). To what extent are persistence and removal of Phac effected by varariation in treatment parameters. Are PhAC present (or detectible) in sewage effluents and at what levels? Development of recommendations for reduction of emissions to the (water) environment.

2C. OCCURRENCE & REMOVAL EFFICIENCY OF PHARMACEUTICALS IN DRINKING WATER TREATMENT

Evaluate removal efficiency of different stages during conventional and advanced treatment technologies in drinking water treatment. The investigations will be made with specific compounds selected in the priority list.

A step-by-step approach should be followed with a careful eye on developments to allow for fine-tuning between the individual issues (2a,b and c).

3. A MULTI-STAKEHOLDER WORKSHOP

This project proposes to organise a multi-stakeholder workshop in order to identify needs and opportunities for risk management: what is the problem, who owns the problem, what should be done. Relevant stakeholders include pharmaceutical industry, regulators, environmental agencies, user groups, water industry.

For each of these themes a project proposal was written by the participants of the workshop. See Annex I for the individual project proposals.

ANNEX I

PROJECT PROPOSALS

1. Project Title:	Development of an International Priority List of Pharmaceuticals				
Name of Proposer & Affiliation:	Djanette Khiari, AwwaRF				
Collaborators:	All				
Estimated Total Cost of Research (Euro)	2004	2005	2006	Beyond	Total
	50 ?				50

Background:	**Justification:** Pharmaceutically active compounds (PhACs) are a family of compounds that includes prescription drugs, over-the-counter medications, drugs used in hospitals and veterinary drugs. Numerous studies in Europe and the United States have shown that a wide variety of pharmaceuticals are present in wastewater effluents, surface waters, and ground waters. The extremely large number of compounds reported in the literature makes it difficult to evaluate the credibility of findings and to assess the impact of all PhACs on the water cycle. *The GWRC members have agreed that the first step of the research agenda be to consolidate the list of* compounds that can be used to judge risks for the water cycle and to be able to compare results.
Consequences if work not carried out:	With no consensus list, it would be difficult, if not impossible to compare results conducted by different research teams and different countries
Benefits to be achieved:	Provide a solid base for the GWRC future endeavours and to build a sound and effective research agenda on PhACs
- Political	Results from this project will help answer public concerns about the safety of drinking water regarding the presence of pharmaceuticals.
- Economic	Narrowing the list of compounds will reduce cost on methods, monitoring and treatment processes.
- Technical	A carefully selected list of indicators will help in a better understanding of all aspects of the study of PhACs (methods, occurrence, fate and transport, mechanisms, treatment) Once a true understanding is achieved, it would be easier to build upon.

	Objectives:
Aiming to achieve:	Develop a GWRC consensus list of representative priority PhACs, that can be used for further studies on analytical methods, occurrence, treatability, and potential risks associated with exposure to PhACs in the water supply. The list will identify compounds that the most likely are to be found in water supplies and that may have significant impact on human health. The use of such a consensus list within the GWRC membership will ensure that research findings are reliable and comparable.
Specific questions answered:	Which PhACs can be used as indicators/surrogate/representative for the drinking and wastewater industry?
Tasks set for contractor:	- Review of available information on the use patterns of PhACs and their metabolites based on published research and searches of various government, private, and public websites. - Select representative priority compounds based on literature and expert judgement. Selection criteria will include Therapeutic use (Antibiotics, Anti-depressants, Anti-inflamants, Lipid regulators, x-ray contract media, psychiatric control., and others) Physico chemical characteristics (octanol/water partitioning coefficient (Kow), acid dissociation constant (pKa), and Henry's law constant (H) and others. Occurrence Reported treatability Analytical methods availability. - Develop a list of priority PhACs for future research on occurrence, treatment, health risks and others.
Deliverables:	The deliverable from this task would be a list of judiciously selected PhACs that may be used in further monitoring studies and additional treatment and assess the health significance of PhACs in water supplies
Completion date to maximise benefits:	2005
Target audience for the output?	Research community, GWRC member organisations, and wastewater and drinking water supplies organizations
Which groups should receive any reports resulting from this work?	GWRC member organisations
Should the output be submitted for independent peer review to add authority to the work?	By GWRC members

2a. Project Title:	**Validated Analytical Techniques for Priority Pharmaceuticals-Part 1**				
Name of Proposer & Affiliation:	A. Bruchet/ M.L. Janex-Habibi, CIRSEE-Suez Environment				
Collaborators:	TZW, Anjou Recherche				
Estimated Total Cost of Research (Euro)	2004	2005	2006	Beyond	Total
	50,000	50,000			100,000 including 50, 000 cash and 50,000 in-kind.

Background:	**Justification:** The presence of drugs in the aquatic Environment is undesirable. Because of the large number of drugs in use, their comprehensive analysis remains out of reach. The Global Water Research Coalition has selected a priority list of about 20 representative pharmaceuticals that will be submitted to further study. These priority pharmaceuticals may also be used as indicators for the drinking and wastewater industries to guarantee consumer health while minimising the cost of monitoring. The implementation of a limited number of validated analytical methods is a prerequisite before conducting further research (occurrence, fate, treatment) in order to ensure : Harmonisation of measurement methods The reliability and comparability of future data collected within the coalition.
Consequences if work not carried out:	If not conducted with validated methods, the results from future research can be questioned by external stakeholders. The whole research effort may hence therefore be at stake.
Benefits to be achieved:	
- Political	Credibility of research data for future lobbying
- Economic	Minimise monitoring cost and avoid duplication of work by laboratories.
- Technical	Validated, cost effective and robust analytical methods using best available Technology

	Objectives:
Aiming to achieve:	A limited set of validated analytical methods for priority pharmaceuticals
Specific questions answered:	Are analytical results on priority pharmaceuticals comparable and accurate?
Tasks set for contractor:	Set up an analytical scheme for priority pharmaceuticals based on existing techniques comprising SPE followed by GC-MS or HPLC-MS. The matrices to be investigated in part 1 of this project will comprise surface waters, ground waters and drinking waters. Minimise the number of techniques. Write detailed analytical protocols. Ensure dissemination of techniques through training workshop. Organise intra and interlaboratory (minimum of 8 participants) exercise. Process the data and write final report
Deliverables:	Detailed Analytical protocols. Intra- and interlaboratory validation data. Stability data.
Completion date to maximise benefits:	1 year after validation of priority list
Target audience for the output?	GWRC and external laboratories
Which groups should receive any reports resulting from this work?	GWRC member organisations
Should the output be submitted for independent peer review to add authority to the work?	Results from this project should be published in peer-reviewed journal.

2b. Project Title:	**Occurrence, transport, fate and removal of Pharmaceuticals and personal care products in waste water**				
Name of Proposer & Affiliation:	Bert Palsma STOWA				
Collaborators:	TZW, EPA, Anjou Recherche, Berlin Wasser, WERF, UKWIR				
Estimated Total Cost of Research (Euro)	**2004**	**2005**	**2006**	**Beyond**	**Total**
	250 K€	250 k€	?	?	500 k€

Background:	**Justification:** The WWTP is the end of pipe treatment for (all) urban wastewater. In order to take part in the discussion concerning surface water quality, sludge disposal or reuse we have to know our sources, processes and emissions. The risk of pharmaceuticals in the (water) environment is not quite clear, WWTP however are one of the point sources and we have to play an active role in understanding provenance, processes and relative contributions.
Consequences if work not carried out:	Possible expensive and ineffective measures (e.g. optimisation of WWTP)
Benefits to be achieved:	
- Political	Active role of responsible stake holders
- Economic	Effective measurements
- Technical	Understanding of processes, cost effective optimisation,

	Objectives:
Aiming to achieve:	Recommendations for reduction of emissions to the (water) environment
Specific questions answered:	Are PhACs present (or detectible) in sewage effluents and at what levels? What is the fate and transport of these compounds through the ww treatment train (ie. from influent to effluent). What effect does varying certain treatment parameters have on their persistence/removal/. What is are the main sources of various PhAC's. Possibilities for source control (separate treatment of e.g. hospitals) and optimisation of WWTP
Tasks set for contractor:	Selection of priority substances (= separate proposal) Selection of representative WWTP Survey of selected treatment processes Source analyses of priority substances Mass balance of emissions: sludge/water partitions Possibility of combined pharmaceuticals and EDC projects should be considered. Note; an analytical method for the determination of pharmaceuticals in sludge should be available
Deliverables:	Selection of representative WWTP Survey of selected treatment processes Estimated contributions of different sources to the influent (households, hospitals, industry, ...)
Completion date to maximise benefits:	1-1-2006
Target audience for the output? **Which groups should receive any reports resulting from this work?**	Water boards, water industries, environmental ministries
Should the output be submitted for independent peer review to add authority to the work?	?

2c. Project Title:	Occurrence and removal efficiency of pharmaceuticals in drinking water treatment				
Name of Proposer & Affiliation:	Margreet Mons & Guus IJpelaar, Kiwa Water Research				
Collaborators:	EPA, Anjou Recherche, AwwaRF, UKWIR, CIRSEE, TZW				
Estimated Total Cost of Research (Euro)	2004	2005	2006	Beyond	Total
	250	250			500

Background:	**Justification:** Research on pharmaceuticals has started in the late 90's and increased ever since. Results show that pharmaceuticals are not always completely removed during drinking water treatment and can be present in drinking water. Mass balances for pharmaceuticals in drinking water treatment plants and data on removal efficiency are not yet available on a large scale.
Consequences if work not carried out:	Without information on the removal efficiency of drinking water treatment plants for pharmaceuticals, optimisation of the treatment processes for complete removal of pharmaceuticals cannot be reached and a safe and healthy drinking water quality cannot be safeguarded.
Benefits to be achieved:	
- Political	Results from this project will help answer public concerns about the safety of drinking water regarding the presence of pharmaceuticals.
- Economic	Results from this project will provide information to allow the selection of cost-effective technologies for removal of pharmaceuticals.
- Technical	Results from this project may help utilities to guide their drinking water treatment plant technology and management practices for optimisation of technologies and selection of most effective technologies for removal of pharmaceuticals.

	Objectives:
Aiming to achieve:	Drinking water that is considered safe by the consumer. Evaluate removal efficiency of different stages during conventional and advanced treatment technologies in drinking water treatment. The investigations will be made with specific compounds selected in the priority list (separate GWRC project). Combination with and contribution to current ongoing research will be made where possible.
Specific questions answered:	Which processes at DWTPs remove pharmaceuticals efficiently? Do these treatment processes (and process conditions) as currently applied by DWTPs form an adequate barrier against pharmaceuticals? At what conditions should the DWTPs be operated? And which processes/systems are cost effective?
Tasks set for contractor:	It is expected that a literature survey coupled with tests at bench scale, pilot scale and full scale will be required to provide information on: Concentrations of pharmaceuticals in raw water and drinking water, if any. Removal efficiencies of different drinking water treatment processes for pharmaceuticals. The mechanics and kinetics of treatment. Options for optimising treatment. Formation of by-products or degradation products, and how to minimise them.
Deliverables:	A report, or series of reports describing: Removal performances of pharmaceuticals in different drinking water treatment plants. Recommendations for future optimisation of drinking water treatment. Presentation at GWRC meeting. Publication in international scientific journal.
Completion date to maximise benefits:	2006
Target audience for the output?	Drinking water (treatment) associations, drinking water research institutes.
Which groups should receive any reports resulting from this work?	GWRC member organisations
Should the output be submitted for independent peer review to add authority to the work?	By GWRC members

3. Project Title:	**Multi-stakeholder workshop on pharmaceuticals**				
Name of Proposer & Affiliation:	Margreet Mons, Kiwa Water Research				
Collaborators:	all GWRC members				
Estimated Total Cost of Research (Euro)	2004	2005	2006	Beyond	Total
		20000			

Background:	**Justification:** A recent GWRC review has documented the presence of a wide variety of substances in pharmaceuticals and personal care products in the environment and in the urban water cycle all over the world. This project proposes to organise a multi-stakeholder workshop in order to identify needs and opportunities for risk management: what is the problem, who owns the problem, what should be done. Relevant stakeholders include pharmaceutical industry, regulators, environmental agencies, user groups, water industry.
Consequences if work not carried out:	Opportunities for effective and efficient risk management for pharmaceuticals in the urban water cycle might be missed
Benefits to be achieved: - Political - Economic - Technical	 Develop integral and coherent policies to minimise the occurrence of pharmaceuticals in the urban water cycle at minimum social costs. Keep consumer confidence in drinking water at high level.

Aiming to achieve: **Specific questions answered:**	**Objectives:** Identify and invite relevant stakeholders Organise workshop Compose report of workshop (position papers, communication material, possible actions towards influential stakeholders)
Tasks set for contractor:	Organisation of multi-stakeholder workshop
Deliverables: **Completion date to maximise benefits**:	Opportunities for risk management of pharmaceuticals in the urban water cycle (e.g. preventive measures by hospitals, pharmaceutical industries, consumers) Report from the multi-stakeholder workshop Communication material on pharmaceuticals 2005
Target audience for the output? **Which groups should receive any reports resulting from this work?** **Should the output be submitted for independent peer review to add authority to the work?**	Water industry, environmental protection agencies, regulators, policy makers, pharmaceutical industry, association of pharmacies, consumer organisations, user groups (human health care, agricultural). GWRC member organisations and target audience No

ANNEX II

WORKSHOP PRESENTATIONS

PROGRAMME

Monday, December 15, 2003:

12.30 Arrival/lunch

Afternoon session:

13.00 Welcome by Kiwa (Theo van den Hoven)

13.05 Welcome bij GWRC (Frans Schulting)

13.10 Scope & set-up of the workshop by Stowa (Bert Palsma)

State of the science: Contributions by GWRC members

13.20 Use & emissions
- Results of Poseidon project by CIRSEE (Marie-Laure Janex-Habibi)
- Contributions from the audience, knowledge gaps

13.45 Occurrence
- Occurrence in waste water and drinking water by AwwaRF Djanette Khiari)
- Occurrence in surfacewater by EPA (Susan Glassmeyer)
- Occurrence in groundwater by TZW (Frank Sacher)
- Contributions from the audience, knowledge gaps

14.45 Analysis
- Presentation by Anjou Recherche (Johanne Bausse)
- Presentation by CIRSEE (Auguste Bruchet)
- Presentation by TZW (Frank Sacher)
- Contributions from the audience, knowledge gaps

15.45 Coffee/tea break

16.15 Removal during treatment
- Removal during waste water treatment by UKWIR (Gordon Wheale)
- Removal during bank infiltration and waste water treatment by Kompetenzzentrum Wasser Berlin (Francis Luck)
- Removal during drinking water treatment / results of Poseidon project by CIRSEE (Marie-Laure Janex-Habibi)
- Contributions from the audience, knowledge gaps

17.15 Effects
- Ecotoxicity by WERF (Jami Montgomery)
- Human Toxicology by UKWIR (John Fawell)
- Contributions from the audience, knowledge gaps

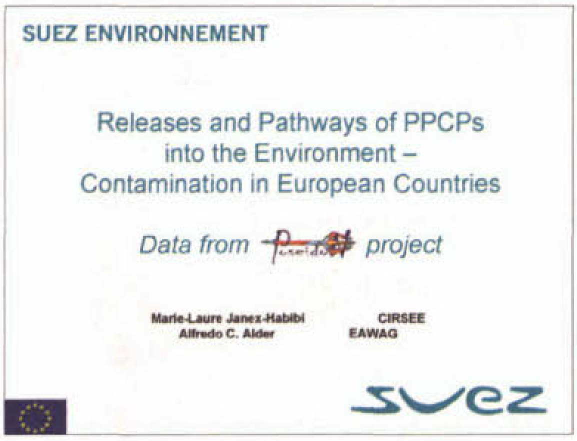
18.00 Closure by Stowa (Bert Palsma)

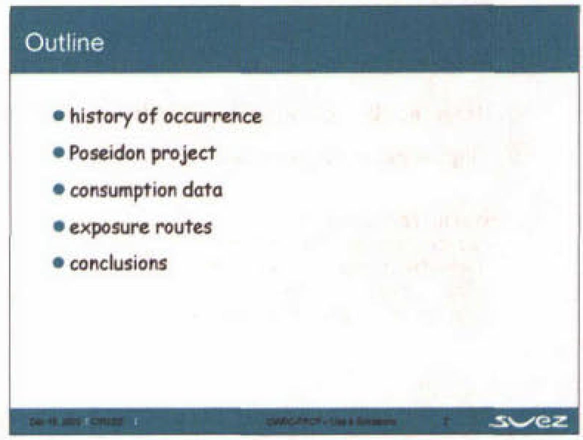
20.00 Diner in the inner city of Utrecht

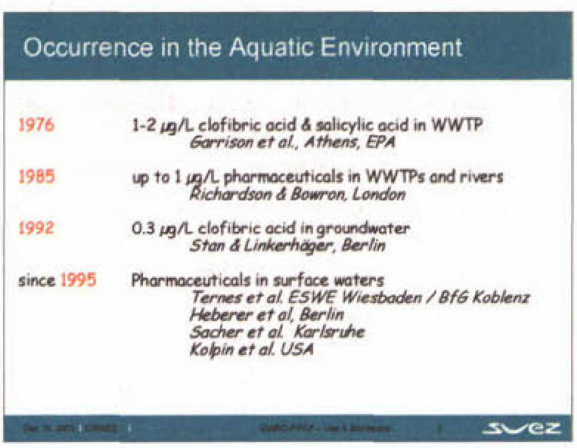
10.30	Coffee break
11.00	Writing of project proposals (in groups)
12.30	Working lunch
	Afternoon session: Project proposals
13.30	Continue writing project proposals (in groups)
14.30	Coffee/tea break
15.00	Presentation & discussion of project proposals
16.30	Wrap up, final remarks by Bert Palsma
17.00	Closure & drinks

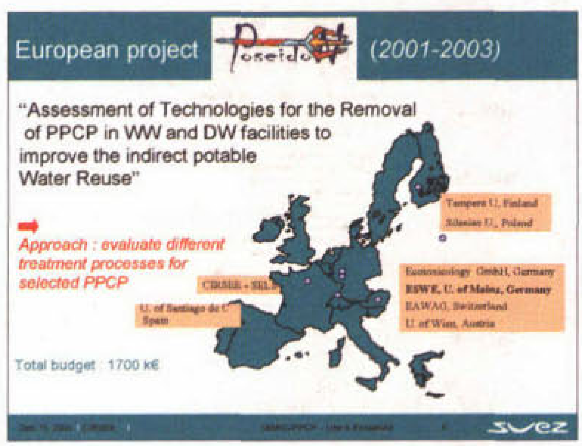
RESULTS OF POSEIDON PROJECT BY CIRSEE

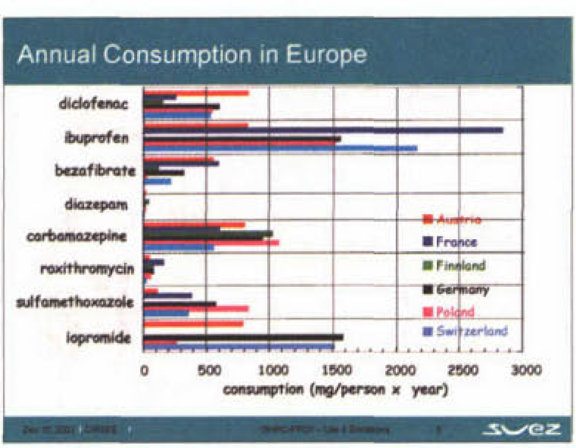
(MARIE-LAURE JANEX-HABIBI)

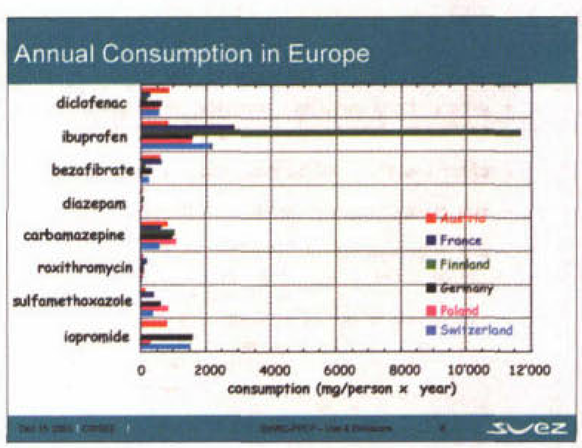












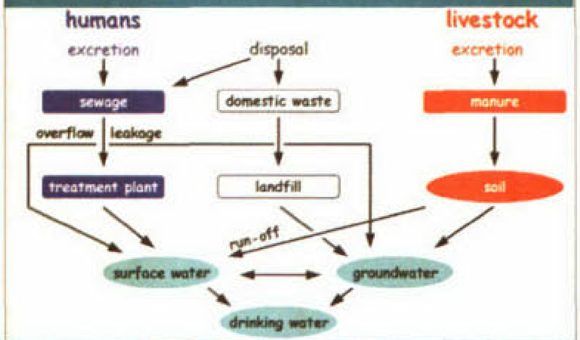
Annual Consumption of Antibiotics

- Veterinary medicine (Therapy / Prophylaxis): 3.494 t
- Antibiotic feed additives: 1.599 t
- Human medicine: 5.400 t

- Total: 10.493 t

Note: Consumption data derived from FEDESA (European Federation of Animal Health) 1998

Exposure Routes

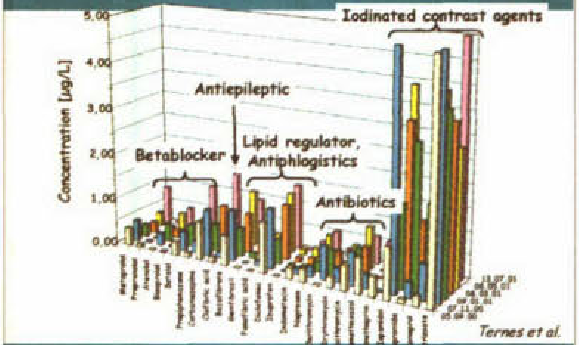


Selection of Pharmaceuticals

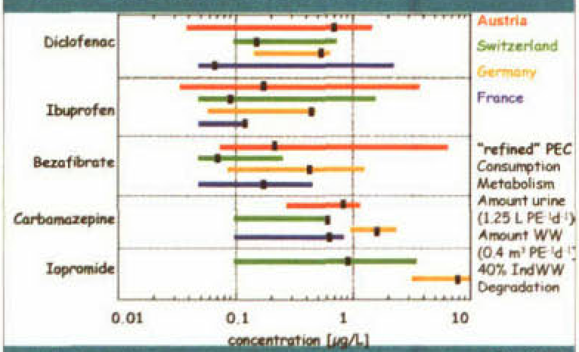
- **large number of pharmaceuticals (ca. 3'000)**
- **high number of excreted metabolites**

criteria for selection
- elevated annual prescriptions
- high effect doses/concentrations
- pharmacokinetic behavior
  (e.g. metabolism, urinary/faecel excretion rates)

Pharmaceuticals in Treated Wastewater



PECs and MECs in WWTP Effluents



Musk Fragrance Ingredients

- **used in fragrances in cosmetics, detergents, fabric softeners, household cleaning products etc.**
- **after use they will be released into wastewater**
- **two groups: (i) nitro musks and (ii) polycyclic musks**
- **use in Europe (IFRA, 1998) in tons:**

- nitro musks	musk xylene	86
	musk ketone	40
- polyclycic musks	galaxolide (HHCB)	1'473
	tonalide (AHTN)	385
	celestolide (ADBI)	18
	phantolide (AHMI)	19

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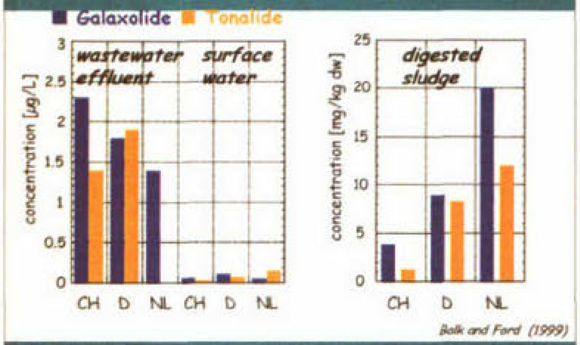
	phantolide (AHMI)	19

Polycyclic Musks (median concentrations)

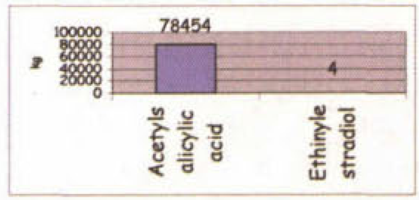


17α-Ethinylestradiol

- Used as contraceptive drug in anti baby pill
- Hormonal active substance (endocrine disruptor)
- Prescribed in very low dosages
- Annual consumption in Austria: 4 kg, Germany 49 kg, Switzerland 4 kg
- Estimated annual excretion rate of 1,7 / 20 kg
- Predicted No Effect Concentration (PNEC) of 0,1 ng/l

SUEZ

Comparison of Consumption in Austria



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Conclusions and Outlook (1)

- **pharmaceuticals and metabolites are ubiquitous in the aquatic environment**
- **the occurrence and behavior of metabolites are greatly unknown**
- **pharmaceuticals do not belong to one chemical group and exhibit different behaviors (e.g.: (bio)degradation, sorption)**

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Conclusions and Outlook (2)

- **how can monitoring data be interpreted?**
  => through understanding of the processes
  - **mass flux in technical and natural systems**
  - **fate in regional studies**
- **high concentration levels do not necessarily mean ecotoxicological risk and vice versa (e.g. 17α-ethinylestradiol, iodinated contrast agents)**
- **in the future chemical methods and biological endpoints should be combined**
  ⇒ effects of subinhibitory concentrations e.g. antibiotic resistance?

SUEZ

Acknowledgements

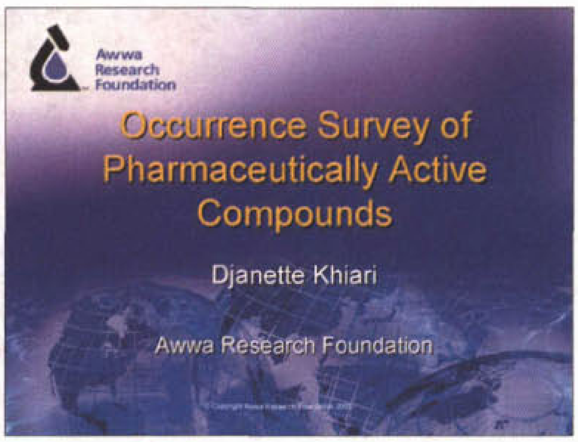
Eva Golet
Oliver Gans
Adriano Joss
Susanna Korhonen
Christa McArdell
Korneliusz Miksch
Hansruedi Siegrist
Thomas Ternes

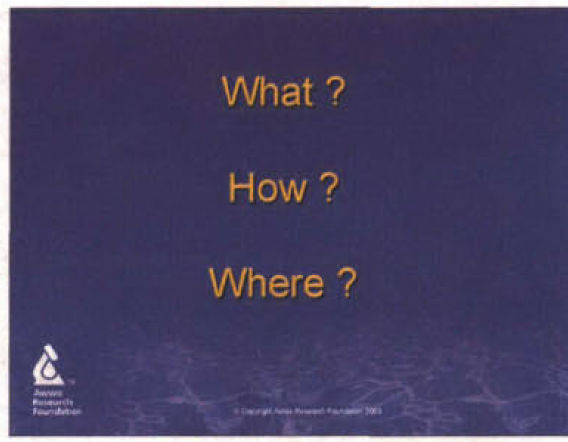
http//www.eu-poseidon.com

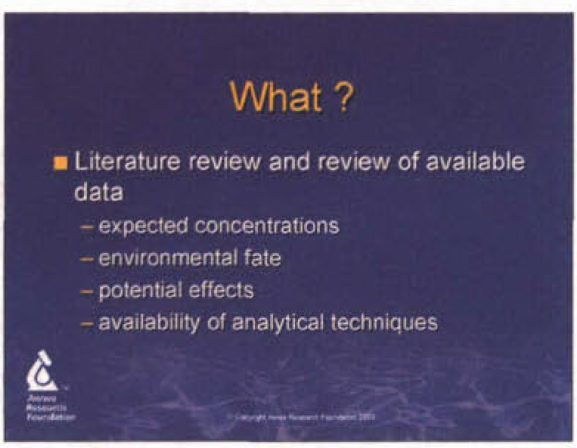
SUEZ

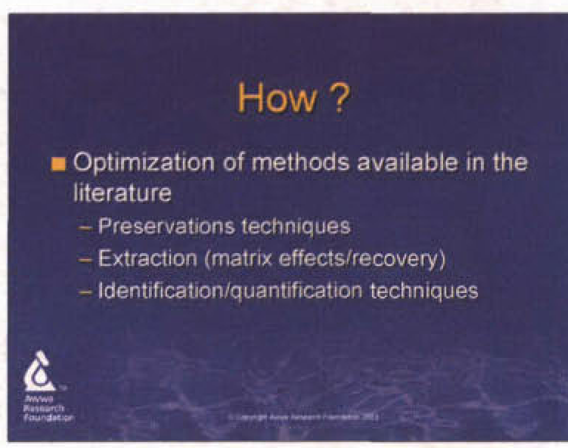
OCCURRENCE IN WASTE WATER AND DRINKING WATER BY AWWARF

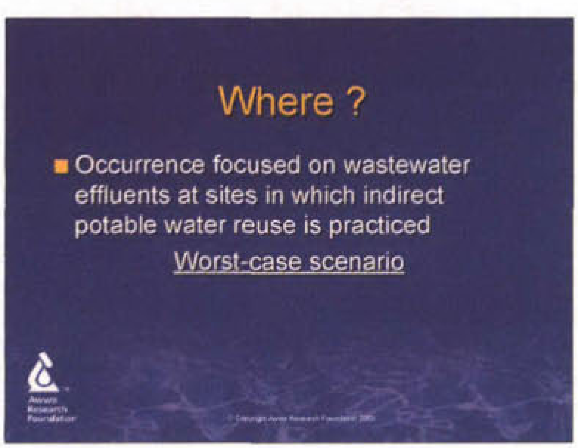
(DJANETTE KHIARI)











Analytical methods

- Acidic drugs and beta-blockers: Solid-phase extraction after derivatization and -GC/MS/MS
- Antibiotics: LC/MS

Occurrence results

Compound	Conc. range (ng/L)
Ciprofloxacin	<30-860
Diclofenac	<10-78
Enrofloxacin	<10-78
Gemfibrozil	92-5500
Ibuprofen	<10-320
Indometacine	10-36
Ketoprofen	10-55
Metoprolol	9-160
Naproxen	100-3200
Norfloxacin	30-150
Ofloxacin	30-600
Propranolol	5-53
Sulfamethazine	30-500
Sulfamethoxazole	30-2000
Trimethoprim	30-1900

Conclusions (I)

- Relatively limited number of compounds can identified
- Monitoring
  - GC/MS
  - HPLC
  - Acidic drugs, beta-blockers, and antibiotic present in municipal wastewater treatment plants (10 -10,000 ng/L)

Conclusions (II)

- PhACs effectively removed by activated carbon and reverse osmosis
- Most PhACs are removed during aquifer treatment
- Little removal in engineered treatment wetlands
- Chlorination of wastewater effluent results in transformation by-products

Recommendations

- Although no known health effects, utilities should be aware that PhACs are likely to be present
- Necessary to monitor PhACs in drinking water sources
- It is important to analyze control samples and matrix recovery samples before monitoring program

Future Research

- Health effects of exposure to low, sub-therapeutic doses of PhACs
- Additional research on occurrence of PhACs in the US
- Additional research on efficacy of treatment (advanced WWTP)
- Additional research on sensitive and robust analytical techniques

OCCURRENCE IN SURFACEWATER BY EPA

(SUSAN GLASSMEYER)

Transport of Chemical and Microbial Contaminants From Known Wastewater Discharges

Susan T. Glassmeyer[1], Edward T. Furlong[2], Dana W. Kolpin[3], Imma Ferrer[3], Jeffery D. Cahill[2], Steven D. Zaugg[2], Stephen L. Werner[2], Michael T. Meyer[4], and David D. Kryak[5]

[1] U.S. Environmental Protection Agency, Office of Research and Development, National Exposure Research Laboratory, Cincinnati, Ohio
[2] U.S. Geological Survey, National Water Quality Laboratory, Denver, Colorado
[3] U.S. Geological Survey, Iowa City, Iowa
[4] U.S. Geological Survey, Kansas
[5] U.S. Environmental Protection Agency, Office of Research and Development, National Exposure Research Laboratory, Research Triangle Park, NC

Weakness of Current Microbial Indicators

- Biological assays require 18- 48 hours to grow and be visualized
- Lack specificity
  - Human v. animal
  - Fecal v. non-fecal
- Do not effectively protect against pathogens
  - Cryptosporidia outbreaks in Texas, Pennsylvania, Wisconsin, and Nevada when the water quality met Federal Standards using current microbial indicators
  - In 12% of the waterborne disease outbreaks in 1997-1998 neither total nor fecal coliform detected.

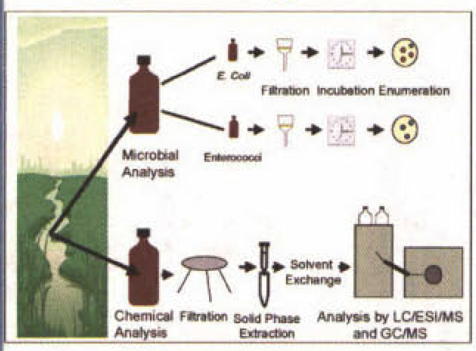
Why use Chemical Indicators?

- Rapid analysis times
- Able to discriminate human from animal fecal material
- Suite of compounds with various physical/ chemical properties may be more impervious to hydrological diversity
- However, must make sure they are persistent enough to survive wastewater treatment, but not so recalcitrant that they become ubiquitous

Sampling Locations- 2002

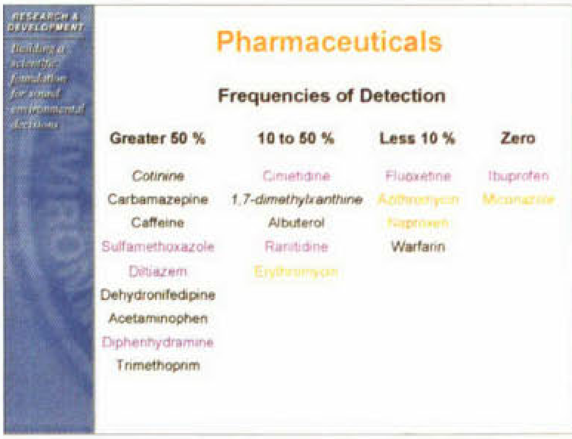
- Focus on wastewater treatment plants
  - One Upstream
  - One Effluent
  - Two Downstream
- Two Background Locations

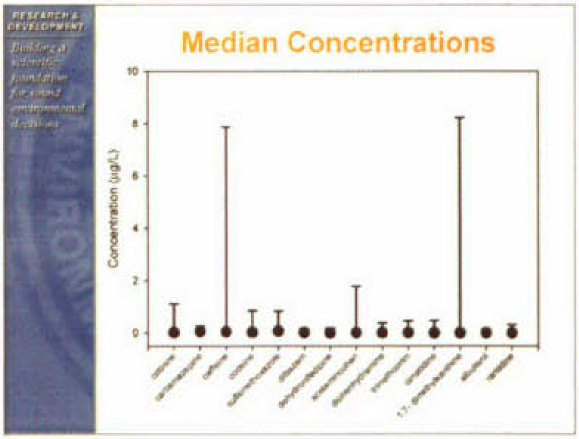
Experimental Approach

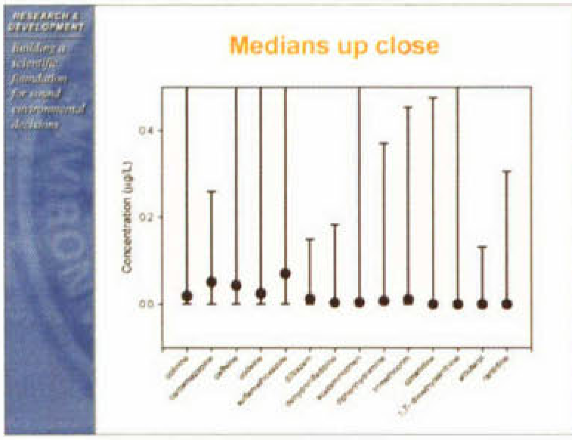


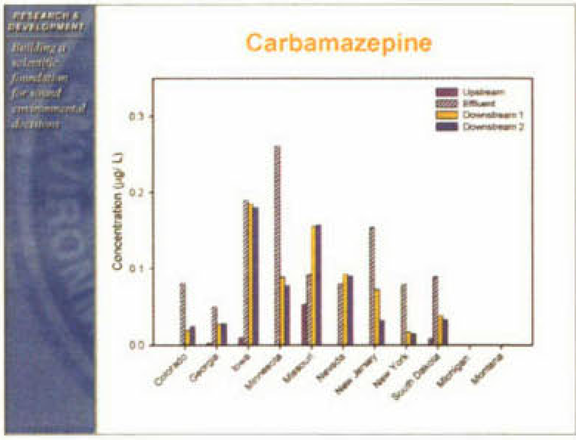
Target Analytes (over 100 total)

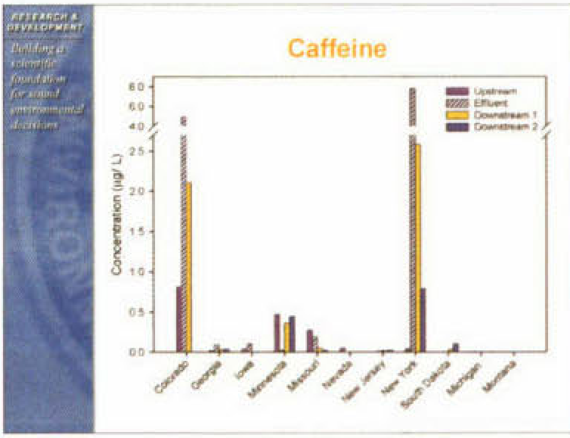
Prescription Drugs and Antibiotics	Nonprescription Drugs	Hormones and Sterols	Other Wastewater Related Compounds
Carbamazepine	Acetaminophen	Coprostanol	DEET
Sulfamethoxazole	Caffeine	Cholesterol	Galaxolide
	Cotinine	β-sitosterol	Tonalide
	Diphenhydromine		Tributylphosphate
	1,7-Dimethylxanthine		Triclosan

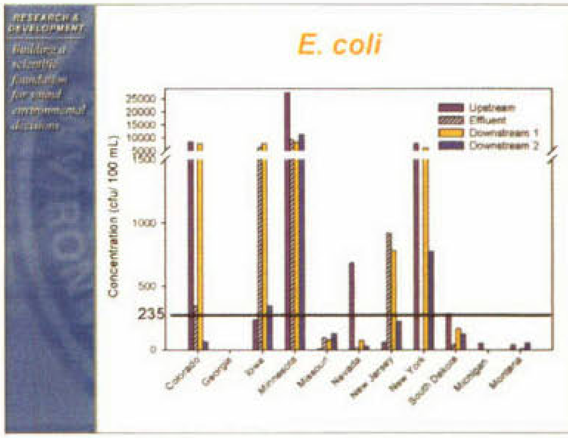

Pharmaceuticals
Frequencies of Detection
Greater 50 %
10 to 50 %
Less 10 %
Zero
Cotinine
Carbamazepine
Caffeine
Sulfamethoxazole
Diltiazem
Dehydronifedipine
Acetaminophen
Diphenhydramine
Trimethoprim
Cimetidine
1,7-dimethylxanthine
Albuterol
Ranitidine
Erythromycin
Fluoxetine
Azithromycin
Naproxen
Warfarin
Ibuprofen
Miconazole

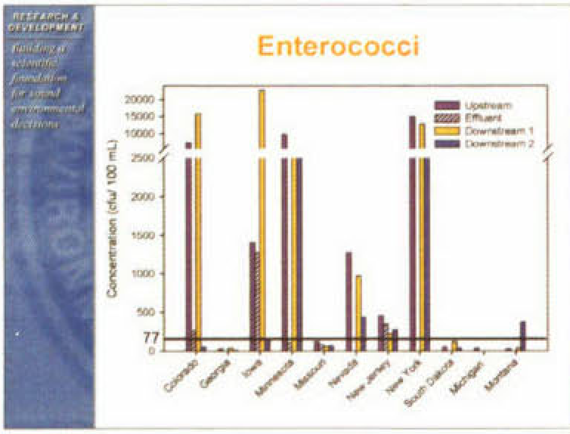

Median Concentrations
Concentration (µg/L)

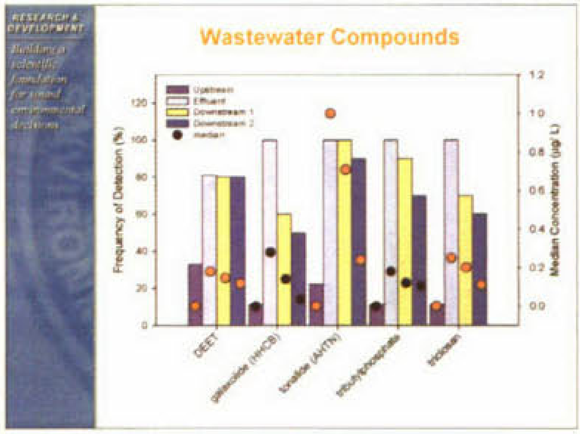

Medians up close
Concentration (µg/L)


Carbamazepine
Concentration (µg/ L)
Upstream
Effluent
Downstream 1
Downstream 2
Colorado
Georgia
Iowa
Minnesota
Missouri
Nevada
New Jersey
New York
South Dakota
Michigan
Montana

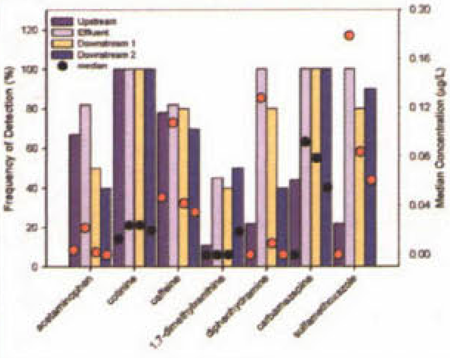

Caffeine
Concentration (µg/ L)
Upstream
Effluent
Downstream 1
Downstream 2
Colorado
Georgia
Iowa
Minnesota
Missouri
Nevada
New Jersey
New York
South Dakota
Michigan
Montana


E. coli
Concentration (cfu/ 100 mL)
Upstream
Effluent
Downstream 1
Downstream 2
235
Colorado
Georgia
Iowa
Minnesota
Missouri
Nevada
New Jersey
New York
South Dakota
Michigan
Montana

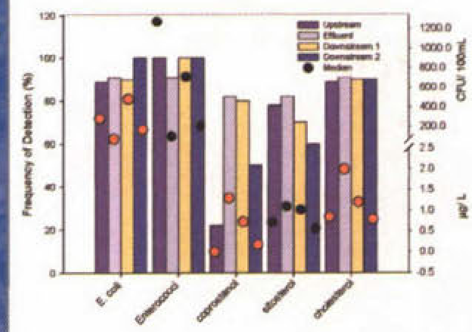

Enterococci
Concentration (cfu/ 100 mL)
Upstream
Effluent
Downstream 1
Downstream 2
77
Colorado
Georgia
Iowa
Minnesota
Missouri
Nevada
New Jersey
New York
South Dakota
Michigan
Montana


Wastewater Compounds
Frequency of Detection (%)
Median Concentration (µg/ L)
Upstream
Effluent
Downstream 1
Downstream 2
median
DEET
galaxolide (HHCB)
tonalide (AHTN)
tributylphosphate
triclosan

Pharmaceuticals



Mammal Source



Preliminary Results

- Pharmaceuticals and other chemicals survive wastewater treatment
- Upstream "background" levels of many of the pharmaceuticals and wastewater compounds are low (especially when compared to the indicator bacteria), and indicate that they are not too ubiquitous
- The downstream samples decrease at different rates for the chemicals
- Pharmaceuticals and other wastewater compounds may be able to be utilized as chemical indicators of human fecal contamination. Factors such as environmental persistence must be considered when preparing compound list.

Current Work

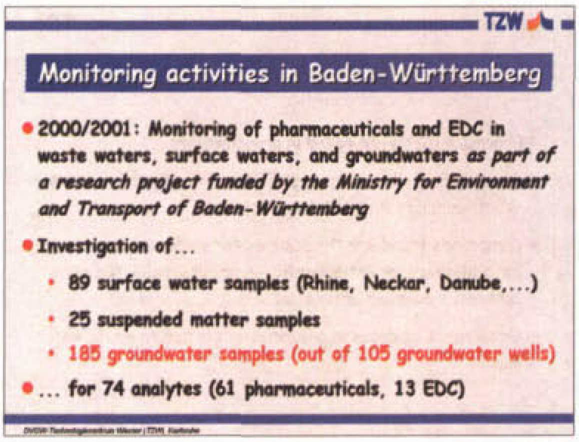
- Lagrangian Studies
- Epidemiology Studies

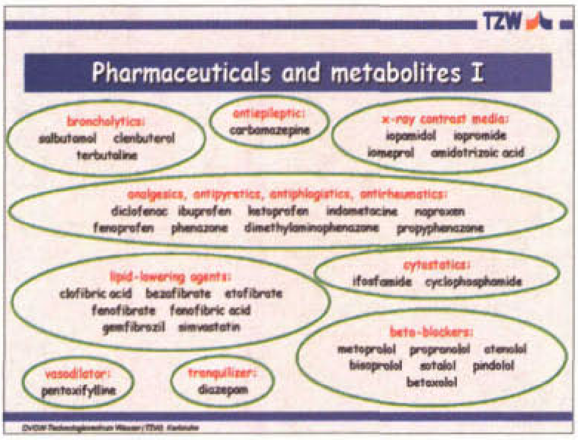
Acknowledgements

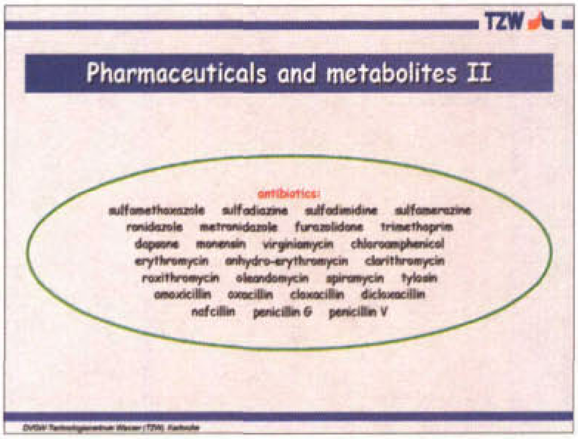
- USGS Field Personnel
- Funded through IAG DW-14-93940201

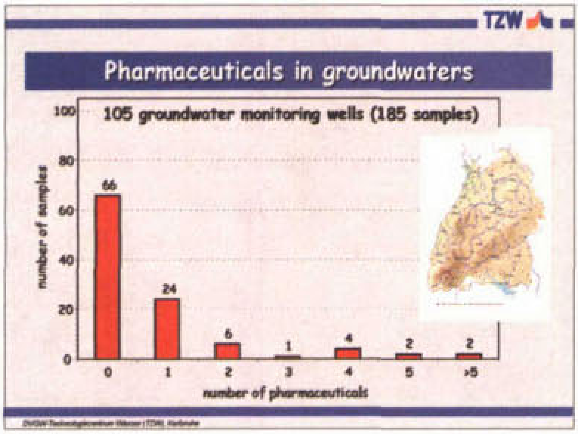
OCCURRENCE IN GROUNDWATER BY TZW

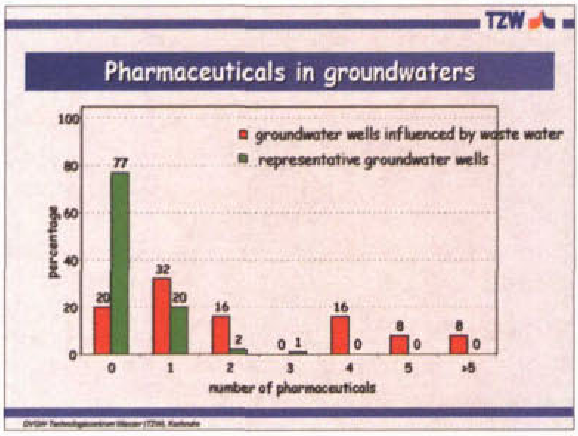
(FRANK SACHER)





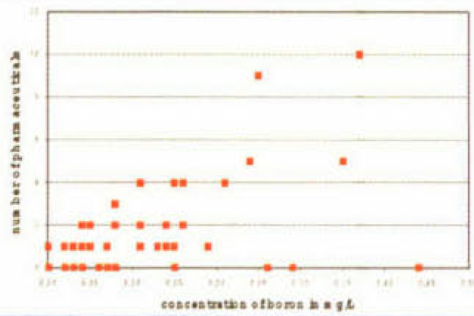






TZW

Correlation to boron concentration



DVGW-Technologiezentrum Wasser (TZW), Karlsruhe

TZW

Pharmaceuticals in groundwaters

	number of positive results	max. concentration in ng/L
sotalol	3	560
phenazone	5	25
diclofenac	4	590
iopamidol	5	300
amidotrizoic acid	21	1100
carbamazepine	13	900
anhydro-erythromycin	10	49
sulfamethoxazole	11	410

DVGW-Technologiezentrum Wasser (TZW), Karlsruhe

TZW

Summary

- Pharmaceuticals are found in groundwaters
- About 1/3 of all groundsamples under investigation in Baden-Württemberg contained drug residues
- Compounds found are the same as for surface waters: mainly beta-blockers, an antiepileptic, analgesics, iodinated x-ray contrast media and antibiotics
- Occurrence of drugs in groundwaters is due to waste water impact

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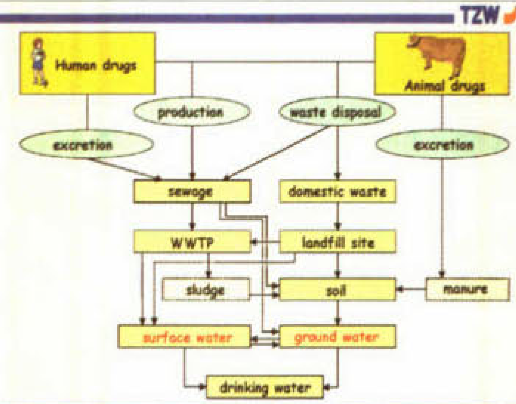
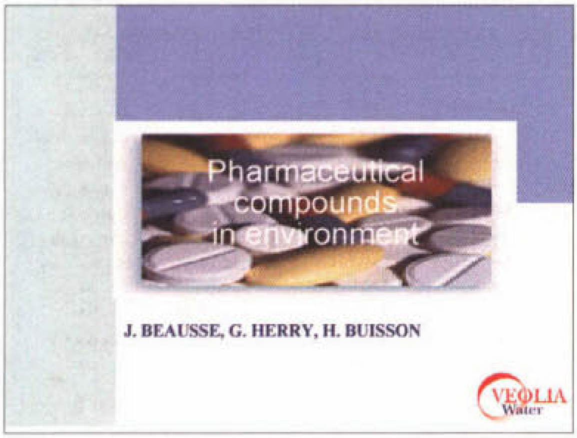
TZW

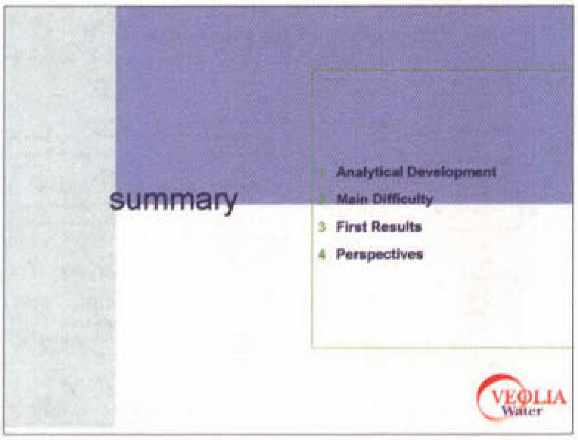


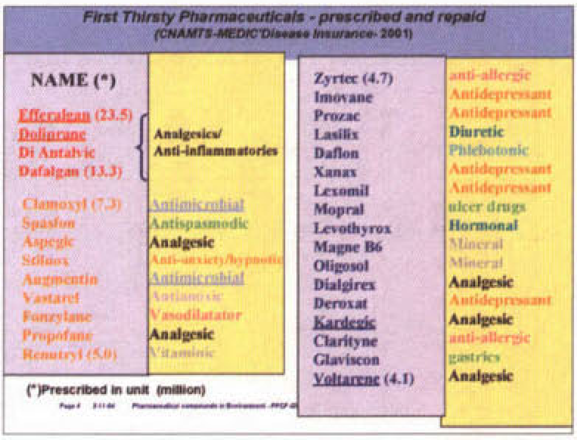
DVGW-Technologiezentrum Wasser (TZW), Karlsruhe

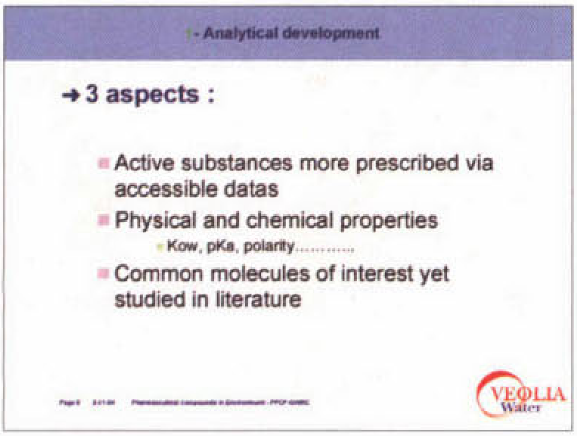
PRESENTATION BY ANJOU RECHERCHE

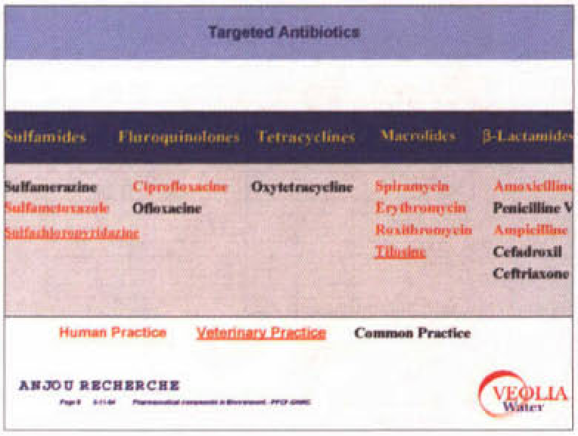
(JOHANNE BAUSSE)











Targeted substances

Analgesics /Anti-infl.	Anti-epileptics	Lipo-regulators	β-Bloquants	Antidepressant
Paracetamol	Carbamazepine	Fenofibrate	Metoprolol	Fluoxetine
Diclofenac	Primidone	Bezafibrate	Propranolol	
Ketoprofen		Gemfibrozil		
Phenazone				
Salicylic Acid				
Ibuprofen				

ANJOU RECHERCHE

VEOLIA Water

CHROMATOGRAPHIC CONDITIONS

- Column: BDS C18 - 2.1 mm
- Mobile phase: Binary grad. H_2O/MeOH, Formate d'NH_4^+ à 10mM
- Flow Rate: 200 µl/min
- Injection Volume: 35 µl
- Column oven: 25°C
- Injector: 4°C
- MS detector: Ion trap

VEOLIA Water

MS and MS-MS parameters : Fragmentation (ESI+)

Antibiotics	Molecular Mass g/mol	Precursor ion	Product Ion
Amoxicilline	365.4	397.9[M+CH$_3$OH+H]$^+$	380.8[-OH]
Penicilline V	350.4	382.9[M+CH$_3$OH+H]$^+$	159.9 (clivage β-lactam)
Ampicilline	349.4	349.9[M+H]$^+$	159.9 (clivage β-lactam
Spyramycine	815/857/871	438.1	365.9
Erythromycine	733.9	734.1[M+H]$^+$	576.1 (-Desosamine)
H_2O- Erythromycine	715.0	716.0[M+H]$^+$	558.0 (-Desosamine)
Roxithromycine	837.1	837.1 [M+H]$^+$	679.1 (-Desosamine)
Tilosine	916.1	948.3[M+CH$_3$OH+H]$^+$	772.2
Ceftriaxone	598.5	554.7[M-COCH$_3$+H]$^+$	295.8
Oxytétracycline	460.4	461.1 [M+H]$^+$	443.0 [-H2O]
Ciprofloxacine	331.4	332.1 [M+H]$^+$	288.1
Ofloxacine	361.4	362.2 [M+H]$^+$	318.1[-CO2]
Sulfaméthoxazole	253.3	254.1 [M+H]$^+$	188.8[-H2SO2]
Sulfamérazine	264.3	265.1 [M+H]$^+$	173.9[-Aminophenyl]
Sulfachloropyridazine	284.7	284.9 [M+H]$^+$	155.9

Cefadroxyl

VEOLIA Water

MS and MS-MS parameters : Fragmentation (ESI+)

Pharmaceuticals	Molecular Mass g/mol	Precursor Ion	Product Ion
Paracetamol	151.2	152.1 [M+H]$^+$	110.0 [-CH$_2$ CO]
Phenazone	188.2	189.2 [M+H]$^+$	146.1 [-CH$_3$ -CO]
Primidone	218.3	235.8 [M+H$_2$O+H]$^+$	219.1 [M+H]$^+$
Metoprolol	267.0	268.1 [M+H]$^+$	116.0
Salicylic Acid	138.1	137.1 [M-H]	93 [-CO$_2$]
Carbamazepine	236.3	237.1 [M+H]$^+$	194 [-CONH]
Ketoprofen	254.3	255.1 [M+H]$^+$	209 [-H$_2$ O -CO]
Bezafibrate	361.8	361.8	316
Diclofenac	295.0	295.9 [M+H]$^+$	278
Gemfibrozil	250.3	267.8 [M+H$_2$O+H]$^+$	251 [M+H]$^+$
Fenofibrate	360.8	360.9	233

Ibuprofen

VEOLIA Water

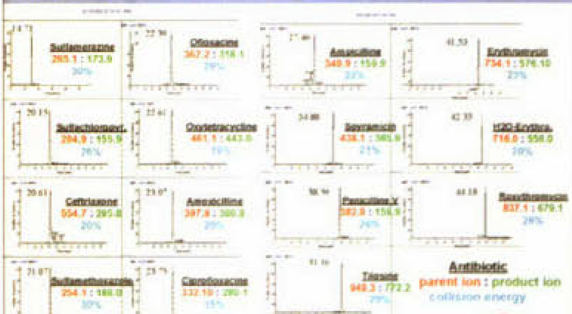
ESI$^+$/MS - MS PARAMETERS

T°Source : 180°C
Sheath Gas : 94
Aux. Gas : 6

VEOLIA Water

ESI$^+$/MS - MS PARAMETERS

T°Source : 200°C
Sheath Gas : 95
Aux. Gas : 14



VEOLIA Water

Stability of Stock solution at - 18°C

compounds	RSD in % on 25 days	compounds	RSD in % on 25days
Ampicilline	13	Paracetamol	11
Penicilline V	19	Phenazone	24
Spyramicin	17	Metoprolol	28
Erythromycin H2O	33	Primidone	55
Roxithromycin	17	Salicylic Acid	55
Tilosine	34	Carbamazepine	14
Ceftriaxone	48	Ketoprofene	27
Oxytetracycline	24	Bezafibrate	28
Ofloxacine	18	Diclofenac	25
Sulfamethoxazole	19	Gemfibrozil	55
Sulfamerazine	11	Propranolol	11
Ciprofloxacine	8	Fluoxetine	11
Amoxicilline	18	Fenofibrate	24
Sulfachloropyridazine	23		

VEOLIA Water

LINEARITY : 5 - 250 ng/L

	R^2	LOD ng/L
Amoxicilline	0.9883	10
Ampicilline	0.9892	5
Penicilline V	0.9806	10
Spyramycin	0.9939	5
Erythromycin-H2O	0.9996	5
Roxithroycin	0.9932	5
Tilosine	0.9987	5
Ceftriaxone	0.9957	5
Oxytétracycline	0.9967	5
Ciprofloxacine	0.9941	5
Ofloxacine	0.9911	5
Sulfaméthoxazole	0.9992	5
Sulfamérazine	0.9995	5
Sulfachloropyridazine	0.9971	5

	R^2	LOD ng/L
Paracetamol	0.9968	10
Diclofenac	0.9981	10
Ketoprofene	0.9968	10
Salicylic Acid	0.9761	10
Metoprolol	0.9971	10
Fenofibrate	0.9937	10
Bezafibrate	0.9937	10
Gemfibrozil	0.9995	25
Carbamazepine	0.9970	10
Primidone	0.9998	25
Phenazone	0.9930	10

VEOLIA Water

Repetability on solvent standard at 200 ng/L (n=10)
External Standard

Antibiotics	RSD % ES	Other substances	RSD % ES
Amoxicilline	11	Paracetamol	10
Penicilline V	6	Diclofenac	17
Spyramycine	9	Ketoprofene	9
H_2O-Erythromycine	7	Acide salicylique	15
Roxithromycine	14	Métoprolol	25
Ceftriaxone	8	Bezafibrate	9
Oxytétracycline	9	Gemfibrozil	11
Ciprofloxacine	na	Carbamazepine	11
Ofloxacine	11	Primidone	13
Sulfaméthoxazole	12	Phenazone	18
Sulfamerazine	4	Propranolol	7
Sulfachloropyridazine	7	Fluoxetine	15
Ampicilline	12	Fenofibrate	6
Tylosine	11		

Page 15 3-11-04 Pharmaceutical compounds in Environment - PPCP-QMRC

VEOLIA Water

Optimization of extraction step

ANTIBIO / PHARMA / BOTH

- Cartridge : C18-SDB-LMS-PPL-HLB-HF-ENV
- Sample Ph : 3 - 7.2 - no ajustment
- Sample volume (mL) : 100-250-500-1000
- Washing step optimisation
- Elution solvent : MeOH- CH3CN-EthAc-Ac
  - alone
  - +NH3
  - +TEA
  - +FA
- Elution Volume (5-10mL) : 6- 8 mL

Page 16 3-11-04 Pharmaceutical compounds in Environment - PPCP-QMRC

VEOLIA Water

Antibiotics

500 mL Water Sample
+Na2EDTA (0.5mg);pH4.9

liquid-solid Extraction
PPL + LMS

1 hour drying

Elution : 4 mL MeOH+ 2% FA
+ 4mL meOH + 5%NH3

Exchange
0.5 mL H_2O/ MeOH (95/5) + EI

EI (50ng/L)

Page 17 3-11-04 Pharmaceutical compounds in Environment - PPCP-QMRC

VEOLIA Water

Pharmaceutical compounds

500 mL Water Sample
pH3

liquid-solid Extraction
HLB

1 hour drying

Elution : 6 mL MeOH

Exchange
0.5 mL H_2O/ MeOH (95/5) + EI

EI (50ng/L)

Page 18 3-11-04 Pharmaceutical compounds in Environment - PPCP-QMRC

VEOLIA Water

Extraction Recovery (%) in spiked spring water
Linear range : 10 - 125 ng/L

compounds	Average Recovery Ratio of slopes	compounds	Average Recovery Ratio of slopes
Ampicilline	61	Paracetamol	62
Peni V & amox	<50	Phenazone	75
Spyramicin	135	Metoprolol	92
Erythromycin-H2O	70	Primidone	50
Roxithromycin	<50	A. Salicylique	122
Tilosine	56	Carbamazepine	75
Ceftriaxone	70	Ketoprofene	42
Oxytetracycline	136	Bezafibrate	75
Ofloxacine	98	Diclofenac	106
Sulfamethoxazole	76	Gemfibrozil	60
Sulfamerazine	78	Propranolol	76
Ciprofloxacine	102	fluoxetine	103
Sulfachloropyridazine	100	Fenofibrate	45

Page 19 3-11-04 Pharmaceutical compounds in Environment - PPCP-QMRC

VEOLIA Water

LOQ in Spring Water (n=5)
25 or 50*ng/L

	RSD % on area	ng/L		RSD % on area	ng/L
Ampicilline	30	24	Paracetamol	15	29
Peni V & Amox	-	-	Diclofenac	22	22
Spyramycine	14	26	Ketoprofene	22	28
Erythromycine-H2O*	25	36	Acide Salicylique*	21	37
Roxithromycine	-	-	Metoprolol	23	24
Tilosine	22	28	Bezafibrate	33	27
Ceftriaxone	29	24	Gemfibrozil	31	30
Oxytétracycline*	30	35	Carbamazepine	20	34
Ciprofloxacine	18	32	Primidone*	30	39
Ofloxacine*	36	36	Phenazone*	20	37
Sulfamethoxazole	30	20	Propranolol	18	28
Sulfamerazine	25	33	Fluoxetine	17	33
Sulfachloropyridazine	29	21	Fenofibrate	19	23

LOD : 10-25 ng/L

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VEOLIA Water

- Main difficulty : Matrix effect
Spiked Raw Water after extraction

50ng/L	Area values: Mineral water	Area values: Raw Water
Spyramicine	19 067 000	4 700 000
Roxythromycine	995 000	102 000
Salicylic A.	551 000	292 000
Ofloxacine	172 402 000	29 211 000
Carbamazepine	14 007 000	4 854 000
Bezafibrate	2 239 000	2 184 000
Ceftriaxone	1 144 000	1 102 000

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VEOLIA Water

Addition of internal standards (50ng/L)

	Before extraction procedure (75<rec.%<125)	At solvent exchange step for analysis
Enrofloxacine		X (Pharma)
Doxycycline Hydrochloride		X
Demeclocycline Hydrochloride	X	
Simetone		X (antibio)
Sulfamethazine - phenyl $^{13}C6$	X (Both)	

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VEOLIA Water

Repetability on solvent standard at 200 ng/L (n=10)
Internal Standard

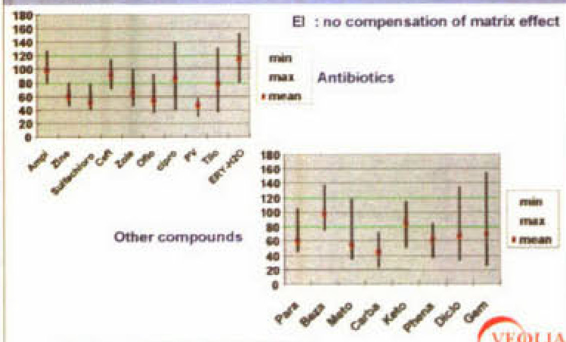
Antibiotics	RSD % IS	Other substances	RSD % IS
Amoxicilline	14	Paracetamol	8
Penicilline V	9	Diclofenac	12
Spyramycine	11	Ketoprofene	10
H_2O-Erythromycine	9	Acide salicylique	15
Roxithromycine	16	Métoprolol	23
Ceftriaxone	9	Bezafibrate	8
Oxytétracycline	8	Gemfibrozil	8
Ciprofloxacine	na	Carbamazepine	15
Ofloxacine	13	Primidone	15
Sulfaméthoxazole	16	Phenazone	19
Sulfamerazine	11	Propranolol	8
Sulfachloropyridazine	10	Fluoxetine	14
Ampicilline	13	Fenofibrate	8
Tylosine	14		

Sulfamethazine C* : 4% Sulfamethazine C* : 3%

IS = Simetone : 9% IS = Enrofloxacine : 4%

VEOLIA Water

Recovery in different real waters spiked at 50 ng/L (n=6)



VEOLIA Water

3- First results

Quantification : addition measured

Area	Capacity	resource	Pre-treatment		CFD	Filtration	refining	disinfection
	(m 3/day)		physical	chemical		sand		
plantA	135 000	river					O3/H2O2 + CAG	
plantB	200 000	river					O3/H2O2 + CAG	
plantC	800 000	river					O3/H2O2 + CAG	

VEOLIA Water

Results of first campaign (nov 2003) in ng/L
Raw water / Drinking water

	Zole	H2O-Ery	Oxy
Plant A	21 / <25	<50/<25	<50
Plant B	25 / <25	65 / 28	56 / <50
Plant C	24 / <25	<50/<25	<50

Not detected (<LOQ)
Sulfamethazine
Spyramycine
Tilosine
Ofloxacine
Ciprofloxacine
Sulfachloropyridazine
Ampicilline
Ceftriaxone

Not available with this method
Penicilline V
Roxythromycine
Amoxicilline

VEOLIA Water

Results of first campaign (nov 2003) in ng/L
Raw water
Drinking water

	Para	Meto	Carba	Beza	Fluox	SA
Plant A	230 <25	<50 <25	66 <25	37 <25	40 <25	<50
Plant B	192 <25	65 <25	60 <25	76 <25	147 41	<50
Plant C	150 <25	<50 <25	<50 <25	25 <25	38 <25	68 <50

Not detected (<LOQ)
Diclofenac
Fenofibrate
Ketoprofen
Propranolol
Gemfobrozil

Not available with this method
Primidone
Phenazone

VEOLIA Water

4- PERSPECTIVES

→ Quantification : Internal Standards?

→ New Campaigns : seasonal or epidemic impact

→ Extension
- New molecules - metabolites
- New matrix : Wastewater and Sludge

VEOLIA Water

PRESENTATION BY CIRSEE

(AUGUSTE BRUCHET)

SUEZ ENVIRONNEMENT

A Broad Spectrum Analytical Scheme for the Screening of Endocrine Disruptors (ED's), Pharmaceuticals and Personal Care Products in Wastewaters and natural waters

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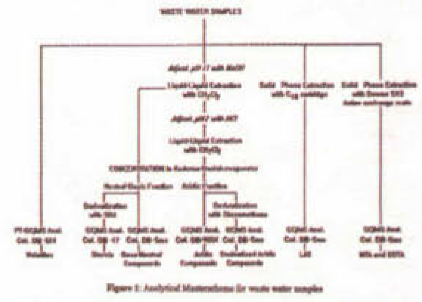
Introduction

- Numerous studies are underway to assess the presence of ED's, pharmaceuticals and personal care products in urban, environmental and drinking waters
- Studies focused on specific target compounds
- A single wastewater sample contains hundreds of micropollutants, some of which could be considered as undesirable in the future.

Objective

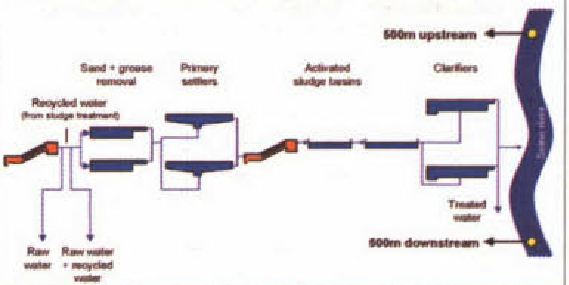
- Implement a broad spectrum analytical scheme capable of identifying as many compounds as possible in a single water sample.
- Screen the identified compounds for ED's, drugs and PPCP's
- Assess the efficiency of wastewater plants

Broad Spectrum Analytical Scheme



First plant investigated

- Paris area, effluents from 250,000 people, ~50,000 m^3 per day.



Identification of Micropollutants

- **Approximately 240 compounds or groups of compounds** (for instance the different isomers of C_3, C_4, C_5-alkylbenzenes, the nonylphenol isomers or the different homologues of LAS were considered as a single compound) **were identified in the raw water at levels above 0.1 µg/L, representing~10% of the DOC.**

Treatment efficiency (µg/l)

Compound	Raw water	Raw water + recycled water	Treated water
2-Butoxyethanol (butylglycol)	110.2	140.6	< 0.1
Butoxyethanol phosphate	15.7	7.8	0.7
2-Méthoxyethyl éther	1.5	< 0.1	0.5
Dipropylene glycol méthyl éther	10.1	24.8	0.6
2-Butoxyethoxyéthanol	317.0	1270.0	< 0.
1,1-Methyl-2-(2-propenyloxy) ethoxy-2-propanol	3.9	< 0.1	< 0.

SUEZ

Glycol ethers

- Water-based products (paints, inks, **cosmetics**, **detergents**...)
- Established reproductive effects on humans
- Series E (Ethylene G.) or P (propylene G.)
- Series E most toxic, classified into 3 groups, two of which (1 and 2) are toxic for reproduction. Reference values for embryo-fœtal development range from 0.1 to 12.4 mg/L (Cicolella et al, 2001)

SUEZ

DRUGS and PCPPs (µg/L)

Compound	Raw water	Raw water + recycled Water	Treated waters
Nicotine	Traces	<0.1	<0.1
Caffeine	34	70	0.3
Camphor	3.5	4.7	<0.1
Sunscreen UV 15 (2-hydroxy-4-methoxy-benzophenone)	1.6	0.9	<0.1

SUEZ

Influence of the Treated effluent on the Seine River (µg/l)

Compound	Treated Effluent	River Upstream	River Downstream
• Diisooctylphtalate	16.3	9.1	14.3
• Butylisobutylphtalate	11.1	3.2	4.4
• β-Sitosterol	<0.1	<0.1	1.2
• LAS	126	35	56
• 1,1,1-trichloroethane	17	0.2	0.8

SUEZ

Presence of Drugs at Plant 2*

Compound	Use water	Raw water	Treated
• caffeine		17.6	5
• Nicotine		2.8	<
• Pentoxiverin	Antitussive	0.5	2
• Clonitazene	Narcotic Analgesic	2.7	<
• Vitamin E acetate	Dietary supplement	15.8	<
• Histadyl	Antihistamine	Traces	~0.1
• Benzyl benzoate	Skin Parasites	3.0	<0.1

*Receives 50% effluents from pharmaceutical industries

SUEZ

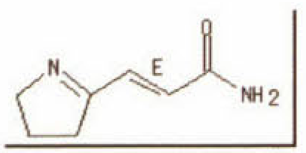
Presence of PPCPs at Plant 2*

Compound	Use	Treated water
• Dodecylguanidine acetate	Fungicide	0.4
• Sunscreen	UV 15	~0.1
• Dimethylethylbarbituric ac.	Tranquillizer	~0.1
• Ethyl ephedrine	Sympathomimetic	0.5
• dihydroprogesterone	Natural Hormone	~0.1
• morpholineethanamine	Synth. Of Antidepressants	~0.1
• butoxyethoxyethanol	Cosmetics, detergents	110
• 3-isothiocyanato-1-propene	Mustard oil	~0.1

SUEZ

Additional Compounds at Plant 3

- Plant 3 released traces (~0.1°g/L) of :

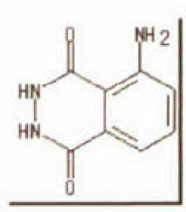


Cyclamidomycin : recent antibiotic effective against Gram+ and Gram- Bacteria, mycobacterium Tuberculosis

SUEZ

Additional Compounds at Plant 3

Luminol (3-aminophtalhydrazide) : Naturally phosphorescent molecule, used in light sticks, in criminology, as a dye in microbiology



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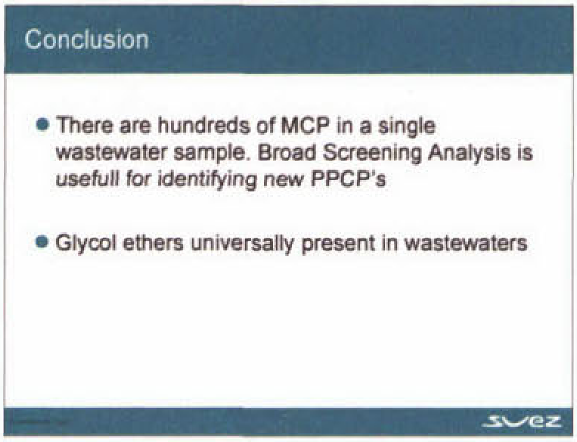
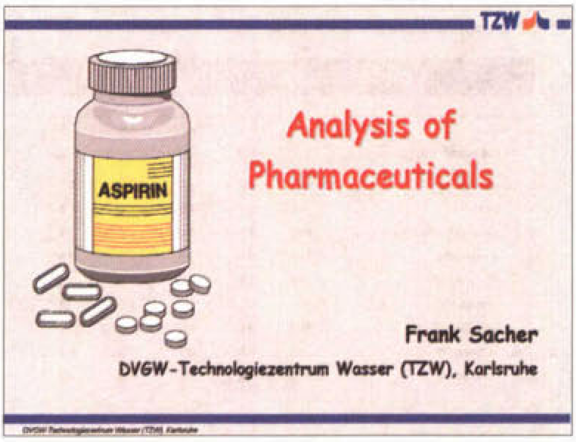
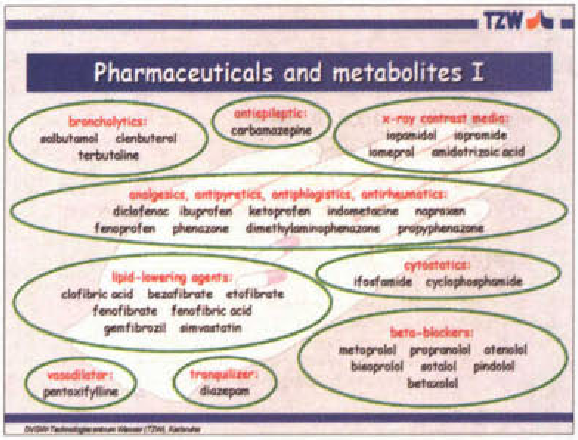
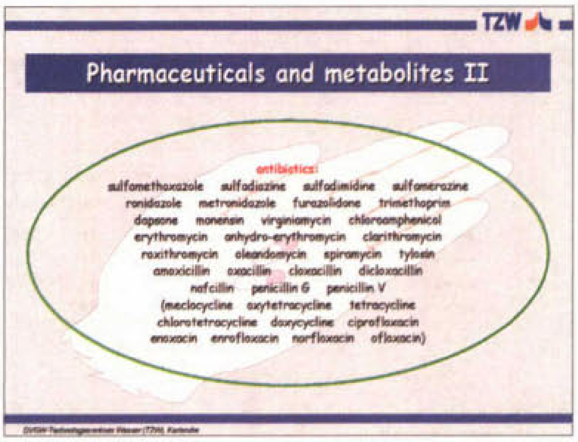

Conclusion
There are hundreds of MCP in a single wastewater sample. Broad Screening Analysis is usefull for identifying new PPCP's
Glycol ethers universally present in wastewaters
suez

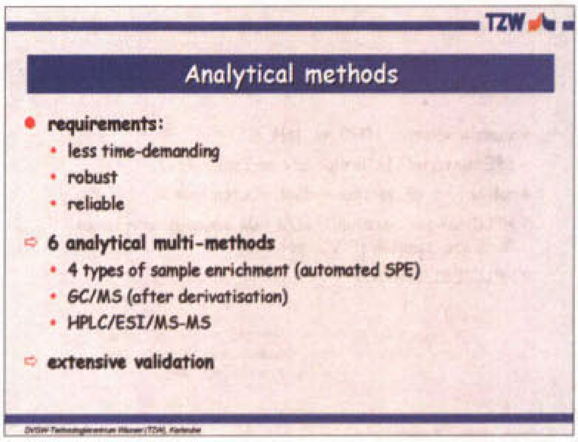
PRESENTATION BY TZW

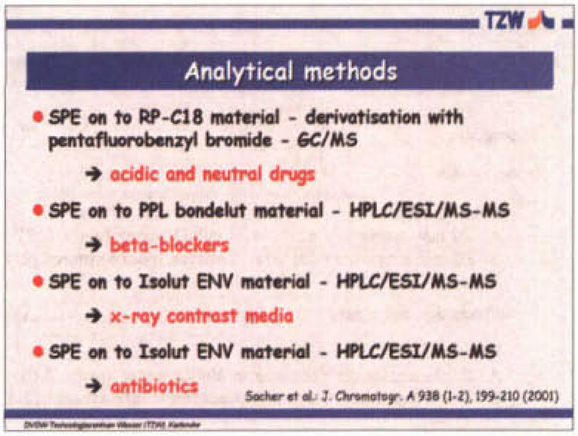
(FRANK SACHER)

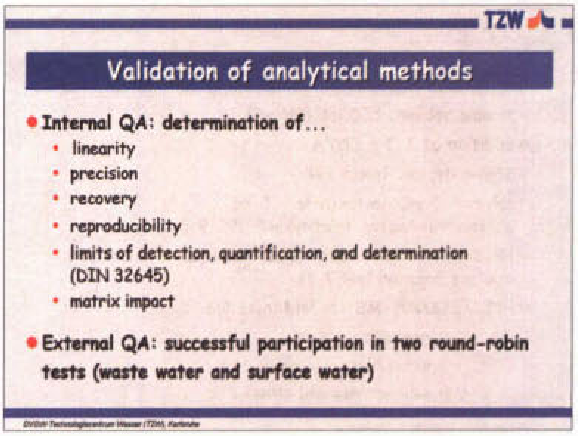












Determination of acidic and neutral drugs

- **sample volume: 1000 mL (pH 3)**
- **SPE material: RP-C18**
- **solvent: acetone (4 mL)**
- **derivatisation: pentafluorobenzyl bromide (2 h at 100 °C)**
- **GC/MS: full-scan mode**

diclofenac, ibuprofen, ketoprofen, indometacine, naproxen, fenoprofen, clofibric acid, bezafibrate, gemfibrozil, etofibrate, fenofibrate, fenofibric acid, carbamazepine, pentoxifylline, diazepam

Validation of acidic and neutral drugs

compound	r	R_{tap} in %	$R_{surface}$ in %	lod in ng/l	LOD in ng/l
bezafibrate	0.985	93	151	7.5	24
carbamazepine	0.976	80	74	9.6	32
clofibric acid	0.991	77	103	5.3	18
diazepam	0.997	73	99	6.9	22
diclofenac	0.979	70	70	8.7	29
gemfibrozil	0.993	49	89	5.2	17
ibuprofen	0.997	67	110	3.5	12
naproxen	0.996	68	105	3.8	13
pentoxifylline	0.989	90	134	6.5	22

Determination of beta-blockers

- **sample volume: 1000 mL (pH ~7)**
- **SPE material: PPL bondelut**
- **solvent: methanol (5 mL)**
- **HPLC solvent: acetonitrile/20 mM aqueous ammonium acetate solution (5:95, pH 7.2)**
- **HPLC/ESI/MS-MS**

metoprolol, propranolol, atenolol, bisoprolol, sotalol, pindolol, betaxolol, salbutamol, clenbuterol, terbutaline, phenazone, dimethylaminophenazone, propyphenazone, ifosfamide, cyclophosphamide, simvastatin

Validation of beta-blockers

compound	r	R_{tap} in %	$R_{surface}$ in %	lod in ng/l	LOD in ng/l
atenolol	0.998	86	67	2.4	8.2
betaxolol	0.996	70	45	3.7	13
dimethylaminophenazone	0.993	72	66	4.3	14
ifosfamide	0.994	87	73	4.2	14
metoprolol	0.998	96	54	2.2	7.9
phenazone	0.996	81	59	3.4	12
propranolol	0.993	84	48	4.6	15
salbutamol	0.998	80	66	2.6	9.1
terbutalin	0.993	44	39	4.5	15

Determination of X-ray contrast media

- **sample volume: 1000 mL (pH 3)**
- **SPE material: LiChrolut EN or Isolut ENV**
- **solvent: 5 mL methanol/5mL acetonitrile**
- **HPLC solvent: acetonitrile/2 mM aqueous ammonium formiate solution (5:95, pH 7.0)**
- **HPLC/ESI/MS-MS**

iopamidol, iopromide, iomeprol, amidotrizoic acid, iodipamide, iohexol, iopanoic acid, iotalamic acid, ioxaglic acid, ioxitalamic acid

Validation of X-ray contrast media

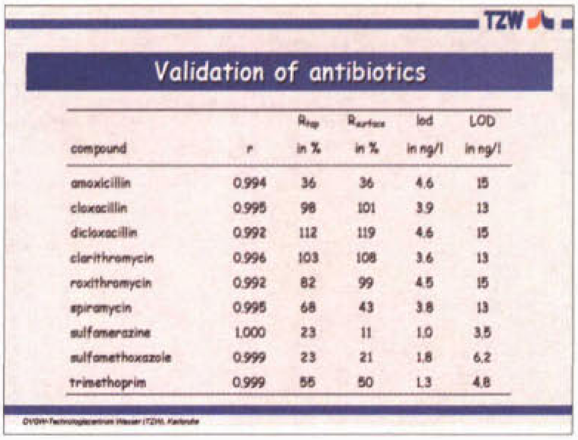
compound	r	R_{tap} in %	$R_{surface}$ in %	lod in ng/l	LOD in ng/l
amidotrizoic acid	0.996	9.0	7.2	3.6	12
iomeprol	0.993	15	7.4	4.8	16
iopamidol	0.992	19	28	4.5	14
iopromide	0.998	46	29	2.3	8.0

Determination of antibiotics

- **sample volume: 500 mL (pH ~5)**
- **addition of 1.3 g EDTA**
- **SPE material: Isolut ENV+**
- **solvent: 5 mL acetonitrile + 5 mL acetonitrile/water/triethylamin (90:9.5:0.5)**
- **HPLC solvent: acetonitrile/20 mM aqueous ammonium acetate solution (pH 7.2)**
- **HPLC/ESI/MS-MS: 3-fold injection**
  1. **penicillins**
  2. **macrolides**
  3. **sulfonamides and others**

HPLC-ESI-MS-MS

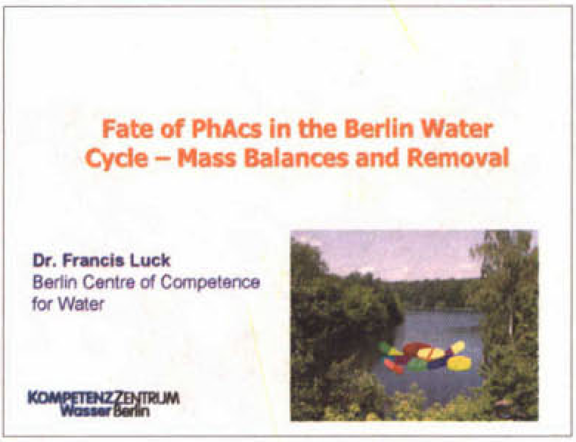
1. **penicillins:** amoxicillin, oxacillin, cloxacillin, dicloxacillin, nafcillin, penicillin G, penicillin V
2. **macrolides:** chloroamphenicol, virginiamycin, oleandomycin, erythromycin, anhydro-erythromycin, roxithromycin, clarithromycin, spiramycin, tylosin
   - **HPLC gradient:**
     A: 20 mM ammonium acetate in MilliQ water (pH = 6.8)
     B: 20 mM ammonium acetate in acetonitrile/methanol (2:1)
3. **sulfonamides and others:** sulfamethoxazole, sulfadiazine, sulfadimidine, sulfamerazine, ronidazole, metronidazole, furazolidone, trimethoprim, dapsone
   - **HPLC gradient:**
     A: 2 mM ammonium formiate in MilliQ water (pH = 7.0)
     B: 2 mM ammonium formiate in acetonitrile/methanol (2:1)

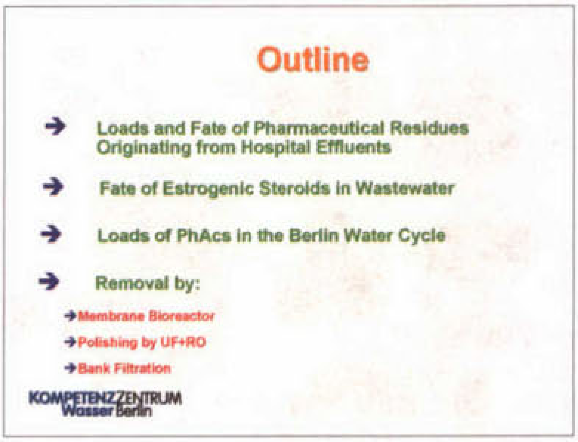


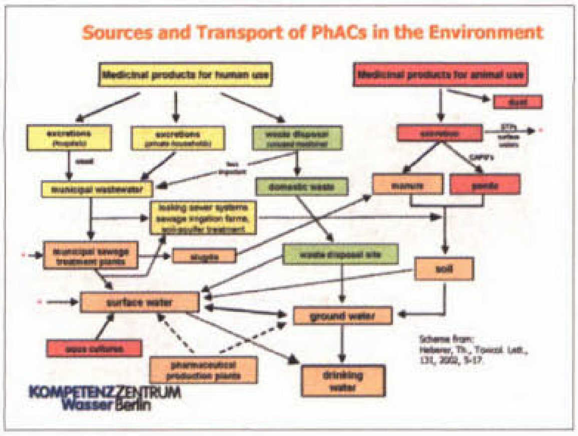
compound	r	R_{tap} in %	$R_{surface}$ in %	lod in ng/l	LOD in ng/l
amoxicillin	0.994	36	36	4.6	15
cloxacillin	0.995	98	101	3.9	13
dicloxacillin	0.992	112	119	4.6	15
clarithromycin	0.996	103	108	3.6	13
roxithromycin	0.992	82	99	4.5	15
spiramycin	0.995	68	43	3.8	13
sulfamerazine	1.000	23	11	1.0	3.5
sulfamethoxazole	0.999	23	21	1.8	6.2
trimethoprim	0.999	55	50	1.3	4.8

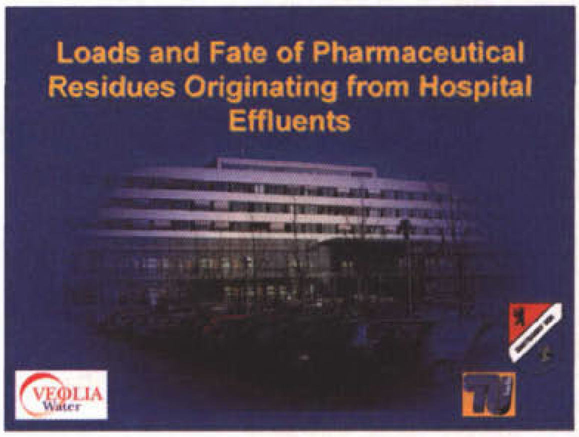
REMOVAL DURING BANK INFILTRATION AND WASTE WATER TREATMENT BY KOMPETENZZENTRUM WASSER BERLIN

(FRANCIS LUCK)









Objectives

➔ Create a model to calculate the expected loads of pharmaceutical residues in urban waste water

➔ Estimate the contribution of pharmaceutical residues originating from hospital wastewater to the total loads found in municipal sewage

➔ Environmental risk assessment (ERA) (PEC / PNEC approach)

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Location of the Berlin Military Hospital

KOMPETENZZENTRUM Wasser Berlin

Pharmaceuticals in the Aquatic Environment

Important prerequisites for the occurrence of pharmaceutical residues from human medical care in the aquatic environment are:

- the amounts administered (prescribed + hospital application + over-the-counter) for a given drug
- mode of application and pharmacokinetics in the human organism (reabsorption/metabolism)
- the behavior of the drug residues during wastewater treatment and in the environment (persistence, sorption, bioaccumulation, metabolism)

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Berlin Military Hospital

- Administered amounts were investigated for the individual pharmaceuticals
- Resorption and metabolism of the individual drugs have been acquired
- Sewage flow rates have been measured and samples have been collected and analyzed at Boyensstr.

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Sewer pipe at Boyensstr.
(collection of composite samples)

Drainage Area

Population: 95677

Pharmacies: 35

Total consumption of pharmaceuticals was calculated by the amounts of prescribed and OTC-drugs sold by the pharmacies

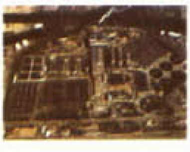
Other Hospitals: 4

Total administration of drugs has been acquired

Sewage Pumping Station

Pumping flow rates were made available by the Berlin waterworks

Sewage Treatment Plants



- The ratio of the sewage-flow towards both STP's is known
- Samples were taken from the influents and the effluents
- Influent samples were taken 6 hours after the sampling in the pumping station
- The effluent samples were taken 32 hours after those from the influents taking into account the residence time of the sewage in the STP's

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Pharmacokinetics

- Pharmacokinetic mechanisms describe the behavior of xenobiotics in the human or veterinary body
- Main processes are resorption, distribution, biotransformation, and elimination
- Pharmacokinetic data for two relevant pharmaceuticals (carbamazepine and diclofenac) will be presented to give an impression of possible problems during such investigations

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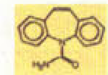
Information / Application

Carbamazepine

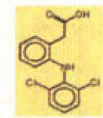


antiepileptic drug

DDD: 1000 mg/day

oral:	tablet, suspension

Diclofenac



non-steroidal anti-inflammatory drug

DDD: 100 mg/day

oral:	tablet, liquid
parenteral:	injection
rectal:	suppository
dermal:	ointment, gel

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Resorption

Carbamazepine

oral:	85 % resorbed, 15 % non resorbed

Diclofenac

oral:	99 % resorbed, 1 % non resorbed
rectal:	99 % resorbed, 1 % non resorbed
parenteral:	100 % resorbed
dermal:	5-10 % resorbed, 90-95 % non resorbed !!!

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Biotransformation

Drug → Phase -1- reaction
- oxidation
- reduction
- hydrolysis

Phase - 1 - metabolite → Phase - 2 - reaction

conjugation with activated
- glucuronic acid
- sulfuric acid
- acetic acid
- amino acids

Phase - 2 - metabolite

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Calculated amounts of drug residues

	Carbamazepine	Diclofenac		
	oral	oral/ rectal	parenteral	dermal
Non-resorbed amount	15 %	1 %	0 %	90 - 95 %
	from the resorbed part of the drug			
Unchanged eliminated amount	1 - 3 %	1 %	1 %	1 %
Glucoronide of the unchanged substance	0 %	15 %	15 %	15 %

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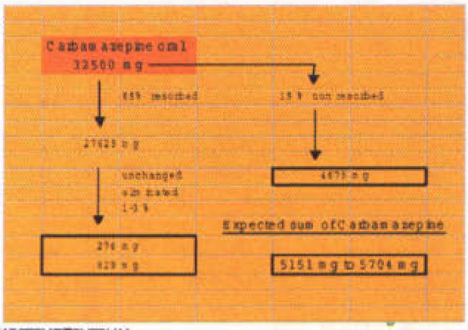
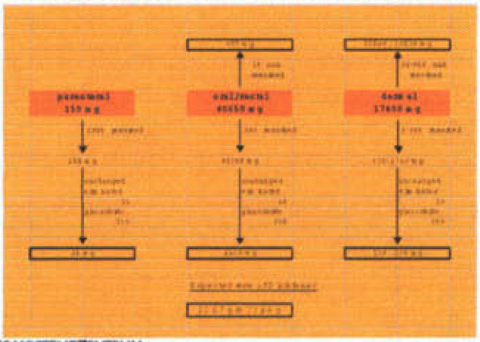
Calculation of Carbamazepine loads



KOMPETENZZENTRUM Wasser Berlin

Calculation of Diclofenac loads



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Results of the wastewater investigations

	Calculated amounts of the residues	Analyzed amounts of the residues	Recovery rate	Load percentage coming from the military hospital
Boyenstr. Carbamazepine	5151 – 5704 mg	3600 mg	63 – 70 %	
Pumping station Carbamazepine	334.7 – 370.6 g	462.6 g	125 – 138 %	0.78 %
STP influents Carbamazepine		2191.7 g		0.16 %

KOMPETENZZENTRUM Wasser Berlin

Results of the waste water investigations

	Calculated amounts of the residues	Analysed amounts of the residues	Recovery rate	Load percentage coming from the military hospital
Boyenstr.				
Carbamazepine	5151 – 5704 mg	5000 mg	53 – 70 %	
Diclofenac	22.7 – 23.7 g	6.2 g	26 – 27 %	
Pumping station				
Carbamazepine	334.7 – 370.6 g	462.6 g	125 – 138 %	0.70 %
Diclofenac	619.8 – 638.4 g	354.3 g	56 - 57 %	1.74 %
STP influents				
Carbamazepine		[illegible] g		[illegible] %
Diclofenac		3218.9 g		0.19 %

KOMPETENZZENTRUM Wasser Berlin

Possible reasons for the low recovery of Diclofenac

- Dermal application of diclofenac: significant parts of the ointment or gel are adsorbed by clothes or bandages. Although diclofenac will appear in the wastewater after the washing of these items, it is not acquired in the study because the laundry of the military hospital is not located inside the drainage area
- Disposal of paper towels and gauze bandages: diclofenac appears in the household waste and not in the wastewater

KOMPETENZZENTRUM Wasser Berlin

Drug residues in effluents from municipal sewage treatment plants in Berlin

Concentrations and removal rates for three drug residues and for caffeine detected in composite samples (24h) of influents (n=10...20) and effluents (n=20...27) from different STPs in Berlin* (Heberer, 2002).

Analyte	Average influent concentration in µg/l	Average effluent concentration in µg/l	Removal rate in %
Carbamazepine	1.78	1.63	8
Clofibric acid	0.46	0.48	0 **
Diclofenac	3.02	2.51	17
Caffeine	230	0.18	> 99.9

* STWs in Berlin: Ruhleben, Schönerlinde, Waßmannsdorf (mixed samples, 24hours) ** ... no removal was observed

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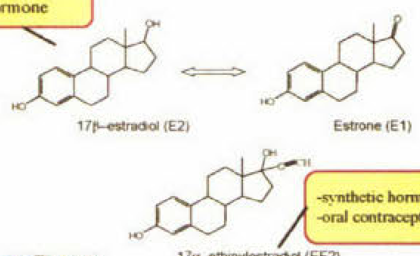
Natural and synthetic estrogens



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Estrogenic steroids in the aquatic environment

- ✓ Estrogenic steroids are excreted unchanged or as conjugates (glucuronides and sulfonides)
- ✓ Conjugates were assumed to be converted into their native forms in the sewage and during sewage treatment
- ✓ Unconjugated steroids possess high endocrine disrupting potentials (0.1 – 1 ng/l)
- ✓ Their behavior during sewage treatment and their fate in the environment are therefore of great concern

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Expected steroid concentrations in raw sewage

Predicted maximum concentration of EE2 in raw sewage in Berlin

50 kg/year in Germany (80 Mio. inhabitants)

~ **2.5 kg/year** in Berlin (3.4 Mio. inhab.)

~ **6.8 g/day** in Berlin (365 days)

about **600,000 m³** raw sewage/day (Berlin)

~ 0.011 mg/m³ in raw sewage or **11 ng/L**

Excretion of the natural estradiol and its main metabolite estrone has been reported with higher values

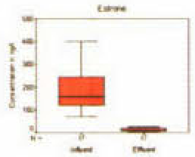
Only minor therapeutic use of estradiol

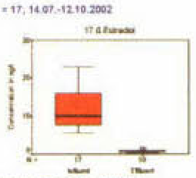
KOMPETENZZENTRUM Wasser Berlin

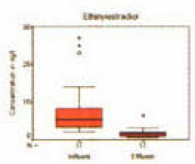
Results WWTP

Compound	Mean conc. [ng/l] influent	Mean conc. [ng/l] effluent	Calculated removal
E1	188 ±91 *	12.6 ±7.6	93.3 %
E2	11.8 ±5.1	[illegible]	[illegible] %
EE2	[illegible]	[illegible]	[illegible] %

n = 17, 14.07.-12.10.2002







KOMPETENZZENTRUM Wasser Berlin

Detections of PhACs in the aquatic environment

Analytes (class of prescription)	Number of compounds detected: Sewage and Surface water	Ground-water	Drinking water
Analgesics, anti-inflammatory drugs + metabolites	26	15	**8**
Antibiotics	31	3 (8 traces)	-
Antiepileptic drugs	2	2	**2**
ß-Blockers	7	1	-
Lipid regulators + metabolites	7	3	**3**
Contrast media + metabolites	8	6	**3**
Cytostatic drugs	2 traces	-	-
Oral contraceptives (Ethinyl estradiol (EE2) +mestranol)	2 (traces)	(1) validity in doubt	(1) validity in doubt
Other PhACs	21	4	-
Total	**106**	**34 (39)**	**16**

Drug residues in effluents from STP's in Berlin

in µg/L

Analyte	Mean effluent concentration in	Analyte	Mean effluent concentration in
4-Acetylamino-antipyrine	1.3 - 4.8*	Pentoxifylline	0.21
4-Formylamino-antipyrine	0.73 - 4.3*	Phenazone	0.41
4-Hydroxy-antipyrine	0.17 - 1.4*	Phenobarbital	0.43
[illegible]	0.026 - 0.21*	Phenytoine	0.1
AMDOPH	0.81	Primidone	0.66
Bezafibrate	0.7	Propyphenazone	0.41
Carbamazepine	1.29	Sulfadiazine	0.08
Clofibric acid	0.31	Sulfamethizole	<0.01
Diclofenac	2.44	Sulfamethoxazole	0.3
Dimethylaminophenazone	0.18	[illegible]	<0.01
Fenofibric acid	1.09	Hormones and other compounds	
Gemfibrozil	0.24	Androsterone	0.08
Ibuprofen	0.14	Cholesterol	4.76
Indometacine	0.31	Coprostanol	3.47
Ketoprofen	0.28	Estrone	0.013
Mefenamic acid	0.01	17α-Ethinylestradiol	0.0017
Metamizole	1.28	17β-Estradiol	0.0008
Metoprolol	1.00	Estriol	0.03
[illegible]	0.019 - 0.289*	[illegible]	1.90
Naproxen	0.21	Caffeine	0.21
Oxazepam	0.18	Salicylic acid	0.06

Loads of PhACs in the Berlin water cycle

- Loads of PhACs in sewage effluents, surface waters, and drinking water were calculated:
  - by measuring concentrations of PhACs in composite water samples *(upstream and downstream of Berlin)*
  - from production values (for all STPs and DWPUs) and measured surface water flows
- Comparison of PhACs loads in sewage effluents and surface waters provides information on:
  - validity of analytical results and study design (representative sampling, analytical methods ...)
  - persistence or degradation of PhACs in surface water

KOMPETENZZENTRUM Wasser Berlin

Results from the surface water monitoring in Berlin

(Monitoring in Berlin 2000-2002)

Positive findings: Results from nine sampling series (June 2000 to June 2002):

Compound	Concentration in ng/L
AMDOPH	ND - 1150
Diclofenac	ND - 1580
Ibuprofen	ND - 130
Indometacine	ND - 160
Ketoprofen	ND - 30
Mefenamic Acid	ND - 20
Naproxen	ND - 130
Propyphenazone	ND - 3350
Tolfenamic Acid	ND - 20
Bezafibrate	ND - 470
Clofibric Acid	ND - 450
Fenofibric Acid	ND - 1165
Gemfibrozil	ND - 45
Diazepam	ND - 123

Compound	Concentration in ng/L
Pentoxifylline	ND - 30
Carbamazepine	ND - 1700
Primidone	ND - 435
Caffeine	ND - 970
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
NBBS*	ND - 1190
TCEP**	20 - 270
TCPP***	65 - 1160

* [illegible]
** Tris-Chlorethyl-Phosphate
*** Tris-Chlorpropyl-Phosphate

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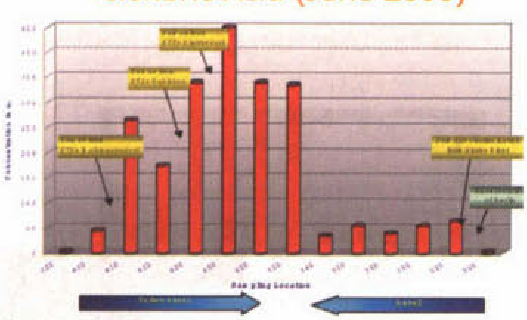
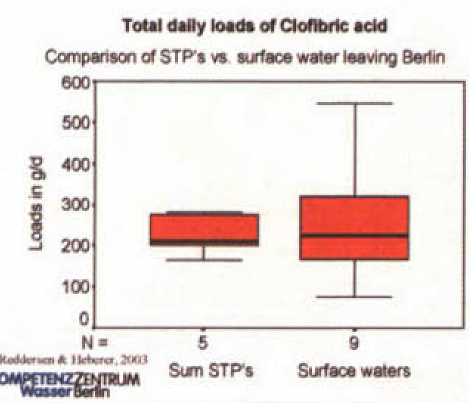
Clofibric Acid (June 2000)

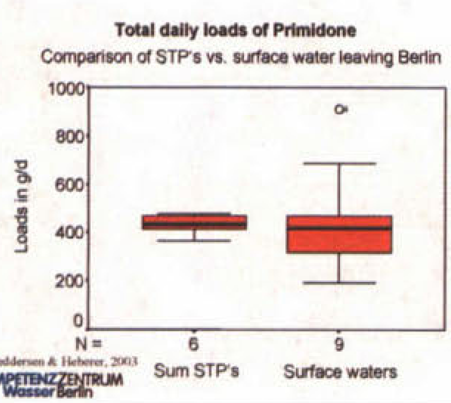


KOMPETENZZENTRUM Wasser Berlin



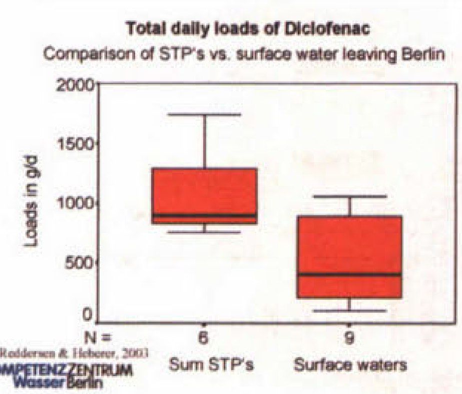
Reddersen & Heberer, 2003

KOMPETENZZENTRUM Wasser Berlin



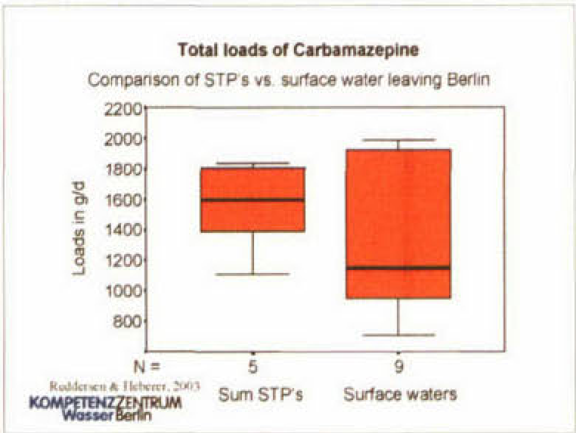
Reddersen & Heberer, 2003

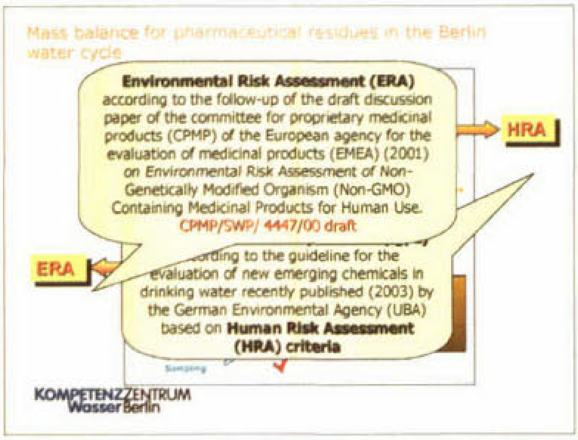
KOMPETENZZENTRUM Wasser Berlin



Reddersen & Heberer, 2003

KOMPETENZZENTRUM Wasser Berlin





Overall Conclusions

- Persistent PhACs are discharged into the aquatic environment from municipal sewage treatment plants acting as point sources.
- Due to their persistence and polarity a small number of specific residues are not significantly adsorbed in the subsoil and can under recharge conditions **leach into ground water.**
- Several PhACs are **excellent indicators** for municipal sewage influences in surface and groundwater

KOMPETENZZENTRUM Wasser Berlin

Conclusions

- For a limited number of compounds (e.g. EE2 or antibiotics) **an environmental risk can not be excluded** at the concentration levels measured in surface waters with high proportions of municipal sewage.
- With regard to the rare positive findings of trace levels of pharmaceuticals in drinking water and with today's knowledge **a risk for humans might almost be excluded.**

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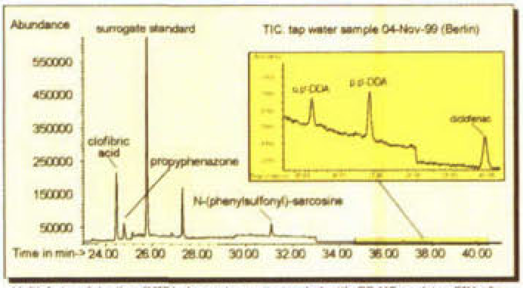
MID : Drinking water sample



Multiple ion detection (MID) chromatogram recorded with GC-MS applying SIM of a derivatized extract of a tap water sample.

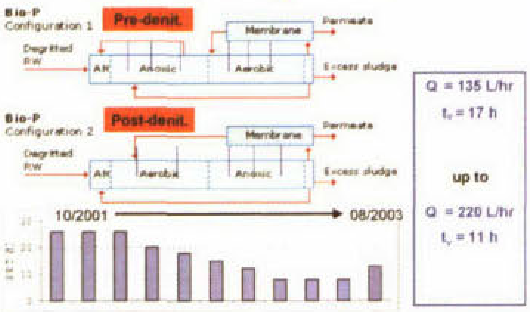
KOMPETENZZENTRUM Wasser Berlin

Long term comparison of trace organics removal performances between conventional and membrane activated sludge processes

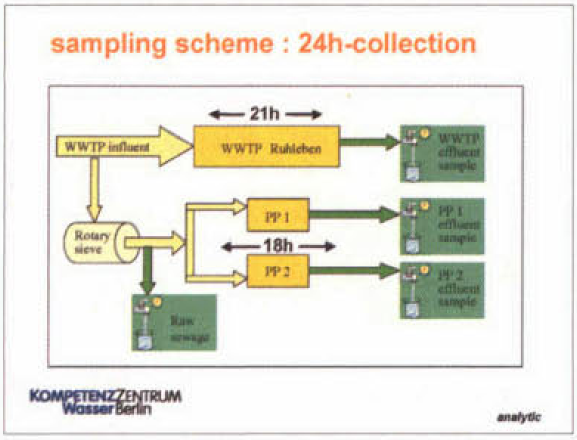
- **MBR – Pilot units**

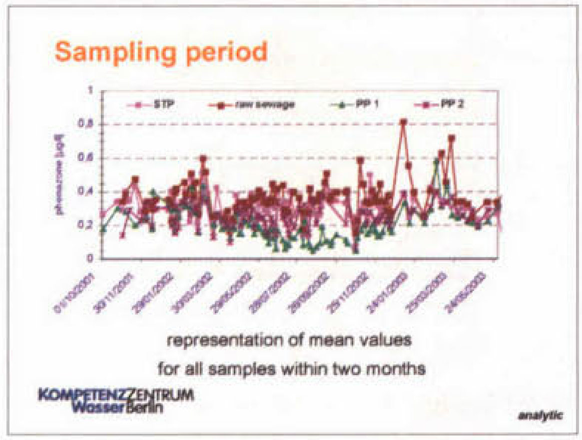
KOMPETENZZENTRUM Wasser Berlin

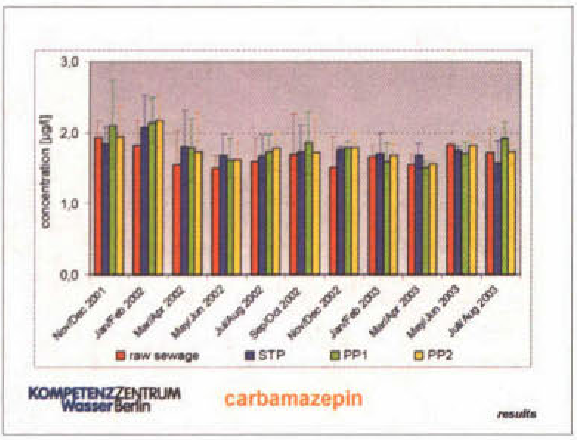
Pilot plant configuration

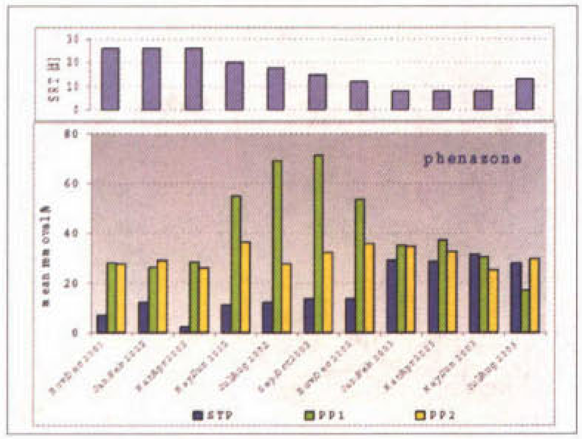


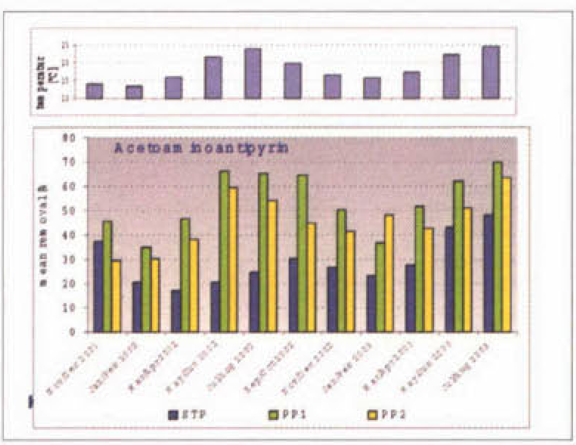
KOMPETENZZENTRUM Wasser Berlin

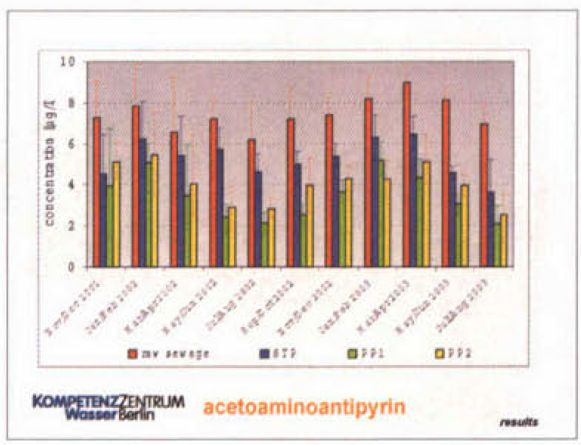

sampling scheme : 24h-collection
21h
WWTP influent
WWTP Ruhleben
WWTP effluent sample
Rotary sieve
PP 1
PP 1 effluent sample
18h
PP 2
PP 2 effluent sample
Raw sewage
KOMPETENZZENTRUM Wasser Berlin
analytic

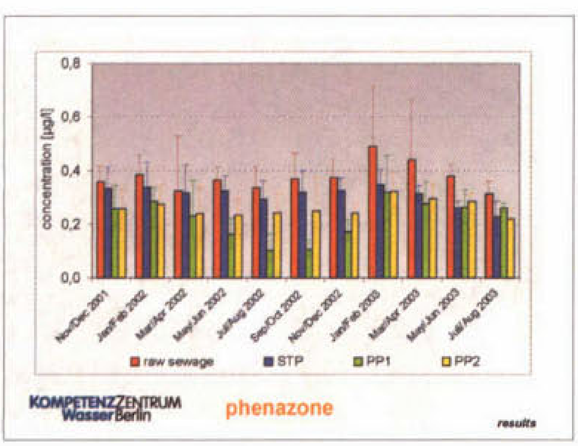

Sampling period
STP
raw sewage
PP 1
PP 2
representation of mean values
for all samples within two months
KOMPETENZZENTRUM Wasser Berlin
analytic

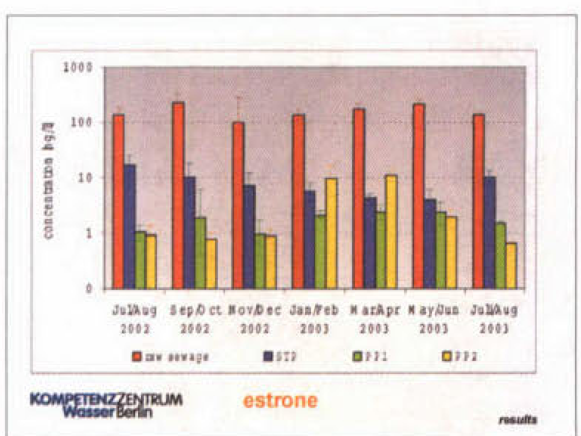

concentration [µg/l]
raw sewage
STP
PP1
PP2
KOMPETENZZENTRUM Wasser Berlin
carbamazepin
results

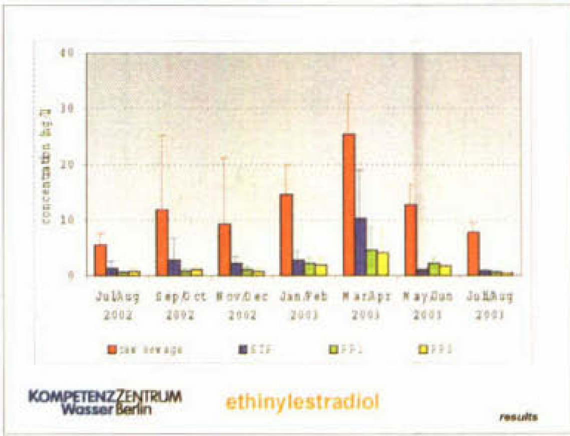

phenazone
STP
PP1
PP2


Acetoaminoantipyrin
STP
PP1
PP2

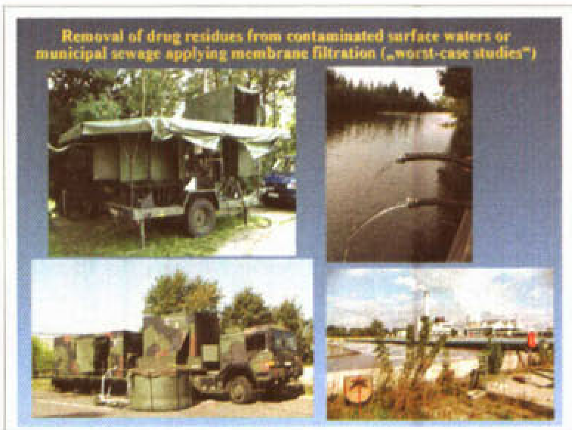

raw sewage
STP
PP1
PP2
KOMPETENZZENTRUM Wasser Berlin
acetoaminoantipyrin
results


concentration [µg/l]
raw sewage
STP
PP1
PP2
KOMPETENZZENTRUM Wasser Berlin
phenazone
results


Jul/Aug 2002
Sep/Oct 2002
Nov/Dec 2002
Jan/Feb 2003
Mar/Apr 2003
May/Jun 2003
Jul/Aug 2003
raw sewage
STP
PP1
PP2
KOMPETENZZENTRUM Wasser Berlin
estrone
results

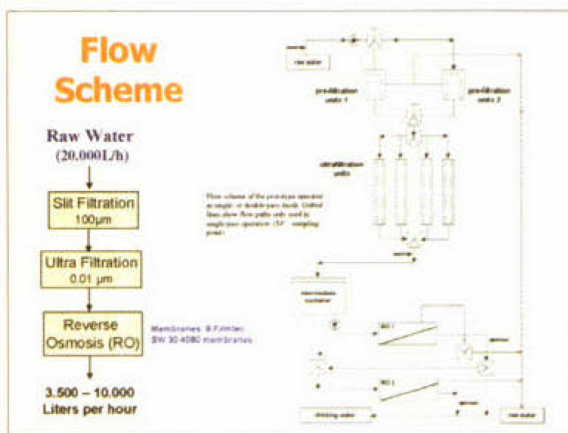

40
30
20
10
0
Jul/Aug 2002
Sep/Oct 2002
Nov/Dec 2002
Jan/Feb 2003
Mar/Apr 2003
May/Jun 2003
Jul/Aug 2003
KOMPETENZZENTRUM Wasser Berlin
ethinylestradiol
results

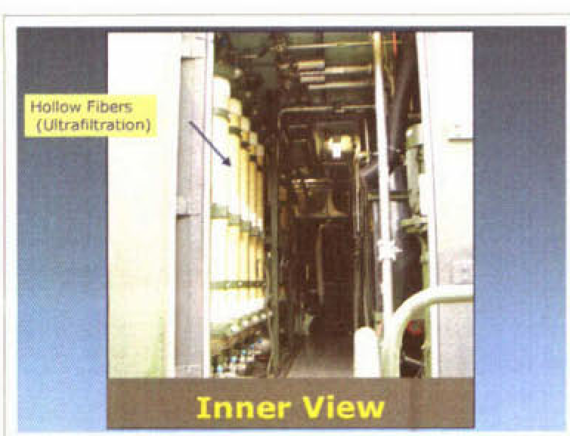

Conclusion
MBR technology was shown to be able to achieve enhanced elimination of different trace organics in comparison to conventional activated sludge treatment
Results justify the needs of long-term investigations when assessing biological processes
MBR technology does not provide any stand-alone solution when extensive or complete removal is required
KOMPETENZZENTRUM Wasser Berlin

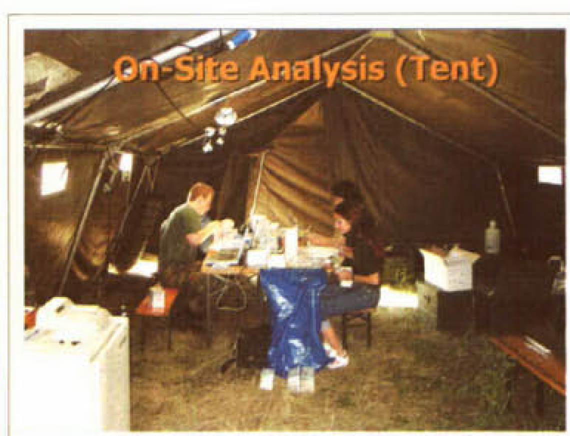

Removal of drug residues from contaminated surface waters or municipal sewage applying membrane filtration („worst-case studies")


location of the field trial in September 2001

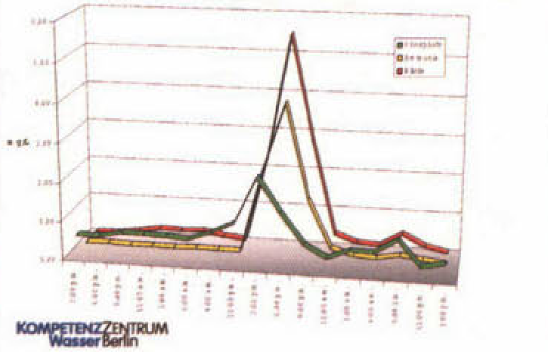

Mobile Drinking Water Purification „Prototype" Unit
Technologies: Membrane filtration with pre-filtration (100 µm), UF (0,2 µm) and RO
Operation: Ultrafiltration, RO: Single- or Double-Pass-Operation
Capacity: 10 m³/hr in UF mode, 5 m³/hr with Single-Pass Mode or 3,5 m³/hr in Double-pass Mode
KOMPETENZZENTRUM Wasser Berlin


Flow Scheme
Raw Water (20.000L/h)
Slit Filtration 100µm
Ultra Filtration 0.01 µm
Reverse Osmosis (RO)
3.500 – 10.000 Liters per hour


Hollow Fibers (Ultrafiltration)
Inner View


On-Site Analysis (Tent)

Raw Water (Sewage Effluents)



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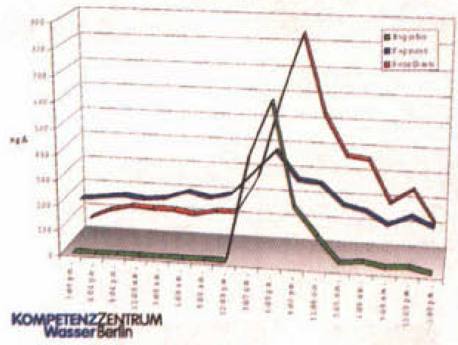
Raw Water (Sewage Effluents)



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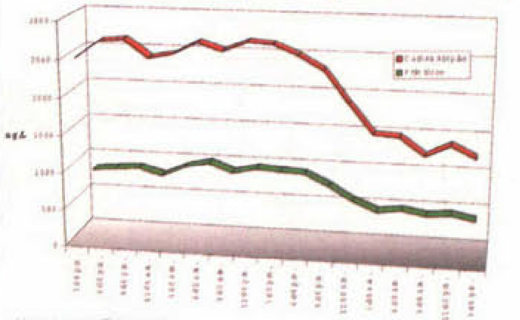
Raw Water (Sewage Effluents)



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Removal of Organic Contaminants

(in double pass mode)

Average concentrations for different persistent organics in sewage and drinking water and the corresponding removal rates during ultrafiltration (UF) and reverse osmosis (RO).

	Raw water	Removal %			Permeate
Parameter	ng/L	UF	RO 1	RO 2	ng/L
AMDOPH	810	32	99.9	99.9	< 1
Carbamazepine	2280	13	99.9	99.9	< 1
Clofibric acid	175	20	99.4	99.4	< 1
Diclofenac	870	44	99.9	99.9	< 1
Naproxen	220	0	98.2	99.5	< 1
Primidone	730	0	99.9	99.9	< 1
Propyphenazone	295	46	99.3	99.7	< 1
Mecoprop	70	0	98.6	98.6	< 1
TCEP	850	34	98.5	99.4	5

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Conclusions

- Reliable continuous operation (over 48 hours)
- Bacteria were already effectively removed by the microfiltration device
- All organics and some inorganic compounds such as nitrate, nitrite, and ammonia were almost totally removed by the system
- Borate and detergents have only partially but sufficiently been removed
- The generated drinking water meets all requirements set by the drinking water regulations (EU, US EPA, STANAG)

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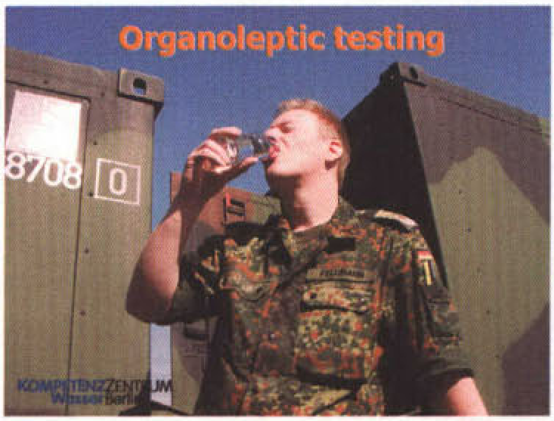

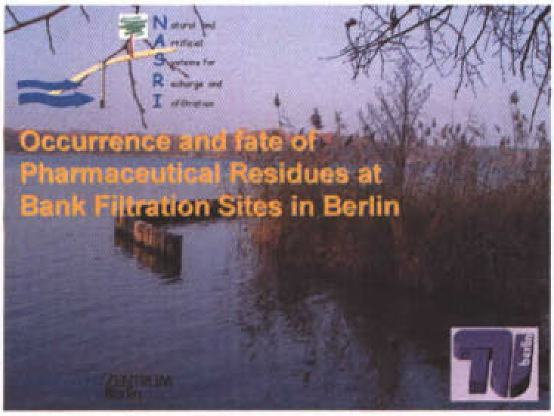

Transect Lake Wannsee

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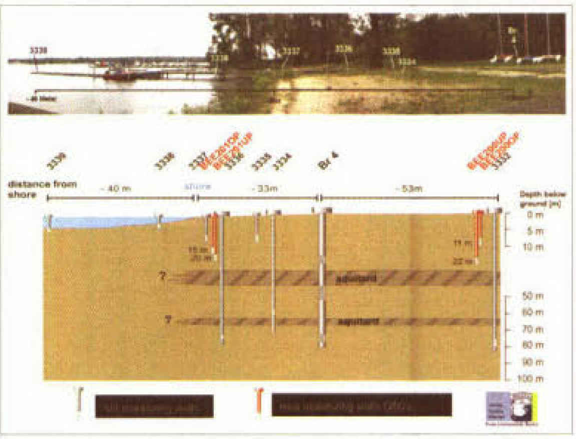

PhACs found at transect "Lake Wannsee"

between May and October 2002 (n=6) (mean concentrations in ng/L)

Transect Wannsee May-Oct.2002	Surface water	shallow monitoring wells				water supply wells		
		3339	3338	3337	3335	Well5	Well4	Well3
Diclofenac	26	29	28	15	18	6	<5	8
Clofibric acid	61	23	22	15	5	121	113	95
Propyphenazone	147	86	100	73	54	104	28	158
AMDOPH	169	116	149	180	175	580	182	332
Carbamazepine	329	217	365	323	362	25	17	68
Primidone	61	68	62	50	58	35	9	42
Indometacine	17	<5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Bezafibrate	65	9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

AMDOPH 1-Acetyl-1-methyl-2-dimethyl-oxamyl-2-phenylhydrazide
BLR Blood lipid regulator
n.d. not detected

KOMPETENZZENTRUM Wasser Berlin

Antibiotic residues at Transect "Lake Wannsee"

Results, September 2001
[ND: not detected; detection level 1 ng/L; data are reported in ng/L]

Compound	Lake	Shallow wells				Deep wells			Water-supply well
		3339	3338	3337	3335	3336	3334	3332	
Clarithromycin	1	1	2	ND	ND	ND	ND	ND	ND
Clindamycin	14	11	23	7	ND	ND	ND	ND	ND
Erythromycin	31	5	15	6	1	ND	ND	ND	ND
Roxithromycin	8	1	5	ND	ND	ND	ND	ND	ND
Sulfadimidine	ND	3	3	2	3	ND	ND	ND	ND
Sulfamethoxazole	106	ND	17	25	17	ND	ND	ND	ND
Trimethoprim	7	ND	ND	ND	ND	ND	ND	ND	ND

Not detected: Amoxicillin, Ampicillin, Azithromycin, Benzylpenicillin, Chlortetracycline, Ciprofloxacin, Cloxacillin, Dicloxacillin, Doxycycline, Flucloxacillin, Methicillin, Mezlocillin, Nafcillin, Ofloxacin, Oxacillin, Oxytetracycline, Phenoxymethylpenicillin, Piperacillin, Spiramycin, Tetracycline, Tylosin, Vancomycin

Analyses carried out at the Institute for Hygiene, University of Bonn (Dr. H. Färber)

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Other organic compounds found at transect "Lake Wannsee"

between May and October 2002 (n=6) (mean concentrations in ng/L)

transect Wannsee May-Oct. 2002		surface water	shallow monitoring wells				water supply wells		
			3339	3338	3337	3335	Well5	Well4	Well3
pesticides									
Bentazone	herbicide	21	22	29	34	20	11	9	14
Mecoprop	herbicide	14	14	18	12	20	10	8	13
p,p'-DDA	DDT-metabolite	19	22	26	21	11	15	10	19
o,p'-DDA	DDT-metabolite	7	7	7	8	<5	<5	<5	<5
industrial chemicals									
NPS	metabolite	19	22	27	24	15	103	56	114
TCEP	flame retardant	314	299	256	496	399	72	95	208
TCIPP	flame retardant	2173	1130	1799	1344	1147	294	192	392

DDT Dichloro diphenyl trichloroethane
DDA Bis(4-chlorophenyl)-acetic acid
NPS N-(Phenylsulfonyl)-sarcosine
TCEP Tris(2-chloroethyl)-phosphate
TCIPP Tris(2-chloroisopropyl)-phosphate

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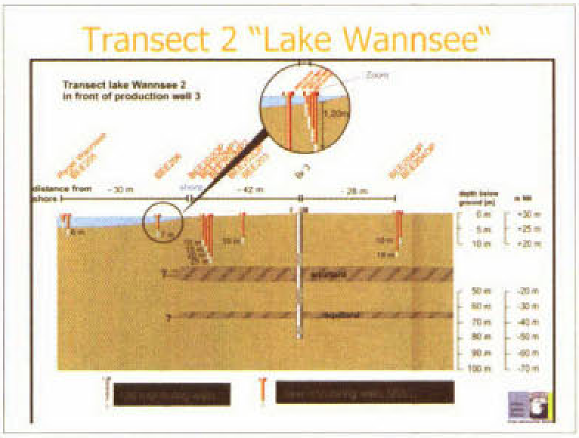

Results for selected PhACs found at transect "Lake Wannsee 2"

January 2003 (concentrations in ng/L)

Transect Wannsee Januar 2003	Surface water	BEE 205	BEE 206	BEE 207 OP	BEE 207 MP1	BEE 207 UP	BEE 202 OP	BEE 202 MP1	BEE 202 MP2	BEE 202 UP	BEE 203	Well 3	BEE 204 UP	BEE 204 OP
Diclofenac	35	30	5	65	65	75	ND	5	15	20	ND	30	ND	ND
Clofibric acid	35	35	20	35	35	30	ND	ND	55	70	ND	60	10	ND
Propyphenazone	115	55	25	85	60	50	25	45	345	480	10	185	25	ND
AMDOPH	205	140	135	135	130	145	145	190	750	1720	175	470	30	ND
Carbamazepine	280	245	170	195	195	190	350	250	45	ND	210	110	10	ND
Primidone	30	80	50	65	65	60	90	100	125	200	100	75	ND	ND

AMDOPH 1-Acetyl-1-methyl-2-dimethyl-oxamyl-2-phenylhydrazide
ND not detected

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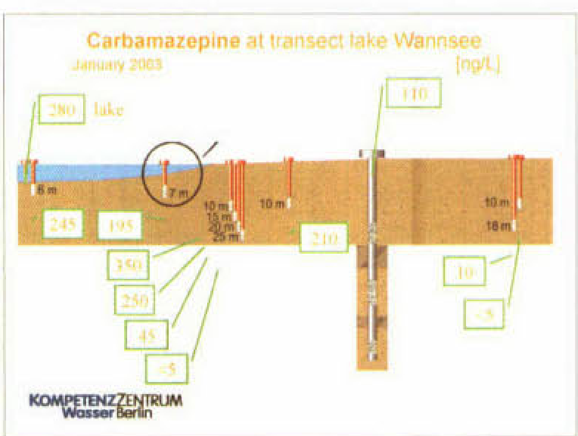
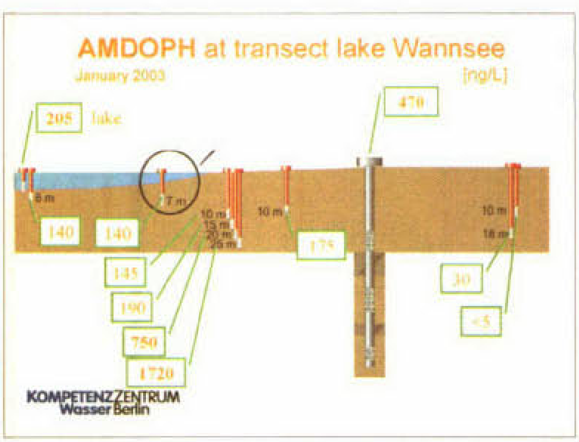
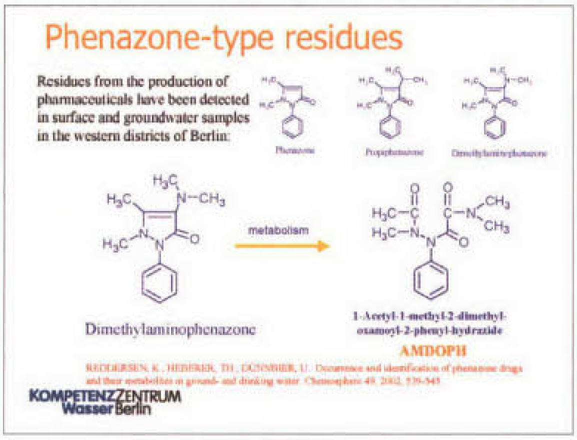
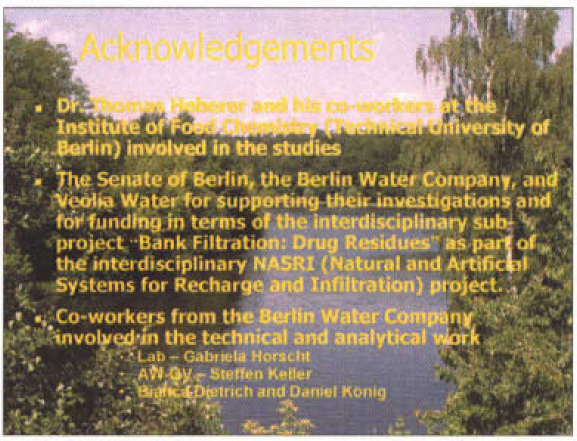





Phenazone-type residues
Residues from the production of pharmaceuticals have been detected in surface and groundwater samples in the western districts of Berlin:
metabolism
Dimethylaminophenazone
1-Acetyl-1-methyl-2-dimethyl-oxamoyl-2-phenyl-hydrazide
AMDOPH
KOMPETENZZENTRUM Wasser Berlin

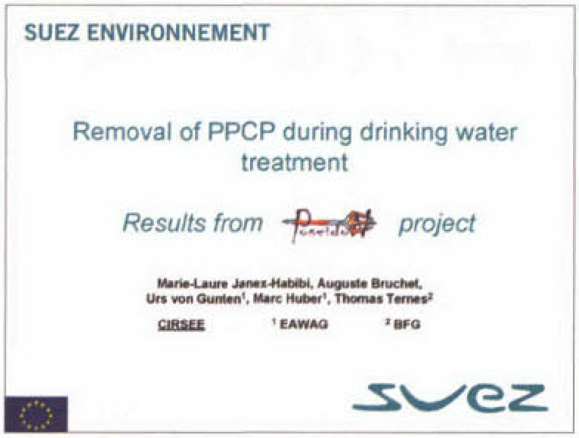

Current results
• Several polar organic compounds, especially several PhACs, are relevant to bank-filtration pre-treatment near urban areas.
• Some PhACs such as bezafibrate, diclofenac, indomethacine, estrogenic steroids or antibiotics seem to be efficiently removed during bank filtration!
• However, other polar compounds, e.g. five PhACs and a few other organic contaminants, are not completely removed and appear in drinking water supply wells.
KOMPETENZZENTRUM Wasser Berlin

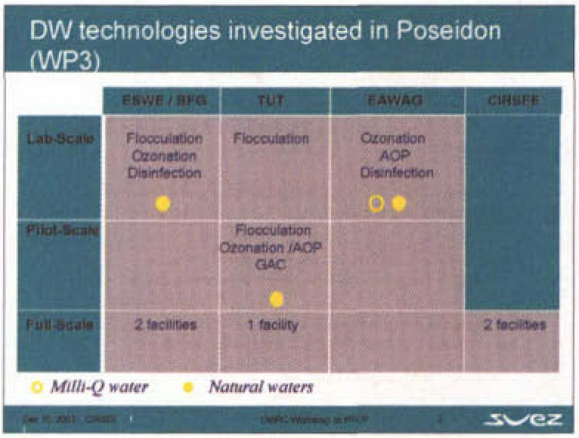

Acknowledgements
▪ Dr. Thomas Heberer and his co-workers at the Institute of Food Chemistry (Technical University of Berlin) involved in the studies
▪ The Senate of Berlin, the Berlin Water Company, and Veolia Water for supporting their investigations and for funding in terms of the interdisciplinary sub-project "Bank Filtration: Drug Residues" as part of the interdisciplinary NASRI (Natural and Artificial Systems for Recharge and Infiltration) project.
▪ Co-workers from the Berlin Water Company involved in the technical and analytical work
• Lab – Gabriela Horscht
• Bianca Dietrich and Daniel Konig

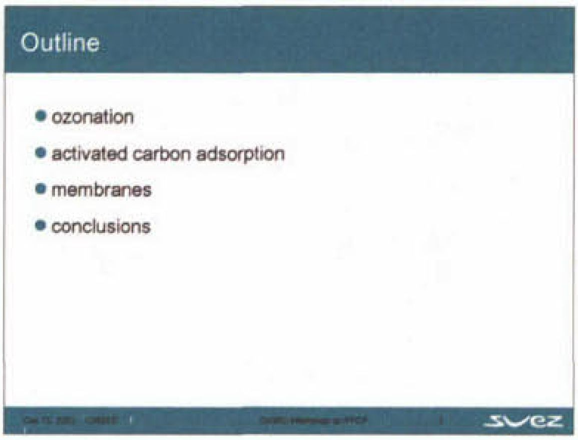

Acknowledgements
▪ Senate Department of Urban Development, Environmental Protection and Technology for providing surface water samples and some additional information
▪ German Ministry of Defense for logistical help and funding
▪ German Research Foundation (DFG) for funding

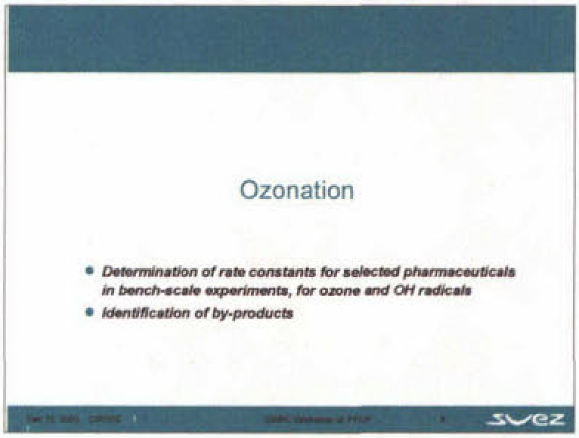
REMOVAL DURING DRINKING WATER TREATMENT/RESULTS OF POSEIDON PROJECT BY CIRSEE

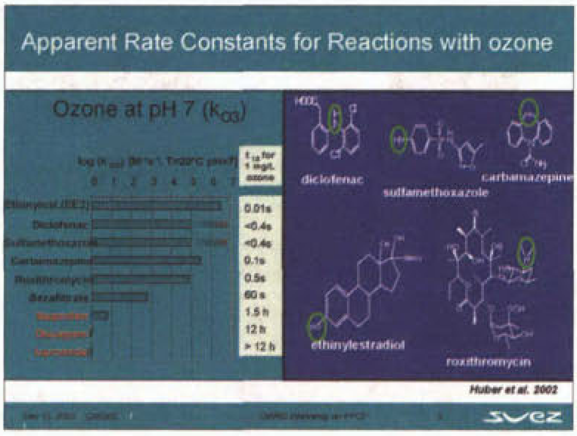
(MARIE-LAURE JANEX-HABIBI)

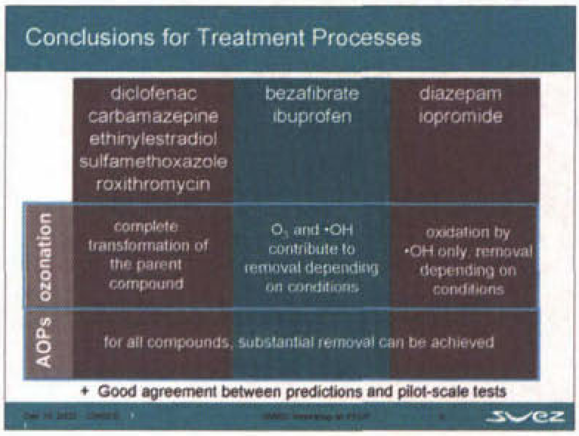


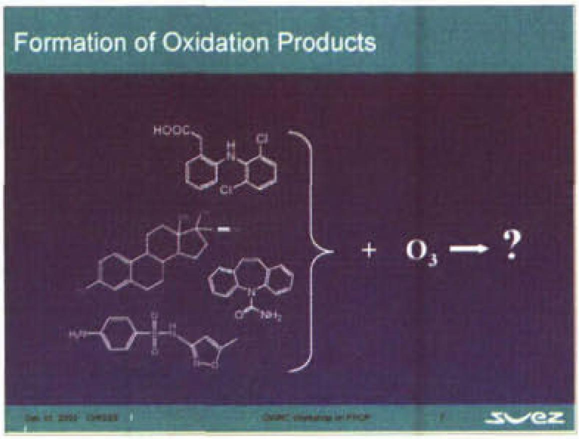


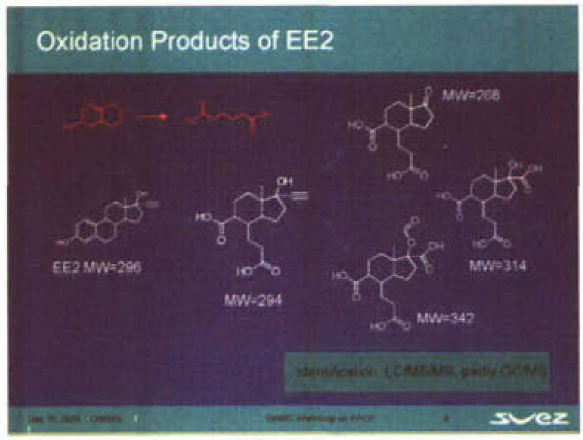


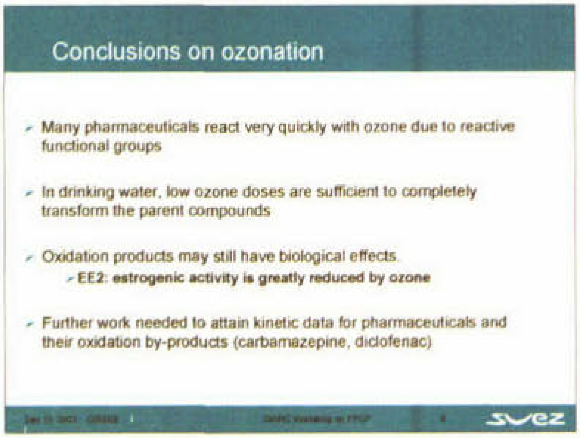


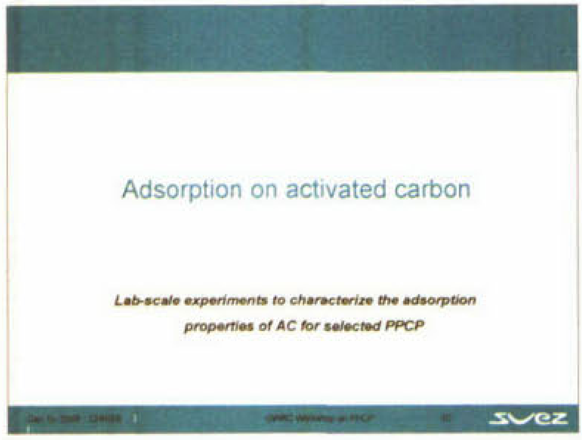


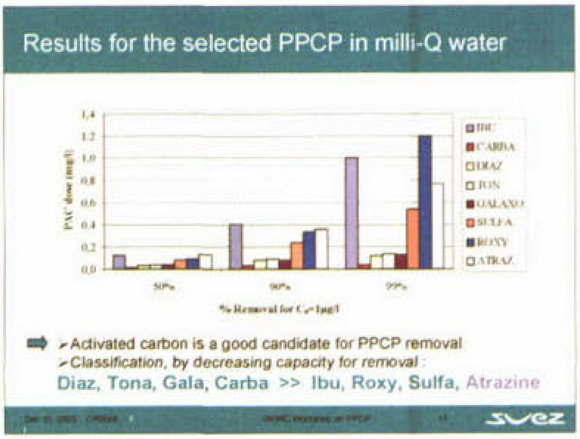


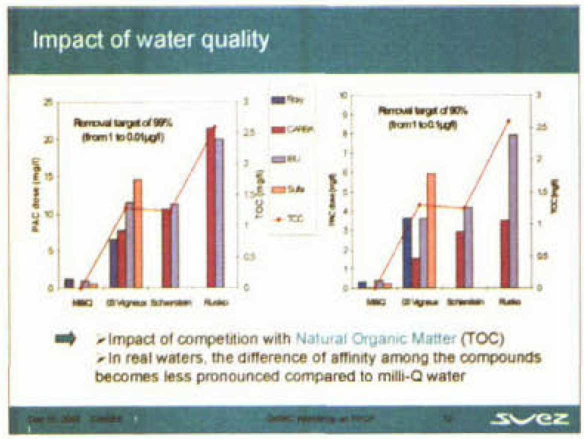

Formation of Oxidation Products
HOOC
Cl
Cl
+ O3 → ?

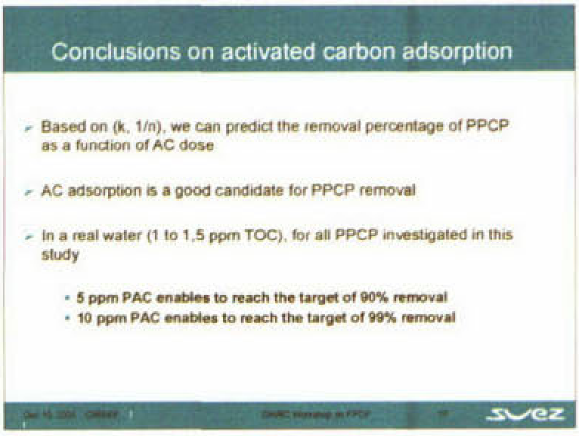

Oxidation Products of EE2
MW=268
EE2 MW=296
MW=294
MW=314
MW=342
Identification: LC/MS/MS, partly GC/MS

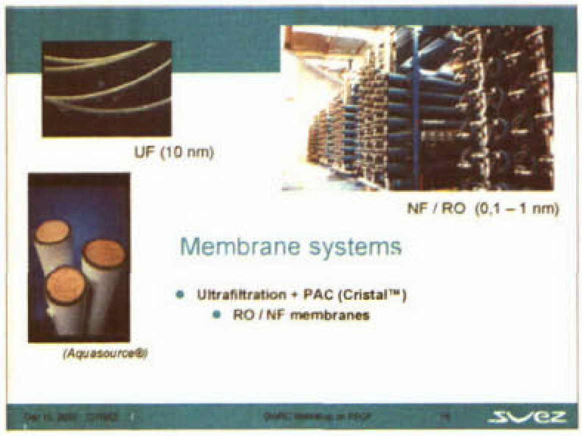

Conclusions on ozonation
Many pharmaceuticals react very quickly with ozone due to reactive functional groups
In drinking water, low ozone doses are sufficient to completely transform the parent compounds
Oxidation products may still have biological effects.
EE2: estrogenic activity is greatly reduced by ozone
Further work needed to attain kinetic data for pharmaceuticals and their oxidation by-products (carbamazepine, diclofenac)


Adsorption on activated carbon
Lab-scale experiments to characterize the adsorption properties of AC for selected PPCP

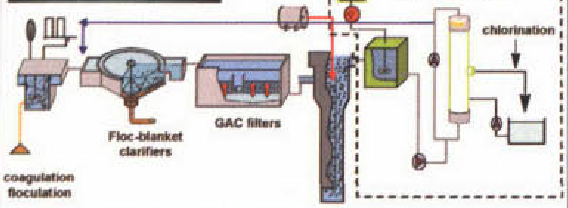

Results for the selected PPCP in milli-Q water
PAC dose (mg/l)
IBU
CARBA
DIAZ
TON
GALAXO
SULFA
ROXY
ATRAZ
50%
90%
99%
Activated carbon is a good candidate for PPCP removal
Classification, by decreasing capacity for removal :
Diaz, Tona, Gala, Carba >> Ibu, Roxy, Sulfa, Atrazine


Impact of water quality
Removal target of 99% (from 1 to 0.01µg/l)
Removal target of 90% (from 1 to 0.1µg/l)
PAC dose (mg/l)
TOC (mg/l)
Roxy
CARBA
IBU
Sulfa
TOC
MilliQ
St Vigneux
Scheinstein
Rudio
Impact of competition with Natural Organic Matter (TOC)
In real waters, the difference of affinity among the compounds becomes less pronounced compared to milli-Q water

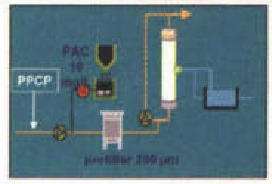

Conclusions on activated carbon adsorption
Based on (k, 1/n), we can predict the removal percentage of PPCP as a function of AC dose
AC adsorption is a good candidate for PPCP removal
In a real water (1 to 1,5 ppm TOC), for all PPCP investigated in this study
5 ppm PAC enables to reach the target of 90% removal
10 ppm PAC enables to reach the target of 99% removal


UF (10 nm)
NF / RO (0,1 – 1 nm)
Membrane systems
Ultrafiltration + PAC (Cristal™)
RO / NF membranes
(Aquasource®)

Vigneux-sur-Seine (55 000 m³/d)



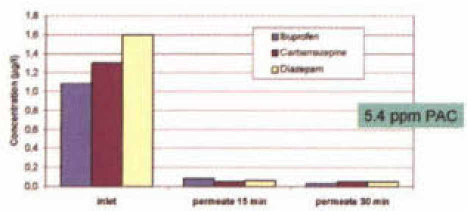
Cristal™ Process at pilot-scale



Tap water spiked with PPCP (a few µg/l)

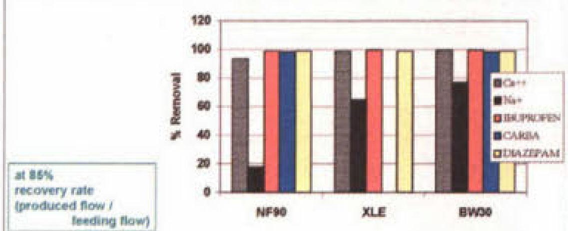
UF pilot

Results of UF / PAC experiments



➡ > 95% removal with 5 ppm PAC
for ibuprofen, carbamazepine, diazepam
(other PPCP not tested yet)

Removal of 3 PPCP by 3 different NF/ RO membranes



➡ > 98% removal (outlet < quantification limit, ie. 0,02 to 0,05 µg/L)
for ibuprofen, carbamazepine, diazepam
(other PPCP not tested yet)

Conclusions on PPCP removal by membranes

Decreasing cut-off →

Parameters	MF	UF	NF	RO
Turbidity	X	X		
Bacteria and cysts (*Giardia, Cryptosporidium*...)	X	X		
Virus		X		
Color		X-PAC	X	X
Organic matter and disinfection by-products		X-PAC	X	
Micropollutants (pesticides, taste+odor, PPCP)		X-PAC	X	X
Hardness			X	X
Sulfates			X	X
Monovalent ions (fluorine, nitrates,...)				X

Drinking Water Technology : conclusions

- Ozonation is a powerful technique to oxidize PPCPs in water treatment. Ozonation products were identified.
- Adsorption on activated carbon is very efficient to remove most PPCPs. All carbons are not equivalent. NOM lowers the adsorption capacity for PPCPs, with a higher impact for neutral than for acidic compounds.
- Nanofiltration, reverse osmosis, or ultrafiltration combined with activated carbon are very appropriate to remove PPCP

Treatment processes are available to avoid a drinking water contamination with PPCPs even at the low ng/L-level

Outlook

- A typical treatment line for **surface water** in Europe should prevent from a PPCP contamination of the drinking water (multi-barrier treatment)
- **Groundwaters** appear as more sensitive : their contamination must be avoided (Water Framework Directive)
- The ICM (iodinated contrast media) could be the exception, with poor adsorption to AC and poor sensitivity to ozone
- Knowing the fate of PPCP through drinking water treatment lines contributes to the risk approach recommended in WHO draft guidelines : identifying and controlling the critical points from the source to the end-product

SUEZ ENVIRONNEMENT

Acknowledgements to the European Commission for support of Poseidon project

suez

Consumption of selected pharmaceuticals in France and analytical method used

Type of drug	Compound	Amount (tons) in France (1998)	Analytical Method
Antiepileptics	Carbamazepine	37,8	GC/MS
Antiphlogistics	Diclofenac	15,2	GC/MS
	Ibuprofen	166,6	GC/MS
Antibiotics	Sulfamethoxazole	23,3	LC/MS/MS
	Roxithromycine	9,5	LC/MS/MS
Tranquilizer	Diazepam	0,4	GC/MS
Contrast Agent	Iopromide	73,4	LC/MS/MS
Musks	Tonalide	-	GC/MS
	Galaxolide	-	GC/MS

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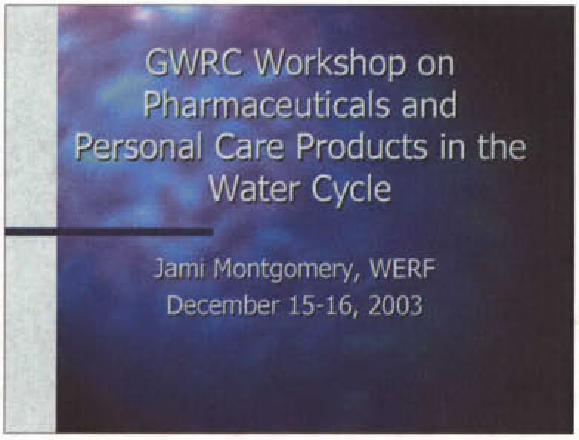
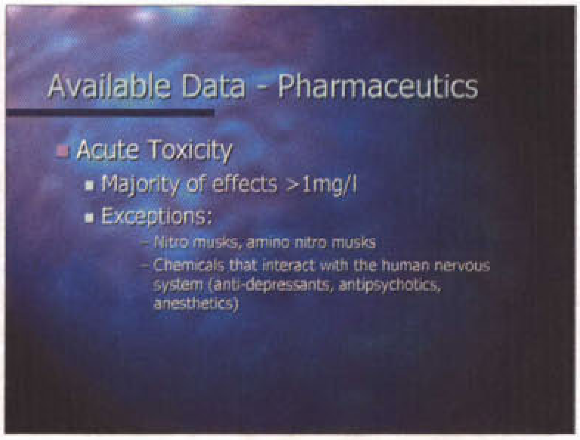
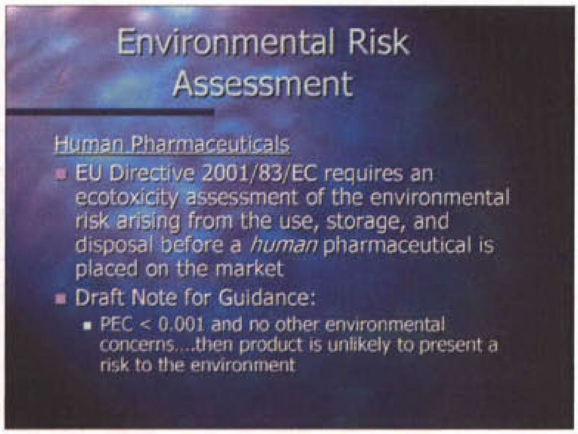
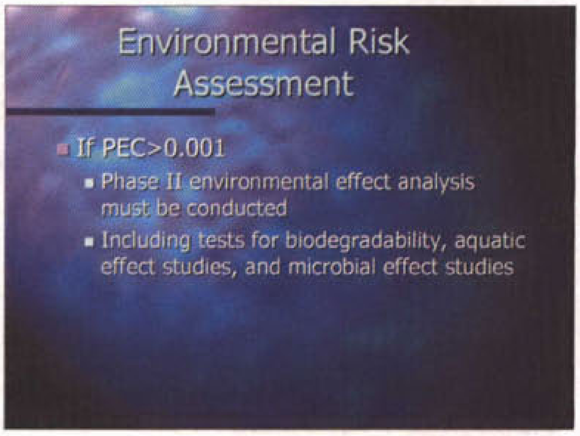
ECOTOXICITY BY WERF

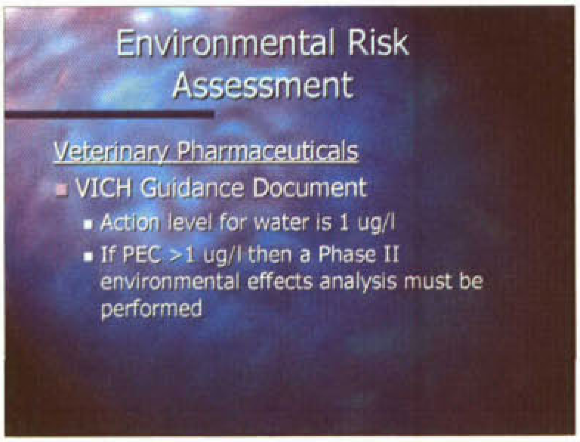
(JAMI MONTGOMERY)

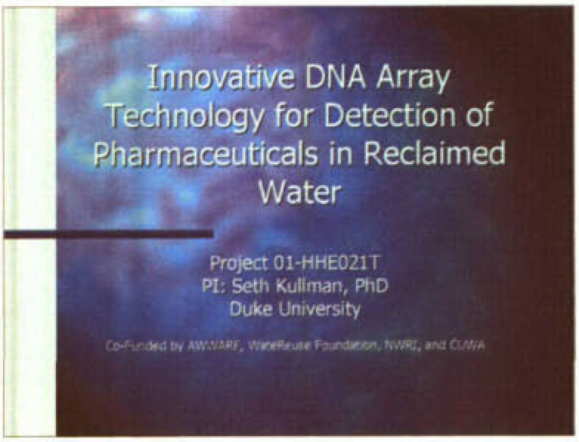




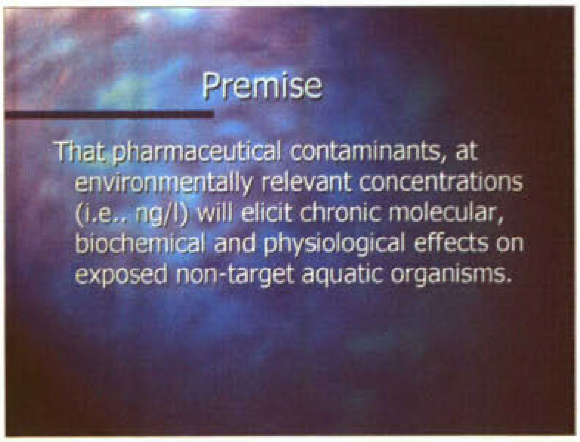


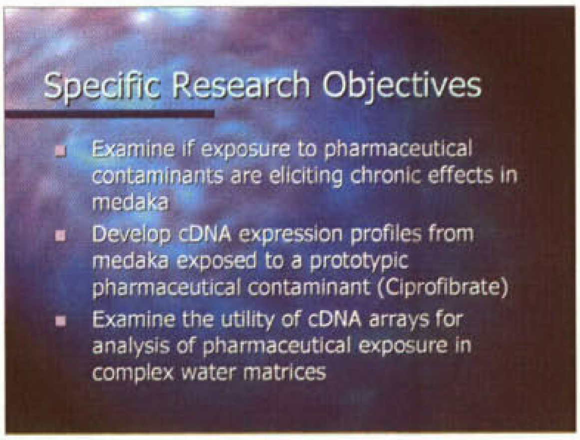


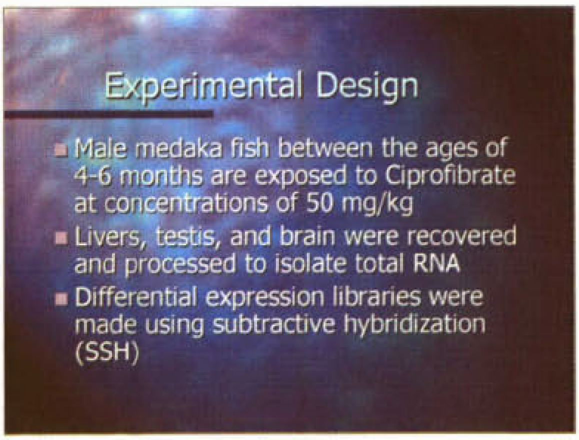

Environmental Risk Assessment
Veterinary Pharmaceuticals
VICH Guidance Document
Action level for water is 1 ug/l
If PEC >1 ug/l then a Phase II environmental effects analysis must be performed

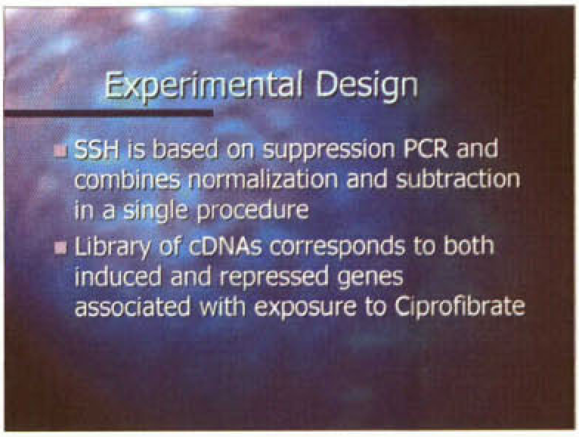

Innovative DNA Array Technology for Detection of Pharmaceuticals in Reclaimed Water
Project 01-HHE021T
PI: Seth Kullman, PhD
Duke University
Co-Funded by AWWARF, WateReuse Foundation, NWRI, and CUWA

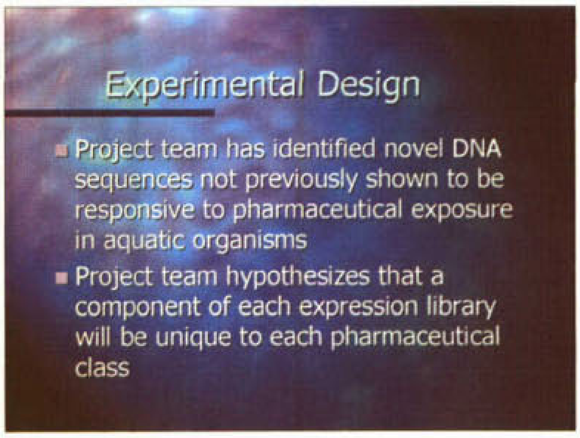

Project Goal
To use pharmaceutical-induced gene expression and repression as means to develop a DNA-array to assess exposure and effect on aquatic organisms


Premise
That pharmaceutical contaminants, at environmentally relevant concentrations (i.e., ng/l) will elicit chronic molecular, biochemical and physiological effects on exposed non-target aquatic organisms.

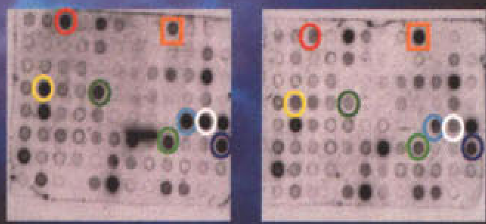

Specific Research Objectives
Examine if exposure to pharmaceutical contaminants are eliciting chronic effects in medaka
Develop cDNA expression profiles from medaka exposed to a prototypic pharmaceutical contaminant (Ciprofibrate)
Examine the utility of cDNA arrays for analysis of pharmaceutical exposure in complex water matrices


Experimental Design
Male medaka fish between the ages of 4-6 months are exposed to Ciprofibrate at concentrations of 50 mg/kg
Livers, testis, and brain were recovered and processed to isolate total RNA
Differential expression libraries were made using subtractive hybridization (SSH)


Experimental Design
SSH is based on suppression PCR and combines normalization and subtraction in a single procedure
Library of cDNAs corresponds to both induced and repressed genes associated with exposure to Ciprofibrate


Experimental Design
Project team has identified novel DNA sequences not previously shown to be responsive to pharmaceutical exposure in aquatic organisms
Project team hypothesizes that a component of each expression library will be unique to each pharmaceutical class

Typical Result



Results to Date

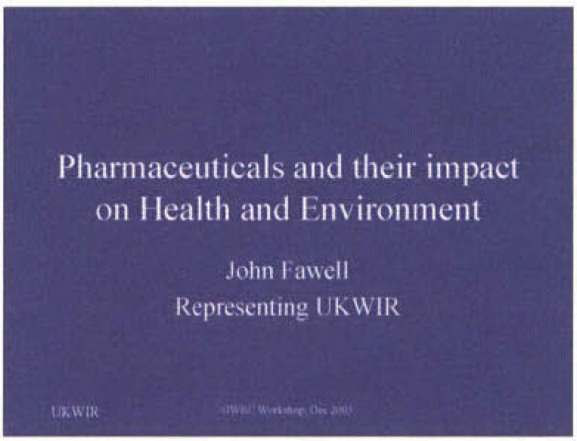
- Ciprofibrate regulates the expression of a number of genes involved in the metabolism and transport of lipids, glucose homeostasis, amino acid metabolism, cell proliferation and differentiation, and apoptosis
- Gene response in the liver also included immune and inflammation response

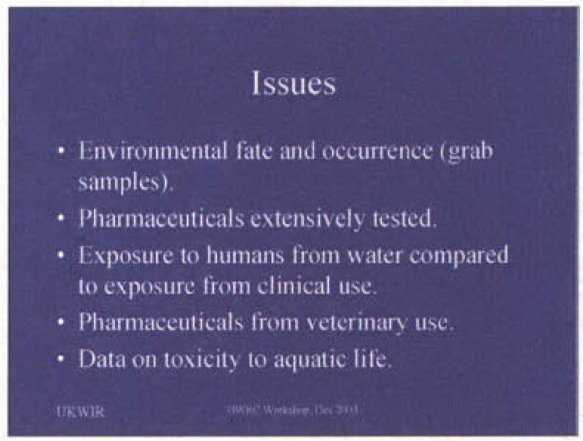
Next Phase

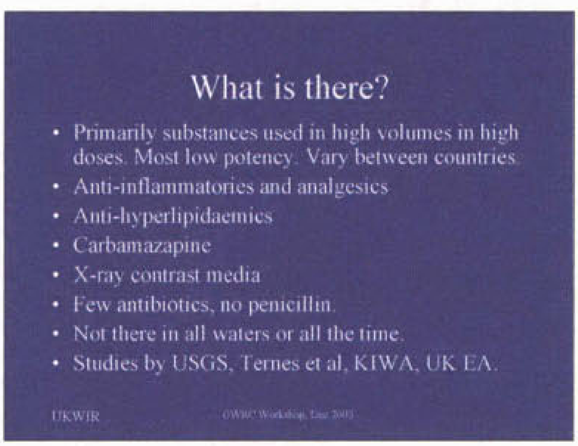
- Use the gene set to establish a macroarray that will be used to characterize differentially expressed cDNAs and gene expression profiles as markers of pharmaceutical exposure
- Project team will then use this method to assess pharmaceutical exposure in reclaimed water and the wastewater treatment process

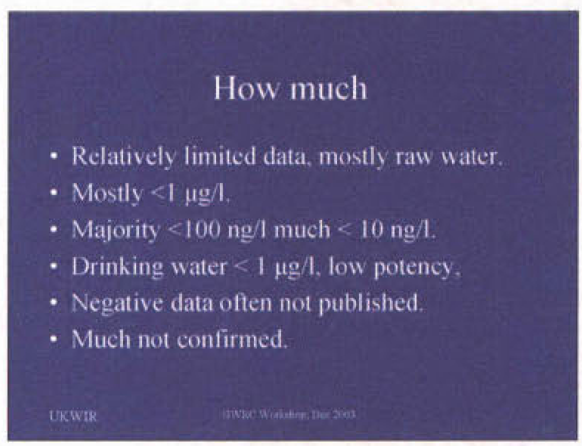
HUMAN TOXICOLOGY BY UKWIR

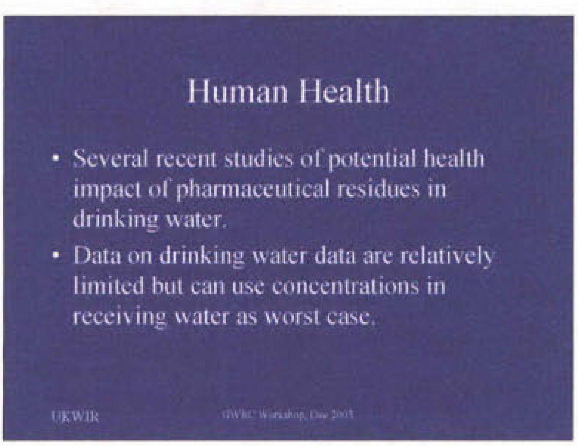
(JOHN FAWELL)

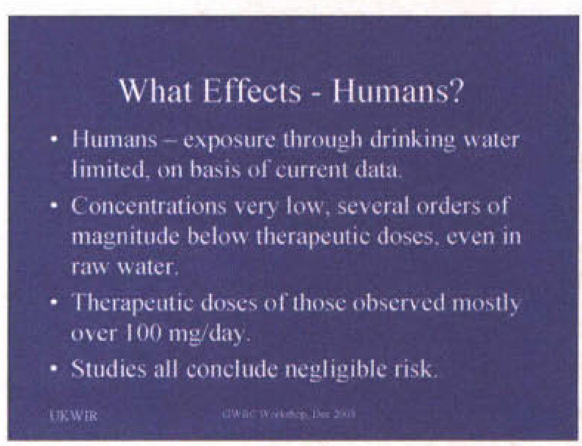


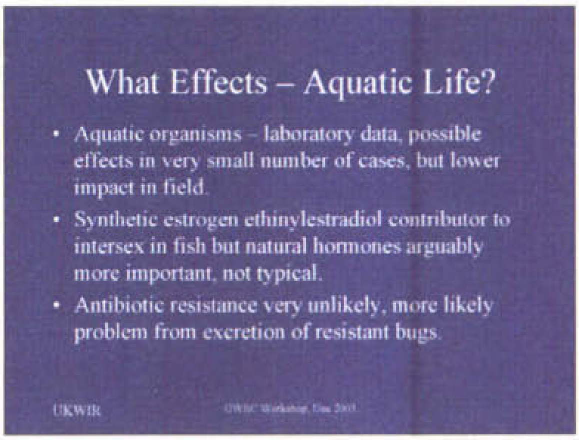











What Effects – Aquatic Life?
• Aquatic organisms – laboratory data, possible effects in very small number of cases, but lower impact in field.
• Synthetic estrogen ethinylestradiol contributor to intersex in fish but natural hormones arguably more important, not typical.
• Antibiotic resistance very unlikely, more likely problem from excretion of resistant bugs.
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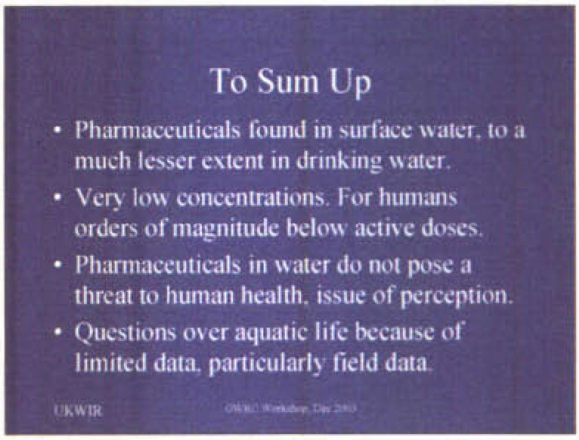
To Sum Up
• Pharmaceuticals found in surface water, to a much lesser extent in drinking water.
• Very low concentrations. For humans orders of magnitude below active doses.
• Pharmaceuticals in water do not pose a threat to human health, issue of perception.
• Questions over aquatic life because of limited data, particularly field data.
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