

# Sampling and Analysis of Emerging Contaminants in the Aquatic Environment: Current and Future Challenges

What are the next generation of emerging compounds?

Cytotoxic drugs in sewage effluents?

Neville Llewellyn

Centre for Ecology and Hydrology - Lancaster  
ceh.ac.uk

# •What are cytotoxic drugs?

- The presence of human pharmaceuticals in the environment is not a new issue (Tabak and Bunch, 1970, US & Aherne and Briggs, 1989 Europe).

- 80s and 90s saw explosion in number of papers addressing the presence, fate and behaviour of pharmaceuticals (Halling-Sorensen et al., 1998; Daughton and Ternes, 1999).

- But.....not so much work on the risks to humans and wildlife either for acute or chronic exposure by single compounds or mixtures.

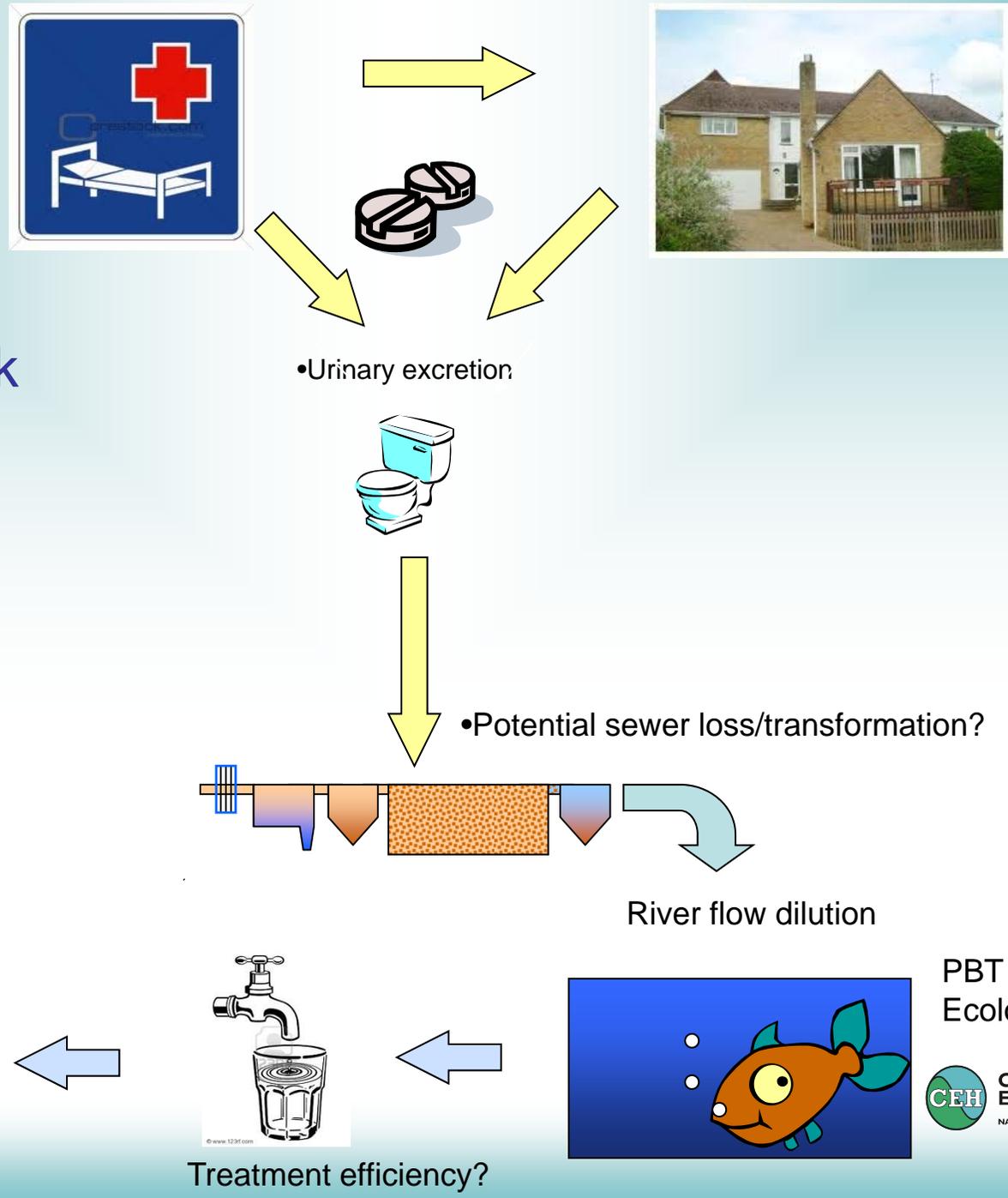
- We can't look at all compounds – better to focus on the most toxic compounds –  
AntiCancer drugs

- AntiCancer drugs. Cytostatic (no DNA interaction) and cytotoxic which interact with DNA and lead to cell death. Reported to exert teratogenic, genotoxic, mutagenic effects. Practically all eukaryotic organisms are vulnerable to damage.

# Common compounds

Drug	Log Kow	Usage (2008, Kg, France)	Fraction released through excretion and WWTP
Hydroxycarbamide	-1.68	6838	0.5
Capectiabine	0.56	5134	0.03
5FU	-0.89	1733	0.2
Cyclophosphamide	0.63	305	>0.25
Ifosfamide	0.86	103	0.5
Methotrexate	-1.28	74	0.90
Carboplatin	-0.46	83	0.3 - 1.0
Usage generally increasing by 10% per year			
Besse et al Env Int 39, (2012), 73-86			
Since 1995 drugs licensed by European Medical Agency			

# The route to the aquatic environment/ ecological and human and risk



Risk to the developing foetus???



Treatment efficiency?

PBT scoring?  
Ecological Risk?

# PHARMAS

Ecological and human health risk assessments of antibiotics  
and anti-cancer drugs found in the environment.



PHARMAS | PHARMA CLUSTER | IDENTIFICATION

ABOUT PHARMAS

THE ISSUE

the issue

POLICY EFFORTS

DOWNLOAD

NEWS

LINKS

CONTACT

## Public information

### Pharmaceuticals in the environment: what are their effects?

This page aims to explain in simple terms some facts about human pharmaceuticals in the environment and in drinking water. Pharmaceuticals are substances that can be found in prescription medicines and over-the-counter therapeutic drugs: high blood pressure medicine, pain relief tablets, cough syrup, eardrops, contraceptive pill, vaccines, the list goes on...

Despite our limited current understanding of this emerging environmental issue, the scientific community tends to agree that **we should already explore ways of limiting the input of PPs into the environment, thus anticipating action needed in the near future.**

# CEH Work with cytotoxics

## Abstract

Journal of Chromatography A

In Press, Accepted Manuscript - Note to users



doi:10.1016/j.chroma.2011.09.061 | [How to Cite or Link Using DOI](#)

[Permissions & Reprints](#)

## Determination of Cyclophosphamide and Ifosfamide in sewage effluent by stable isotope-dilution liquid chromatography-tandem mass spectrometry

N. Llewellyn<sup>a</sup>, , , P. Lloyd<sup>b</sup>, M.D. Jürgens<sup>c</sup>, A.C. Johnson<sup>c</sup>

<sup>a</sup> Centre for Ecology and Hydrology-Lancaster, Lancaster Environment Centre, Library Avenue, Bailrigg, Lancaster, Lancashire, LA1 4AP, United Kingdom

<sup>b</sup> Wallingford Hydrosolutions, Maclean building, Crowmarsh Gifford, Wallingford, Oxfordshire, OX10 8BB, United Kingdom

<sup>c</sup> Centre for Ecology and Hydrology-Wallingford, Maclean building, Crowmarsh Gifford, Wallingford, Oxfordshire, OX10 8BB, United Kingdom

Received 1 March 2011; revised 20 September 2011; Accepted 22 September 2011. Available online 28 September 2011.

### Abstract

A reliable and specific method was developed for the determination of the cytotoxic drugs cyclophosphamide and ifosfamide in sewage effluent. The most successful combination was found to be Strata-X solid-phase extraction followed by Florisil<sup>®</sup> clean-up with analysis by liquid chromatography-tandem mass spectrometry. Quantification by internal standardisation was achieved using custom synthesised d4-cyclophosphamide. The mass spectrometer was operated in highly selective reaction monitoring (HSRM) mode, which significantly reduced matrix noise and improved sensitivity. Although it suffered from some ionisation suppression, electrospray ionisation (ESI) was found to give an order of magnitude better sensitivity in terms of limit of detection than atmospheric pressure chemical ionisation (APCI).

Using final effluent from two different sewage treatment plants, the method was validated following official European guidelines and shown to be a high performance tool for routine analysis at the sub-nanogram per litre level. Depending on the matrix, the limit of detection for cyclophosphamide was between 0.03–0.12 ng/L and for ifosfamide between 0.05 - 0.09 ng/L. For cyclophosphamide the accuracy and precision, tested at 1.7 ng/L, were 98-109% and  $\leq$  13% CV respectively. For ifosfamide the accuracy and precision, tested at 1.1 ng/L, were 98-113% and  $\leq$  15% CV respectively. Depending on the sample matrix the absolute recovery of the internal standard was between 57 and 70%.

# Sewage Works data



The impact of a chemical pollutant will be modified by the amount of dilution available



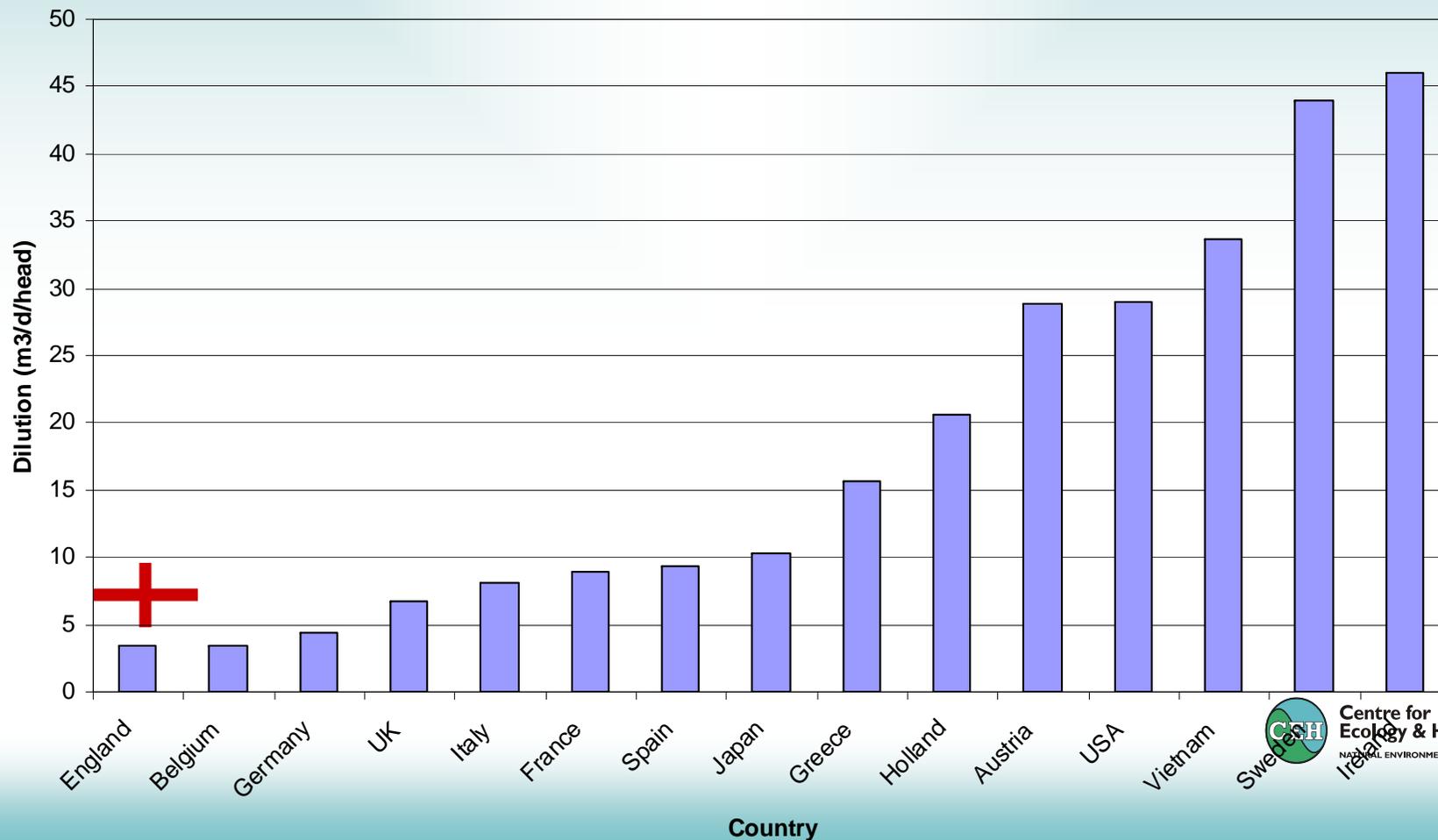
•Waste products



•How much water do we have in the UK have to dilute our daily waste?

# Calculating the amount of natural flow available per person at a national scale

Dilution available per head per day •(Calculated from mean annual runoff)





"This project received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n. 265264"



- Project
- Partners
- News and Events
- Scientific publications
- Dissemination
- Links
- PHARMA CLUSTER



Search...

### Project Menu

- > Summary
- > [Objectives](#)
- > Work Programme
- > Results and impacts

### Login Form

User Name

Password

Remember Me

- [Forgot your password?](#)
- [Forgot your username?](#)

### Objectives



- 1.To develop new analytical methods for assessment of the occurrence and fate of cytostatic pharmaceuticals, their metabolites and transformation products in water treatment systems and in the environment.
- 2.To explore potential delayed and irreversible effects of cytostatic pharmaceuticals at environmentally relevant concentrations in aquatic experimental models, and compare the data to those obtained in human experimental models.
- 3.To explore combined effects of mixtures of cytostatic pharmaceuticals, their excreted metabolites and transformation products formed in the environment and/or waste water treatment.
- 4.To develop, based on the obtained results, guidance on how to improve the environmental and human risk assessment of cytostatics released into the environment.



Designed by [Net Kreczja](#) Valid [XHTML](#) and [CSS](#)

- The study, carried out at the Centre for Ecology and Hydrology in Wallingford, Oxfordshire, examined the risks posed by chemotherapy drugs that escape into the environment through sewage.
- The researchers estimated that an adult drinking more than three pints of water a day would receive a weekly dose of between 300 and 30,000 times lower than recommended safety levels.
- They warn that a developing foetus would also be exposed to the drugs in the womb.
- Andrew Johnson, the scientist who led the Wallingford study, said: "In the foetus, which is rapidly growing and comparatively tiny, the dose would be relatively higher and any damage to its cells could be far more serious.
- "There is not evidence to show that drinking water treatment removes all these drugs, so while we are not wanting to alarm people, it would be foolish to assume there is no risk."

What are cytotoxics?

Common compounds

Route to the environment – Ecological and human risks

EU Studies

CEH Work