Environmental Side Effects of Medication

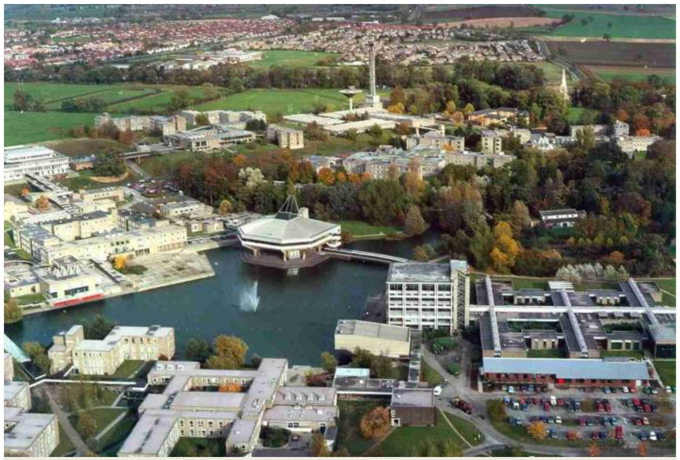
Alistair B A Boxall
Environment Department

Location

- North East of England
- 1 Hour 40 minutes to London – (high – speed train)
- Close to International Airports
    - Leeds/Bradford
    - Manchester International
    - London

A Campus University

University Campus



"There are few universities that can combine beautiful views, historic buildings and high quality education. But York does!"

Fei Fei Cao (China) York Student


Environment


The City of York and Yorkshire

"York has a unique blend of small-town and cosmopolitan atmospheres, giving it the feeling of a cosy, bustling town."

Shannon Dennison (USA), York Student

A jewel in England's crown

195,000 inhabitants

A city rich in history and culture

Social and cultural activities

Good transport link to nearby cities

Highly accessible to the rest of the UK, Europe and rest of world

Environmental Side Effects of Medication

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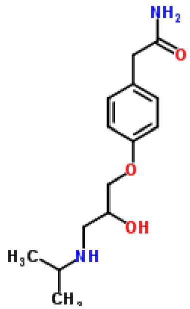
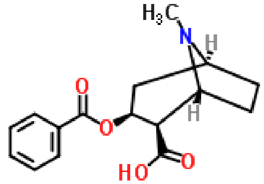
Environment Department

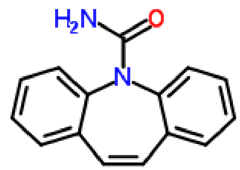

CVS
BIOGLAN
Sleep Well
RAHUA
NUXE
M
LAB.
Aesop.
PerioWash
Complete Oral Care
Cool Mint
DailyCare
fresh


5

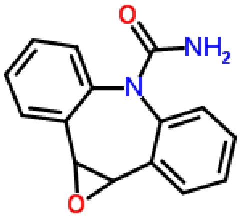


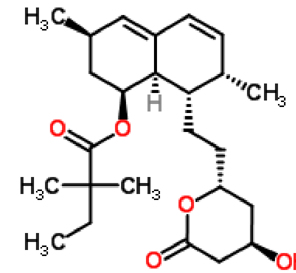
benzoylecgonine





carbamazepine epoxide

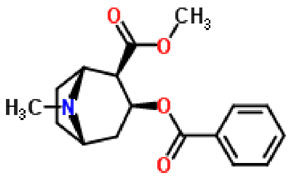


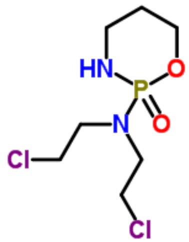


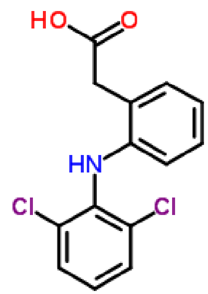
simvastatin

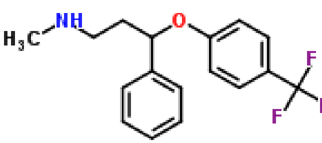
carbamazepine

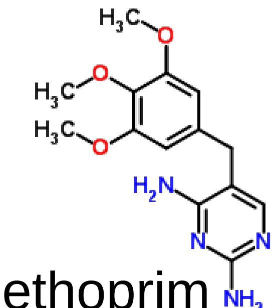
atenolol











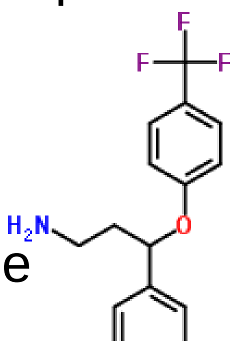
trimethoprim

fluoxetine

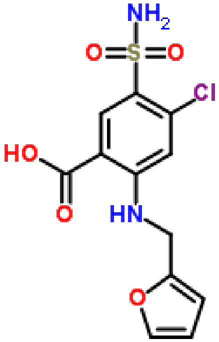
cocaine

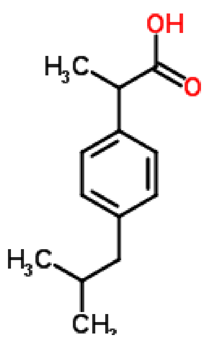
cyclophosphamide

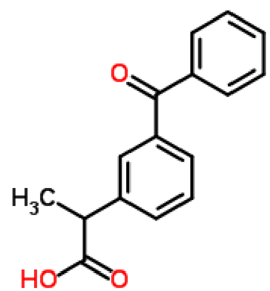
diclofenac

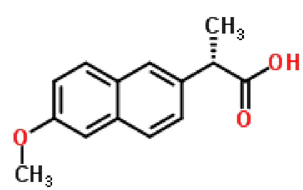


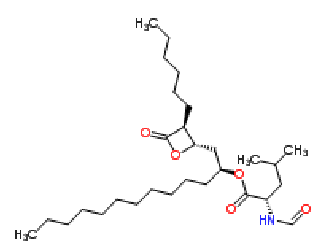
norfluoxetine











furosemide

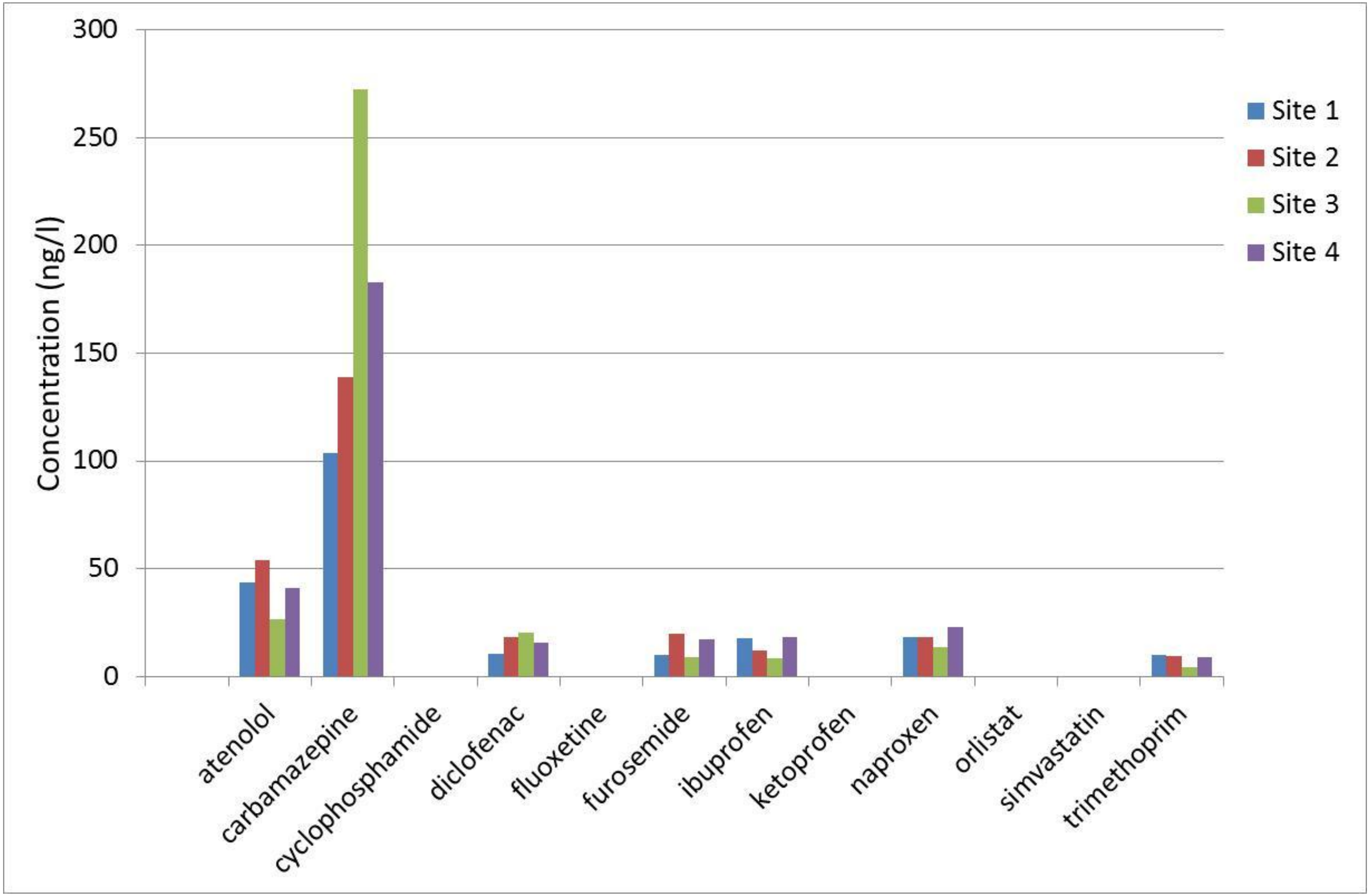
ibuprofen

ketoprofen

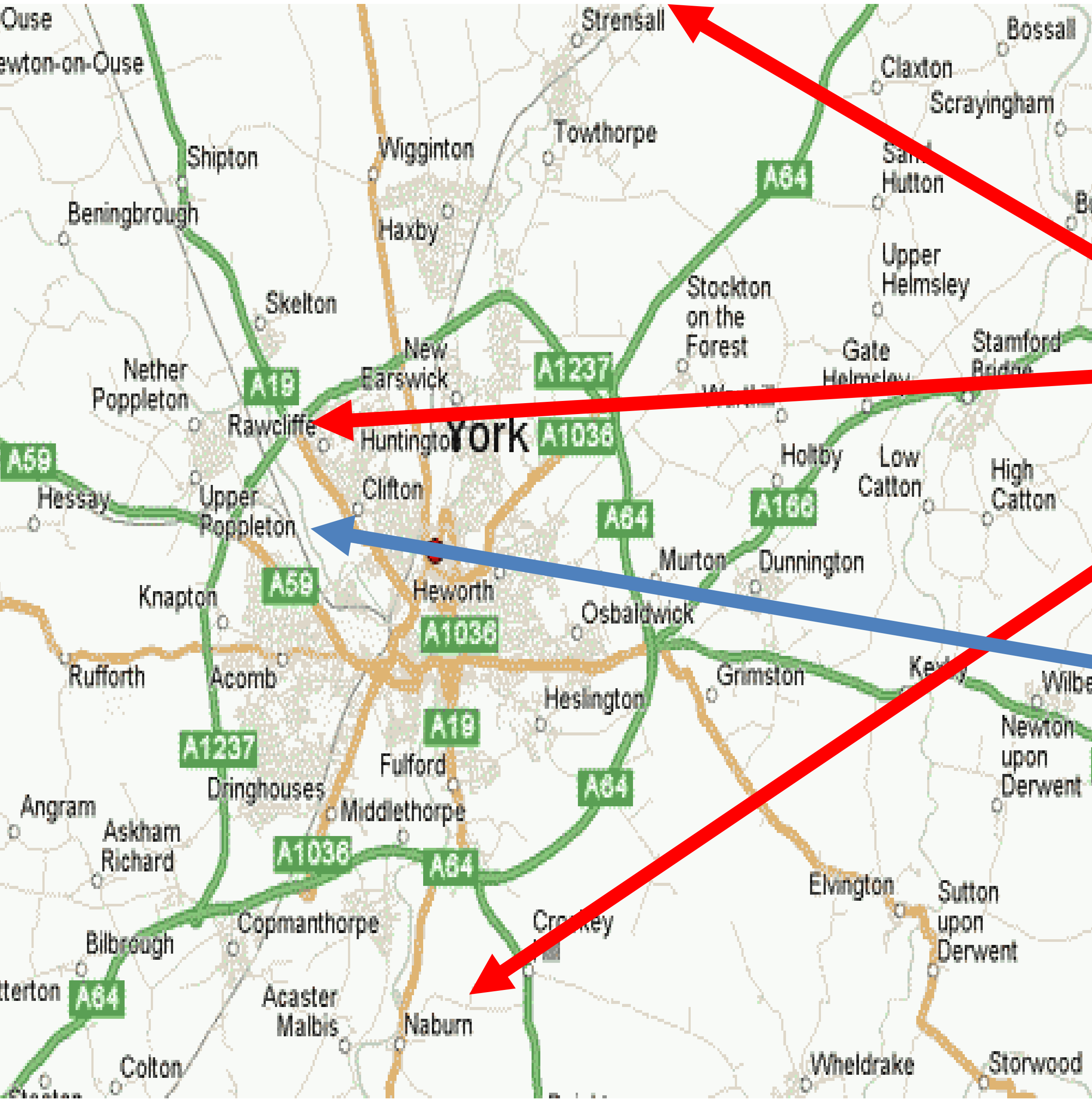
naproxen

orlistat

Occurrence in UK rivers



Situation in York



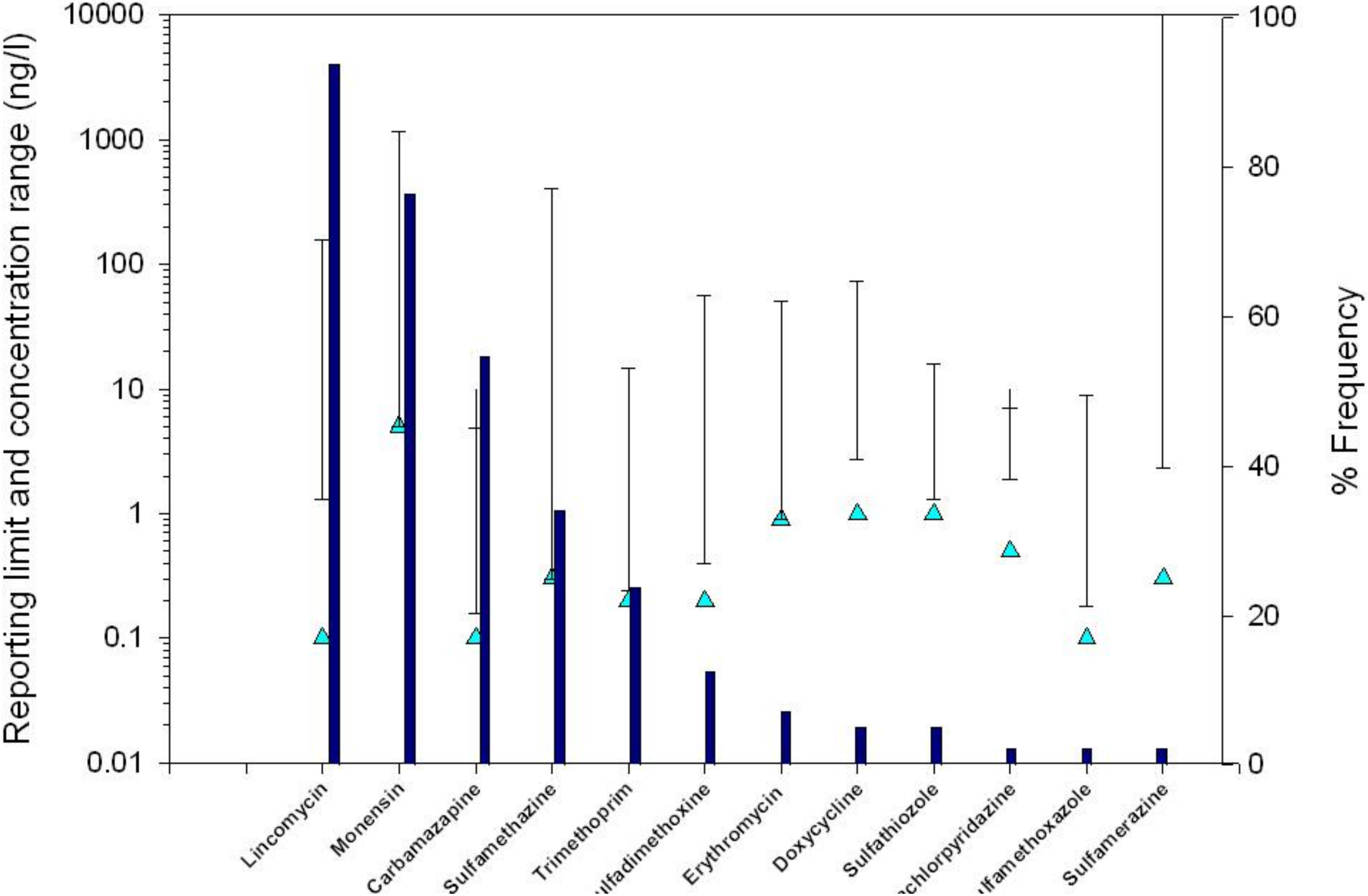
- STPs
  - Walbutts
  - Rawcliffe
  - Naburn
- Drinking water

Monitoring results

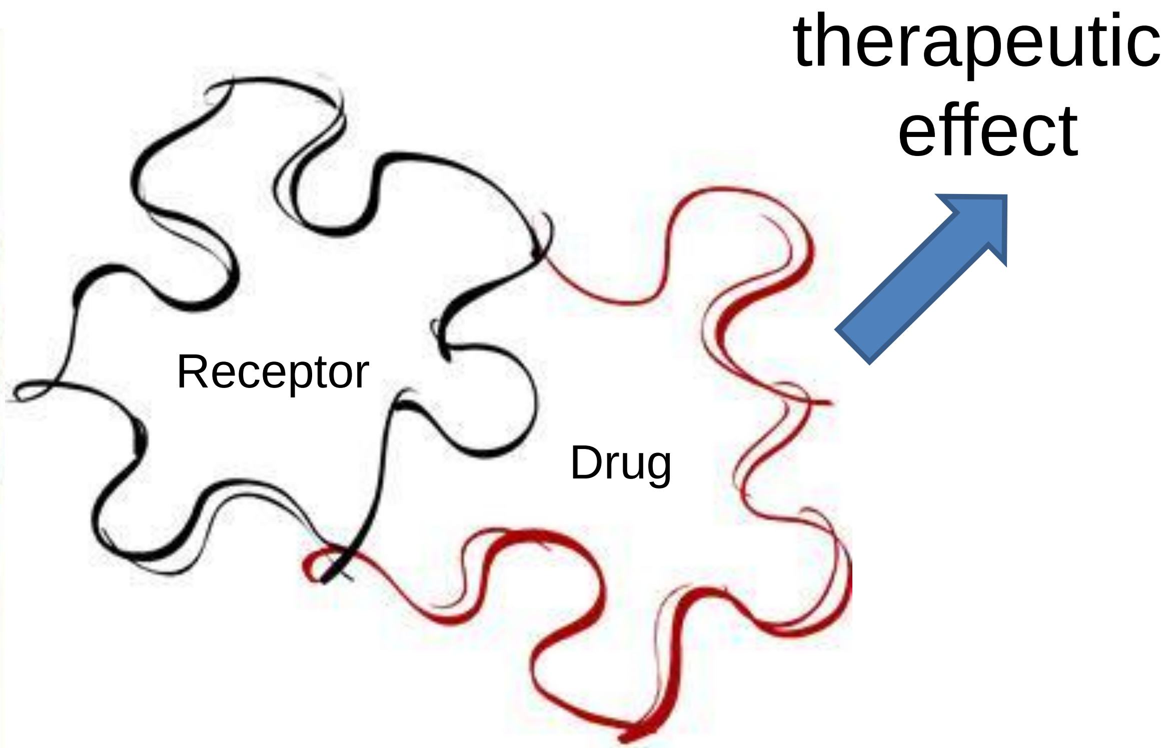
- River waters
  - 36 pharmaceuticals detected and quantifiable
  - 26 pharmaceuticals detected
  - 26 pharmaceuticals not detected
- Drinking water
  - 6 pharmaceuticals detected: metformin, nicotine, acetominophen, carbamazepine, cotinine, triamterene

A significant contributor to pharmaceutical use - around 290 tonnes of antibiotics are used in veterinary medicine each year in the UK

Agricultural Surface Waters (n=97)



Drug receptors



Many receptors also occur in organisms in the natural environment

Effects on behaviour

Rebecca Klaper, Great Lakes Water Institute

Fathead minnow -

Lifecycle exposure

to Fluoxetine

100 ng/L

Behavioural change – males sitting under tiles, not pursuing females. Time spent on breeding behaviours was very low.

‘Nine species of vultures in the wild numbered 40 million birds in the early 1980s. Today, only about 60,000 birds are left’

(Vibhu Prakash, Bombay Natural History Society)

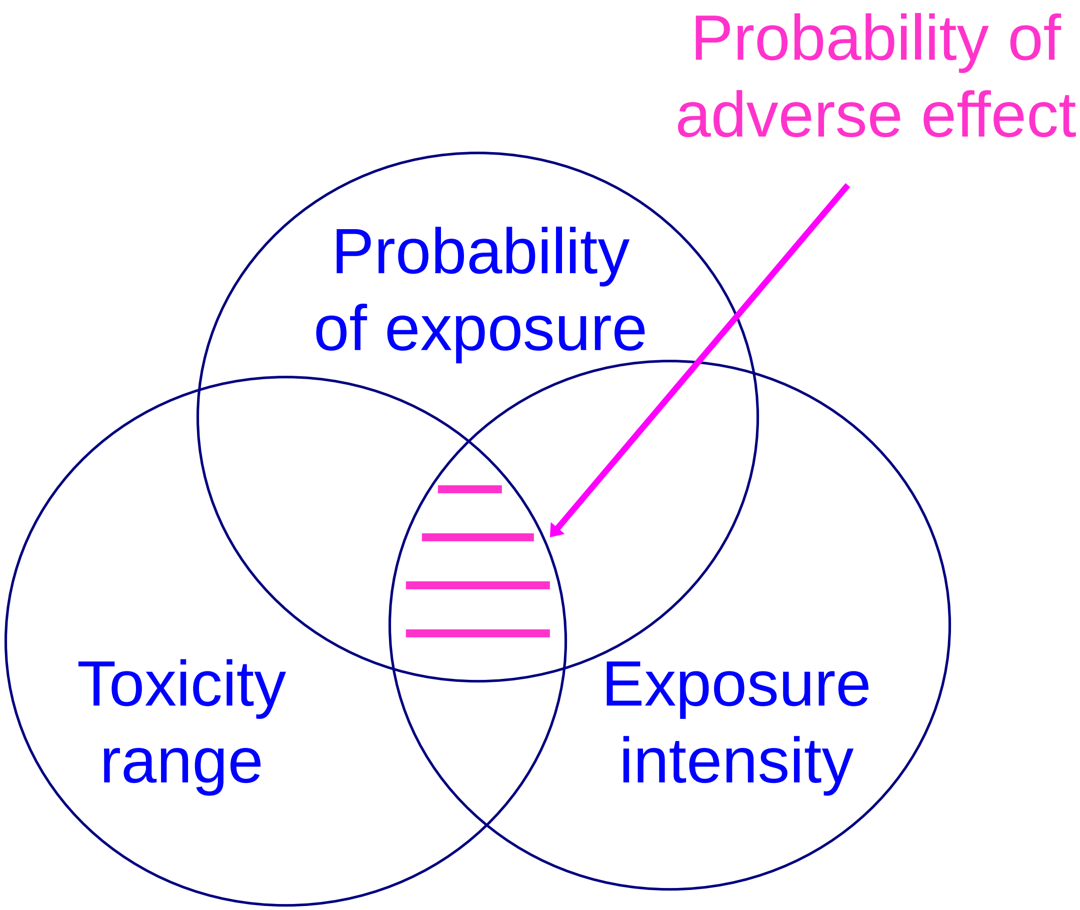
Effects on Aquatic Organisms

Impacts on reproduction, histology, growth, behaviour, histology…

Klaus Steifel

What are the risks?

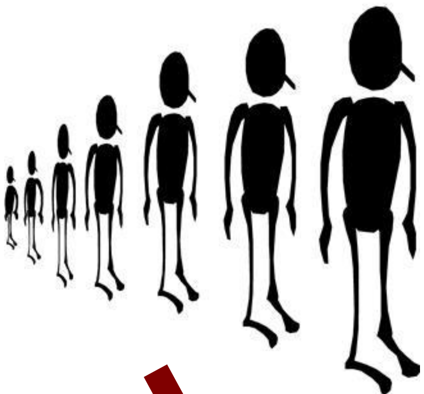
- Human pharmaceuticals across England and Wales
- Mixtures of veterinary antibiotics



Assessment of risks across the UK landscape

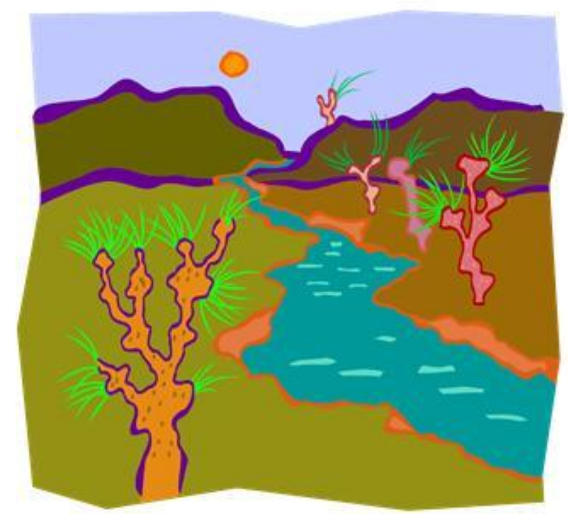
- 22 large catchments across England and Wales
- Serving a population of 21 M people
- Exposure predictions obtained for 3117 river reaches
- Predictions compared to predicted no effect concentrations (and proposed quality standards) derived from available ecotoxicity data

Exposure modelling



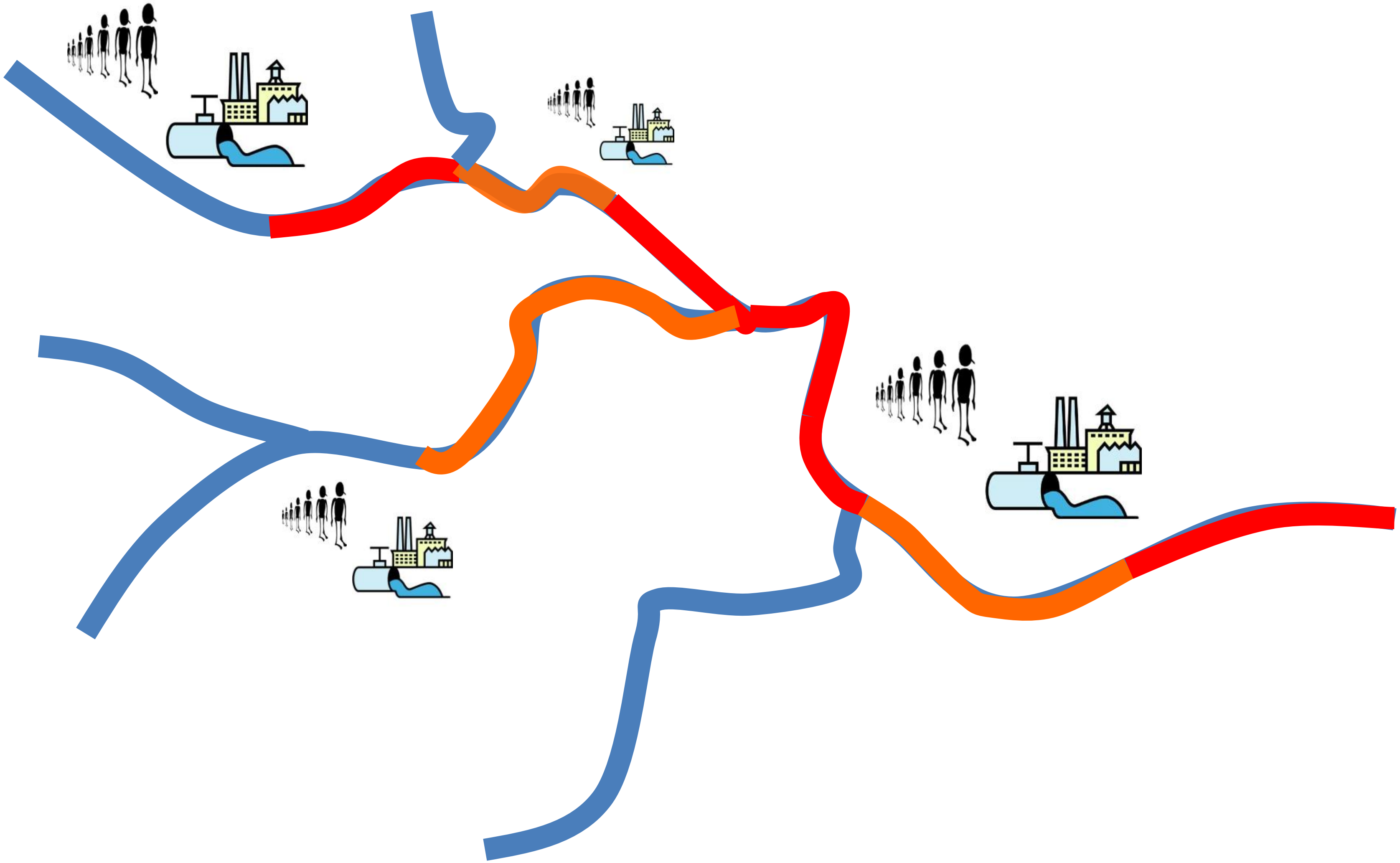
Removal: fraction removed
Wastewater flow: $m^3\ d^{-1}$

River flow: $m^3\ d^{-1}$
In-river dissipation rates: d^{-1}

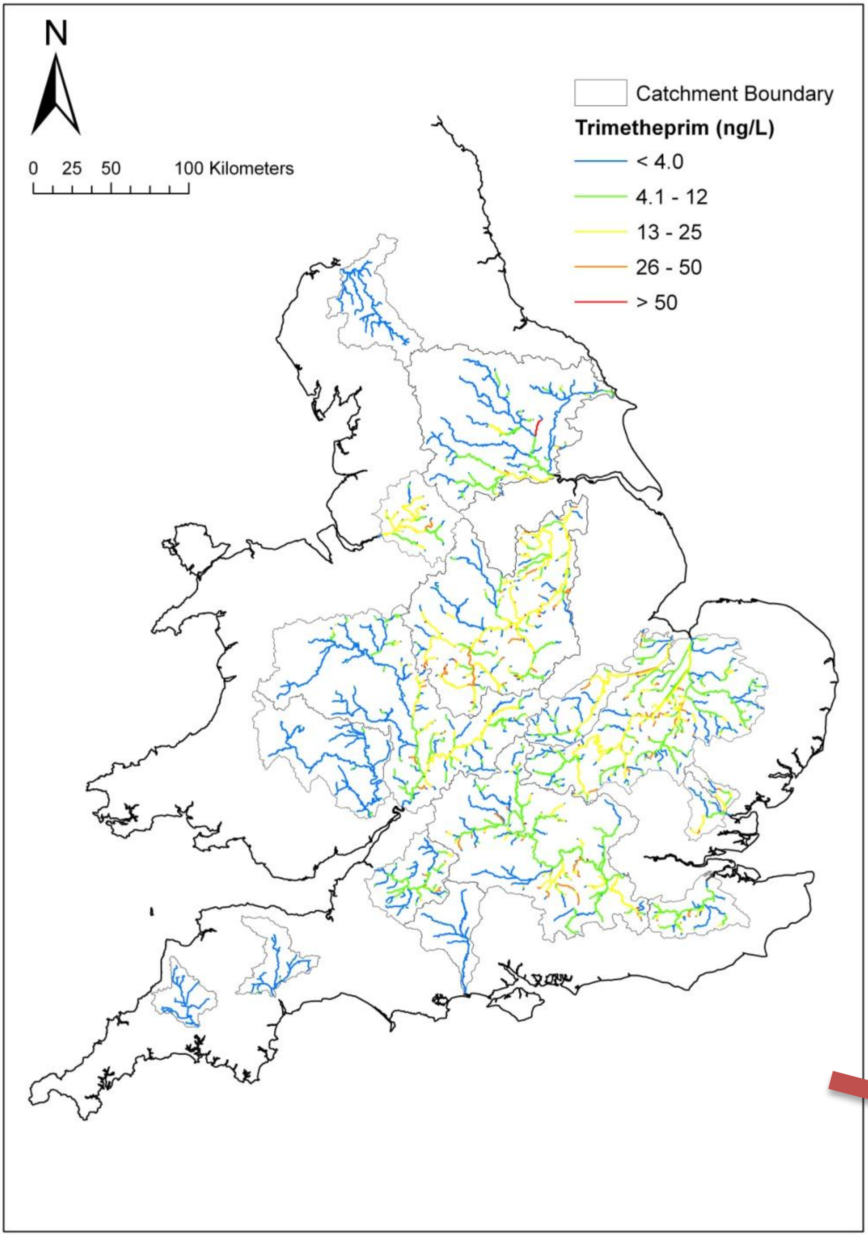


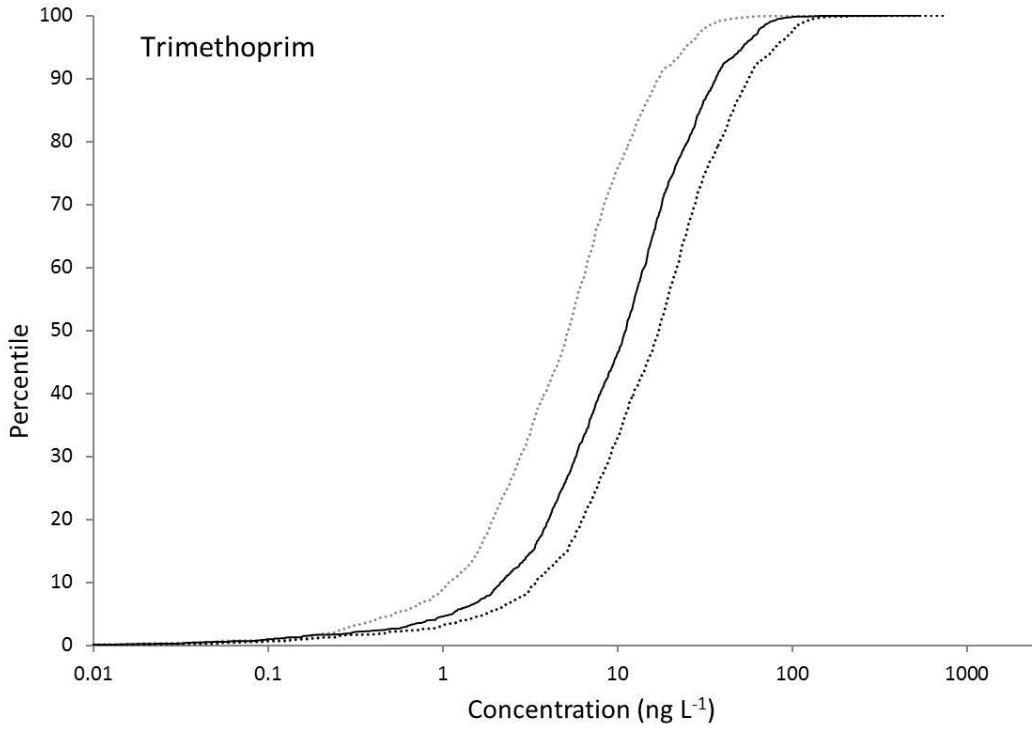
Usage: mg $person^{-1}\ d^{-1}$
Metabolism: fraction excreted
Population size: persons

Low Flows 2000 WQX Model

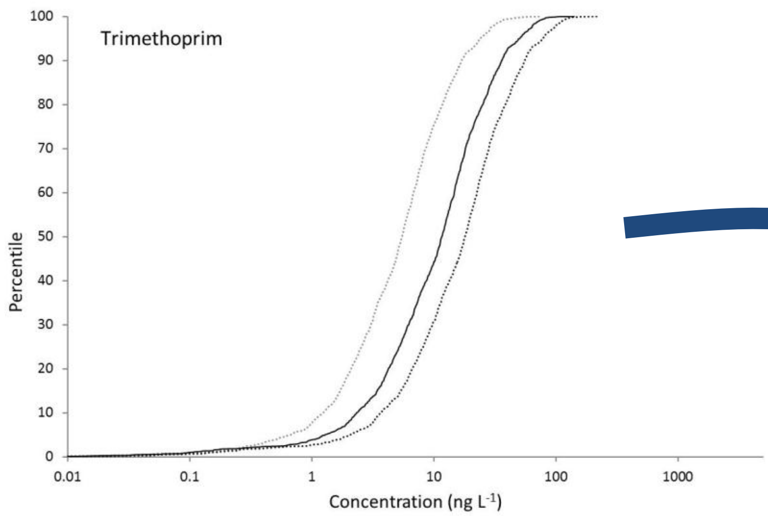


Exposure distributions

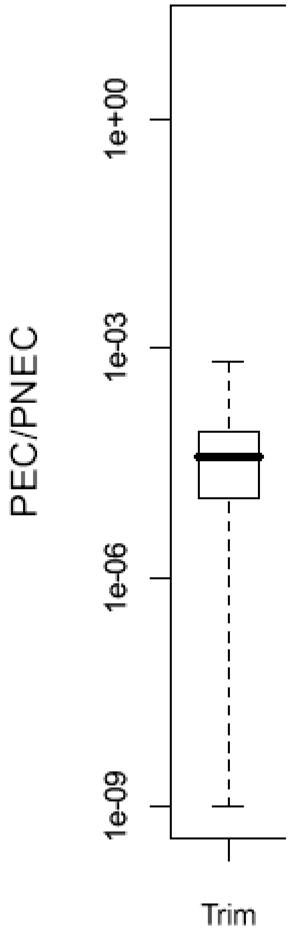




Risk characterisation



$$RCR = \frac{PEC}{PNEC}$$

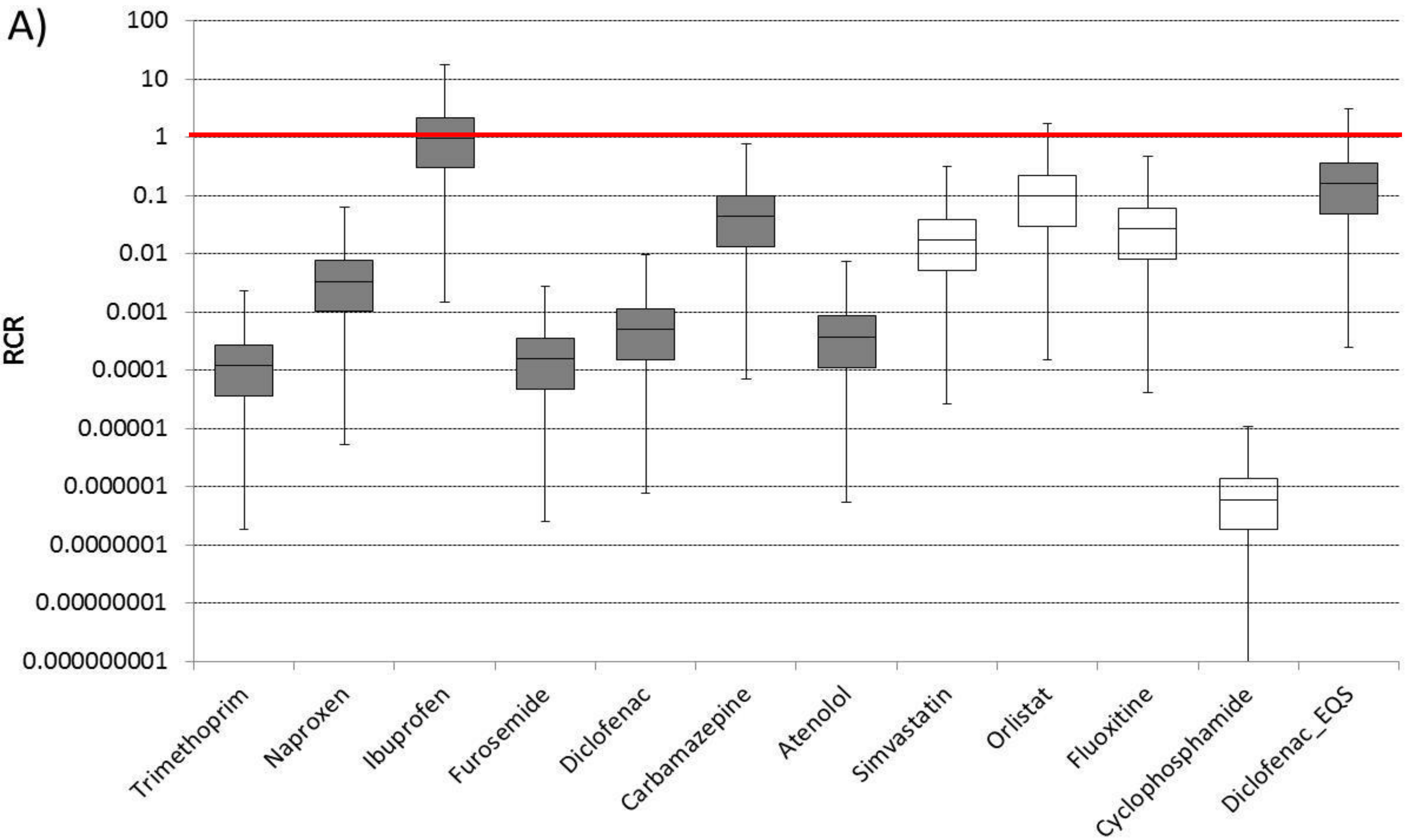


$$PNEC = \frac{ECx}{AF}$$

Or

WFD proposed EQS

Risk to UK Waters



THE INDEPENDENT

September 29, 2008

Tests for drugs in tap water

By Steve Connor, Science editor

Drinking water supplies are to be tested for the presence of prescription drugs amid fears that rivers are being contaminated by the growing quantity of pharmaceuticals flushed unwittingly down the drain.

The Government has commissioned scientists to test river water at intake points where it is abstracted for human consumption, The Independent can reveal. They will also test drinking water after it has been through the water-treatment cycle.

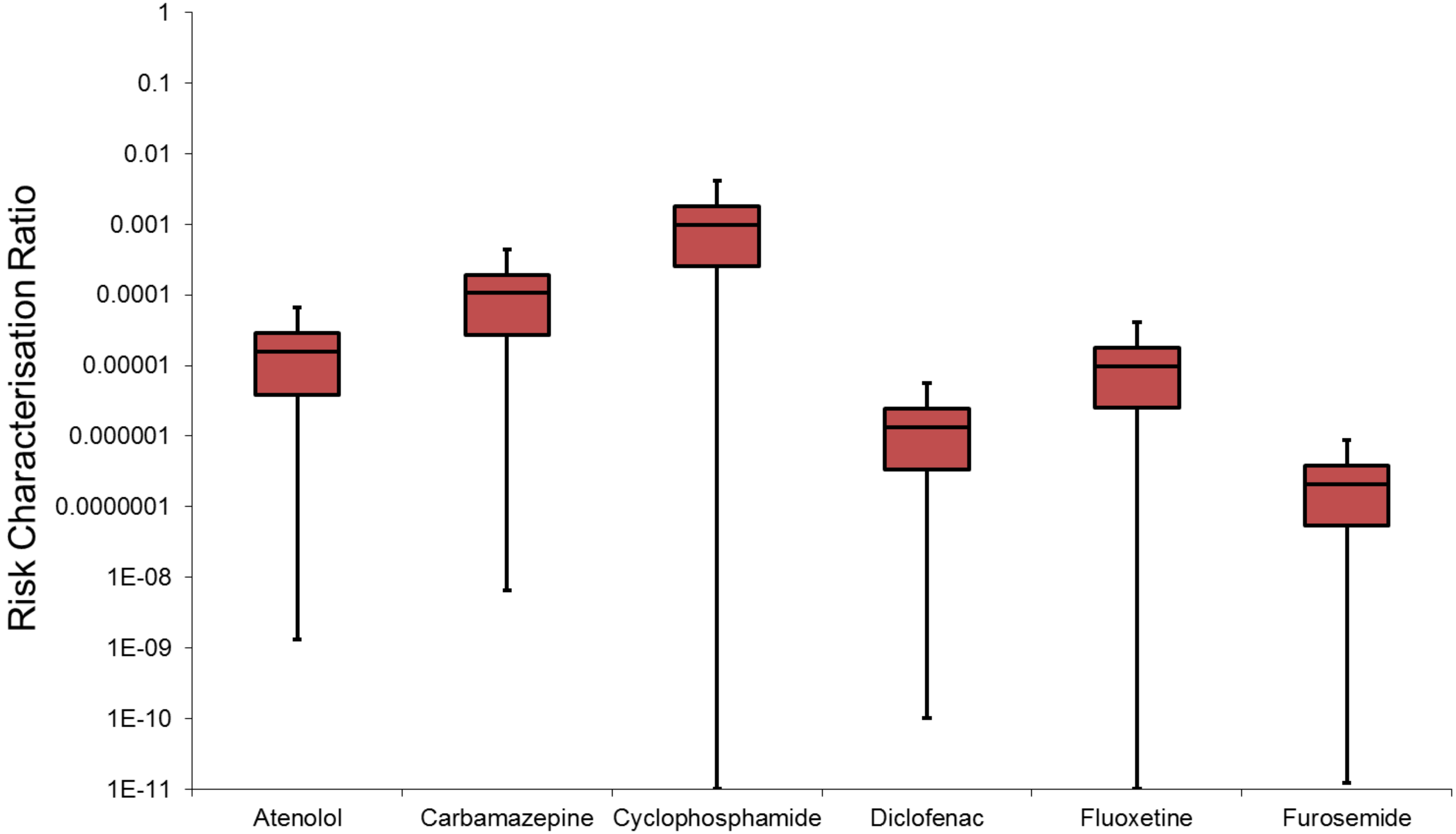
Under a pilot project to begin next year, supplies will be examined for about five of the most common and potentially dangerous prescription drugs. The experts will meet over the next few weeks to decide which drugs to look for and where testing should be carried out. However, an insider said this was likely to be at selected sites on the river Thames because its water-catchment area covered the most densely populated part of the country.

Powerful anti-cancer drugs are of particular concern as they can be excreted unaltered from the body into the sewerage system. They are thought to be potentially dangerous because they are highly toxic to dividing cells, are easily dissolved in water and are difficult to destroy by conventional water-treatment techniques.

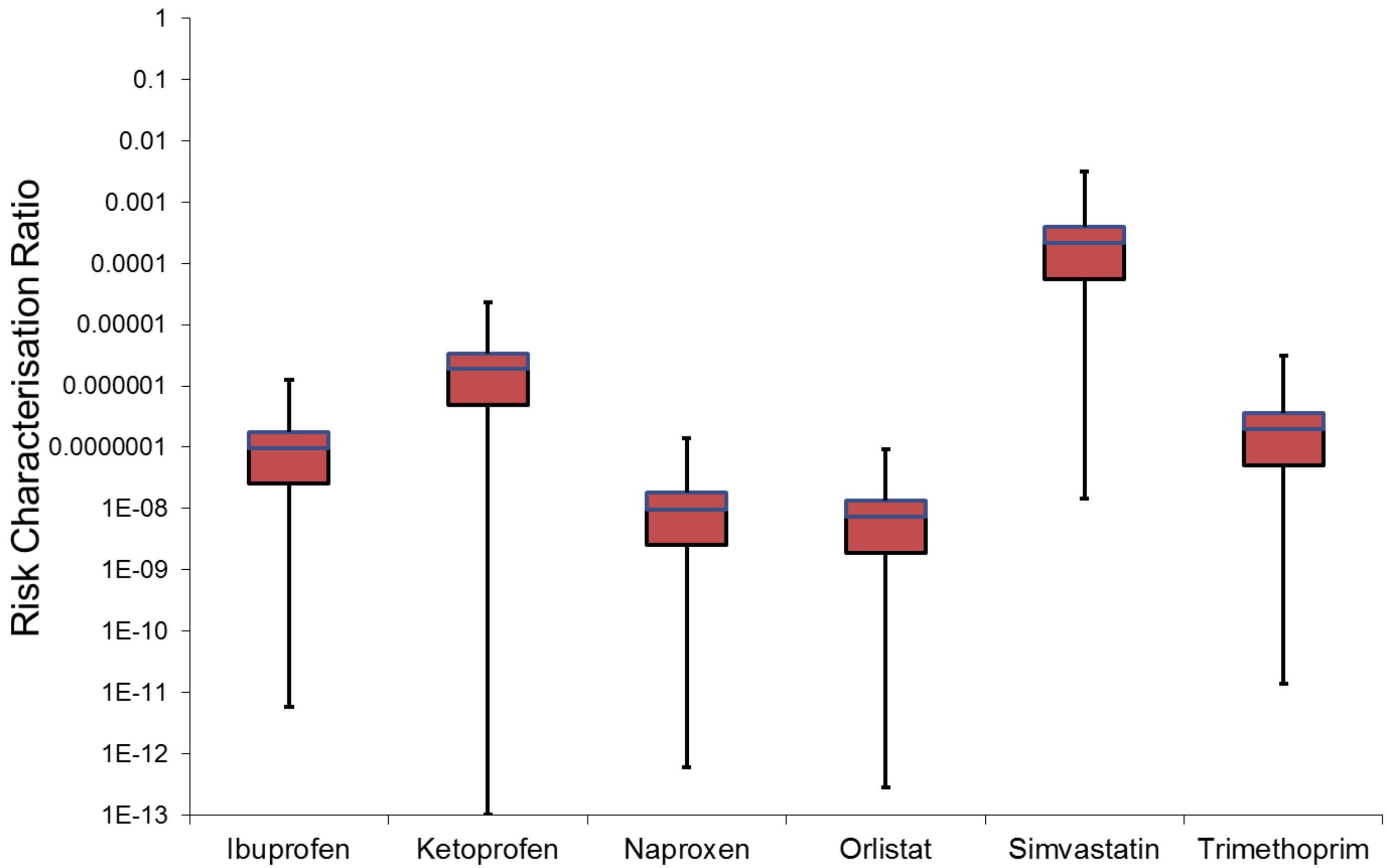
Risk to human health?

- 100 drinking water plants in the modelled river network
- Predictions of point of abstraction combined with DW treatment removal rates to estimate tap water levels
- Assumed individuals consumed 2 L of water per day and then compared estimated exposure to ADI

Human health risks



Human health risks



Human Pharmaceutical Risks

45% of UK river reaches have levels of ibuprofen shown in the laboratory to affect fish hatching; 4.5% have levels of diclofenac shown to affect fish histology; Low risk to human health

Klaus Steifel

A significant contributor to pharmaceutical use - around 290 tonnes of antibiotics are used in veterinary medicine each year in the UK

Blue green algae and antibiotics

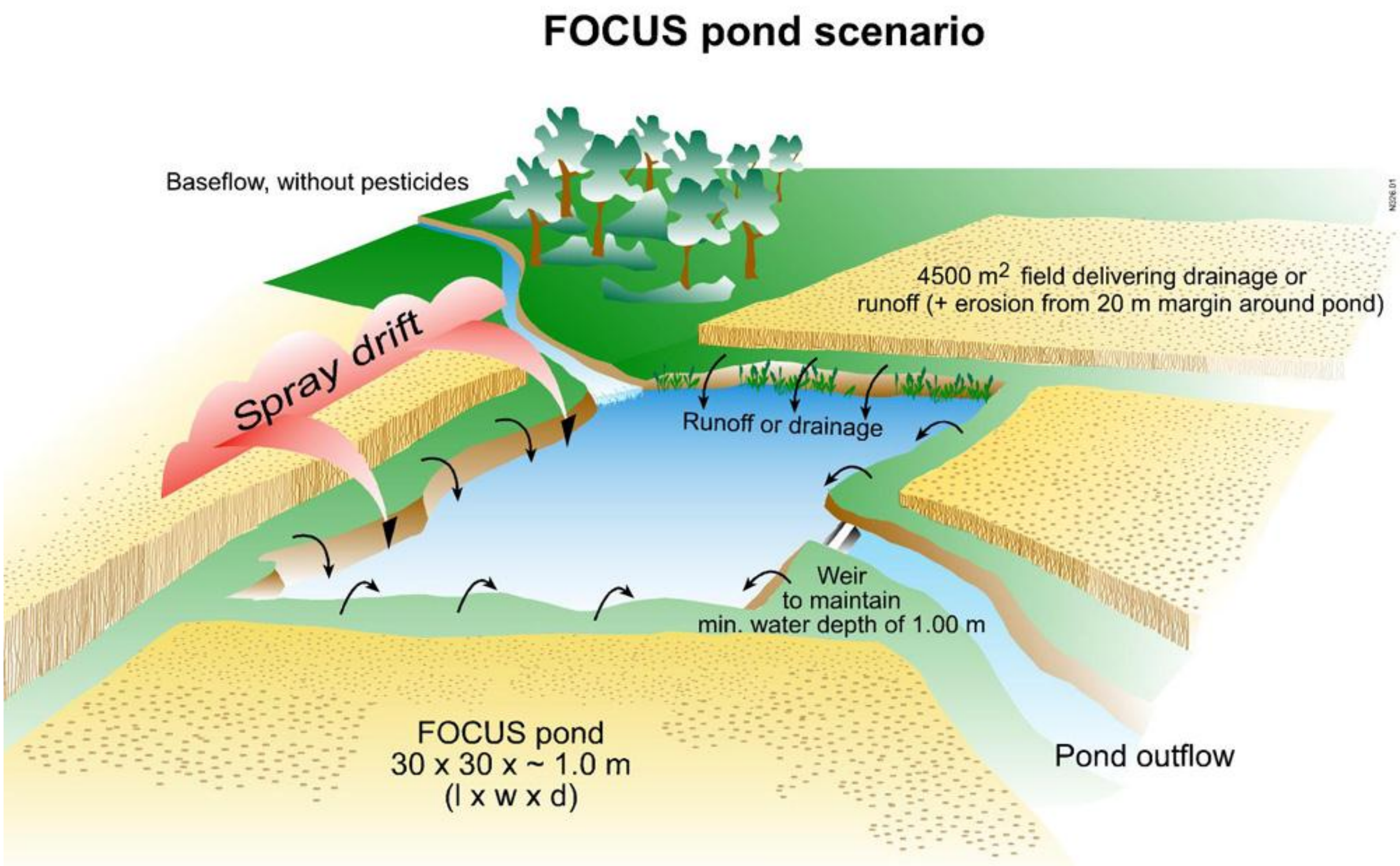
	M. aeruginosa		
	Tested concentration levels (mg/l)	EC_{50} (mg/l)	95% confidence limit
Benzylpenicillin (penicillin G)	0.002–0.01	0.006	0.004–0.012
Chlortetracycline	0.002–10	0.05	0.03–0.10
Olaquindox	0.5–10	5.1	4.5–5.6
Spiramycin	0.002–10	0.005	0.001–0.018
Streptomycin	0.002–10	0.007	0.006–0.008
Tetracycline	0.003–10	0.09	0.08–0.10
Tiamulin	0.0025–0.02	0.003	0.002–0.004
Tylosin	0.002–1.25	0.034	0.024–0.048
$K_2Cr_2O_7$		0.211	–
$\mu_{control}$, d^{-1}		0.6	

Halling Sorensen, 2000

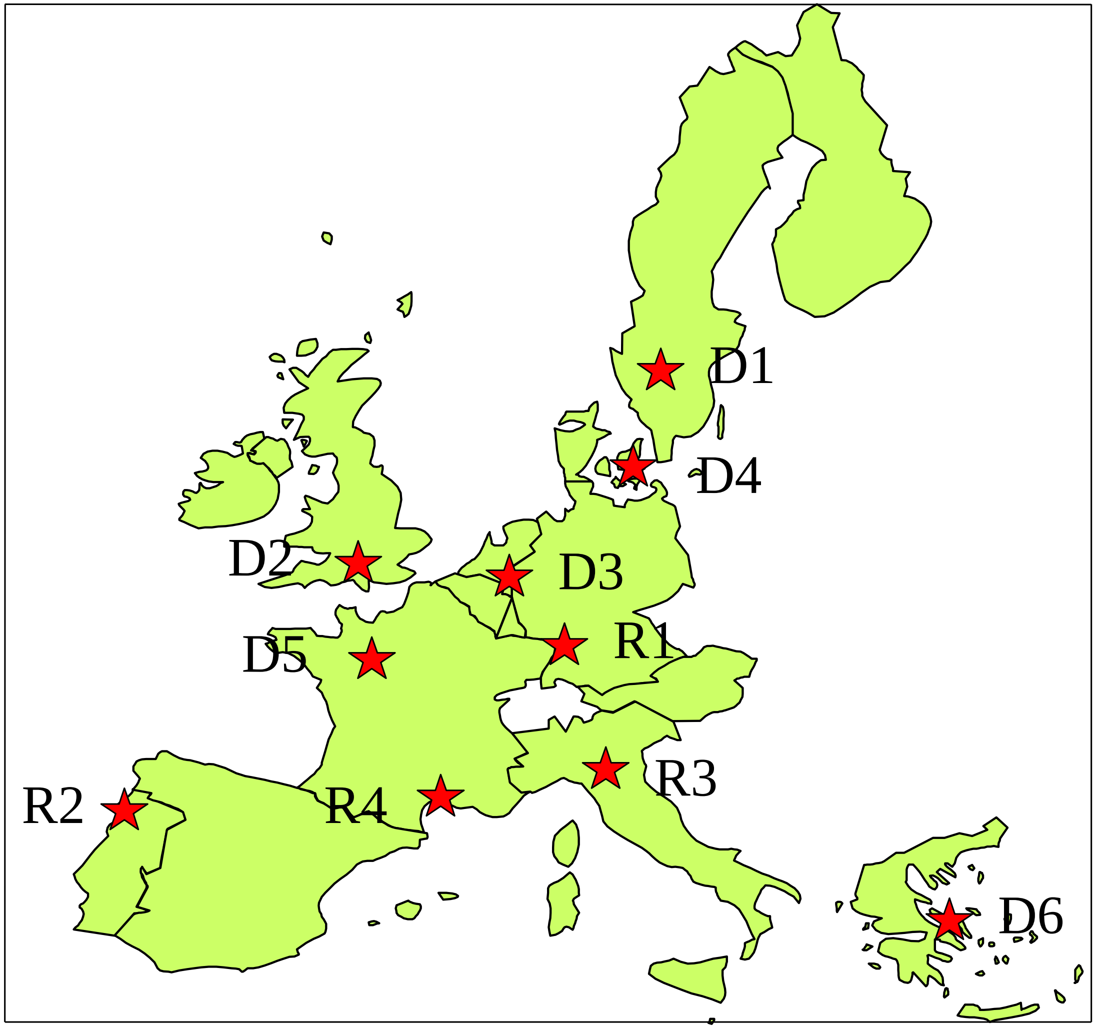
Risks of veterinary antibiotic mixtures

- Tylosin, lincomycin and trimethoprim
- Focus on algae (the most sensitive taxonomic group)
- Exposure modelled for range of European scenarios
- SSDs used to assess hazard levels for algal communities
- Mixture models used to estimate hazard of antibiotic combinations

Surface water exposure



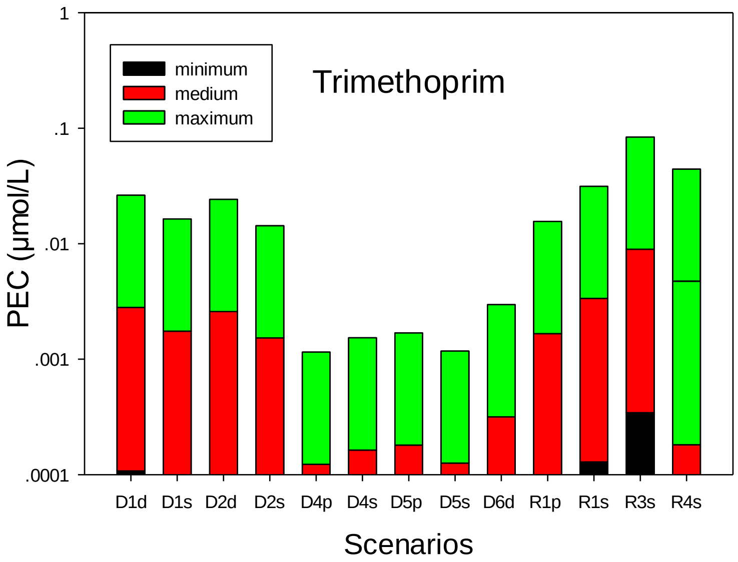
Surface water scenarios

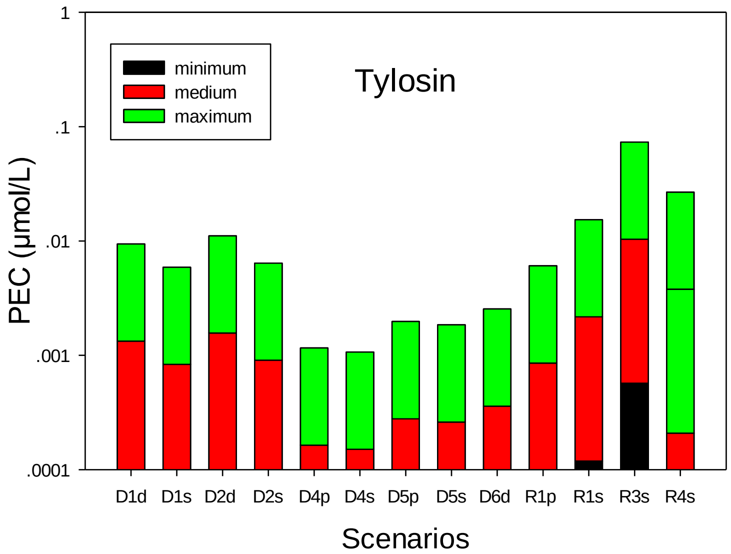


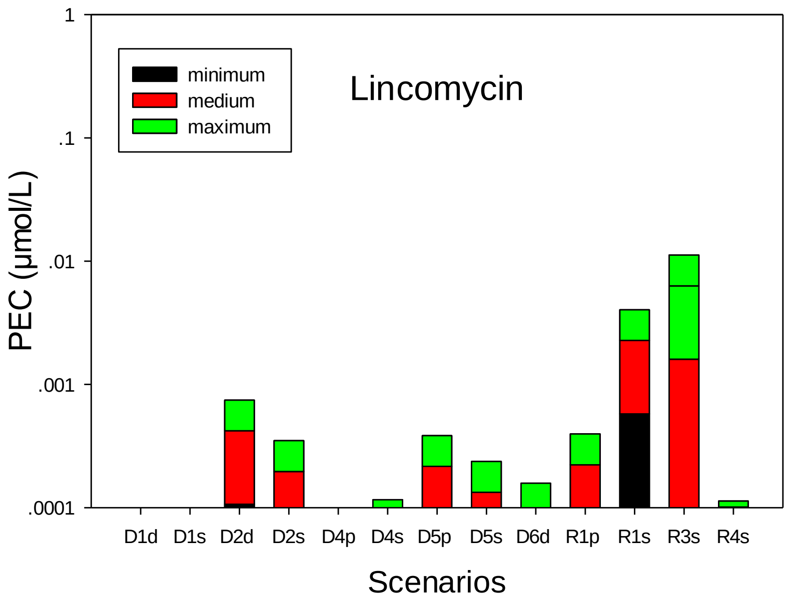
D = Drainage Scenario

R = Runoff scenario

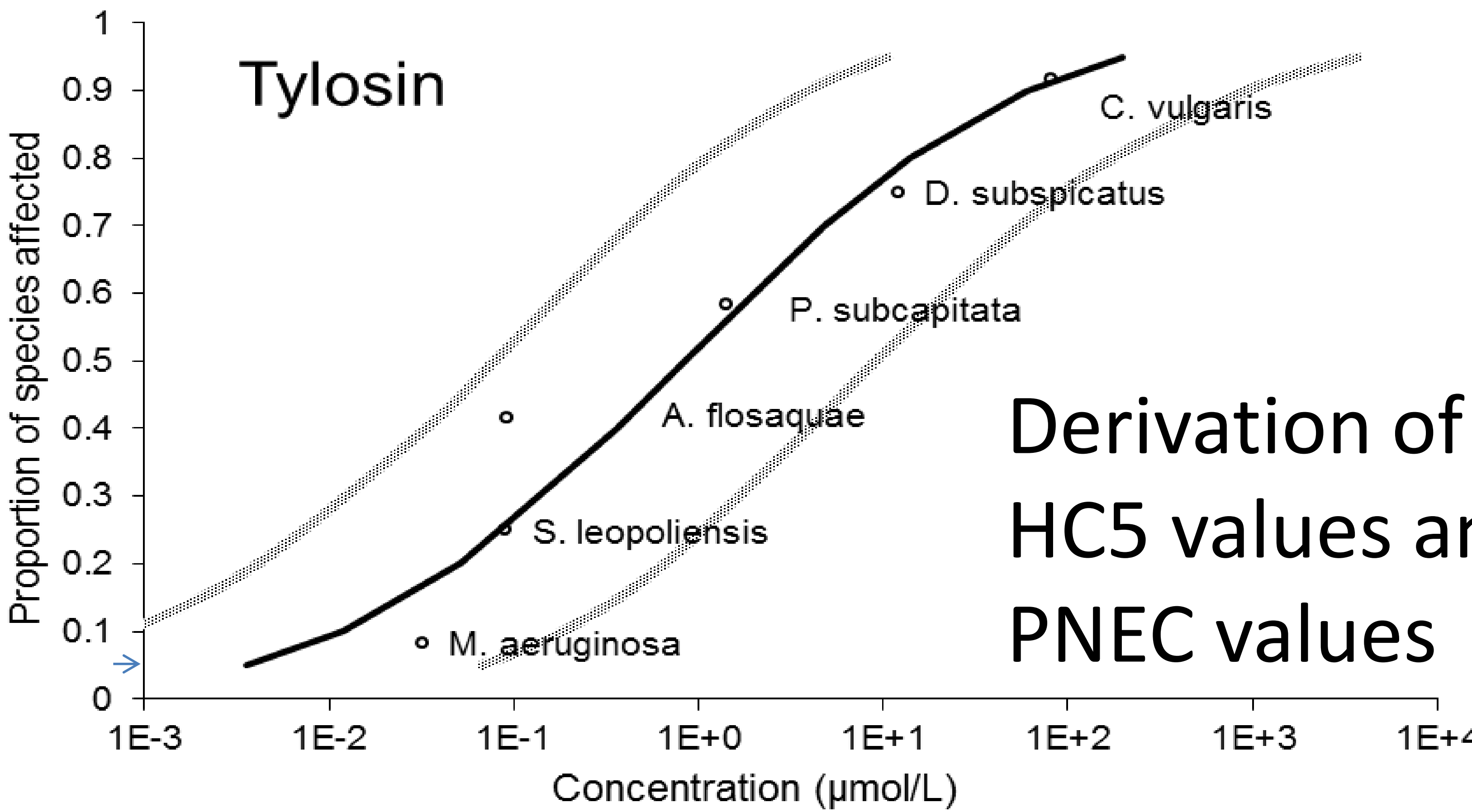
Exposure predictions





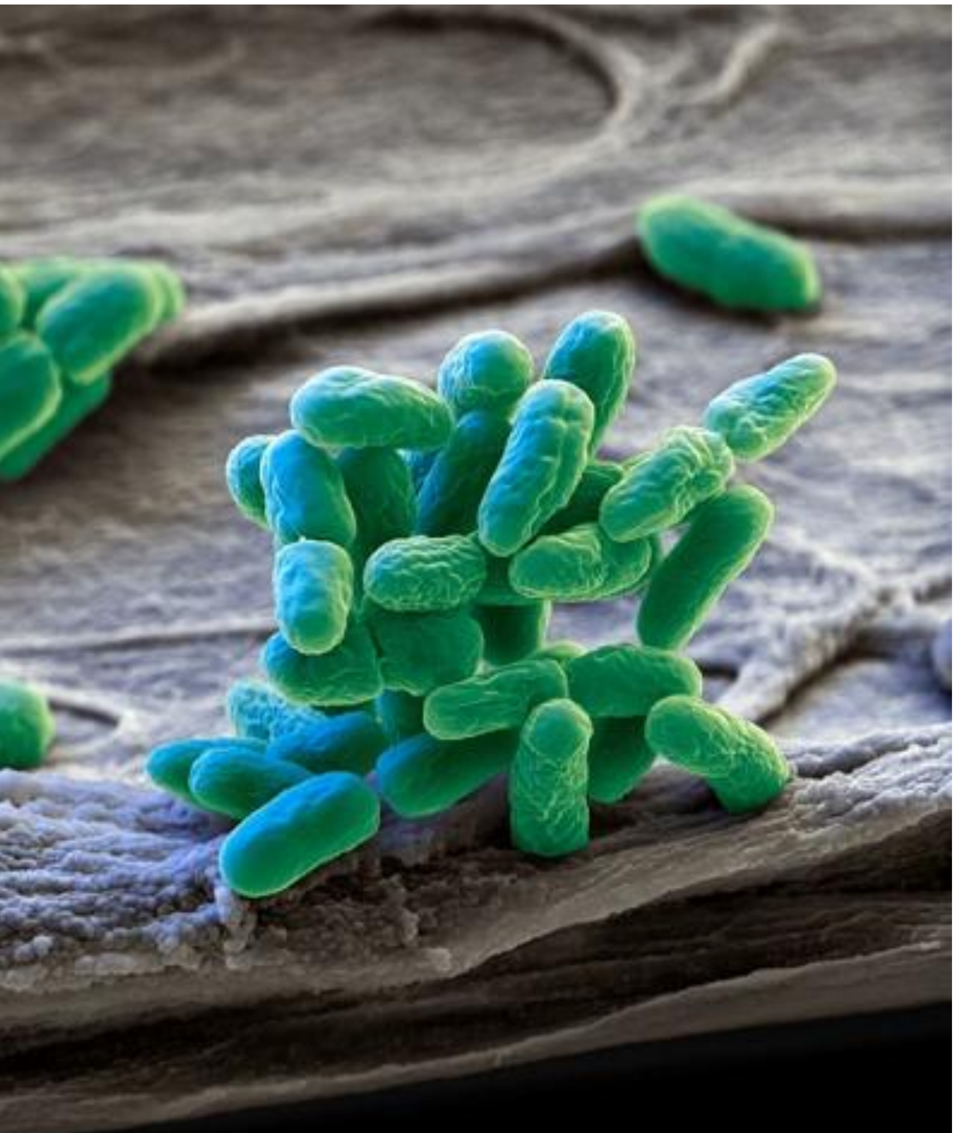


Species sensitivity distribution



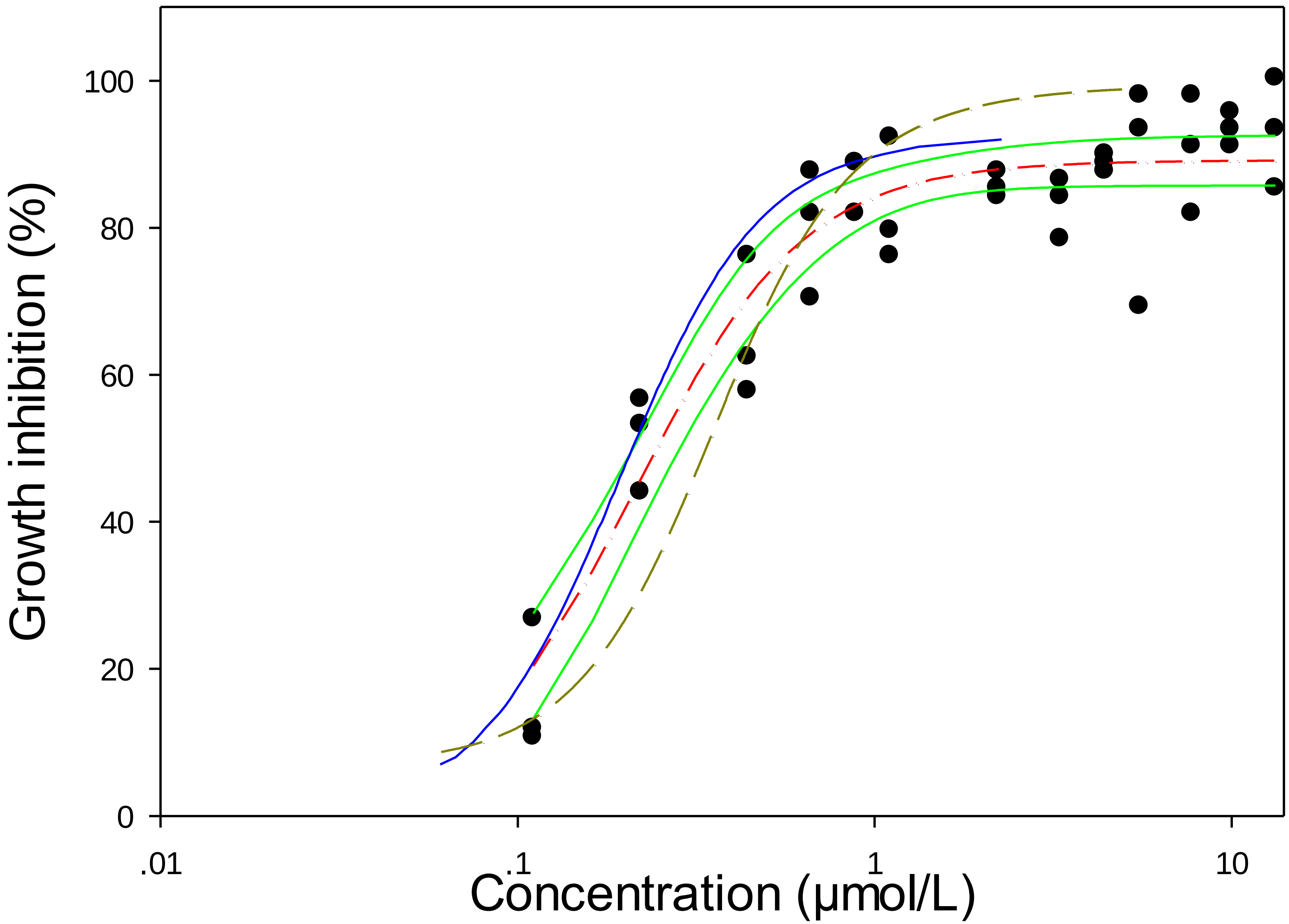
Derivation of HC5 values and PNEC values

Evaluation of Mixture Interactions

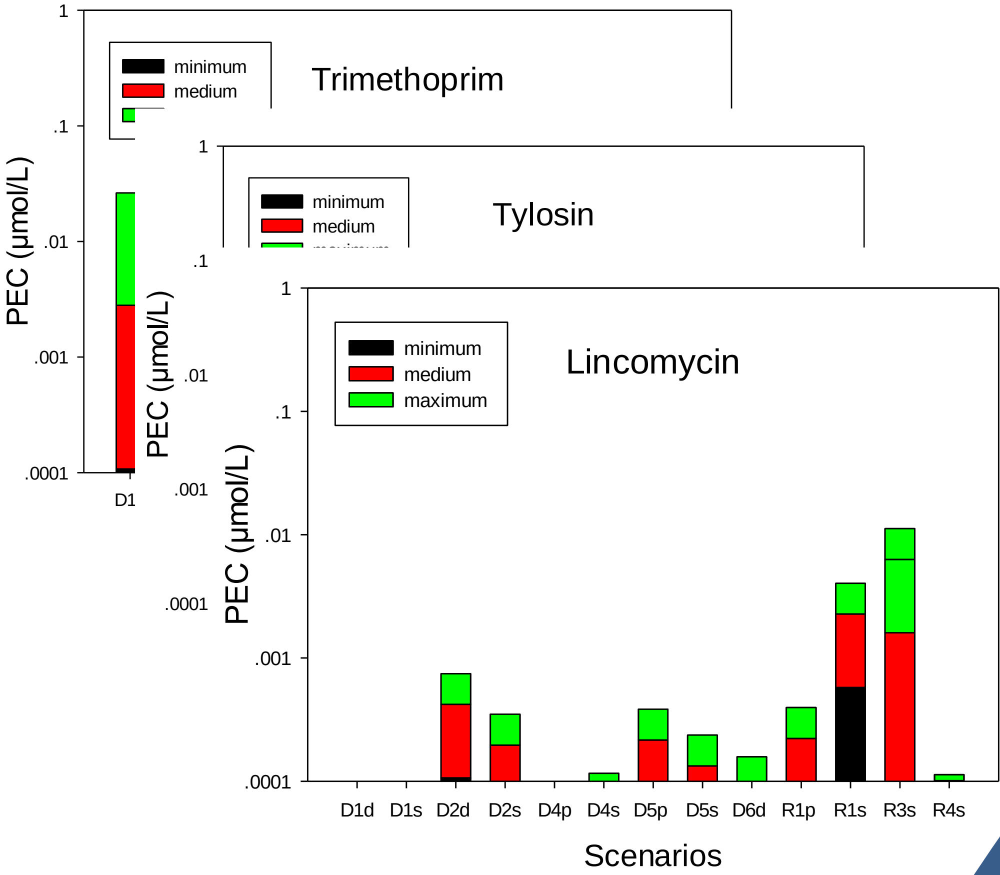


- Single and mixture studies using blue green algae
- Data used to evaluate the concentration addition and independent action models

Modelling effects of mixtures



Risk Characterisation



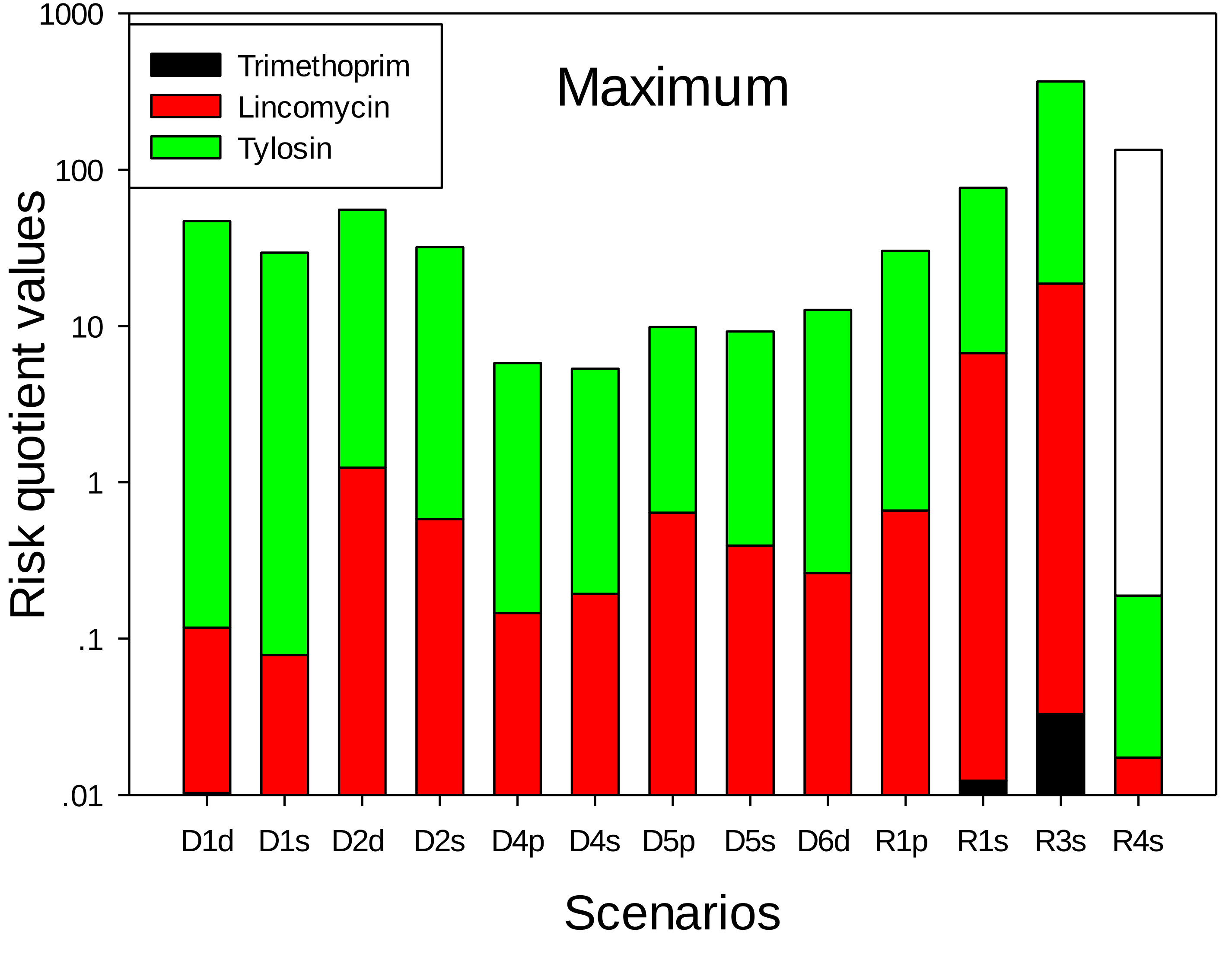
CA Model

PNEC$_{tylosin}$

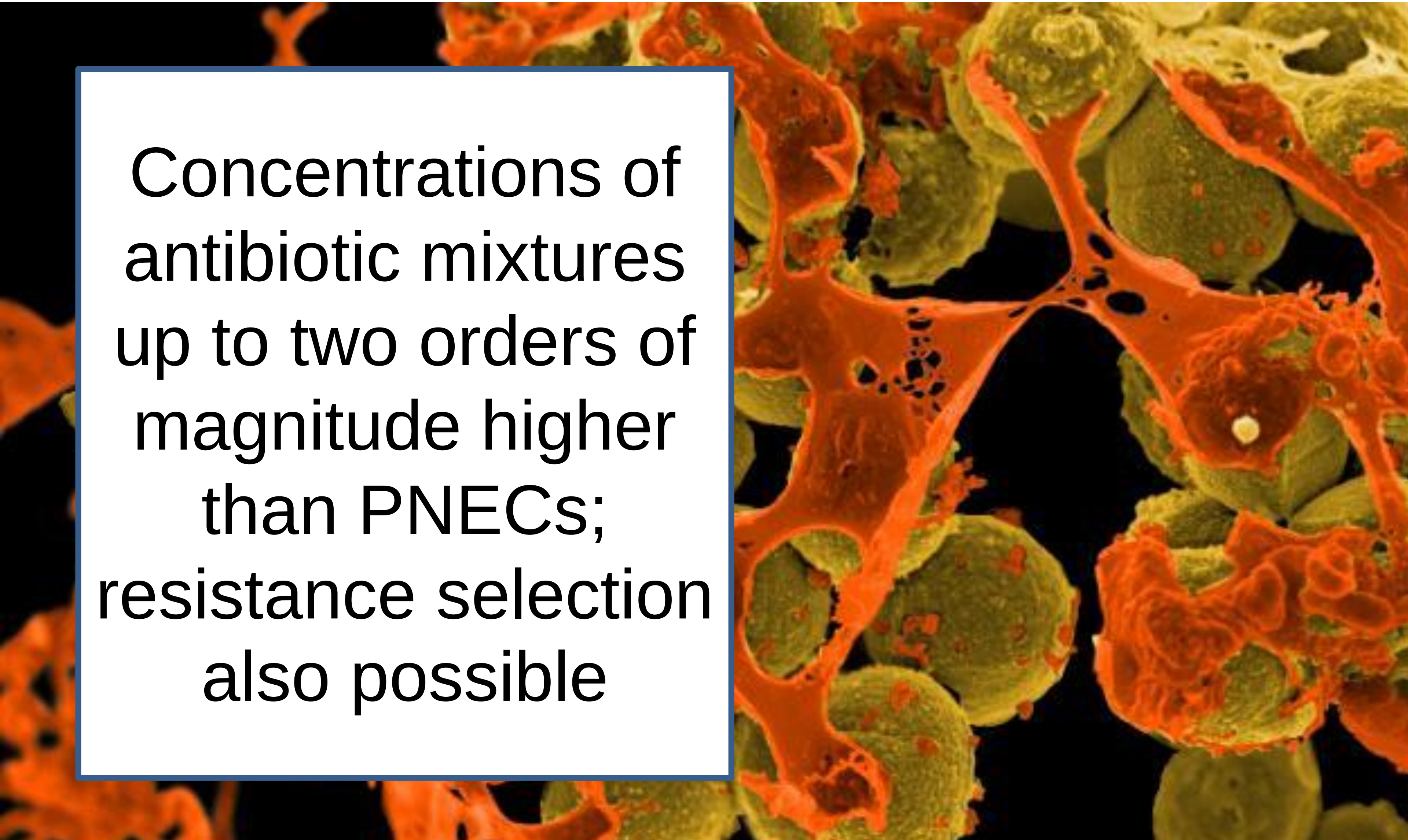
PNEC$_{lincomycin}$

PNEC$_{trimethoprim}$

Is there a risk?



Mixture study conclusions



Concentrations of antibiotic mixtures up to two orders of magnitude higher than PNECs; resistance selection also possible

What is all this telling us?

- The majority of medicines we use are unlikely to be having impacts
- Evidence that a handful of substances could be impacting ecosystems
  - Up to 45.5% of modelled river reaches in England and Wales have concentrations of ibuprofen of concern
  - Antibiotics may be impacting primary production (and selecting for resistance!)
  - Significant proportion of rivers have levels of estrogens of concern
- Risk to human health is low in Europe/N. America
- Increasing evidences of effects on wildlife such as birds and bats
- What can be done to control the risks?

Benign by design

www.ourgreenlab.com

Upgrade sewage treatment plants

Reduced Pharmaceuticals Impacts

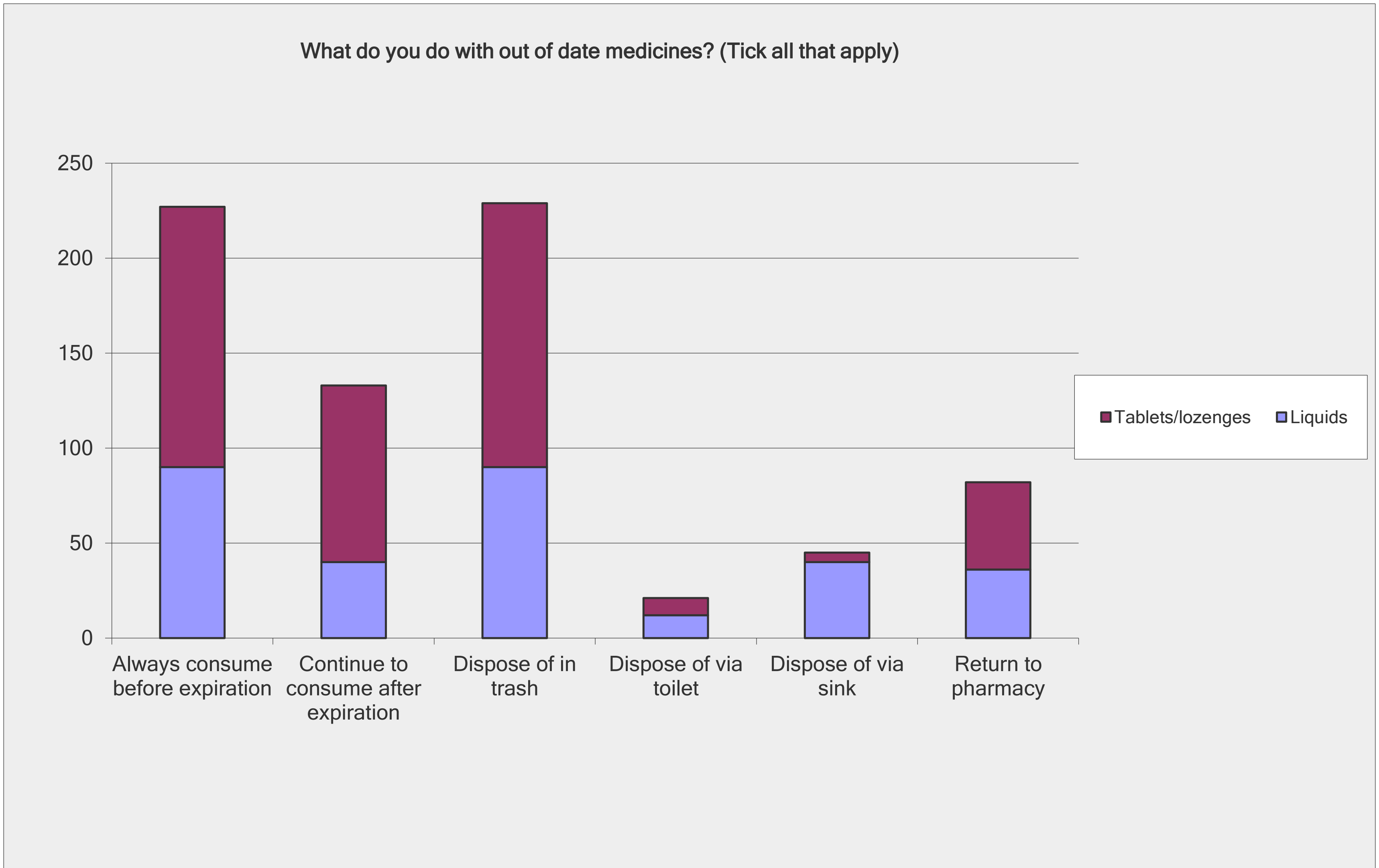
Change the way we use drugs

Stewardship schemes

www.ourlocal pharmacy.com

Drug disposal part of the problem

3-64% of pharmaceuticals not used

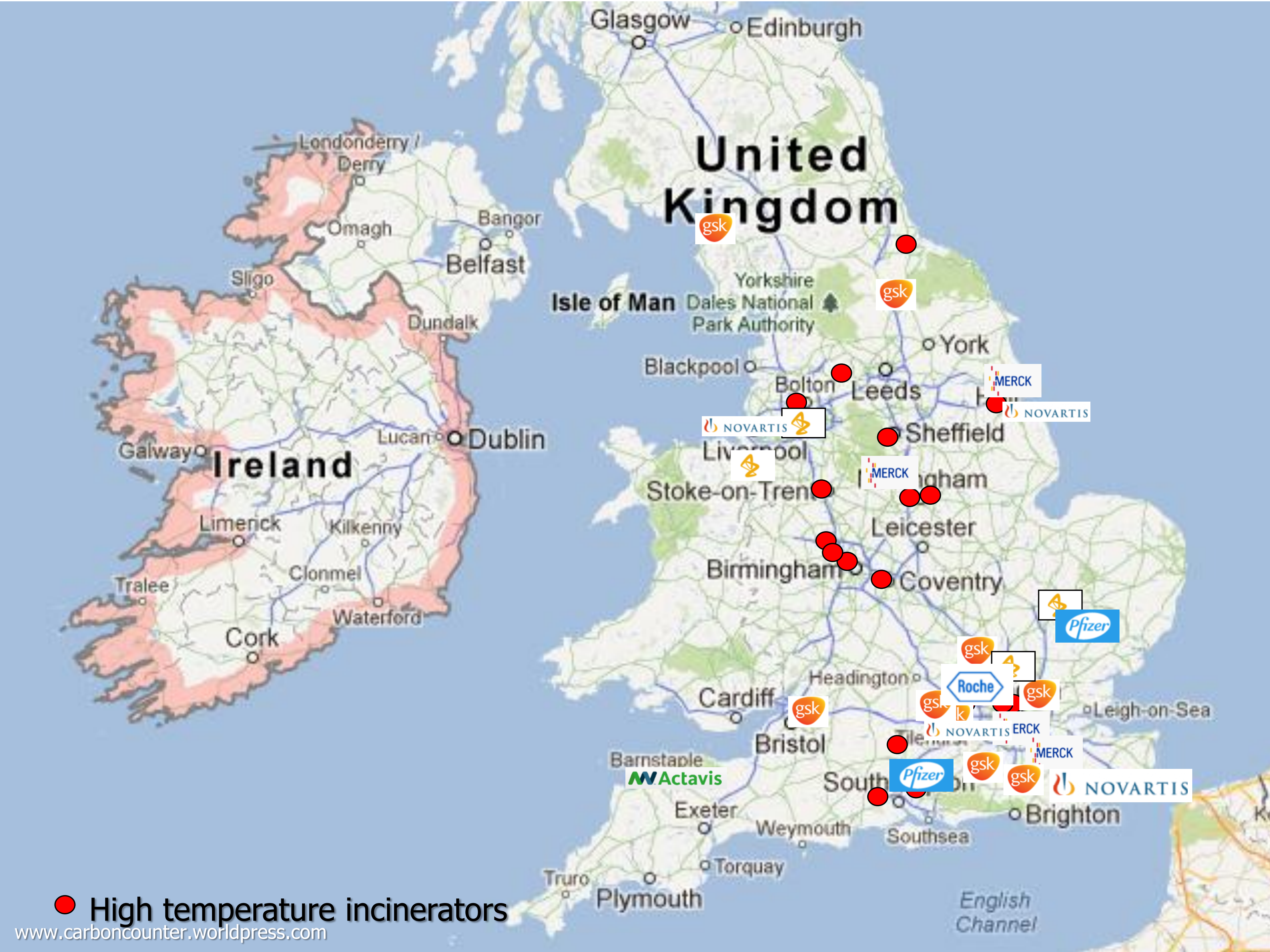


How can I dispose of medicines safely?

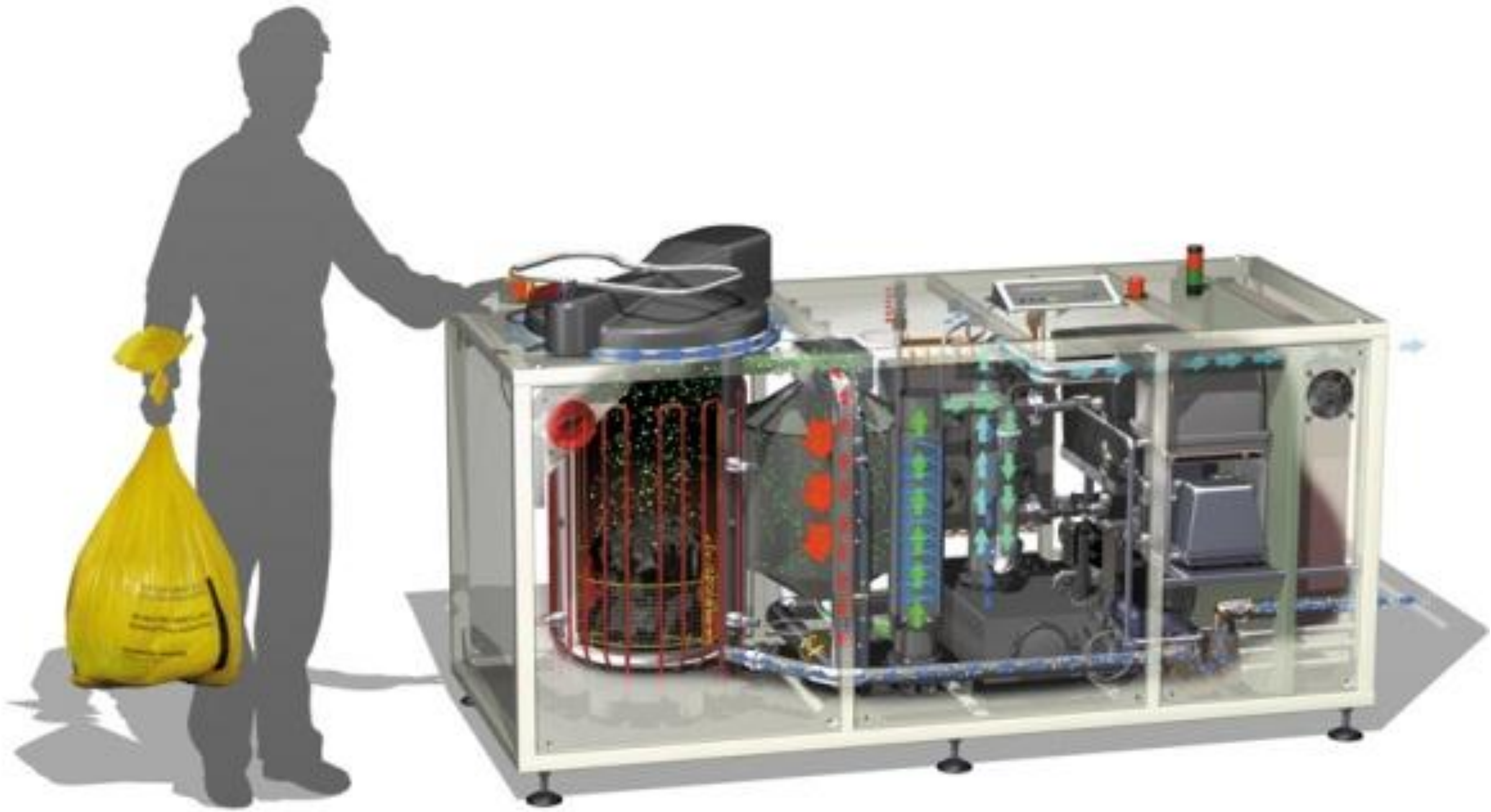
The best way to dispose of medicines that are no longer needed is to return them to your pharmacist.

This service is available at every pharmacy, it is free-of-charge and some pharmacies may even carry out local collections. Try to return unwanted medicines in their original packaging where possible, as some medicines need special handling.

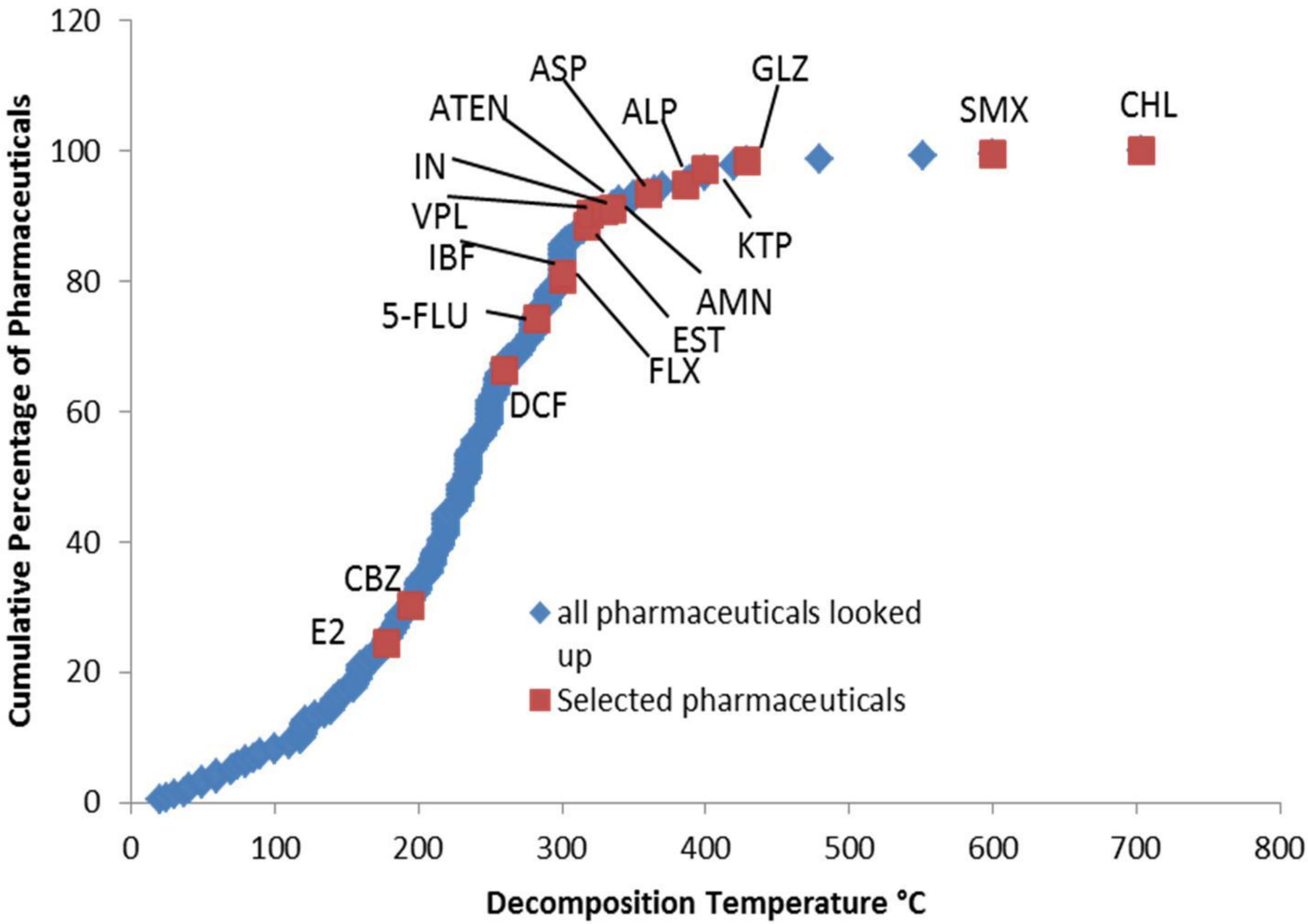
Never dispose of medicines down the toilet or sink. Medicines disposed of in this way can become a hazard to the environment and water supply.


United Kingdom
Ireland
Glasgow
Edinburgh
Londonderry / Derry
Omagh
Bangor
Belfast
Sligo
Dundalk
Isle of Man
Yorkshire Dales National Park Authority
York
Blackpool
Bolton
Leeds
Hull
Sheffield
Liverpool
Stoke-on-Trent
Lucan
Dublin
Galway
Limerick
Kilkenny
Clonmel
Tralee
Waterford
Cork
Leicester
Birmingham
Coventry
Headington
Cardiff
Bristol
Barnstaple
Exeter
Weymouth
Southsea
Brighton
Leigh-on-Sea
Torquay
Truro
Plymouth
English Channel
gsk
MERCK
NOVARTIS
Pfizer
Roche
Actavis
High temperature incinerators

Pyropure – an in situ system for hazardous waste treatment



Stability of study compounds



17 Pharmaceuticals selected

Decomposition Range 195-704°C

Non Steroidal Anti-Inflammatory Drugs

- Ketoprofen
- Ibuprofen
- Diclofenac
- Indomethacin

Analgesic

Ca-channel blocker: Verapamil

Beta-blocker: Atenolol

Anti-Parkinsons: Amantadine

Antidepressant: Fluoxetine

Anti-cancer: 5-fluorouracil

Hormones

- Estradiol
- Ethinyl-estradiol

Anti-gout:
Allopurinol

Antibiotics

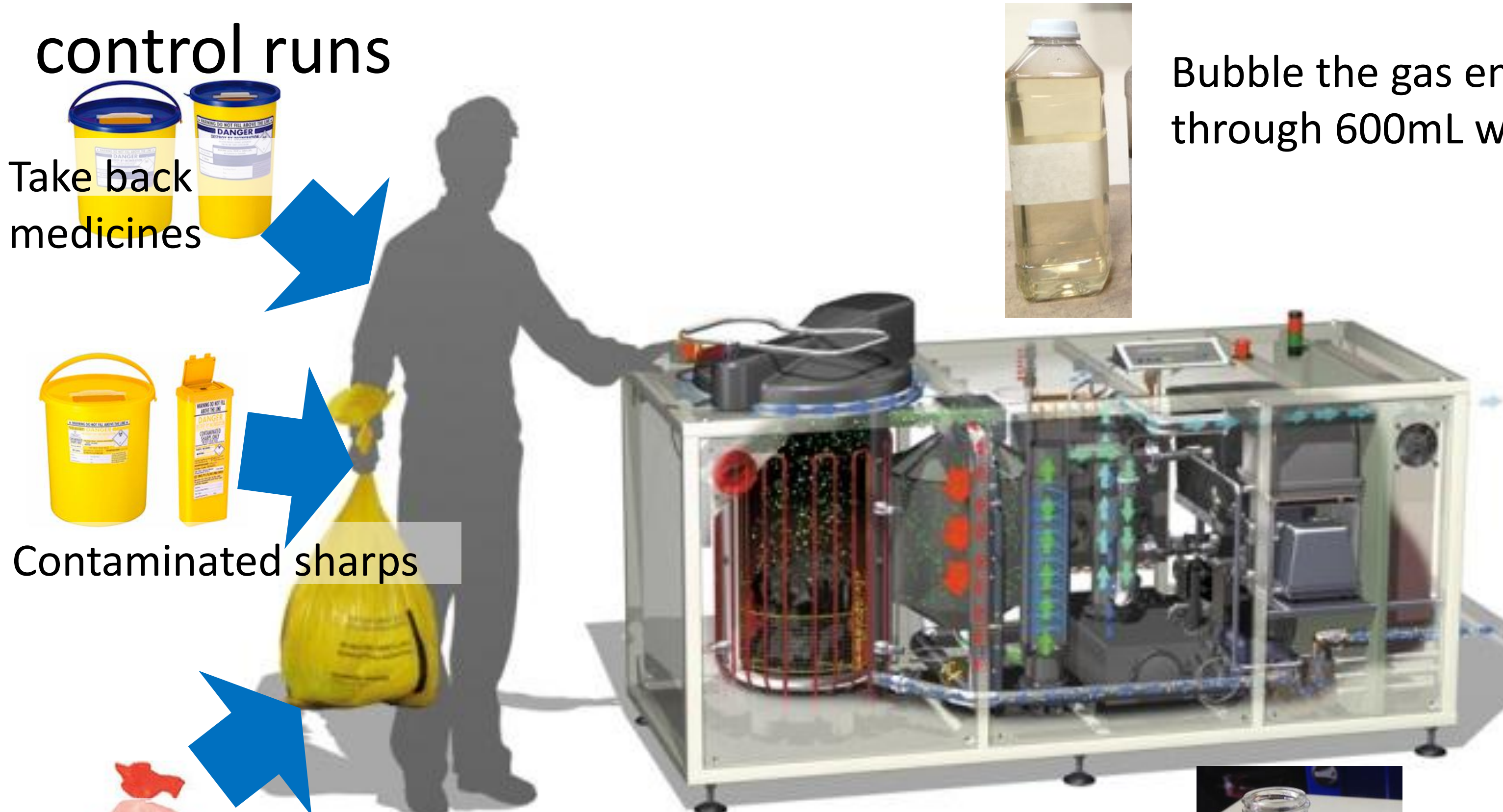
- Chloramphenicol
- Sulfamethoxazole

Anti-diabetes:
Gliclazide

Anti-epilepsy: Carbamzepine

Experimental structure

3 Waste streams: For each 3 Pharmaceutical runs and 2 control runs



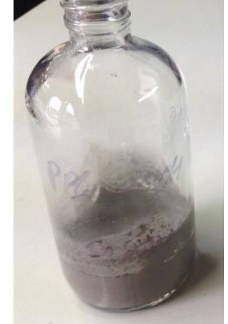
Take back medicines

Contaminated sharps

Contaminated manufacturing waste

Bubble the gas emission through 600mL water

3 effluent samples per run



Collect all the solids (sludge)

Total of 15 runs: 5 for each waste stream

Analytical methods

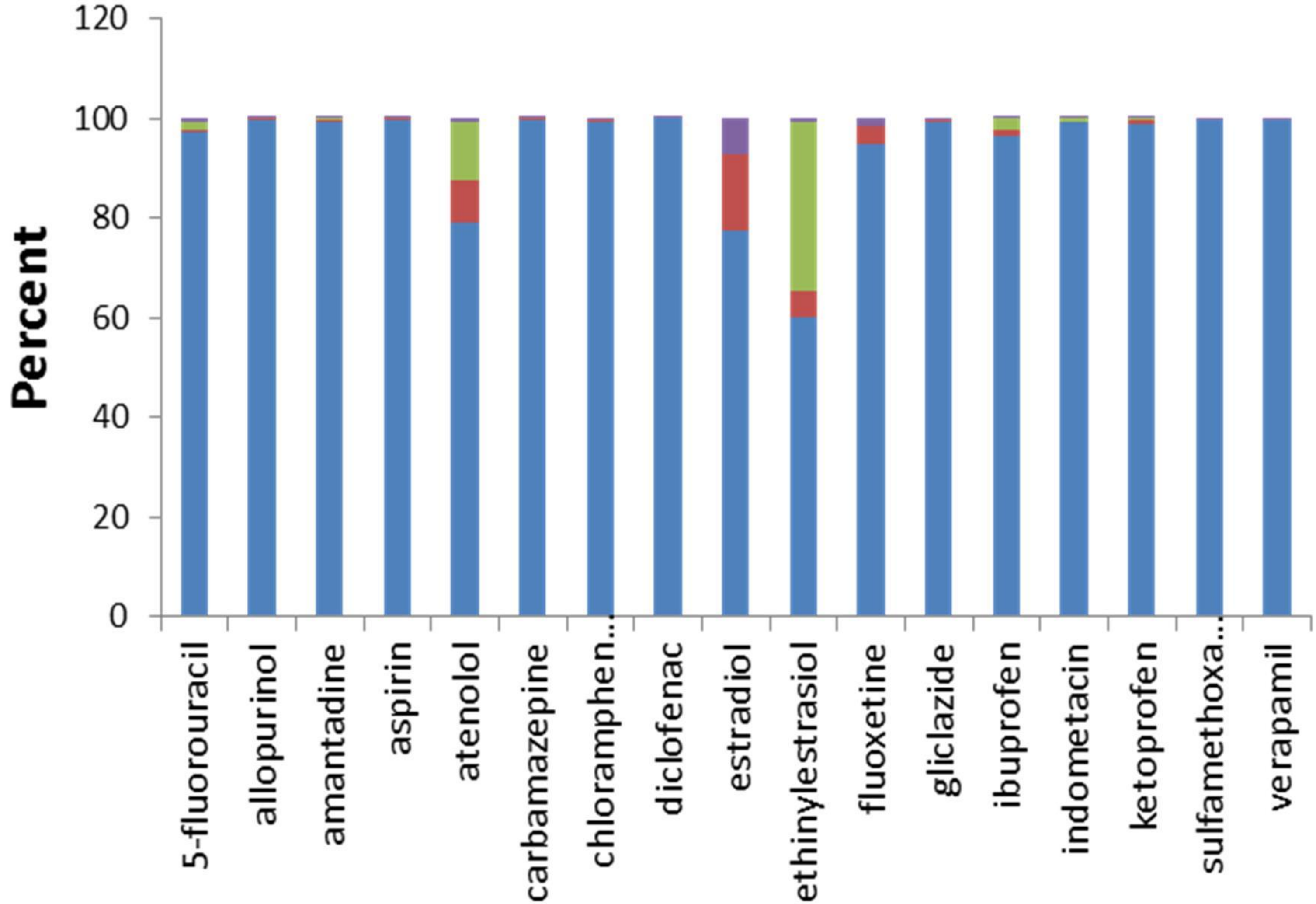
Parent Compounds

Liquid Chromatography Triple Quadrupole mass spectrometry

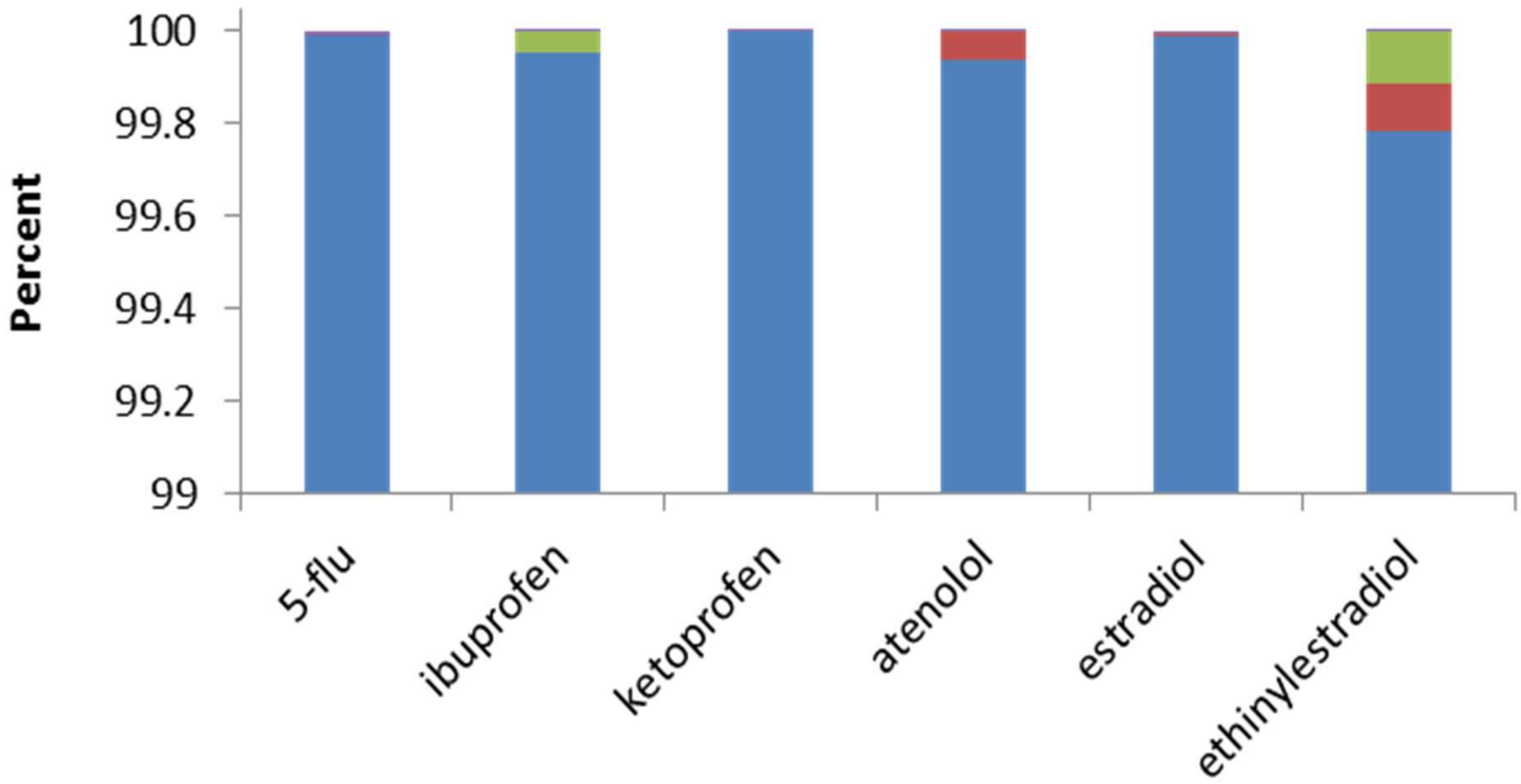
Transformation products

Fourier Transform Mass Spectrometry

Results - Phase 1



Results - Phase 2



Main results

- Greater than 99% destruction of all pharmaceuticals achieved in all waste simulations
- No known degradation products seen

Summary

- Major concerns over pharmaceuticals in the environment
- A significant proportion of river reaches in the UK may be at risk so some compounds require further scrutiny
- Impacts on wildlife also possible
- A range of management options available - there is a need for an integrated approach
- Still many open questions

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NERC
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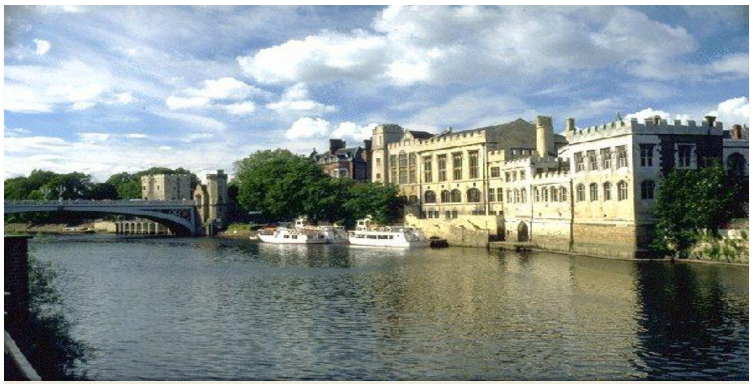

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