The Food and Environment Research Agency

The Risk to the UK Population of Pesticide Metabolites in Drinking Water

Chris Sinclair

Thursday 19th November

NORMAN Workshop

Presentation overview

- Metabolites in drinking water
- Monitoring data in UK
- Identifying those for further study
- Estimating concentrations in raw water
- Fate during drinking water treatment

UK Drinking Water Regulations

The Food and Environment Research Agency

- The Water Supply (Water Quality) Regulations 2000
  - Consumer tap water should not exceed:
  - 0.1 µg/L for individual pesticides and related products, including their relevant metabolites, degradation and reaction products
  - 0.5 µg/L total sum of pesticide concentrations
  - 0.03 µg/L for aldrin, dieldrin, heptachlor and heptachlor epoxide

- DWI Guidance Document
  - relevant = similar pesticidal properties to their parent pesticide
  - "no evidence at the present time that any pesticide metabolites….are active pesticides or represent a risk to health and therefore no additional monitoring is required"

Metabolites in drinking water

- Scientific literature
  - No data relating to pesticide metabolites in UK waters
- Environment Agency
  - Jan 2003 to Dec 2007
  - ~50,000 surface water, ~44,000 ground water

Metabolite	Parent pesticide	% of analysis	Max. concentration (µg/L)
deisopropylatrazine	atrazine	0.4	0.54
pp-TDE	DDT	34.1	0.31
deethylatrazine	atrazine	0.4	0.07
op-TDE	DDT	10.5	0.5
heptachlor epoxide	heptachlor	9.6	0.05
pp-DDE	DDT	34.2	0.1
op-DDE	DDT	9.4	0.01
dementon-S-methyl sulphone	dementon-S-methyl	1.4	1

Metabolites in drinking water

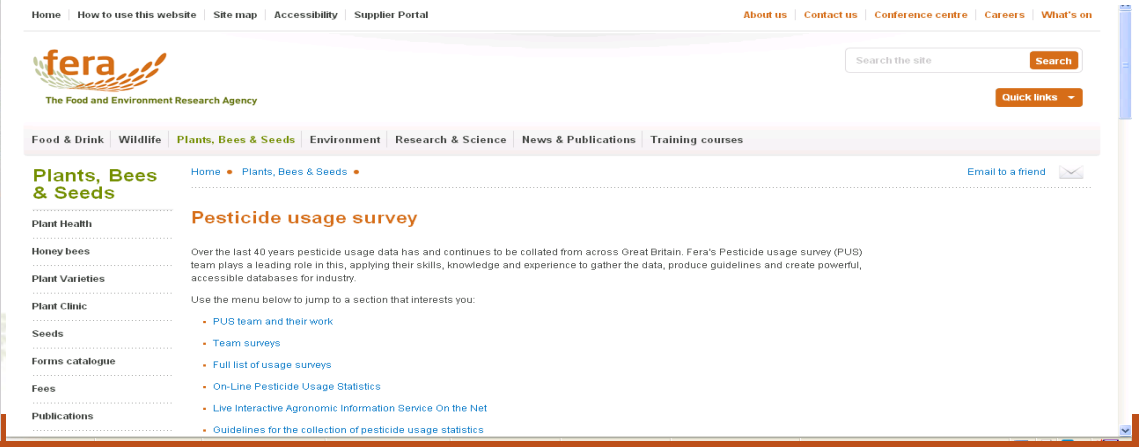
- Water companies
  - Water provision is private in UK, 27 companies contacted
  - 6 did not reply, 12 indicated they had no metabolite data and 9 provided data

Metabolite	Parent Pesticide	Max. concentration (µg/L)	
		Raw water	Treated water
deethylatrazine	atrazine	1.02	0.0575
deisopropylatrazine	atrazine	0.914	0.0124
op-DDE	DDT	0.01	0.004
op-TDE	DDT	0.02	0.004
pp-DDE	DDT	0.016	0.004
pp-TDE	DDT	0.012	0.006
heptachlor epoxide	heptachlor	0.0133	0.01

Identification of pesticides

- Identification of pesticides whose metabolites could contaminate abstracted waters
  - Fera Liasion database (liaison.csl.gov.uk)
  - 276 pesticides with current approval and 33 that lost approval in last three years

  - Pesticide Usage Survey statistics (agricultural pesticide usages)
  - Zero usage?: 1, not used or 2, to new to be encountered



Identification of metabolites

- Identified pesticides refined to remove:
  - inorganic (e.g. sulphuric acid)
  - undefined chemistry (e.g. fatty acids)
  - biological (e.g. *Bacillus thuringiensis)*
- Metabolites identified from soil degradation studies
  - 25 pesticides had no major metabolites formed
  - 76 no suitable degradation studies identified
- Data collated from different sources
- 523 metabolites from 185 pesticides
  - 485 metabolites with structural representation

Metabolites for further study

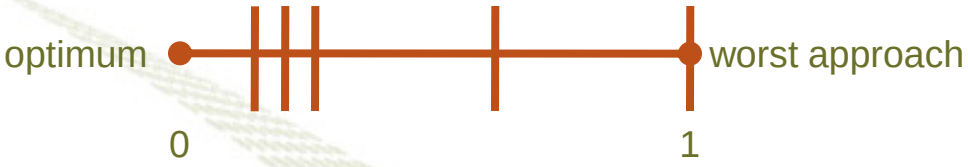
- Identified ~50 metabolites for further study
  - Ranked on the basis of potential to contaminate raw source waters
  - Identified those with potential toxicological concerns (QSAR)
  - Those that may exhibit pesticidal activity

- Metabolites were ranked on their potential to contaminate raw source waters (Sinclair et al, 2006)
  - Pesticide usage, extent of formation, persistence and mobility
  - Experimental data used but limited (31% Koc and 21% DT50)
  - Koc estimated from estimated Kow using QSPR
  - No suitable DT50 estimation methodology so default of 30d (27d is 75th percentile of collated metabolite DT50 data)
  - Those pesticides not encountered estimated by PUS team

Data gap filling - Hydrophobicity

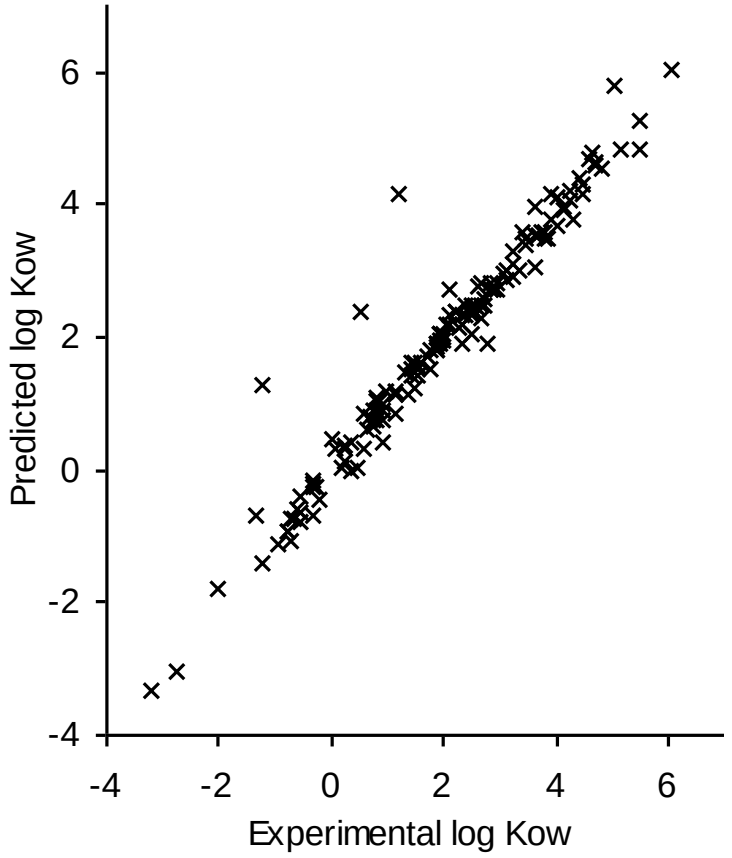
- Evaluation of six K_{ow} QSPRs using experimental K_{ow} data for 160 metabolites
  - KOWWIN, ClogP, ALogPS, miLogP, XLogP & LogP

- Ability measured using six statistical parameters
  - Number of compounds estimate generated
  - % positive deviation
  - Mean absolute deviation
  - Mean squared absolute deviation
  - % compounds < 1 OoM from experimental values
  - Pearson correlation coefficient



Data gap filling - Hydrophobicity

- 4 approaches quivalent performance (0.4-0.49)
- 2 poorly performing (0.8-0.91)
- Combining techniques?
- Mean estimate from KOWWIN, CLogP and ALogPS best perfroming
- >98% to within 1OoM
- Relationship of Kanazawa (1989) to estimate Koc



Metabolites with potential toxicological concerns

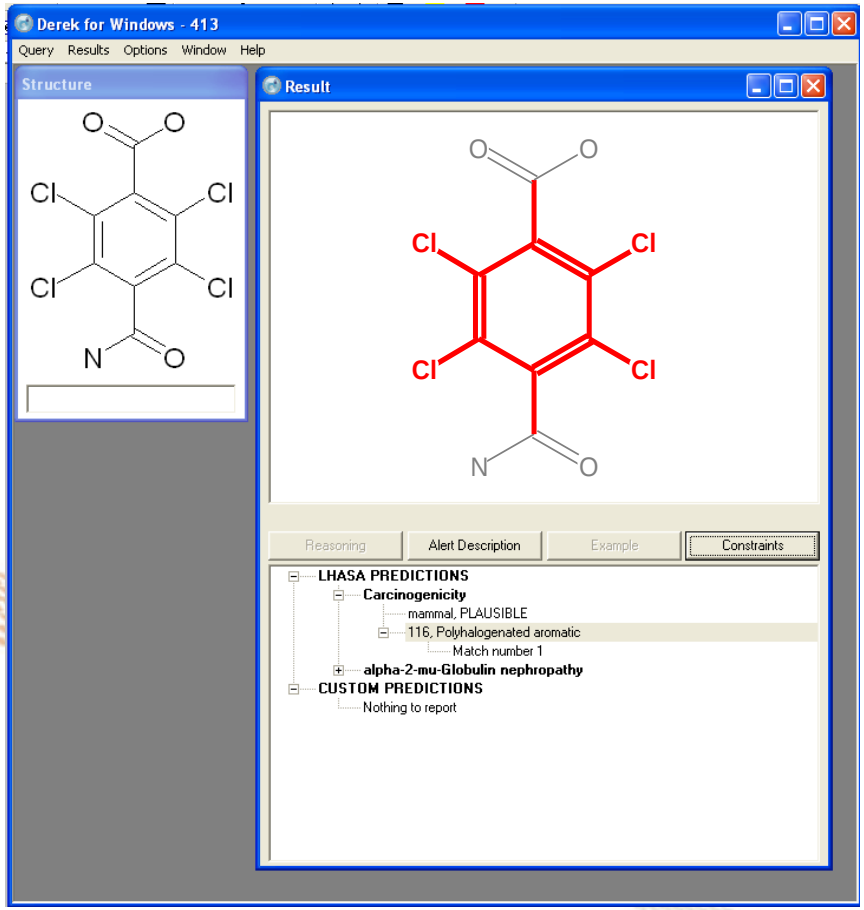
The Food and Environment Research Agency

- Predictive techniques used – TOPKAT and DEREK
- Used to estimate a selection of end-points:
  - Carcinogenicity, mutagenicity, developmental toxicity, potent rat oral LD50, teratogenicity and thyroid toxicity

- Predictive ability of approaches previously assessed for some end-points for some chemical types but not for pesticides and/or metabolites

- Examined ability to estimate the most abundant metabolite experimentally determined toxicological end-points (mutagenicity and rat oral LD50)

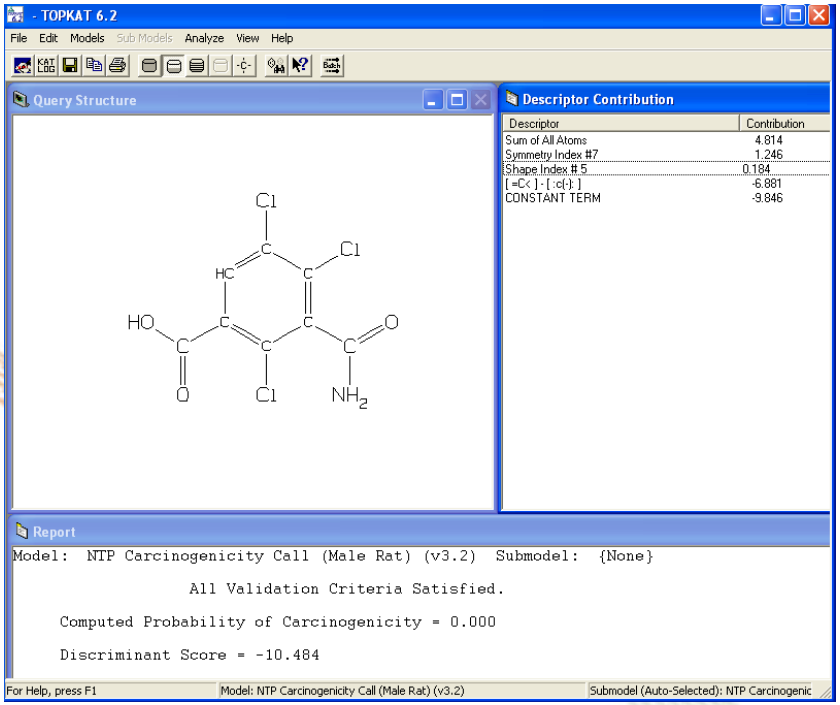
DEREK

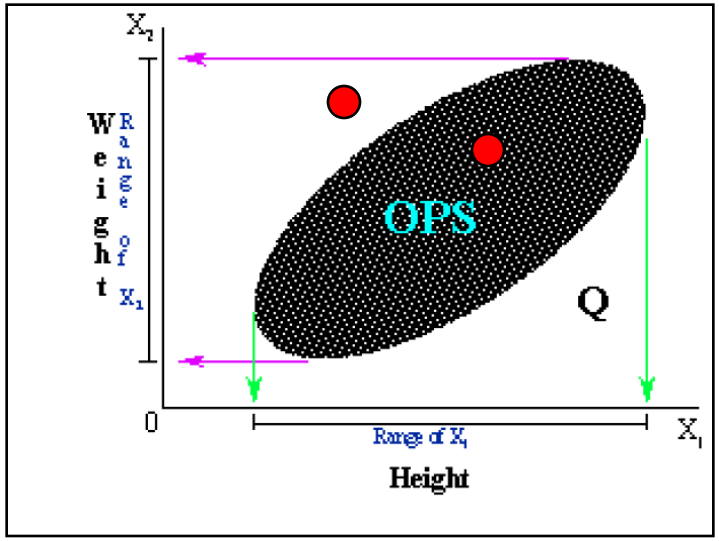


- DEduction of Risk from Existing Knowledge (DEREK) - Lhasa Ltd
- Expert system based on structural alerts
- Qualitative likelihood that molecule will exhibit effect
- If alert present and likelihood plausible, probable or certain

TOPKAT

- Multivariate statistical relationships for a range of mammalian toxicities (Acclerys Inc.)
- Probability estimates (e.g. Ames mutagenicity test)
- Quantitative estimates (e.g. rat oral LD50)





From Accelrys Inc, 2004

Mutagenicity of metabolites

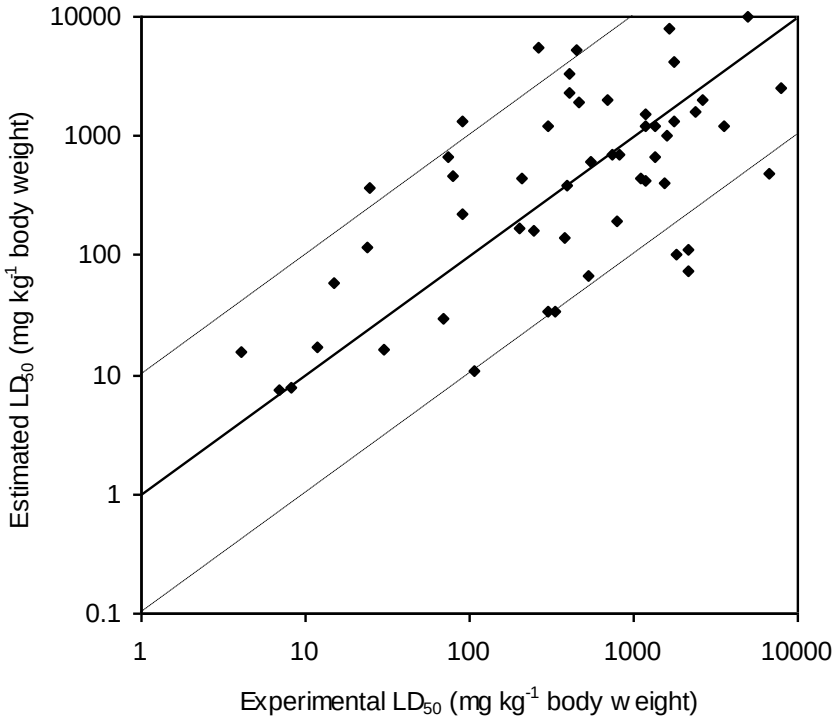
- DEREK and TOPKAT evaluated with experimental data on 120 metabolites (18 positive)
- Experimental inter-lab concordance is ~80%

Exp. data		DEREK		TOPKAT		
		concordant	discordant	concordant	discordant	OOPS
-'ve	102	95	7	57	12	26
+'ve	18	3	15	2	13	1

- Predictive ability can be improved, decreasing false negatives to one by:
  - Considering the mutagenicity of parent
  - Combining both approaches
  - Consider DEREK mutagenicity and chromosome damage alerts

Rat oral LD50 of metabolites

- TOPKAT evaluated with experimental data for 115 metabolites
- 82% within an order of magnitude of exp. values
- Similar to evaluation of Danish EPA (81%)
- ‘Appropriate to give approximation of toxicity’



Pesticidal activity

- 2D structures examined for parent ‘toxicophore’
- 184 did not contain parental toxicophore
- Mode of action literature used to determine if metabolite active
- 82 may act via a pesticidal mode of action

Sinclair and Boxall 2003

Metabolites selected for further study

The Food and Environment Research Agency

- Highest ranked metabolites according to their potential to contaminate raw source water where selected if they were estimated to exhibit:
  - Pesticidal activity (15)
  - Carcinogenicity (10)
  - Mutagenicity (10)
  - Developmental toxicity (10)
  - High rat oral toxicity (10)
  - Thyroid toxicity (5)
  - Tetratogenicity (5)

- In total 53 metabolites were selected for further study

Raw source water estimates

- Metabolite concentrations estimated in 3 catchments
  - high risk to pesticide contamination
  - EA monitoring data for the catchment
- Empirical relationship used to estimate concentrations (previously developed for pesticides)
  - interval between pesticide application and first drainage event
  - metabolite sorption (Kd)
  - clay content of soil (%)
  - metabolite degradation rate in soil (DT50)
  - Catchment scenerios developed with GIS (agricultural statistics, land cover, soil types, ward and catchment boundaries)
- Concentrations in SW a cumulative result of all drained fields were parent was applied, diluted with metabolite free solution from other areas

Raw source water estimates

- Conservative estimate
  - Pesticide applied to all approved crops at the maximum rate e.g. all cereals, default DT50 300d and 3 days between peak metabolite formation and leaching
- Refined estimates
  - Pesticide usage data for the catchment from PUS, more realistic DT50 of 30d and real application timing data for pesticide

Active ingredient	Catchment C	
	Max usage (kg)	Actual usage (kg)
Asulam*	113	645*
Carbendazim	14707	4.9
Chlorothalonil	77234	105

Raw source water estimates

The Food and Environment Research Agency

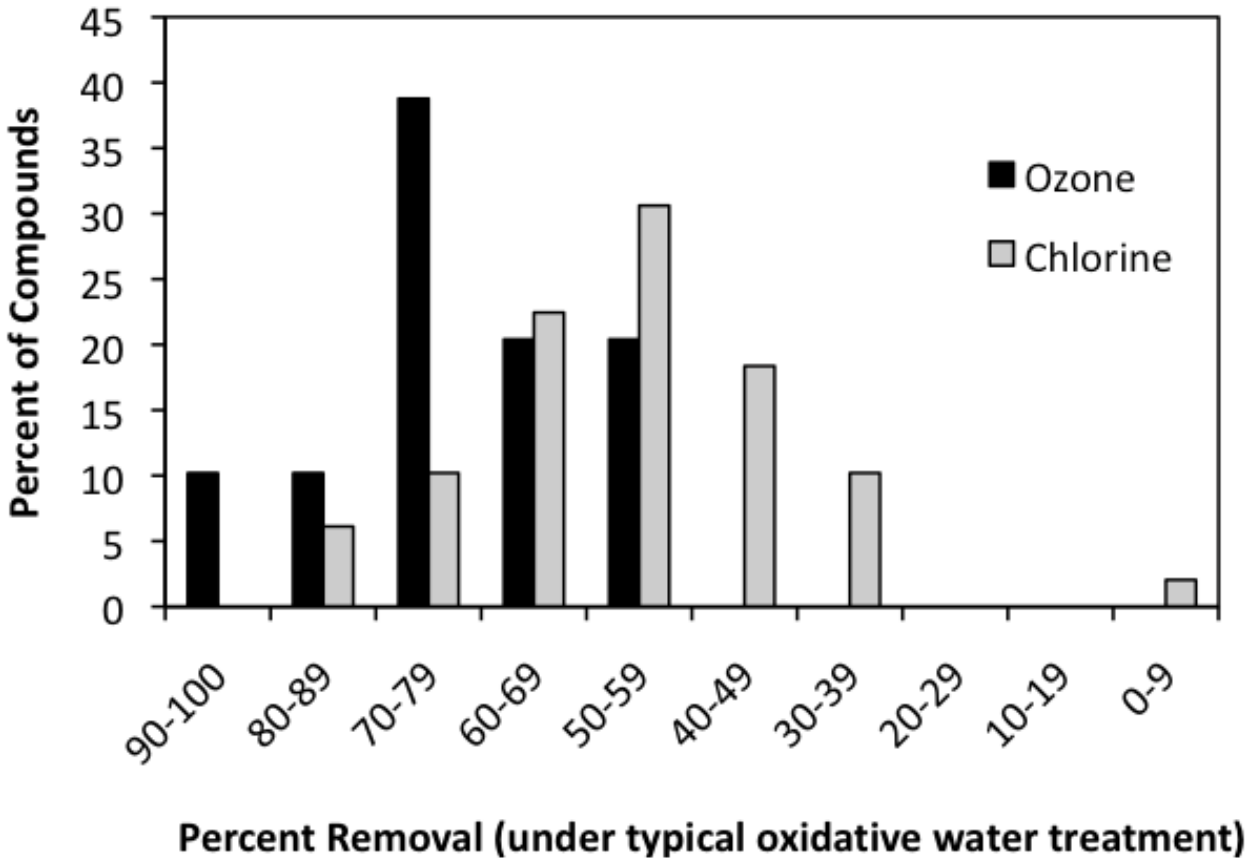
Metabolite	Parent pesticide	Conservative Estimate	Refined Estimate I (DT50)	Refined Estimate II (Pesticide usage)
R417888	Chlorothalonil	53.25	53.25	0.06
diisopropylamine	Tri-allate	41.37	24.57	0.00
3-carbamyl-1,2,4,5-tetrachlorobezoic acid	Chlorothalonil	33.83	22.02	0.04
cyanazine acid	Cyanazine	30.70	11.92	0.00
methomyl	Thiodicarb	23.14	23.14	0.00
metazachlor sulfonic acid	Metazachlor	18.09	7.68	1.61
cis-3-chloroprop-2-enoic acid	1,3-dichloropropene	16.81	8.78	0.00
trans-3-chloroprop-2-enoic acid	1,3-dichloropropene	16.81	8.78	0.00
aldicarb sulfone	Aldicarb	16.01	3.63	0.00
2-aminobenzimidazole	Carbendazim	14.20	7.68	0.01
3-(3-chloro-p-tolyl)-1-methylurea	Chlorotoluron	13.03	10.33	0.12
3-carbamyl-2,4,5-trichlorobenzoic acid	Chlorothalonil	12.45	12.45	0.01
acetaldehyde	Metaldehyde	9.18	3.48	0.04
metazachlor oxalic acid	Metazachlor	7.18	4.05	0.64
methiocarb sulfoxide	Methiocarb	6.62	3.67	0.09

Removal during treatment

- Limited data on metabolite removal during DWTP
- Removal in specific treatments estimated using physical chemical properties
- Processes considered: coagulation, activated carbon, ozonation and chlorination

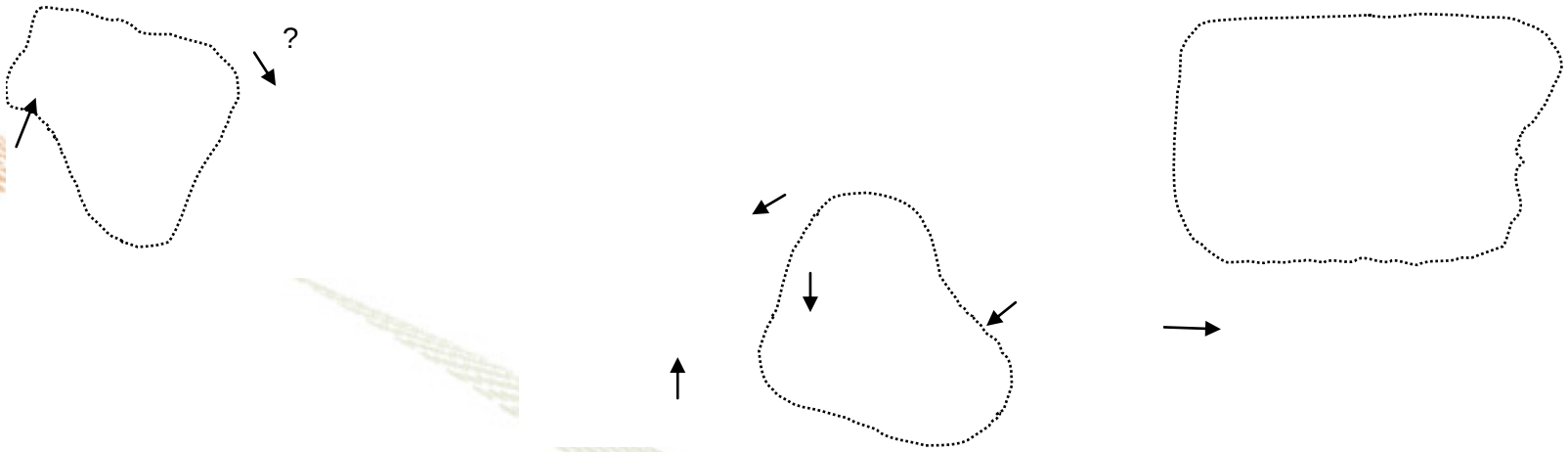
Metabolite	Removal with coagulation (%)	Removal with PAC (%)	Removal with chlorination (%)
aldicarb sulfone	0	15	39
aldicarb sulfoxide	0	15	46
sulfanilamide	0	15	69.5
deethylatrazine	25	50	47.7
reference compound 10	25	50	73.4
2-aminobenzimidazole	0	50	70.9

Removal with chlorination



Effect of ozonation and chlorination

- Susceptible sites to electrophilic attack by chlorine
- Compared tox. moities with sus. moieties
  - Those likely to be oxidized in water treatment by ozone or chlorine
  - Those whose water treatment degradates might be detoxified during oxidation (21) versus those that might be expected to retain their toxicity (11)



Current on-going work

- Estimate daily intakes of metabolites
- Develop project specific derived values (PSDV) in absence of ADI's for metabolites
- Evaluation proportion of PSDV/ADI for a metabolite that the daily intake represents
- Consider the potential toxicity hazard and determine whether any of the metabolites considered pose a risk to the UK population

Acknowledgements

Fera
- Wendy van Beinum, Miles Thomas

University of York
- Guy Buamann

Cranfield University
- Simon Parsons, Emma Goslan, Ruth Bevan and Len Levy

Kansus University
- Craig Adams

Thank you for listening

fera
The Food and Environment Research Agency