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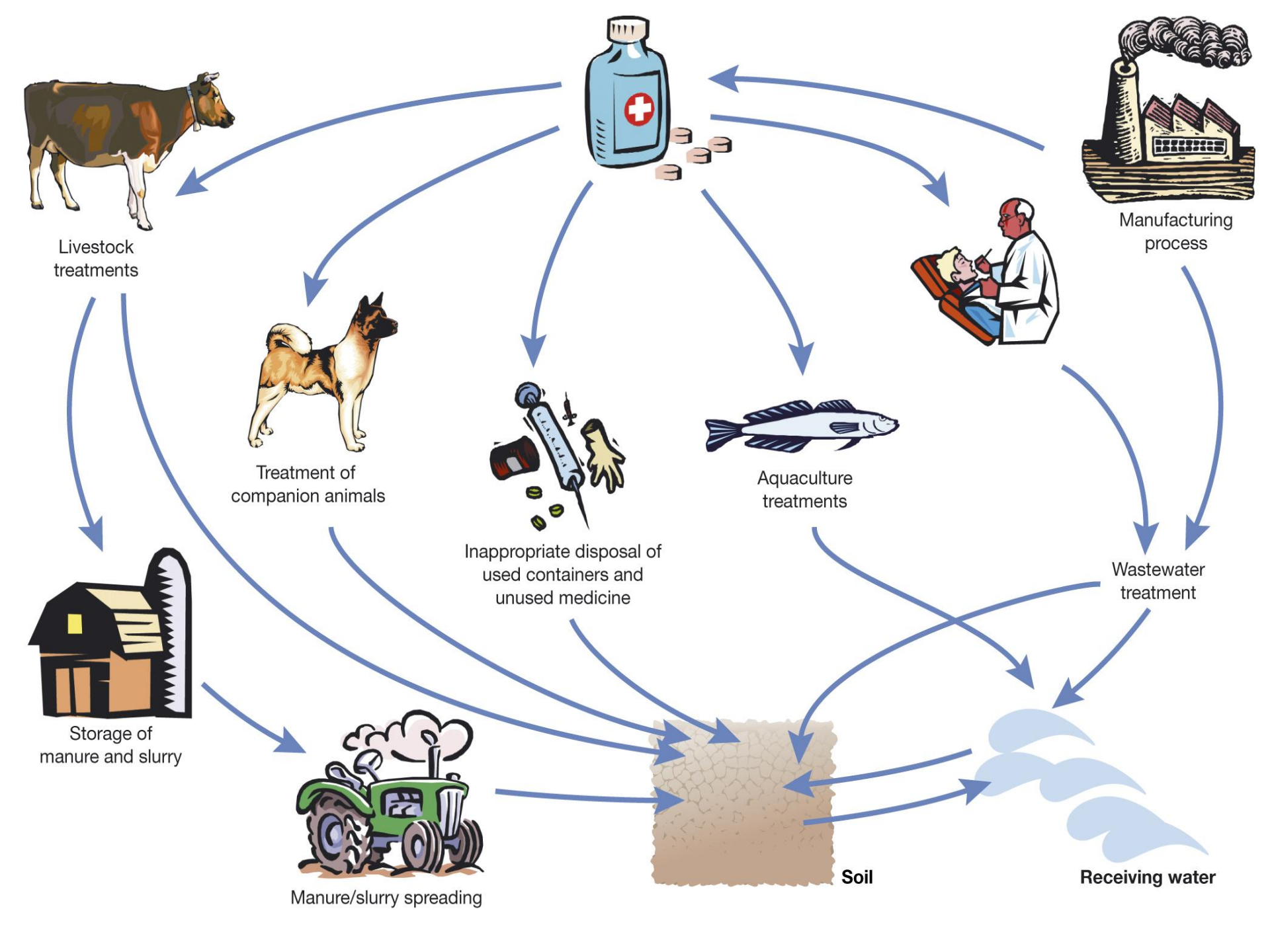
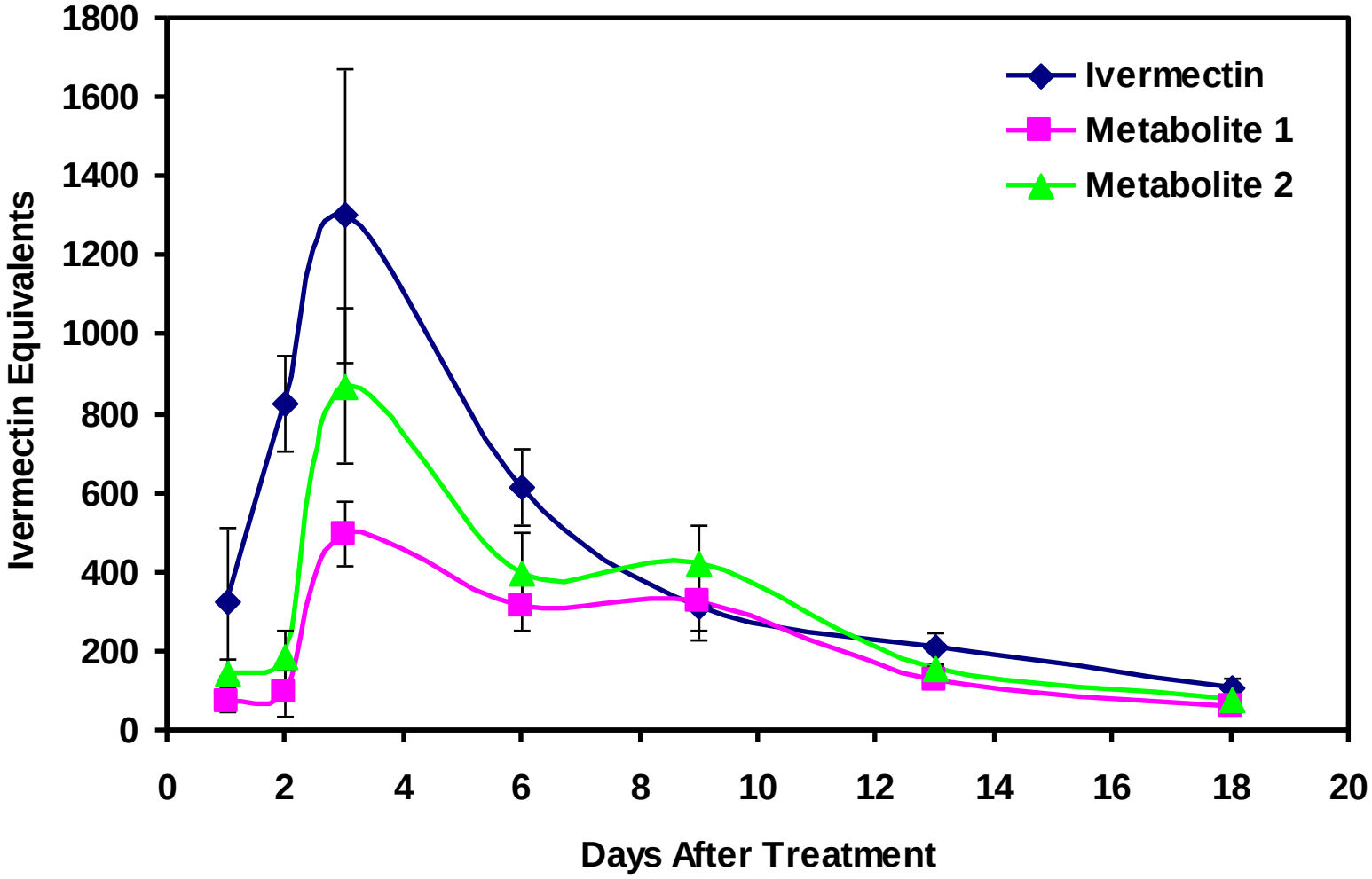
Are Veterinary Medicines Causing Environmental Risks?

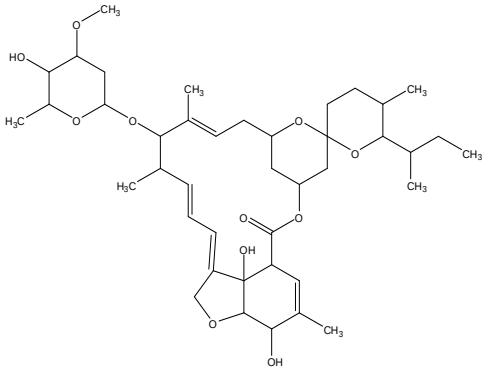
Nine species of vultures in the wild numbered 40 million birds in the early 1980s. Today, only about 60,000 birds are left'

(Vibhu Prakash, Bombay Natural History Society)

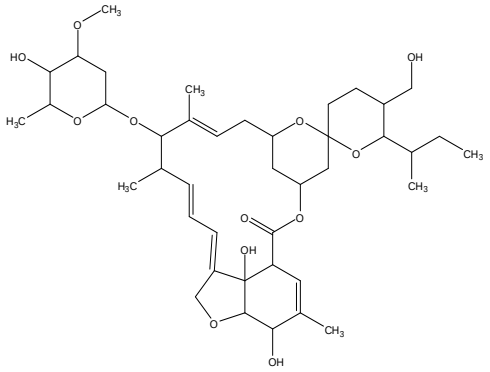

Livestock treatments
Manufacturing process
Treatment of companion animals
Inappropriate disposal of used containers and unused medicine
Aquaculture treatments
Wastewater treatment
Storage of manure and slurry
Manure/slurry spreading
Soil
Receiving water

Excretion Profile

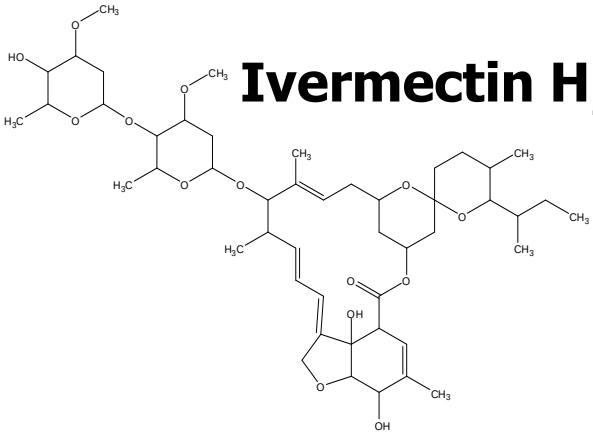




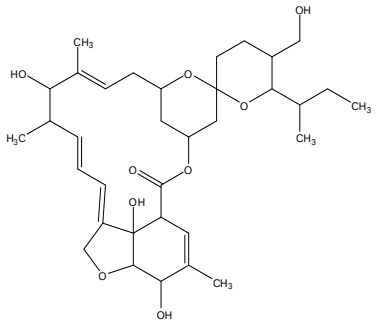
H_2B_{1a} Monosaccharide



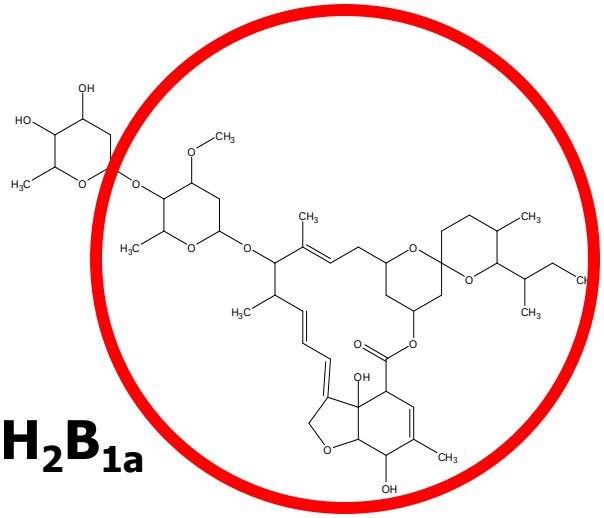
24 Hydroxymethyl H_2B_{1a} Monosaccharide



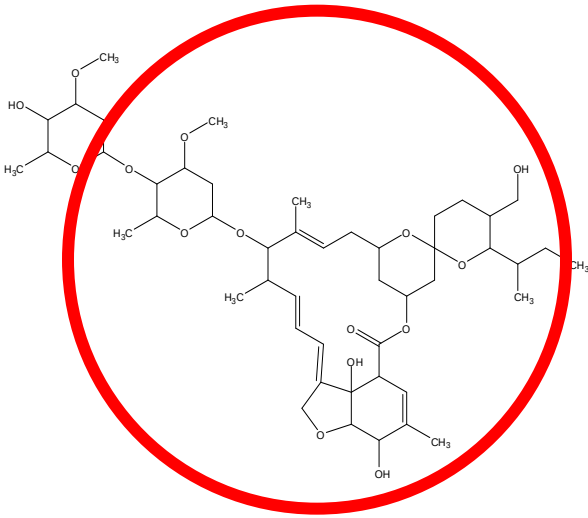
Ivermectin H_2B_{1a}



Aglycone



3”-O-Desmethyl H_2B_{1a}



24 Hydroxymethyl H_2B_{1a}

Dissipation in the Field

- Dung collected 3 days after treatment
- 500 ml dung pats

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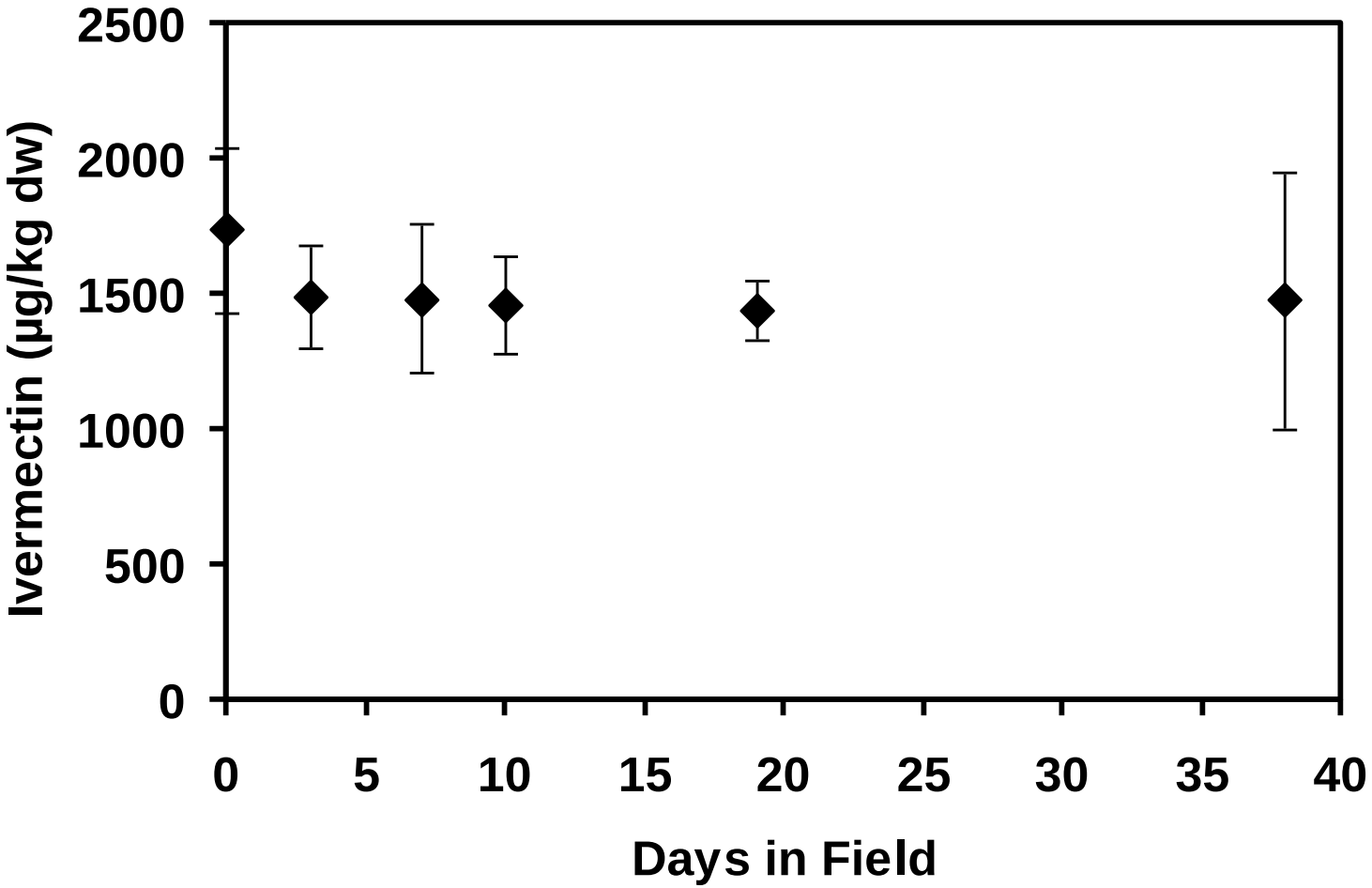
Ivermectin Persistence in Dung



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Transfer of Ivermectin to soil

- Soil sampled directly beneath pats
- 3 depths
  - 0-1cm
  - 1-3cm
  - 3-5cm
- For each pat and each time point

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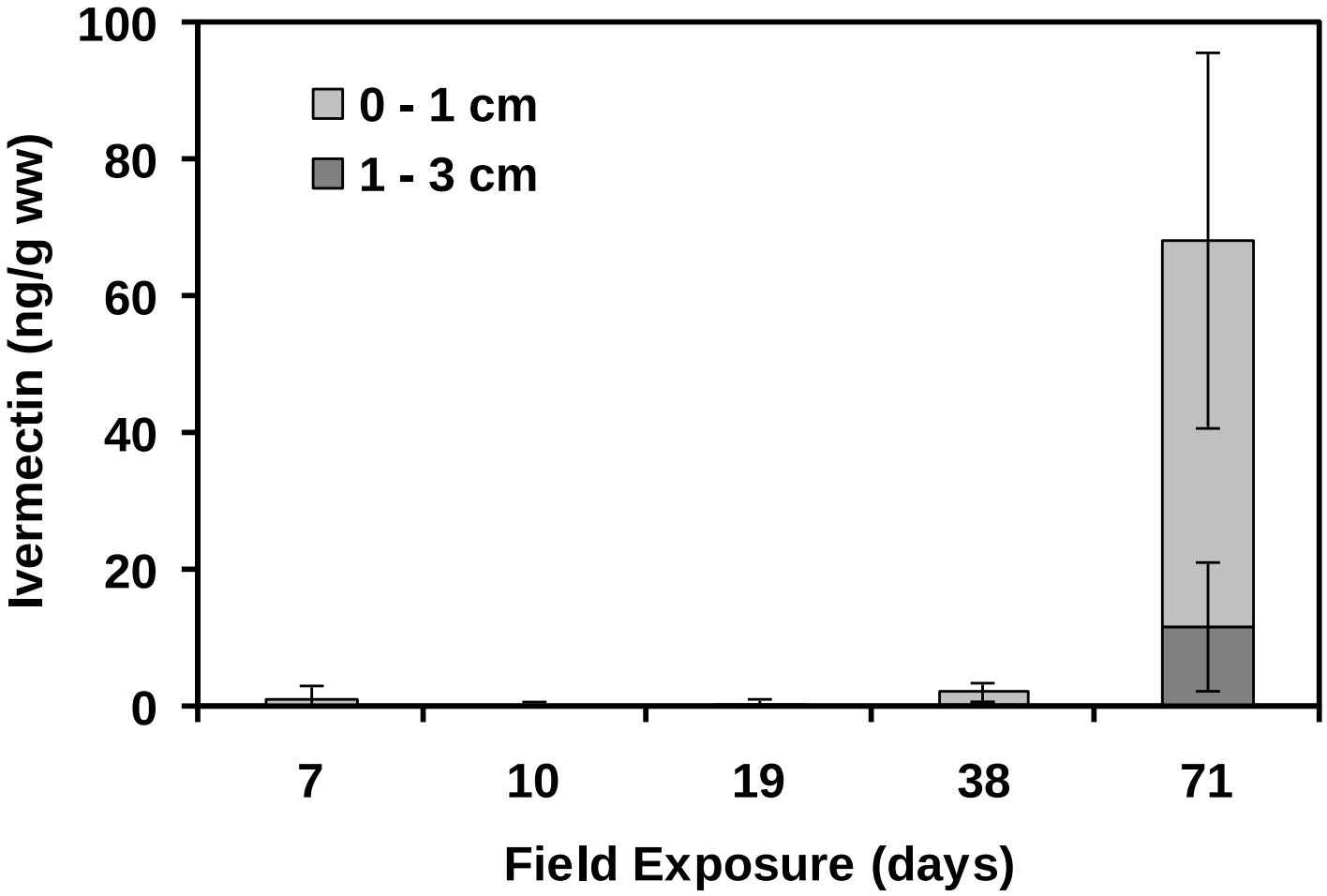
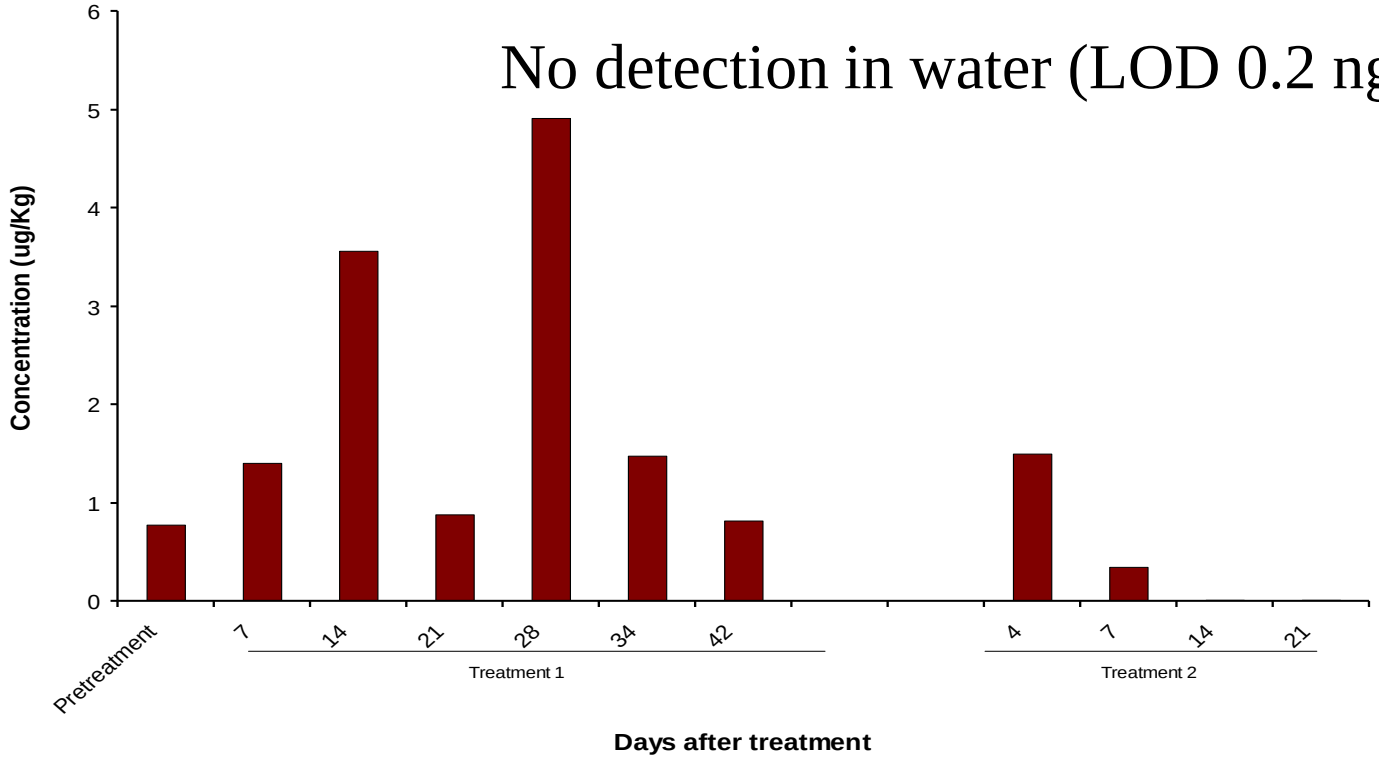
Transfer of Ivermectin to soil



Direct excretion into water

- Ivermectin
- Dung, water, sediment
- Two treatment cycles

No detection in water (LOD 0.2 ng/l)



Antibiotics

Sulfonamides

Tetracyclines

Fluoroquinolones

Lincosamides

Antiparasitics

Macrocyclic lactones

Benzimidazoles

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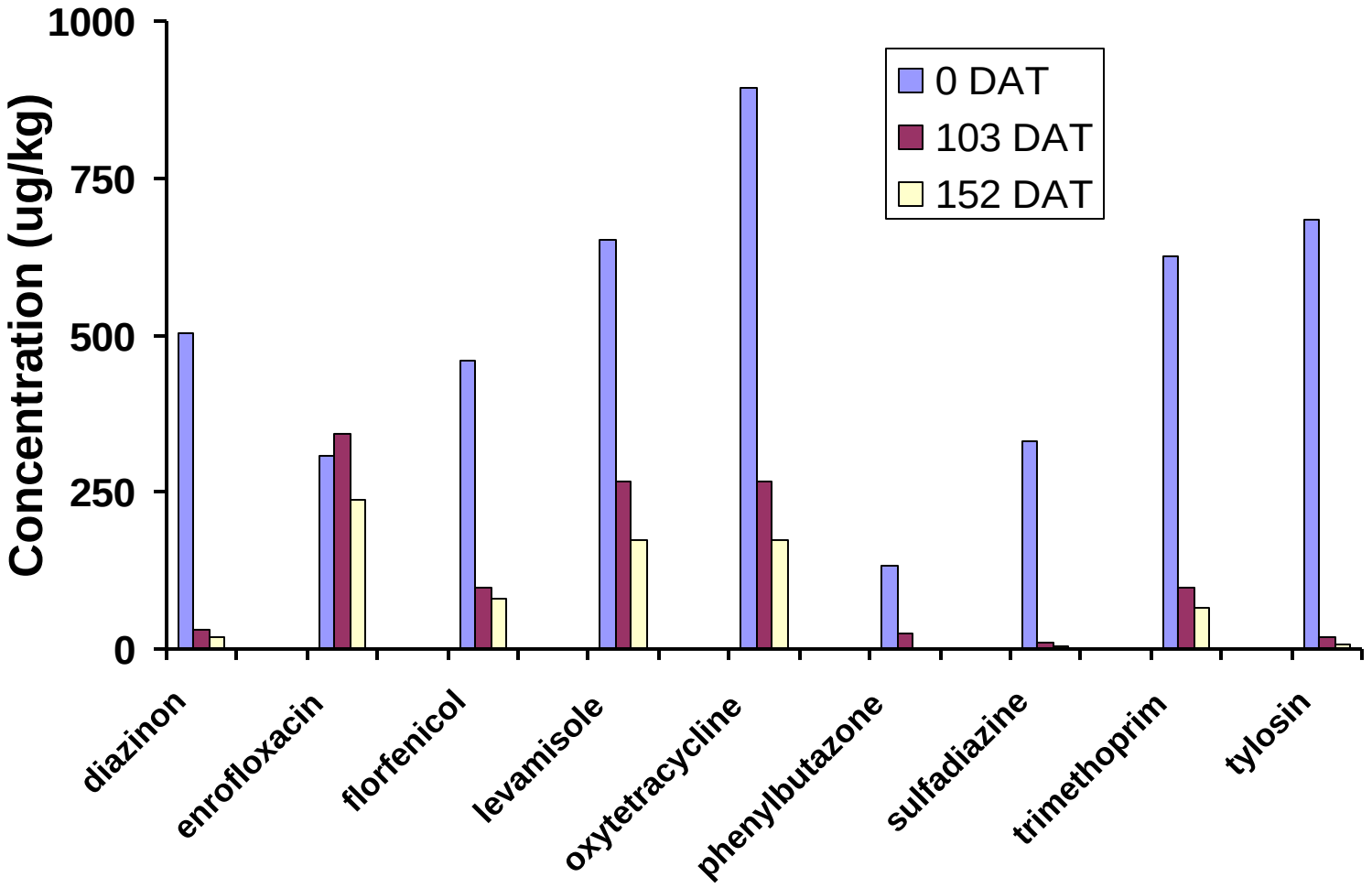
Persistence in soils



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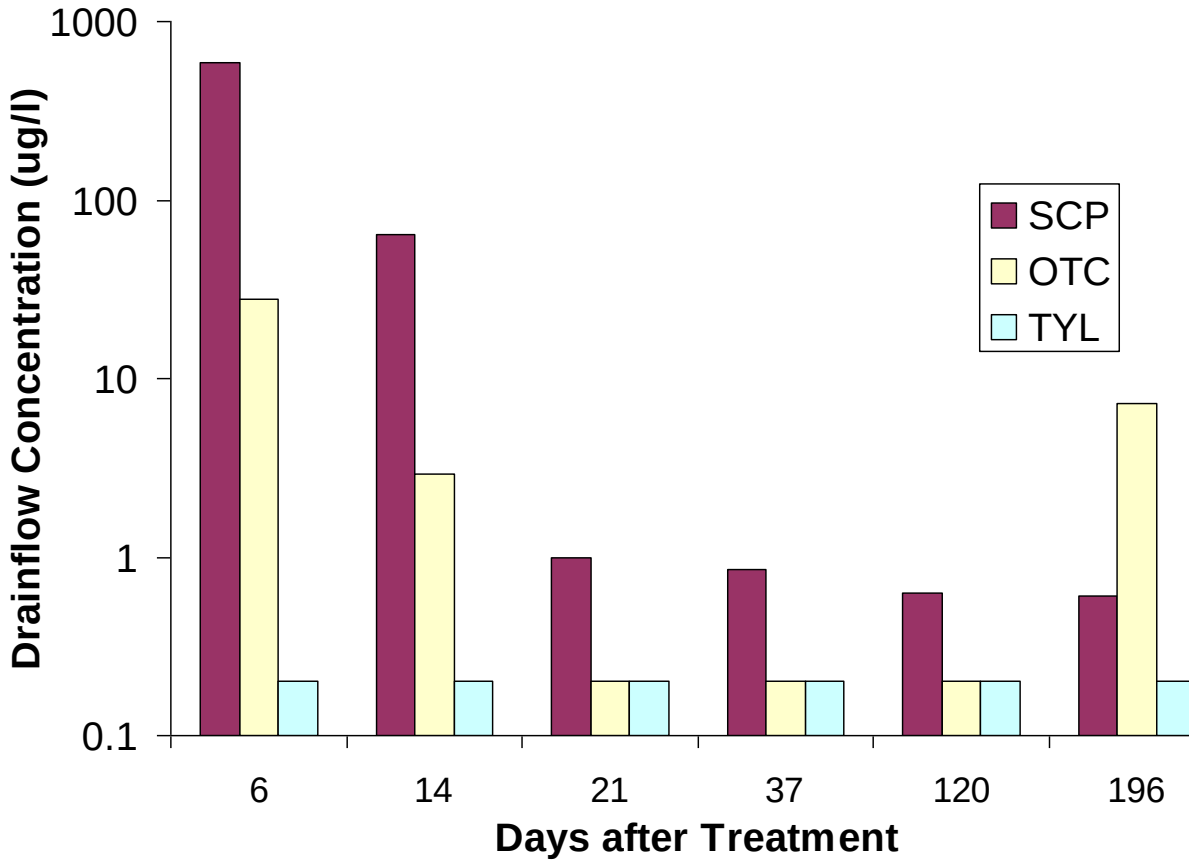
Concentrations in drainflow



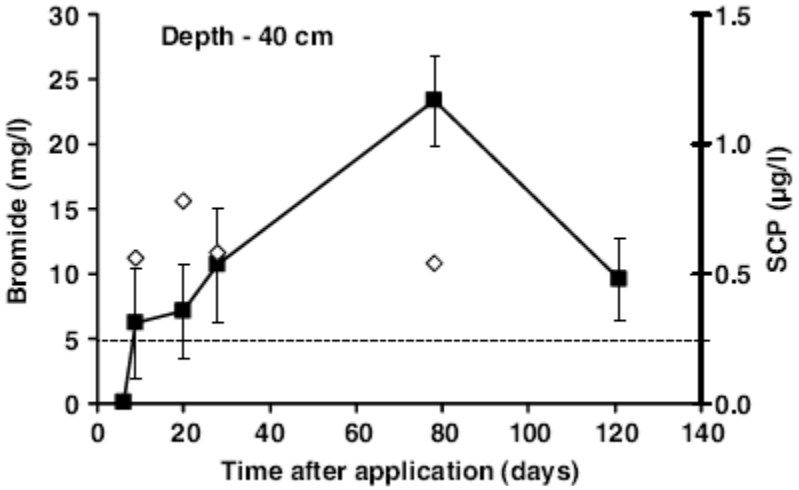
Surface runoff

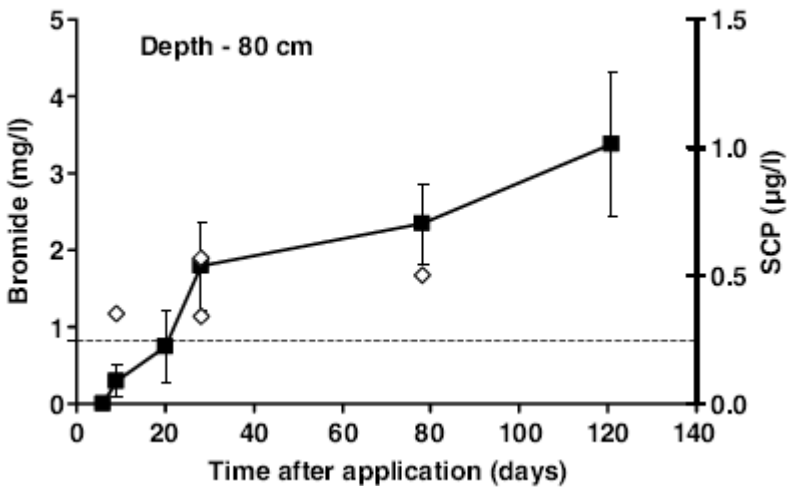
- 2 days after slurry application:
  - 47 µg/l SCP (dissolved phase)
  - 8 µg/l OTC (dissolved phase)
- 50 days after application:
  - Less than 0.5 µg/l of both SCP and OTC
- Much greater runoff generated by plot containing tractor wheelings
- Lots of sediment transported in surface runoff - high concentrations of OTC likely

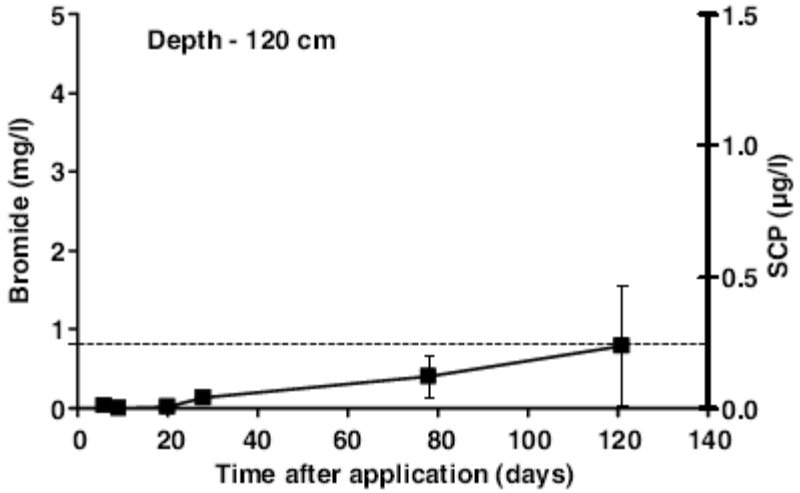
Leaching to groundwater

- Sampled throughout the soil profile using suction cups
- Intercepts leaching water
- Analysed for antibiotics and bromide tracer
- 3 depths (40, 80, 120 cm)

Field leaching studies







Tylosin and oxytetracycline not detected

Blackwell et al., Chemosphere2007

Pharmaceuticals in groundwater

Class	Examples
antiinflammatories	diclofenac
antibiotics	erythromycin, sulfadiazine, oxytetracyline
antiepileptics	carbamazepine
B-blockers	sotalol
X-ray contrast media	iopromide
hormones	estradiol, ethinylestradiol
lipid regulators	bezafibrate

Monteiro and Boxall, 2010

Inputs to aquatic systems

- Cattle treated with ivermectin pour on
- Runoff from farmyard monitored continuously
- Concentrations of ivermectin in runoff detemined by HPLC-FD

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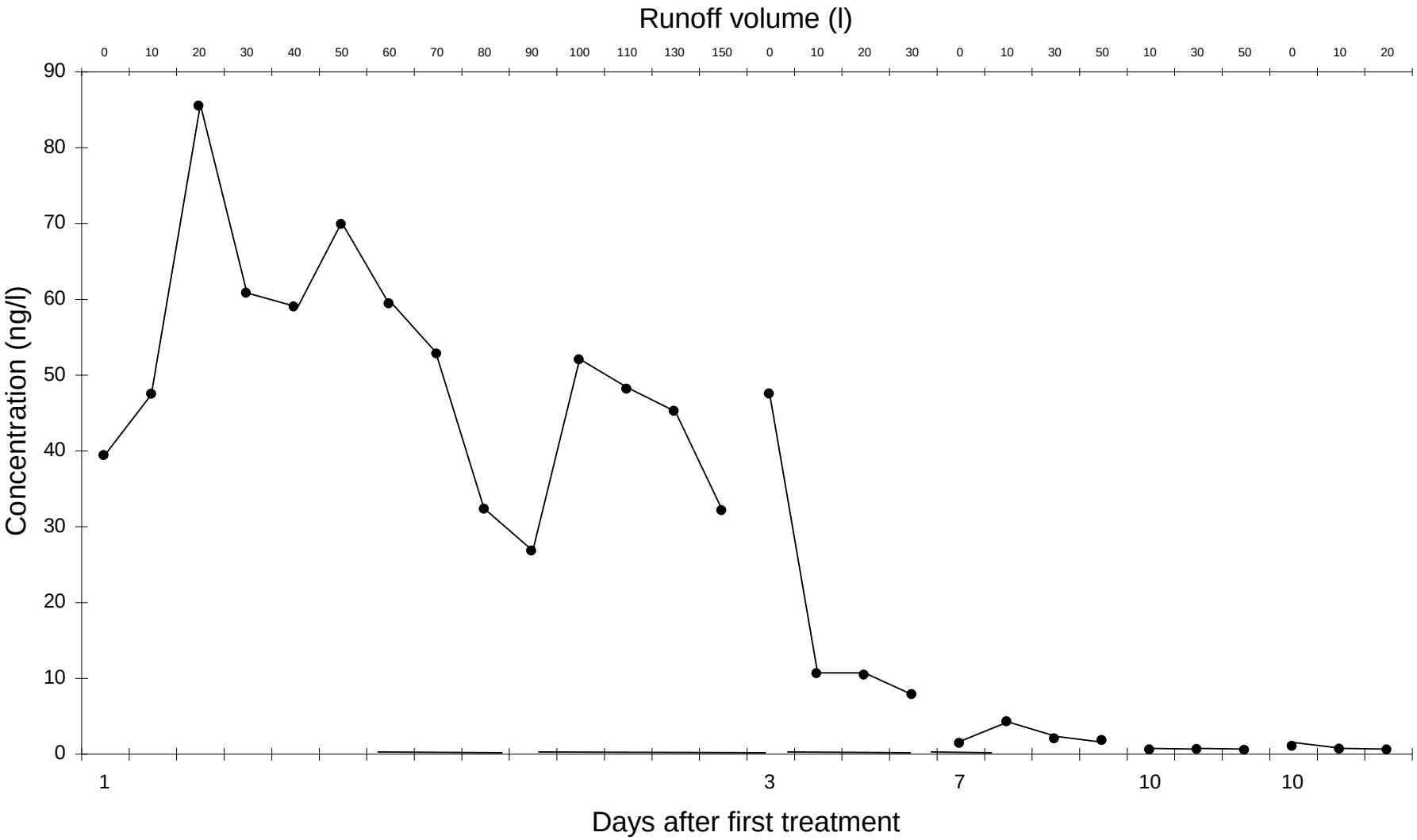
Runoff results



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Peak concentrations in farmyard runoff

Study site/Active	Concentration of active in product	Maximum measured concentration in runoff ($\mu g\ L^{-1}$)
Site 1		
dicyclanil	50 g/L	441.7
ivermectin	8 g/L	0.120
deltamethrin	1 g/L	<0.100
cyromazine	6 g/L	104.0
Site 2		
ivermectin	5 g/L	0.085

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Uptake into crops

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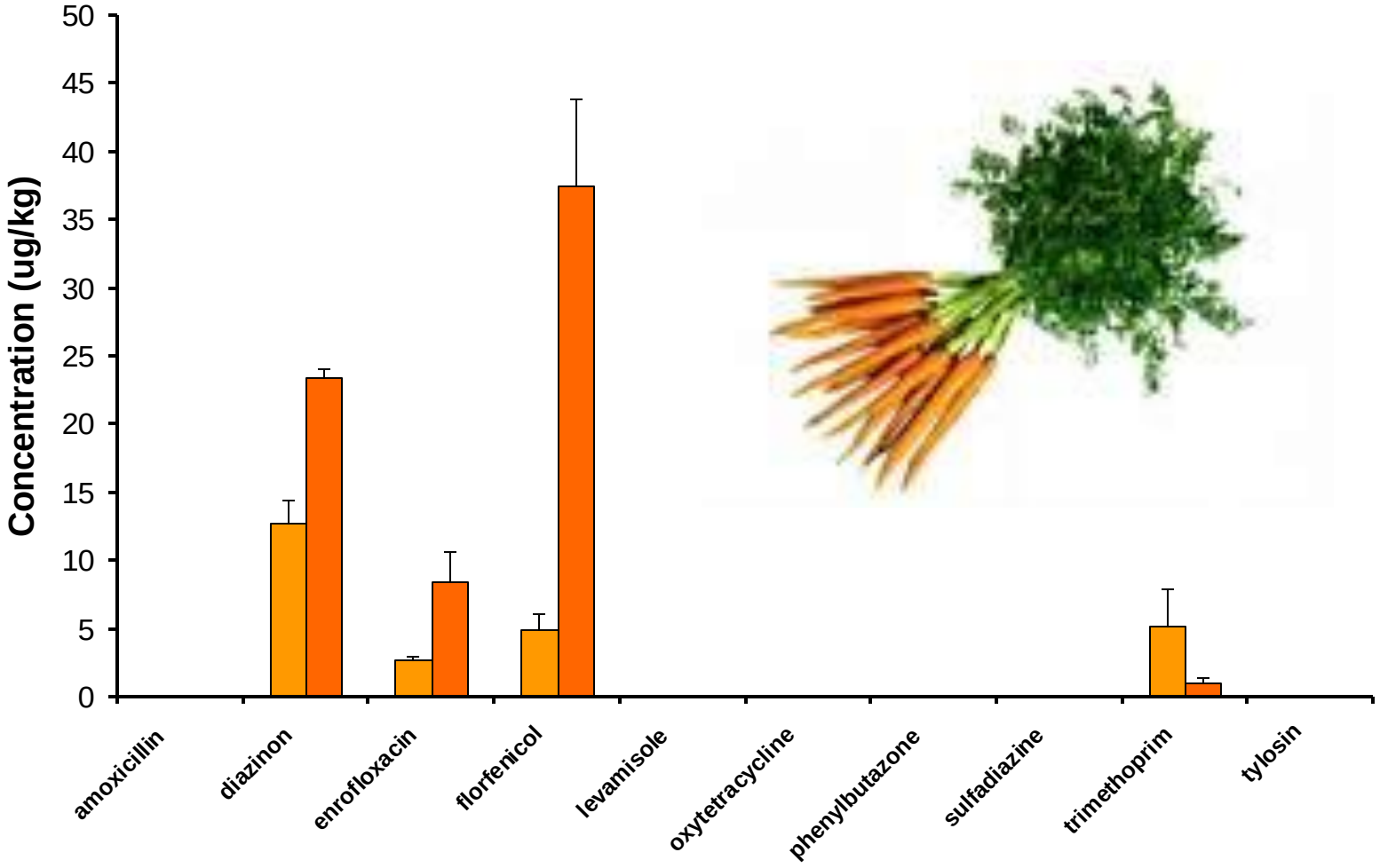
Uptake into crops



Boxall et al., JAFC (2006)

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Effects on organisms?

- Limited toxicity to fish, invertebrates and green algae
- High toxicity to cyanobacteria
- Some antibiotics appear to be very toxic to terrestrial and aquatic plants
- Few impacts seen in standard C&N mineralisation studies with soils
- Effects on microbes can lead to impacts on key ecosystem processes (e.g. degradation of other substances)
- Human exposure very low

	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	

Is their a risk

Table 4.2 Comparison of maximum measured concentrations in surface waters with PNECs

Compound	Most sensitive endpoint	EC50 (mg l^{-1})	Calculated PNEC (µg l^{-1})	Maximum measured concentration (µg l^{-1})	MEC:PNEC
oxytetracycline	*S. capricornutum* 72 h EC50	4.5	45	4.49	0.10
sulfadiazine	*S. capricornutum* 72 h EC50	3.49	34.9	4.13	0.12
trimethoprim	*S. capricornutum* 72 h EC50	16	16	0.02*	0.001*
ivermectin	*Daphnia magna* 48 h EC50	0.000025	0.00025	<0.0002	<0.8
doramectin	*Daphnia magna* 48 h EC50	0.0001	0.001	<0.001	<1
lincomycin	*Daphnia magna* 48 h EC50	379.4	379	21.1	0.056

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Peak concentrations in farmyard runoff

Study site/Active	Concentration of active in product	Maximum measured concentration in runoff (μg L^{-1})
Site 1		
dicyclanil	50 g/L	441.7
ivermectin		0.120
deltamethrin		<0.100
cyromazine	6 g/L	104.0
Site 2		
ivermectin	5 g/L	0.085

LOEC of 0.00001 μg/L (Garric 2007)

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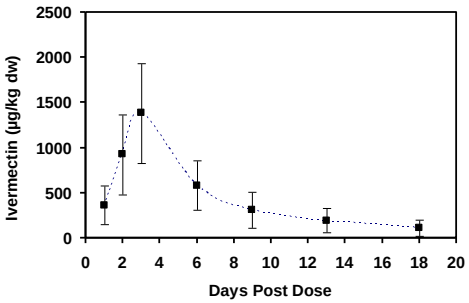
Toxicity to dung organisms

Taken from Forster et al., 2010
RCR = 9000 (field study >8)

Test organism	Test method	Effect concentration[a]	Reference
Musca autumnalis (dung fly)	OECD (2008a)	*$EC50_{21\ d,\ emergence\ rate}$ = 4.65 µg/kg dung fresh wt*	Römbke, Barrett, et al. (2010)
Scathophaga stercoraria (dung fly)	OECD (2008a)	$LC50_{28\ d}$ = 20.9 µg/kg dung fresh wt	Römbke et al. (2009)
		$NOEC_{28\ d,\ development\ time}$ = 0.84 µg/kg dung fresh wt	
	Specific test design (acute toxicity)	$LC50_{48\ h,\ larvae}$ = 36 µg/kg dung fresh wt	Strong and James (1993)
		$EC50_{3–4\ w.,\ emergence}$ = 1.0 µg/kg dung fresh wt	
Aphodius constans (dung beetle)	OECD draft (2009)	*$LC50_{21\ d}$ = 176 µg/kg dung fresh wt*	Hempel et al. (2006)
		$LC50_{21\ d}$ = 880 µg/kg dung dry wt	
		$NOEC_{21\ d,\ larval\ survival}$ = 320 µg/kg dung dry wt	
Aphodius constans (dung beetle)	OECD draft (2009), modified	$LC50_{21\ d}$ = 100 µg/kg dung fresh wt[b]	Lumaret et al. (2007)
		$LC50_{21\ d}$ = 590 µg/kg dung dry wt	

Modelling reality

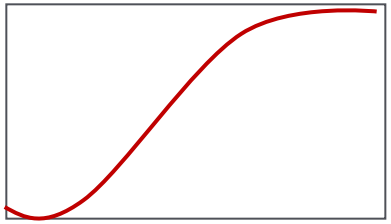


Excretion profile

Medicine use patterns

Husbandry practices

Impact on population



Compound dose response

Insect life cycle and behaviour

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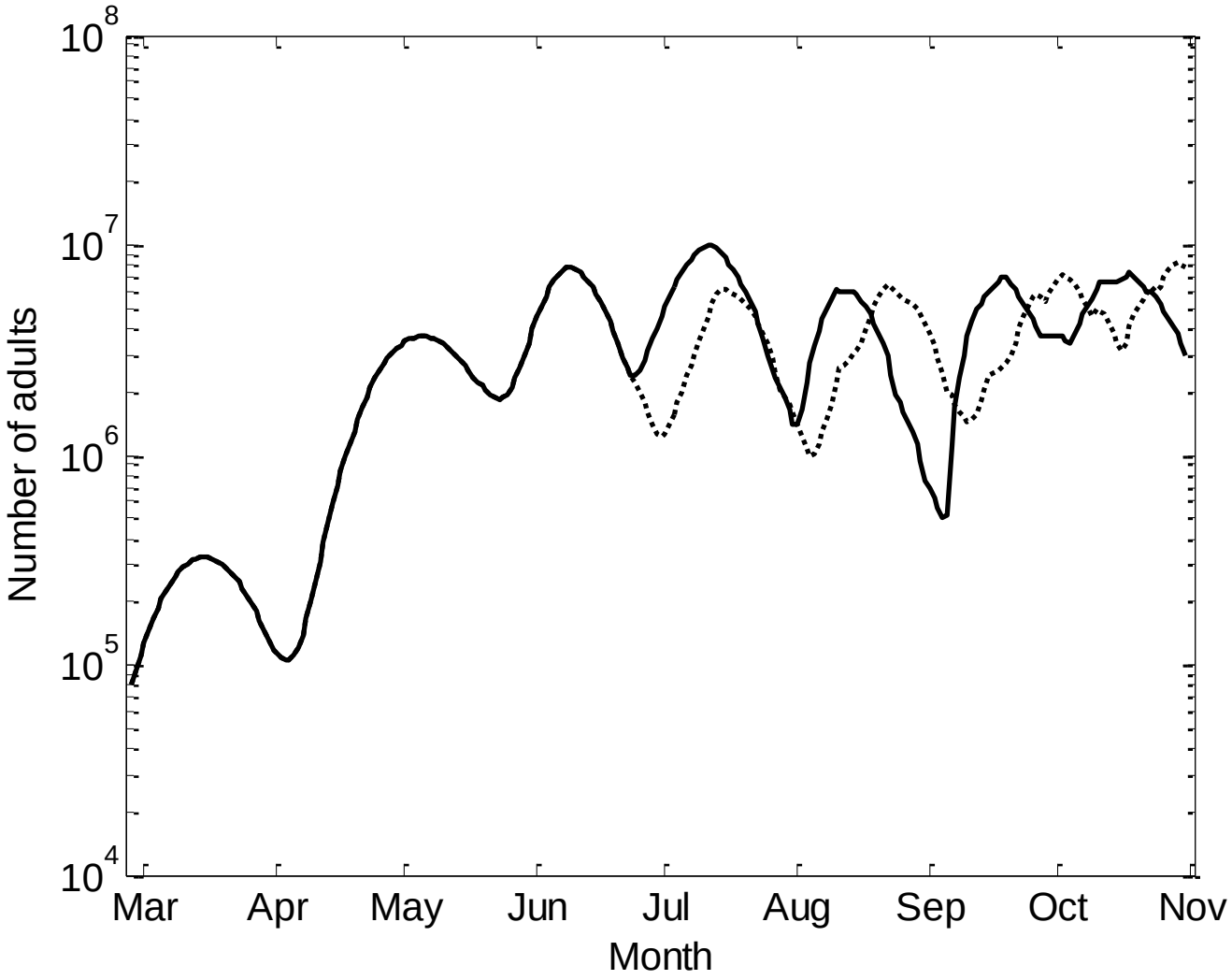
Are effects caused at the farm scale? - modelling insect numbers



Antibiotic resistance

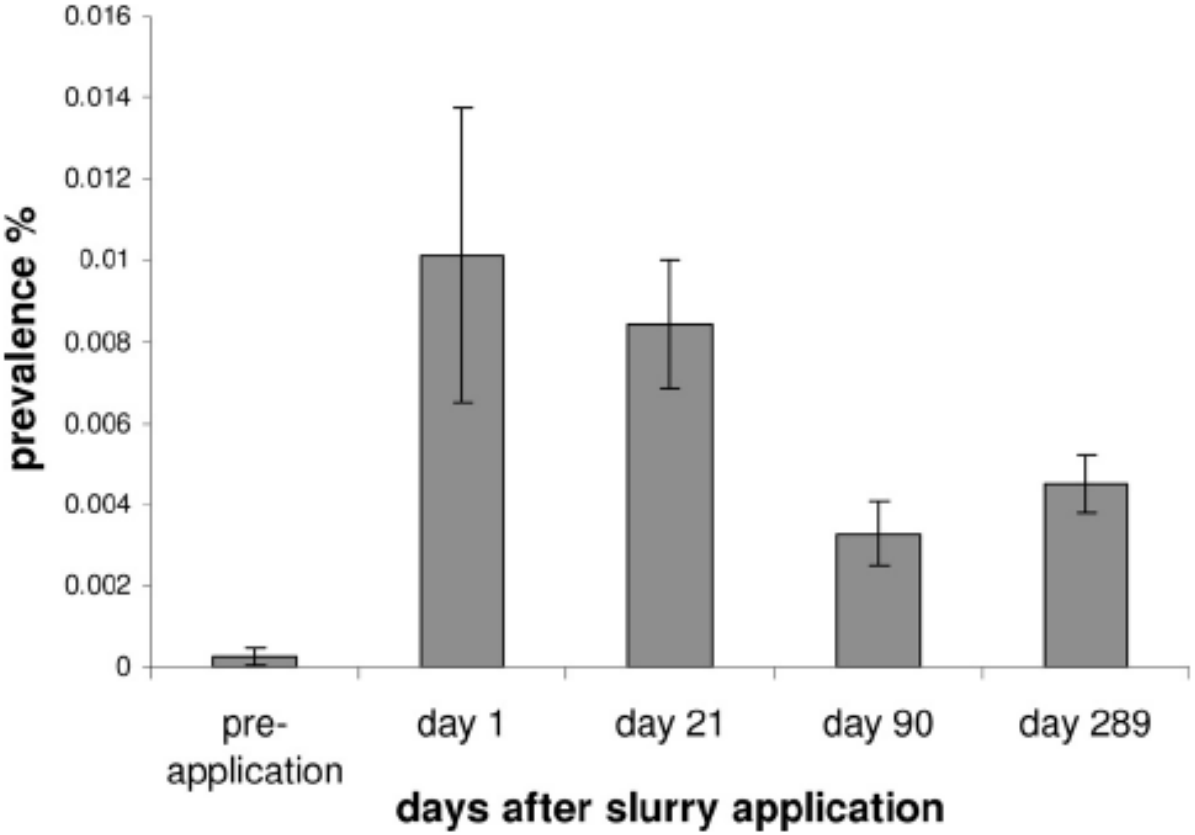


FIG. 1. Molecular prevalence of *intI1* in soil amended with pig slurry. Error bars represent standard errors of the results for three replicate samples (four in preapplication soil); the prevalences are statistically significantly different from one another at all time points (chi-square test, $P < 0.0001$).

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Conclusions

- Veterinary medicines and their metabolites released to and occur in the environment
- We now have a very detailed understanding of the fate and standard effects of many veterinary drugs in the environment
- Standard risk assessment approaches suggest limited risk but…….
- We may be missing the important pathways and important endpoints
- More ‘intelligent’ approaches could help