Salmonella and *Campylobacter* control on the farm: the role of rodents

BRITISH VETERINARY POULTRY ASSOCIATION

Spring Meeting, 12-13th March 2020

Dr Alan Buckle, Chairman Campaign for Responsible Rodenticide Use UK and Visiting Research Fellow University of Reading

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What is CRRU?

- Not-for-profit company limited by guarantee
- 14 funding companies, all rodenticide manufacturers/authorisation holders
- Provides the only rodenticide stewardship framework that meets HSE 'High-level principles' https://www.hse.gov.uk/biocides/eu-bpr/rodenticides.htm
- All who hold UK authorisations for professional rodenticides must be members
- CRRU offers "guidance" (e.g. CoBP and farm assurance scheme standards) but holds no statutory powers
- But CRRU guidance carries regulatory weight because of label phrases such as:
  - *"For supply to and use only by professional users holding certification demonstrating that they have been trained according to the UK second generation anticoagulant rodenticide (SGAR) stewardship programme requirements."*
  - *"Read the label before use. Using this product in a manner that is inconsistent with the label may be an offence. Refer to the CRRU UK Code of Best Practice (or equivalent) for guidance."*
  - *"For permanent baiting follow any additional instructions provided by the CRRU Guidance on Permanent Baiting"*

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Rodents, *Salmonella* and *Campylobacter*

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Disease organisms present in UK Norway rats – University of Oxford study

Disease Agent	Disease of Man/Animals	% infected/infested rats
Ectoparasites		
Fleas	-	100
Mites	-	67
Lice	-	38
Helminths		
Capillaria spp	Capillariasis	23
Hymenolepis diminuta	Rodent tapeworm	22
Toxocara cati	Toxocariasis	15
Hymenolepis nana	Rodent/human tapeworm	11
Rickettsia		
Coxiella burnetti	Q fever	34

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Disease organisms present in UK Norway rats – University of Oxford study

Disease Agent	Disease of Man	% rats carrying disease
Bacteria		
Leptospira spp	Weil's disease	14
Listeria spp	Listeriosis	11
Yersinia entericolitica	Yersiniosis	11
Pateurella spp	Pasteurellosis	6
Pseudomonas spp	several pathologies	4
Salmonella spp	Salmonellosis	0
Protozoa		
Cryptosporidium parvum	Cryptosporidiosis	63
Toxoplasma gondii	Toxoplasmosis	35
Viruses		
Hanta virus	Hantaan-fever	4

Webster, J. P. and D. W. Macdonald (1995). Parasites of wild brown rats (*Rattus norvegicus*) on UK farms. Parasitology 109: 37-43.

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Salmonella

Salmonella sp.

- **Only occasionally isolated from rodents**
- **8% of rat faecal samples positive for *Salmonella* in urban rats in the West Midlands (Hilton *et al.*, 2002)**
- **Bacteria in rat faeces remain viable for >80 days**
- **Transmitted from animals to humans, often via meat-based food products**
  - *Salmonella* Enteriditis (mild)
  - *Salmonella* Typhimurium (mild)
  - *Salmonella* Typhi (Typhoid fever, aggressive)
- **During outbreaks rodents may also be important in mechanical transmission**
- **Many animal specific strains that rats transmit at animal husbandry units (poultry particularly affected)**

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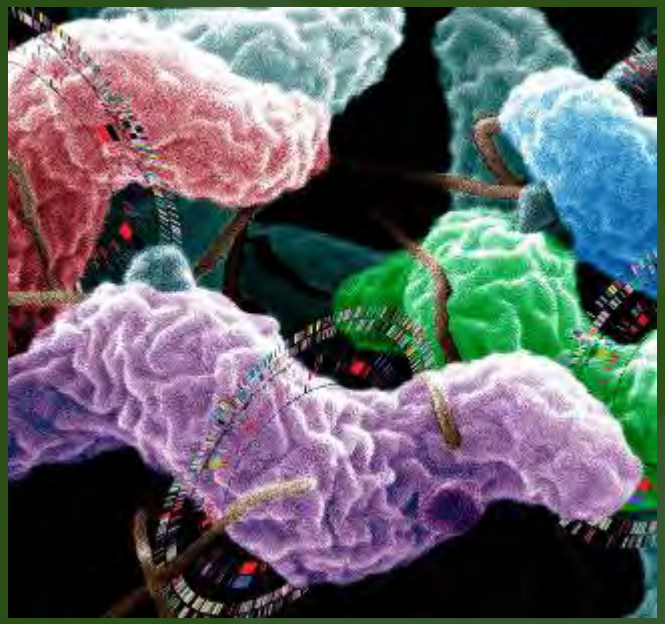
Campylobacter



Campylobacter sp.

- **The most common food-borne disease, with significant increases in last 15 years**
- **Present in a wide range of animals, poultry, cattle, pigs, pets**
- **No adverse effects in most animal hosts**
- **Transmitted from animals to humans, often via meat-based food products:**
  - *Campylobacter jejuni*
  - *Campylobacter coli*
- **Infections usually mild but may be serious for immuno-supressed and young**
- **During outbreaks rodents may be important in mechanical transmission**

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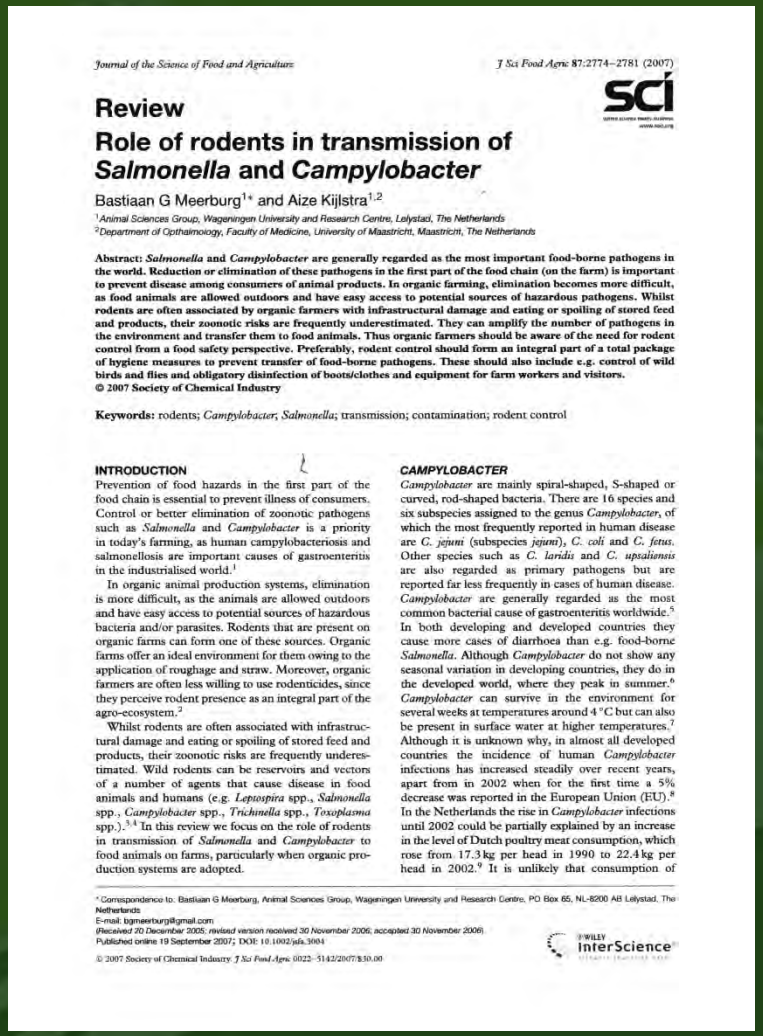
Role of rodents in disease transmission



Journal of the Science of Food and Agriculture J Sci Food Agric 87:2774–2781 (2007)

Review

Role of rodents in transmission of *Salmonella* and *Campylobacter*

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[2]Department of Opthalmology, Faculty of Medicine, University of Maastricht, Maastricht, The Netherlands

Abstract: ***Salmonella*** **and** ***Campylobacter*** **are generally regarded as the most important food-borne pathogens in the world. Reduction or elimination of these pathogens in the first part of the food chain (on the farm) is important to prevent disease among consumers of animal products. In organic farming, elimination becomes more difficult, as food animals are allowed outdoors and have easy access to potential sources of hazardous pathogens. Whilst rodents are often associated by organic farmers with infrastructural damage and eating or spoiling of stored feed and products, their zoonotic risks are frequently underestimated. They can amplify the number of pathogens in the environment and transfer them to food animals. Thus organic farmers should be aware of the need for rodent control from a food safety perspective. Preferably, rodent control should form an integral part of a total package of hygiene measures to prevent transfer of food-borne pathogens. These should also include e.g. control of wild birds and flies and obligatory disinfection of boots/clothes and equipment for farm workers and visitors.**

Keywords: rodents; *Campylobacter*; *Salmonella*; transmission; contamination; rodent control

INTRODUCTION

Prevention of food hazards in the first part of the food chain is essential to prevent illness of consumers. Control or better elimination of zoonotic pathogens such as *Salmonella* and *Campylobacter* is a priority in today's farming, as human campylobacteriosis and salmonellosis are important causes of gastroenteritis in the industrialised world.[1]

In organic animal production systems, elimination is more difficult, as the animals are allowed outdoors and have easy access to potential sources of hazardous bacteria and/or parasites. Rodents that are present on organic farms can form one of these sources. Organic farms offer an ideal environment for them owing to the application of roughage and straw. Moreover, organic farmers are often less willing to use rodenticides, since they perceive rodent presence as an integral part of the agro-ecosystem.[2]

Whilst rodents are often associated with infrastructural damage and eating or spoiling of stored feed and products, their zoonotic risks are frequently underestimated. Wild rodents can be reservoirs and vectors of a number of agents that cause disease in food animals and humans (e.g. *Leptospira* spp., *Salmonella* spp., *Campylobacter* spp., *Trichinella* spp., *Toxoplasma* spp.).[3,4] In this review we focus on the role of rodents in transmission of *Salmonella* and *Campylobacter* to food animals on farms, particularly when organic production systems are adopted.

CAMPYLOBACTER

Campylobacter are mainly spiral-shaped, S-shaped or curved, rod-shaped bacteria. There are 16 species and six subspecies assigned to the genus *Campylobacter*, of which the most frequently reported in human disease are *C. jejuni* (subspecies *jejuni*), *C. coli* and *C. fetus*. Other species such as *C. laridis* and *C. upsaliensis* are also regarded as primary pathogens but are reported far less frequently in cases of human disease. *Campylobacter* are generally regarded as the most common bacterial cause of gastroenteritis worldwide.[5] In both developing and developed countries they cause more cases of diarrhoea than e.g. food-borne *Salmonella*. Although *Campylobacter* do not show any seasonal variation in developing countries, they do in the developed world, where they peak in summer.[6] *Campylobacter* can survive in the environment for several weeks at temperatures around 4 °C but can also be present in surface water at higher temperatures.[7] Although it is unknown why, in almost all developed countries the incidence of human *Campylobacter* infections has increased steadily over recent years, apart from in 2002 when for the first time a 5% decrease was reported in the European Union (EU).[8] In the Netherlands the rise in *Campylobacter* infections until 2002 could be partially explained by an increase in the level of Dutch poultry meat consumption, which rose from 17.3 kg per head in 1990 to 22.4 kg per head in 2002.[9] It is unlikely that consumption of

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- *Salmonella* and *Campylobacter* - "*…the most important food-borne pathogens in the world*"
- "*Prevention of food hazards in the first part of the food chain is essential to prevent illness of consumers*"
- A relationship (causative?) between EU increases in poultry meat consumption and *Campylobacter* infections
- Mice as important in transmission as rats

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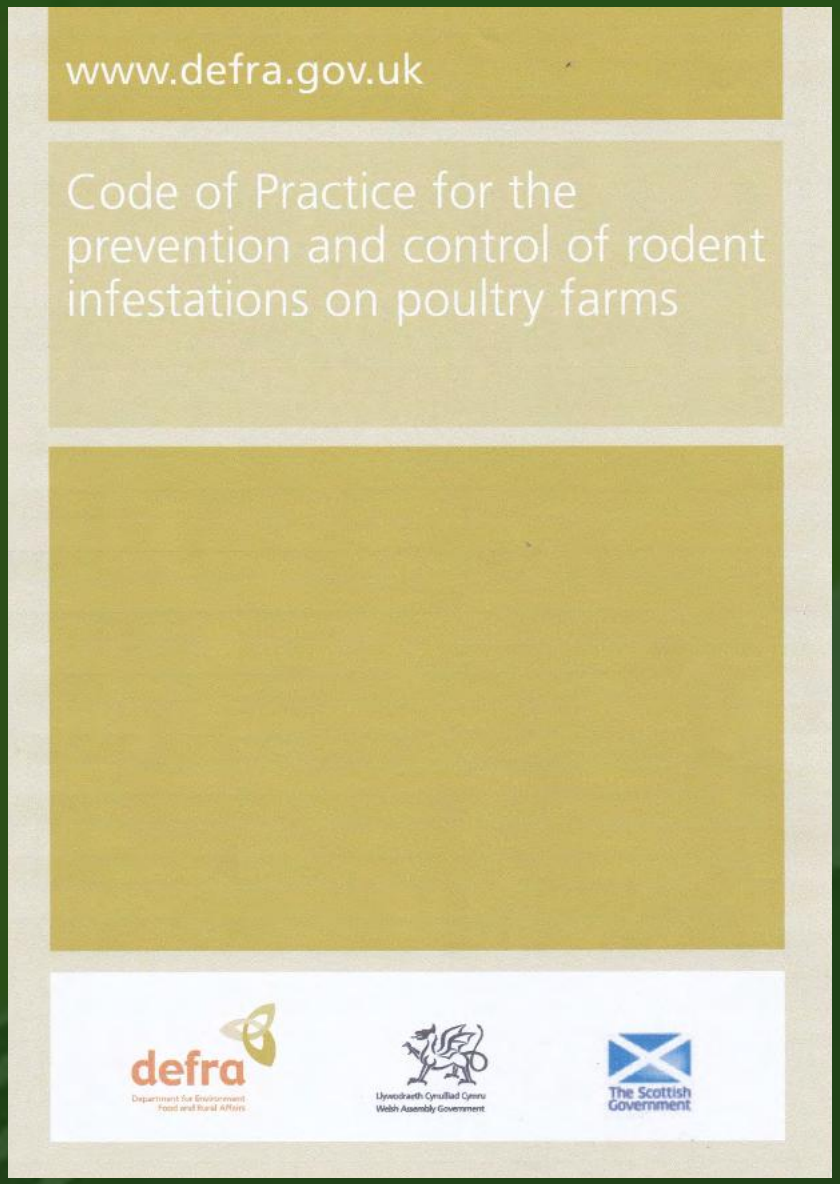
Defra Code of Practice - 2009



- Much excellent advice on prevention and control options
- Useful statements on importance of rodents in transmission
- Complete revision of rodenticide authorisations and use practices since 2009, so…
- Content is out of date about all rodenticide interventions

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From the Defra Code

- *"Research findings in several countries, especially the UK and USA, have confirmed that rodents play a major part in the maintenance of Salmonella Enteritidis and Typhimurium on poultry farms*
- *"Rodents are important in Salmonella control because they can act as the main driver of infection on a poultry unit – in fact on many units Salmonella will clear from flocks if rodent infestations are eliminated.*

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From the Defra Code

- *"Rodents can be infected with a very low dose of Salmonella and then multiply it up so as to be excreting millions of organisms per day at the peak of infection*
- *"They can also remain infected for months*
- *"Because rodents can excrete so much Salmonella, the protective effect of vaccination may be overwhelmed so even well managed flocks, which have been properly vaccinated, may still succumb*

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From the Defra Code

- *"When Salmonella is known to be present on a poultry site, it will be necessary to virtually eradicate all rodents from positive houses and ensure that there are no breeding populations if control of infection is to be successful*
- *"The appropriate techniques for controlling most rodent infestations involve the use of toxic rodenticides presented in edible bait formulations. The majority of the products currently available for use against rats and mice are anticoagulant based.*
- *"The use of methods other than those based on rodenticides have limitations in the control of rodents in poultry units and are unlikely to form a significant part of an overall strategy."*

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The Problem with Anticoagulants

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The Active Substances

Active substance	Comment
First-generation anticoagulant (FGAR)	
Warfarin	No longer available in UK
Chlorophacinone	No longer available in UK
Coumatetralyl	
Second-generation anticoagulant (SGAR)	
Difenacoum	Less-potent, some resistance
Bromadiolone	Less-potent, some resistance
Brodifacoum	No practical resistance
Difethialone	No practical resistance
Flocoumafen	No practical resistance

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Rodent control with rodenticides is virtually totally reliant on anticoagulants in the EU

- No new technology on the horizon – (though there is a "new" a.i. coming, cholecalciferol)
- Anticoagulant Resistance
- Three significant regulatory challenges ('exclusion criteria') - drivers for stewardship
- All anticoagulants are candidates for substitution = "we would ban them if we could!"
- All are subject to "Comparative Assessment"

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Challenge 1. PEC/PNEC ratios >1

Poisoning Type	Rodenticide	PEC/PNEC Ratios
Primary poisoning	FGAR	10.3 – 271,875
	SGAR	1,700 – 1,582,031
Secondary Poisoning	FGAR	0.9 – 15,000
	SGAR	77 – 8,555,855

PEC = Potential environmental conc.
PNEC = Potential no-effect conc.

FGAR = First-generation anticoagulant rodenticide
SGAR = Second-generation anticoagulant rodenticide

PEC/PNEC >1 is an exclusion criterion unless mitigation measures are applied

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Challenge 2. Persistent/Bioaccumulative/Toxic

SGAR active substance	PBT status
Brodifacoum	Potential PBT
Bromadiolone	Potential PBT
Difethialone	Potential PBT/vPvB
Difenacoum	Potential PBT/vPvB
Flocoumafen	Potential PBT/vPvB

PBT and vPvB are Biocidal Products Regulation (BPR) ‘exclusion criteria’

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Challenge 3. RAC Opinion and SCL

- **ECHA Risk Assessment Committee opinion "all anticoagulant active substances are 'toxic to reproduction'" – another exclusion criterion for products that contain them**
- **Specific Concentration Limit (SCL) - 30 ppm in baits is proposed for all anticoagulants**
  - no use by 'general public' of baits exceeding SCL
  - professional use significantly curtailed
- **Current concentrations employed:**
  - FGARs >250-500 ppm – no efficacy at 30 ppm
  - SGARs generally 50 ppm – possible negative effects on efficacy/resistance?
- Many new SGAR products are <30 ppm now

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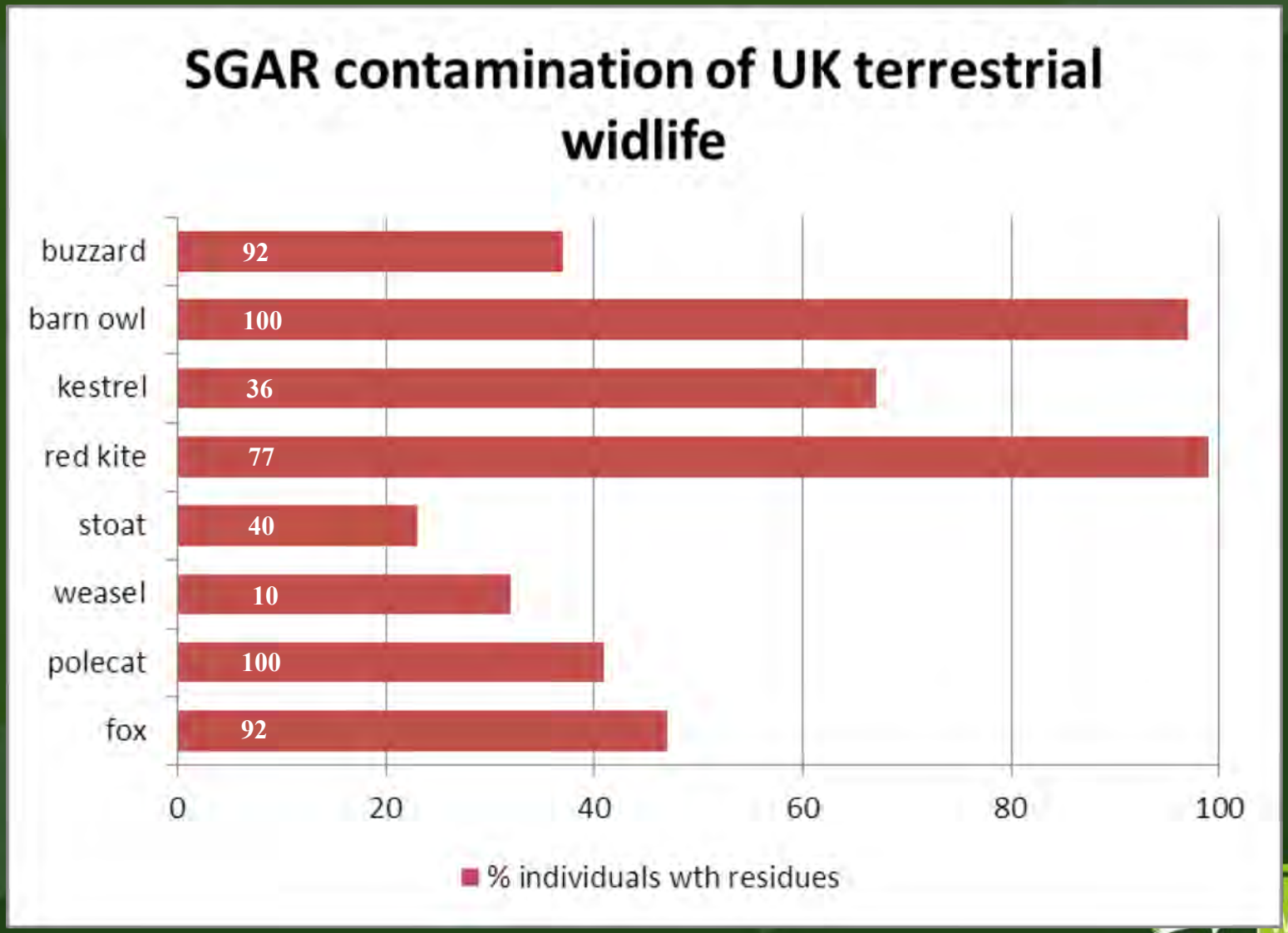
Current use patterns contaminates wildlife



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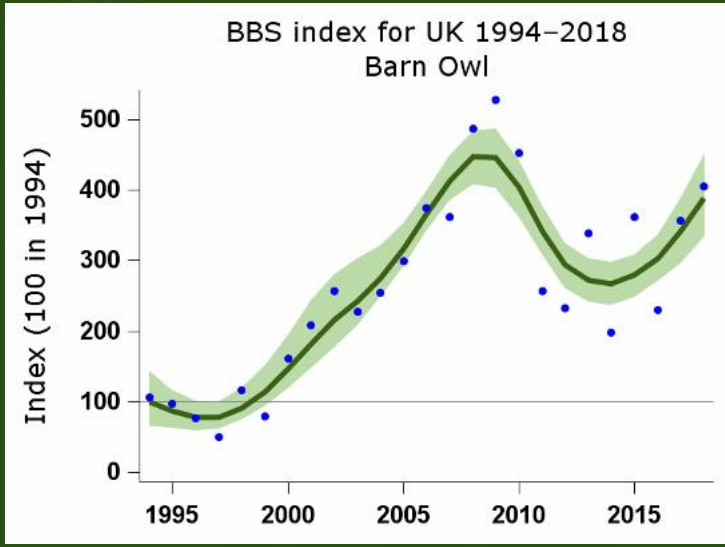
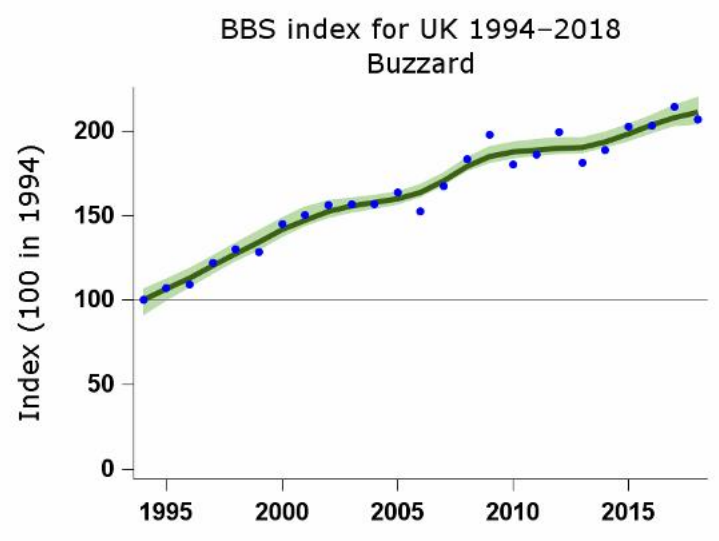
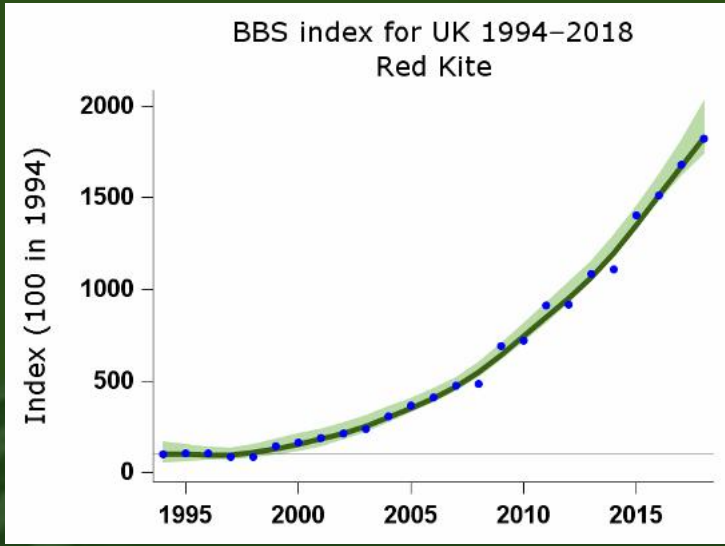
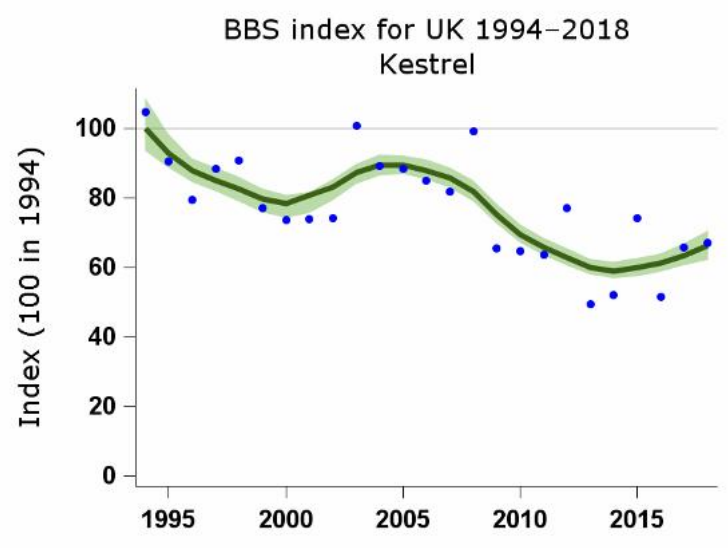
But what is happening to exposed populations?









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Rodenticide Stewardship

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Summary Stewardship Time-line (1)

- April 2013 HSE held a meeting with manufacturers, stakeholders and environmental groups – main outcome is a requirement for a stewardship programme
  - HSE position was that in the forthcoming regulatory review of SGAR authorisations no outdoor use would be permitted without stewardship = virtually no use for rat control
- June 2013 HSE invites CRRU UK to organise and co-ordinate a stewardship programme – CRRU accepts
- 2013-2015 – period of CRRU negotiation with stakeholder groups and HSE to create an acceptable framework for the "UK Rodenticide Stewardship Regime"
- March 2015 – CRRU publishes new Code of Best Practice
- July 2015 - HSE publishes "High Level Principles" setting out the requirements of an acceptable stewardship scheme

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Summary Stewardship Time-line (2)

- January 2016 – HSE publishes targets for reduction of wildlife exposure to SGARs
- April 2016 – first products come to the market that require proof of professional competence for purchase and carry stewardship label phrases AND allow outdoor use of 3 resistance busters
- April 2016 – CRRU publishes "CRRU Guidance Permanent Baiting"
- January 2017 – CRRU publishes "2016 Annual Report of Stewardship". And annually thereafter
- March 2017 – HSE/GOG states that the regime is fit for purpose
- 2020 – HSE and Government Oversight Group conduct a review after 5 years to see if targets are met

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Implementation Structure for Stewardship Regime

Oversight Group:

HSE (Chair), Public Health England, Defra, Natural England, representatives from Devolved Administrations

CRRU UK Task Force: (Chair Alan Buckle, Reading University)

CRRU UK member companies, CRRU technical advisors, representatives Stakeholder Organisations

Now 33 stakeholder agencies and >60 individuals

Work Group 1:

Best Practice (Dee Ward-Thompson, BPCA)

Work Group 3: Regulatory (Sarah Bull, BASF)

Work Group 5: Monitoring (Richard Moseley, Bayer)

Work Group 2: Training & Certification (Matthew Davies, Killgerm)

Work Group 4: Point-of-Sale (Rupert Broome, Killgerm)

Work Group 6: Communication (Phil Christopher, RedRock)

Participants invited from any agency with legitimate interest and expertise

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Critical Elements of Stewardship

- Competent workforce:
  - Training certification from an awarding organisation (BASIS, Lantra, H&G, NPTC)
  - Membership of an approved farm assurance scheme whose standards comply with the CRRU CoBP
- Proof of competence at point-of-sale for all professional rodenticides
- Programme of monitoring effectiveness
  - Key measure is levels of residues in sentinel species (barn owl)
- Annual review by Government Oversight Group (HSE, Defra, Natural England, Public Health England and Devolved Administrations)
- Full review after five years i.e. 2020
- Further restrictions if progress towards goals is judged inadequate

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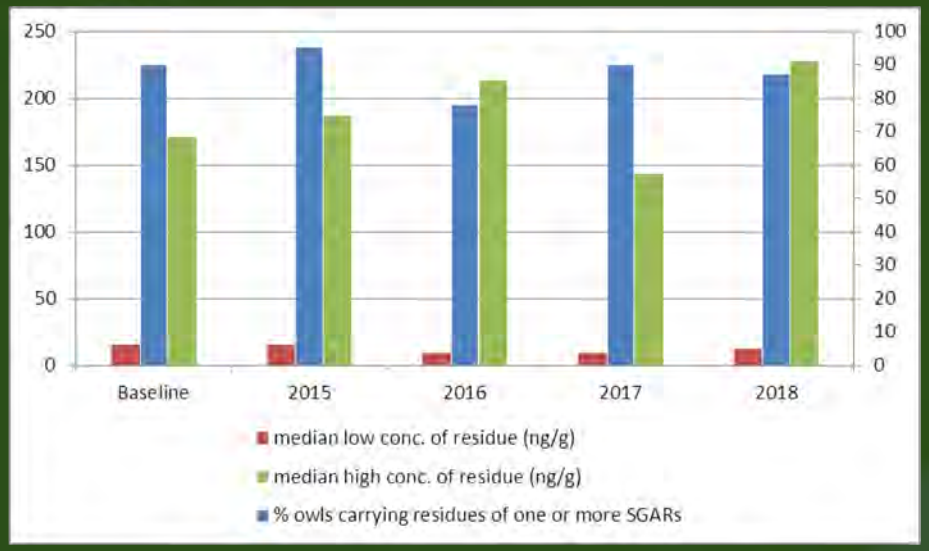
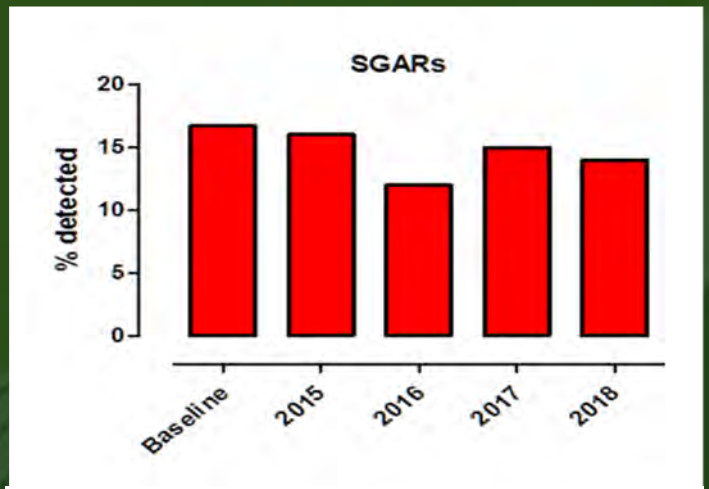
Monitoring is CRUCIAL to stewardship

	Required data by HSE/GOG	Data to be provided
1	Environmental Impacts (Monitoring Compliance)	1. Centre for Ecology & Hydrology annual survey of residues in livers of 100 barn owls
		2. Annual survey of barn owl breeding performance
		3. Annual review of WIIS incidents
2	Whether the rodenticides are effective (Competent Workforce)	1. Annual report of training uptake and award of certification/ qualification by CRRU-approved awarding bodies
		2. Annual report of number of members of CRRU-approved farm assurance schemes
		3. Provision of up to date, relevant best practice guidance documents
		4.Promotion of regime objectives and raising awareness by stakeholder organisations
3	Resistance monitoring (Competent Workforce).	1. Annual report of status of resistance monitoring in UK and elsewhere in EU
4	Awareness using the Knowledge, Attitude and Practice (KAP) survey (Competent Workforce/Monitoring Compliance)	1. KAP survey baseline study (published)
		2. Repeated KAP surveys in 2017 and 2019
5	Point of sale information (Supply Chain Governance)	1. Examination of options for point of sale compliance audits by independent organisations
6	Training (Competent Workforce)	(see point 2 above)

Residues in barn owls – all SGARs combined





% birds with 'high' residues

- Residue levels:
  - 'High' >100 ng/g ww
  - 'Low '<100 ng/g ww
- No statistically significant changes
- Most birds (>85%) carry 'low' residues
- 300 birds checked in the last three years and none was killed by SGARs

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But there is an issue with red kites too!

- High conservation status because of NE re-establishment projects
- Co-ordinated studies by Fera, SASA, Inst of Zoology, CEH, NE etc
- 100% of red kites contaminated
- On average every bird carries 2 different SGARs
- 20% found dead are attributed to SGARs
- Eat TARGET rodents – cannot be protected by stewardship

SASA Helping Scotland Grow

ZSL INSTITUTE OF ZOOLOGY

fera

NATURAL ENGLAND

CEH Centre for Ecology & Hydrology
NATURAL ENVIRONMENT RESEARCH COUNCIL

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THE NEW PRODUCT LABELS AND ‘PERMANENT BAITING’

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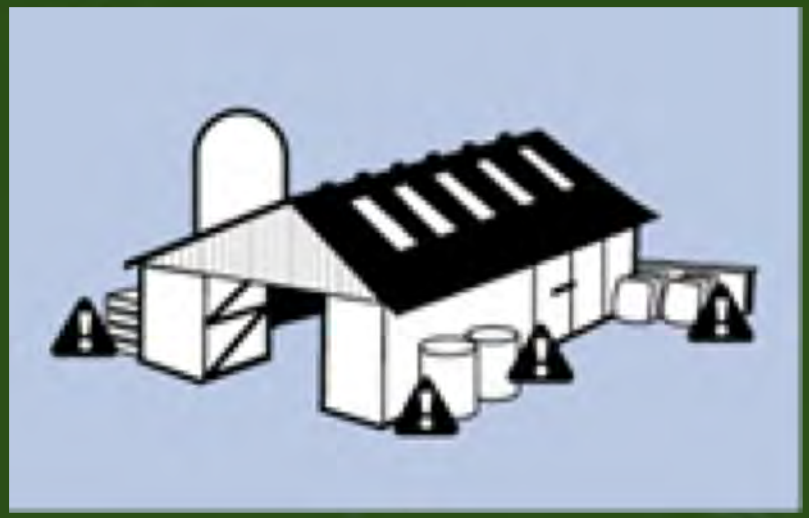
Permanent Baiting (also perimeter baiting)



- Widely used in all farming enterprises
- Baits left out permanently
  - Detects new infestations
  - Protects against infestation increase
- Many Farm Assurance Scheme Standards REQUIRED this measure
- Probably the single most important source of wildlife exposure
- New labels want to reduce it!

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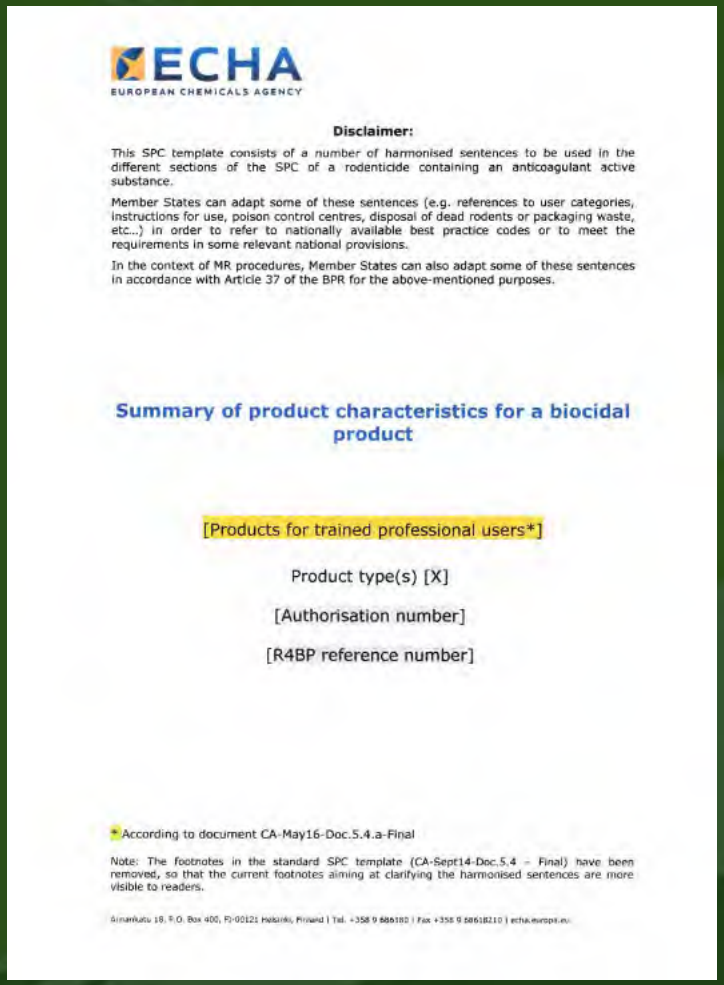
EC Summary of Product Characteristics (SPC)



ECHA
EUROPEAN CHEMICALS AGENCY

Disclaimer:

This SPC template consists of a number of harmonised sentences to be used in the different sections of the SPC of a rodenticide containing an anticoagulant active substance.

Member States can adapt some of these sentences (e.g. references to user categories, instructions for use, poison control centres, disposal of dead rodents or packaging waste, etc...) in order to refer to nationally available best practice codes or to meet the requirements in some relevant national provisions.

In the context of MR procedures, Member States can also adapt some of these sentences in accordance with Article 37 of the BPR for the above-mentioned purposes.

Summary of product characteristics for a biocidal product

[Products for trained professional users*]

Product type(s) [X]

[Authorisation number]

[R4BP reference number]

* According to document CA-May16-Doc.5.4.a-Final

Note: The footnotes in the standard SPC template (CA-Sept14-Doc.5.4 – Final) have been removed, so that the current footnotes aiming at clarifying the harmonised sentences are more visible to readers.

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- SPC templates issued by the Biocidal Products Committee of ECHA
- Each product must have an SPC
- Different SPCs for SAME product if sold to amateurs and professionals
- ‘Letter of the law’ on how product can be used
- New wording on ‘non-standard uses’ i.e. permanent baiting, burrow baiting and use of covered bait points
- Brexit will not change anything quickly

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New Rules on Permanent Baiting (1)

- ***Labels on products that CAN be used for permanent baiting say this (i.e. ONLY SOME bromadiolone and difenacoum products):***
  - *Permanent baiting is strictly limited to sites with a high potential for reinvasion when other methods of control have proven insufficient.*
  - *The permanent baiting strategy shall be periodically reviewed in the context of integrated pest management (IPM) and the assessment of the risk for re-infestation.*
  - *Sites under a permanent baiting regime should be inspected regularly in accordance with product label directions. The period between visits should be determined by the technician in charge but will not be longer than every four weeks when permanent baiting is conducted outdoors.*
  - *For permanent baiting follow any additional instructions provided by the CRRU Guidance on Permanent Baiting*

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New Rules on Permanent Baiting (2)

- ***Labels on products that CANNOT be used for permanent baiting say this (i.e. all other anticoagulants, including brodifacoum, difethialone and flocoumafen):***
  - *Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.*
  - *If after a treatment period of 35 days baits continue to be consumed and no decline in rodent activity is observed, the likely cause must be determined. Where other elements have been excluded, it is likely that there are resistant rodents so consider the use of a non-anticoagulant rodenticide, where available, or a more potent anticoagulant rodenticide. Also consider the use of traps as an alternative control measure.*
  - *Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment.*

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Permanent Baiting

- Permanent baiting ONLY happens when bait is put out where there are no rodents
- Permanent baiting is not banned
- Can only be used with baits containing bromadiolone and difenacoum (resistance!)
- Outdoor permanent bait points must be checked every four weeks
- Brodifacoum/difethialone/flocoumafen baits can be used over extended periods (long-term baiting). But conditions apply

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ANTICOAGULANT RESISTANCE

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The main UK rat and mouse resistance mutations

Species	Mutation	Abbrev.	Severity	Where present
NR	Leucine128Glutamine	L128Q	**	Central Southern Scotland, Yorkshire, Lancashire
NR	Tyrosine139Serine	Y139S	***	Anglo-Welsh border and recently elsewhere
NR	Leucine120Glutamine	L120Q	*****	Hampshire, Berkshire, Essex, Norfolk and elsewhere
NR	Tyrosine139Cysteine	Y139C	****	Gloucestershire, Norfolk, Lincolnshire, Yorkshire, SW Scotland and elsewhere
NR	Tyrosine139Phenylalanine	Y139F	****	Kent, Sussex, Norfolk, Suffolk
HM	Tyrosine139Cysteine	Y139C	*****	Widespread
HM	Leucine128Serine	L128S	***	Widespread

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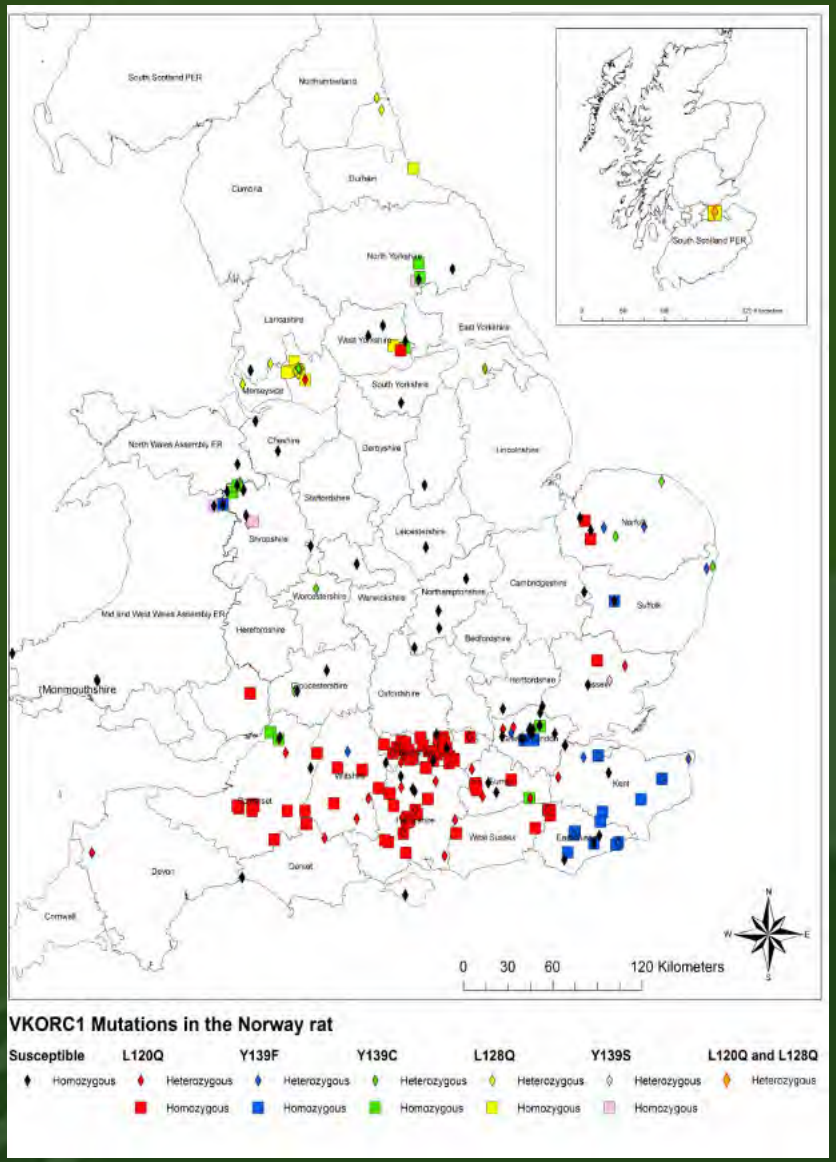
Norway rats - Resistance to anticoagulants (2019)



- Severity and distribution severely effected by 30-year ban on ‘resistance busters’
- Few animals testes that do not possess a resistance gene
- Majority of rats tested are homozygous = severe selection pressure
- L120Q = RED, Y139F = BLUE, Y139C = GREEN
- Many “new” foci, some jump hundreds of miles from nearest occurrence of the same mutation e.g. new Y139C and Y139F foci in Welsh resistance area
- Multiple new L120Q foci. Probably across the whole of south and east England
- Limited data from much of central England, Scotland, Wales and NI

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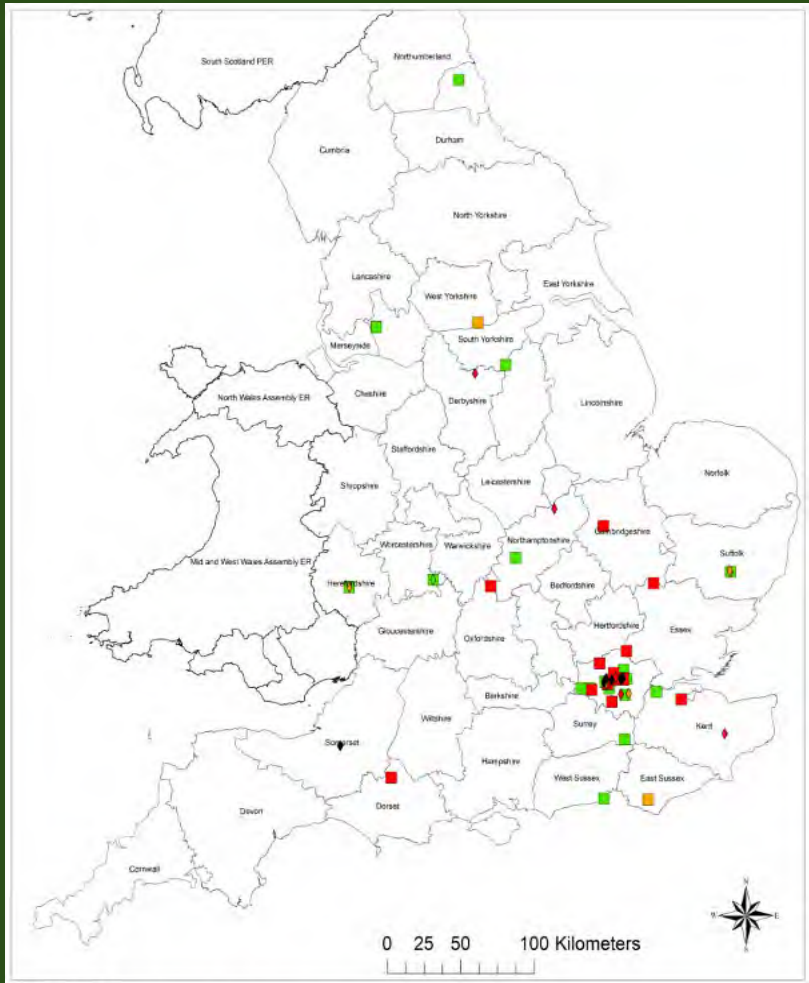
House mouse - Resistance to anticoagulants (2019)



- Intrinsically less susceptible
- Two main resistance mutations:
  - Y139C = resistant to bromadiolone and difenacoum
  - L128S = resistant to bromadiolone, difenacoum efficacy also impaired
- Among all mouse samples (n = 53):
  - 88.7% resistant
  - 60.0% homozygous resistant
  - 3 individuals carried both mutations (additive effect is unknown)
- UK Rodenticide Resistance Action Group (RRAG) advice is only to use brodifacoum, difethialone and flocoumafen against house mice

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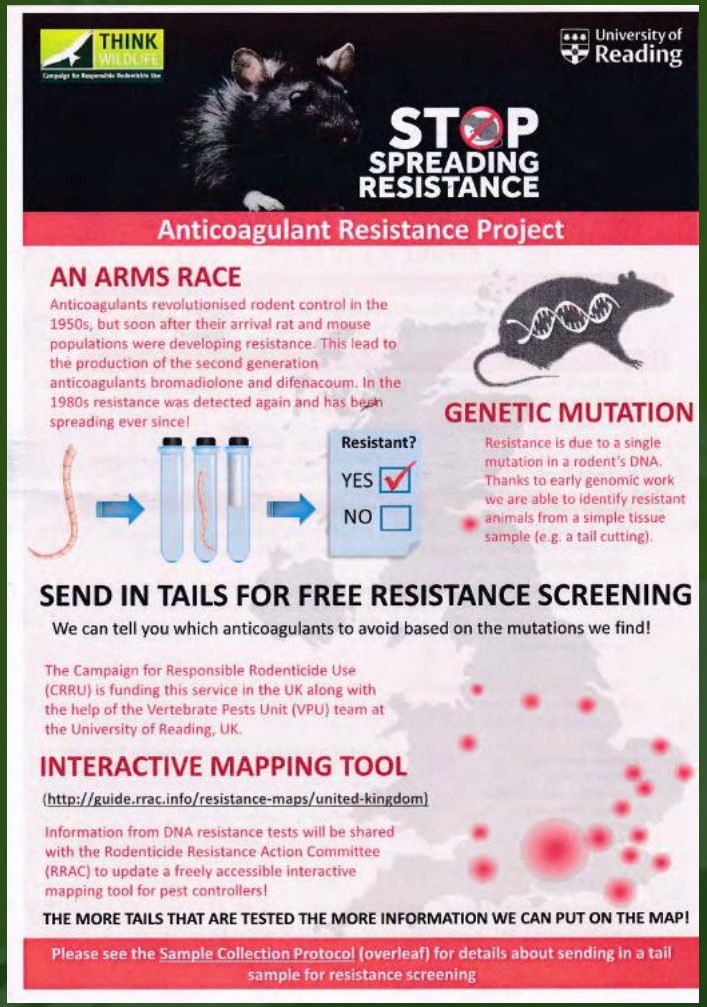
University of Reading: Send us your tails!



- CRRU is funding 150 genetic resistance tests at the University of Reading in 2020
- Send a tail and you will find out resistance status of your infestation and be given advice
- Locations are disguised in published maps using on 10 x 10 km squares
- All information confidential
- Maps of existing resistance foci using Google heat-map technology free at: https://guide.rrac.info/resistance-maps/norway-rat/europe/united-kingdom.html

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Anticoagulant resistance in Norway rats

Active Substance	Resistance mutation and where found				
	L128Q	Y139S	Y139C	L120Q	Y139F
	Scotland, Yorkshire, Lancashire	Anglo-Welsh border	Gloucestershire, Norfolk, Lincolnshire, Yorkshire, SW Scotland	Hampshire, Berkshire and elsewhere	Kent, Sussex and elsewhere
warfarin					
chlorophacinone					
coumatetralyl					
difenacoum					
bromadiolone					
brodifacoum					
difethialone					
flocoumafen					

Do not use

Better avoid

Should work

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Permanent baiting and resistance

- **Resistance to bromadiolone and difenacoum is widespread in UK in both rats and mice (more later)**
- **Cannot use potent resistance-breaking actives for permanent baiting**
- **BUT these words allow 'long-term baiting' under certain circumstances:**
  - *Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment*
- **What "evaluation" might justify long-term baiting with brodifacoum, difethialone, flocoumafen?**

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Justifying long-term baiting with resistance-busting actives – CRRU position

- No permanent baiting with brodifacoum, difethialone, flocoumafen = resistance busters
- But can be used "long-term" if……
- Clear ongoing threat to human health and hygiene or animal health and biosecurity
- Proof of the presence of rodents resistant to bromadiolone and/or difenacoum
- Explanation that other measures either have not been or, if used, are unlikely to be fully effective
- All would need to be documented and frequently reviewed

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Round up

- Effective rodent control essential to flock biosecurity
- Defra guidance document is generally excellent but rodenticide sections need to be updated
- Current use practices result in widespread wildlife contamination
- Permanent baiting is NOT BANNED
- But new product labels restrict use of this intervention and it is NO LONGER an audit requirement
- Pay close attention to resistance status of rats
- Only use most potent three substance against house mice
- Stewardship will be reviewed by government this year and there may be more restrictions

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