

**ADVISORY COMMITTEE ON ANIMAL FEEDINGSTUFFS**

**64th Meeting of ACAF on 9 May 2014**

Presentation Paper  
Phil Sketchley – Chief Executive NOAH

**EUROPEAN INITIATIVES TO MONITOR ANTIBIOTIC RESISTANCE  
AND USAGE AND INDUSTRY PERSPECTIVES FOR THE FUTURE**

**Secretariat  
April 2014**



# European initiatives to monitor antibiotic resistance and usage and industry perspectives for the future

**Phil Sketchley**  
Chief executive, NOAH



# NOAH

- The National Office of Animal Health (NOAH) represents the UK animal medicines industry
- Represents UK industry with the regulatory agencies and at IFAH Europe
- Aim is to promote the benefits of safe, effective, quality medicines for the treatment and welfare of all animals.
- 23 Corporate Members, approximately 90% of UK vet medicines industry
- Member of RUMA (Responsible Use of Medicines in Agriculture Alliance)



# Industry Perspective on Antimicrobial Resistance

- General points on Antimicrobial Resistance and the UK perspective
- European perspective-actions taken to date in different Member States
- European Legislative review
- Industry perspective on antimicrobial resistance and the future legislation changes



# General Points on Antimicrobial resistance

- Industry wants for its products to remain effective for as long as possible- best achieved by the promotion of and adherence to responsible use by vets and farmers
- Appropriate regulatory climate is needed to encourage industry to continue to invest in R and D in animal health
- High costs to market- c. 150 million euros to develop a livestock medicine- need confidence that ROI achievable



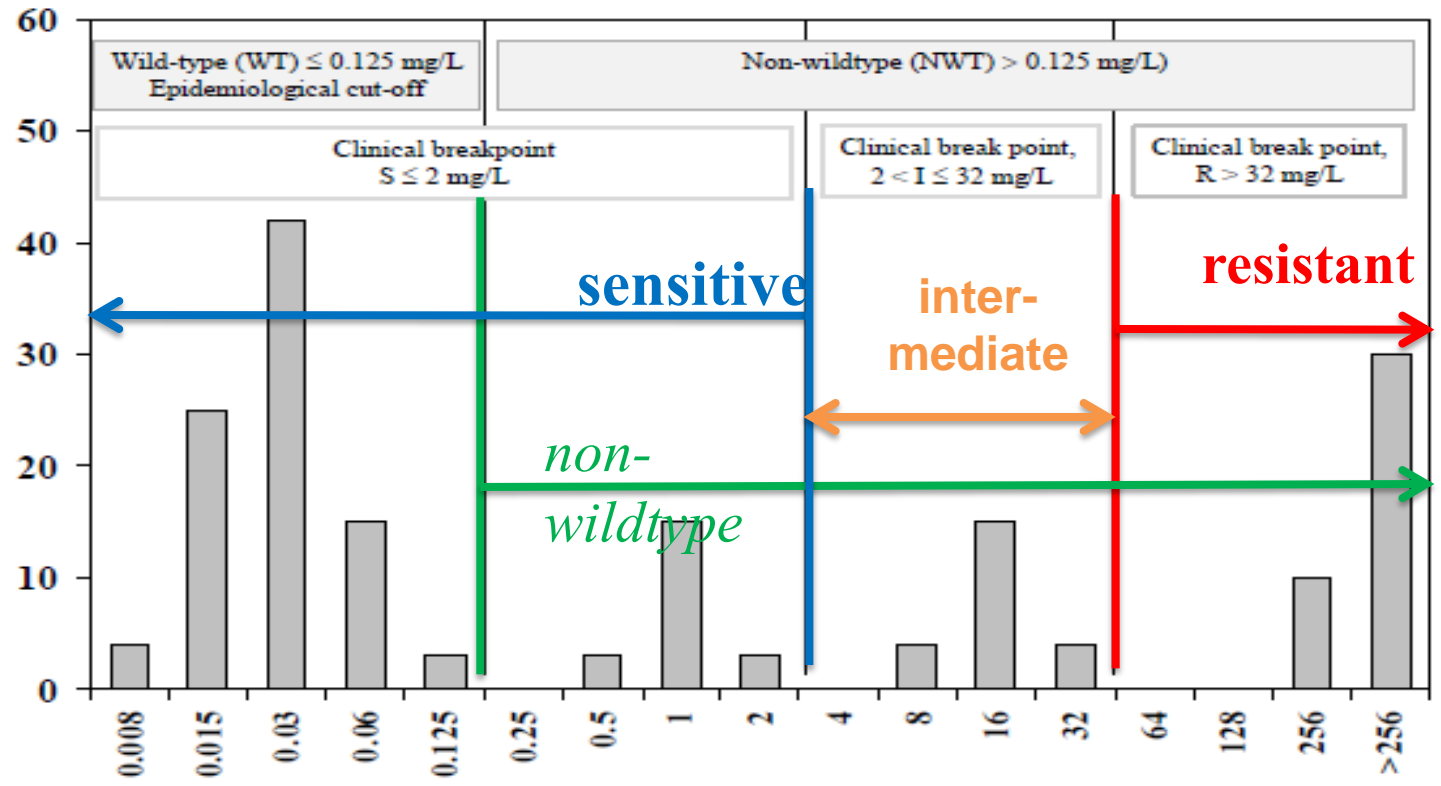
# General Points on Antimicrobial resistance

- Measurement of resistance across EU Member States and in different reports - little consensus - different countries/institutions gather data and measure resistance in different ways
- Makes comparisons between reports and between Member States' data difficult - Clinical Resistance vs Epidemiological Cut-off Values
- ECV- reduced susceptibility, true clinical resistance is the clinical break points
- Lab detected 'reduced susceptibility' - often referred to as 'resistance' in some reports



# Clinical breakpoints vs epidemiological cut-off values

- “Epidemiological resistance” not necessarily clinically relevant!



WT = Wild type organisms, i.e micro-organisms without phenotypically detectable antimicrobial resistance to the drug in question  
 S = Susceptible; I = Intermediate; R = Resistant



Selected References: EU Community Reference Laboratory – Antimicrobial Resistance newsletter No 2 2007



## Antibiotic resistance - UK

- UK Department of Health 5 year strategy on AMR published Sept 2013
- UK Parliament Science and Technology Committee inquiry into AMR - awaiting report
- International dimension of resistance acknowledged - people and foodstuffs moving all over world - little control in developing world
- Strategy acknowledges human use the main driver of human resistance problems;
- *'Increasing scientific evidence suggests that the clinical issues with antimicrobial resistance that we face in human medicine are primarily the result of antibiotic use in people, rather than antibiotics in animals'.*





# Antibiotic resistance - UK

- Recent scientific papers from Mather et al (2013) on Salmonella, Wu et al (2013) on ESBLs in poultry support the D o H view
- Resistance in vet pathogens rare - unusual for a sick animal with bacterial infection to fail to respond to treatment where the appropriate antibiotic is used
- More research is needed on resistance surveillance and transmission pathways (likely to be included in new EU Vet med legislation)

## References;

Wu G, Day MJ, Mafura MT, Nunez-Garcia J, Fenner JJ, et al. (2013) Comparative Analysis of ESBL-Positive *Escherichia coli* Isolates from Animals and Humans from the UK, The Netherlands and Germany. *PLoS ONE* 8(9): e75392. doi:10.1371/journal.pone.0075392

Mather AE, Reid SWJ et al, (2013) Distinguishable epidemics of multidrug-resistant *Salmonella* Typhimurium DT104 in different hosts. *Science* 341, 1514-1517.

# Implementation of the UK 5 year strategy

- RUMA action plan to implement launched and published – will be reviewed quarterly

## UK 5 YEAR ANTIMICROBIAL RESISTANCE (AMR) STRATEGY

### ACTION PLAN FOR THE RESPONSIBLE USE OF MEDICINES IN AGRICULTURE ALLIANCE (RUMA) AND ITS INDIVIDUAL MEMBERS

1. The UK 5 year AMR Strategy was launched on 10 September 2013. RUMA, a unique alliance of 23 organisations across the whole UK livestock sector, was among the groups that welcomed and supported the strategy.
2. The Alliance has discussed the actions that will be required to implement the strategy and has developed this action plan, based on the detailed actions in Annex B of the Strategy, to set out the actions that RUMA and/or its members will take. Inevitably, the plan is still at an early stage. RUMA members have agreed to review and record progress against the plan at RUMA's quarterly meetings and to publish the plan and its subsequent revisions to provide an open report on how this work is developing. During these reviews new actions will be added to the plan including any identified by the high level steering group made up of DARC, ARHAI and ACSMF members who the strategy says will agree an action plan to implement the strategy.
3. A list of RUMA members and the acronyms used in this plan are at Annex A.
4. If you have any comments on the plan please send them to RUMA's Secretary General, John FitzGerald, at [rumasec@btinternet.com](mailto:rumasec@btinternet.com).

RUMA  
April 2014

Strategy actions – Annex B	Section 5.6 Actions for Animal Health (Bold added by RUMA)	RUMA/members' action	Progress
<p><b>Key area 1: improving infection prevention and control practices</b> Actions needed to further improve infection prevention and control in human and animal systems are:</p>	<p>- considering the use of farm assurance schemes as a mechanism to increase adherence to best husbandry including isolation of sick animals, testing of new stock and responsible use of antibiotic principles, while ensuring animal health and welfare, <b>NFU, Species Groups, Red Tractor</b> - encouraging retailers to review their standards for meat and animal products and to set clear specifications, concerning bio-security, antimicrobial stewardship and good</p>	<p><b>RUMA</b> will need to help develop improved infection prevention and control practices and to disseminate advice on them through RUMA Guidelines or advice notes.</p> <p><b>RUMA</b> to develop protocols for members' advisory staff to ensure they are able to provide up to date advice on antibiotic resistance and responsible use when they interact with farmers.</p>	

# Antibiotic resistance- restriction of classes

- Class related restrictions- comments from human sector, submission from Public Health England to UK Parliament Science and Technology Committee inquiry;
- *One major uncertainty, despite the agreed need for antimicrobial stewardship to prevent and slow resistance, is exactly what good stewardship looks like. **There is a tendency in the UK to equate stewardship with simply minimising use of antibiotics such as cephalosporins and fluoroquinolones.** Consequently, there have been major increases in the use of a very narrow range of alternative antibiotics, especially an antibiotic called piperacillin-tazobactam. **This can be equated to 'squeezing the balloon' by potentially creating a resistance problem elsewhere.** Rather than 'swinging the pendulum' away from use of what might be the most effective antibiotic for the patient (e.g. use of cephalosporins), **improving knowledge about appropriate prescribing is required.***

Source-

<http://data.parliament.uk/writtenevidence/WrittenEvidence.svc/EvidenceHtml/3415>



# Antibiotic resistance- regulatory climate

- Antibiotic resistance one of the issues under consideration as part of EU revision of the Veterinary Medicines legislation
- Animal health industry- great concern that a new veterinary antibiotic would be unlikely to be licensed by regulators or would have requirements in authorisation that would severely limit the use
- Regulatory uncertainty around antibiotic resistance acts as major disincentive for companies considering research pipeline
- Precautionary approach rather than evidence based



# Antibiotic resistance- regulatory climate

- Veterinary bodies and industry- all wish to retain use of Critically Important Antibiotics (CIA) for veterinary use
- What is classed as CIA varies depending on what body you consult with and also changes over time - ban on CIAs could really limit future vet antibiotics
- Ban on CIAs can lead to overuse of remaining classes - lead to resistance to remaining products
- Necessary to retain all classes for animal health and welfare reasons



# European Legislative Review

- Review of the EU regulatory framework for veterinary medicines underway
- Antimicrobial resistance and the implications for human and animal health one of the matters under consideration
- The regulatory “package”;
  - 2001/82 – veterinary medicines
  - 1990/167 – medicated feeding-stuffs



# European Legislative Review

- Impact assessment and draft legislation for new Veterinary Medicines Regulation/Directive and Medicated Feed Directive expected in late Summer or early Autumn 2014
- Process will then be delayed because of EP elections
- Co – decision process follows, amendments etc.
- Will take effect ‘on the ground’ in late 2017/early 2018



# European Legislative review

- Current European legislation is a Directive
- Transposed into national legislation through the Veterinary Medicines Regulations (VMR)
- If new legislation were to be a directive – would be transposed into national legislation through new VMR
- BUT understand new legislation will be a Regulation to be applied directly across EU - means no national ‘tweaking’
- Will remain in place for approx. 10 -15 years





# Proposals from different sources

- Proposals to ban prophylactic use from NGOs, UK based MPs, MEPs from Nordics
- RUMA view (supported by NOAH)- Therapy, control and preventive tx needed in vet sector
- *Preventive treatment (sometimes referred to as Prophylaxis)*
  - *Treatment of an animal or a group of animals, before clinical signs of disease, in order to prevent the occurrence of disease or infection.*
  - *Preventive treatment with antibiotics should:*
    - *only be applied to animals diagnosed at high risk of bacterial disease, and*
    - *only occur under prescription by a veterinarian on the basis of epidemiological and clinical knowledge, and not be applied routinely, and*
    - ***not be used to compensate for poor hygiene or for inadequate husbandry conditions.***



# Proposals from different sources

- Decoupling dispensing by the vet from prescribing - latest information NOAH has is this will **not** be in draft legislation
- However- highly likely that will be proposed as amendments by MEPs, or Member States
- Currently, Nordics, Spain, Italy have decoupled prescribing and dispensing- still large variations in volumes used
- Many Member States oppose splitting prescribing and dispensing as does the OIE



# NOAH and IFAH Europe proposals

- Use existing legislation to counter inappropriate use
- Minimise preventative use (not prohibit!) - justifiable under some circumstances – **but never to prop up bad husbandry**
- Biosecurity, husbandry, to prevent disease
- RUMA guidelines on responsible use an example
- Increased communication and training – increase activity and budget for RUMA and EPRUMA
- Need to retain all available classes for vet use i.e. hope to avoid any bans on critically important antibiotics
- Necessary for animal health and welfare that vets retain access to existing authorised medicines



# NOAH and IFAH Europe proposals

- Review seen as an opportunity to help improve availability of veterinary medicines across EU
- Increased data protection to promote innovation in the veterinary medicines sector (animal pharma only c. 2% of human pharma market), only 10 years for ROI currently
- Data protection also needed for new claims as well as new molecules e.g. new species
- Many pioneer companies also involved in human pharma
- Regulatory uncertainty and negative climate for vet use likely to encourage even more focus on human medicines



# NOAH and IFAH Europe proposals

- On the whole - UK vets prescribe responsibly - transparency at use phase needed
- Gather more data at vet and farm level - identify high users and the reasons for high use compared to their peers
- Are the reasons for the high use valid? If not, advice and guidance on measures to reduce use?
- Likely that vets and farmers will need to submit data on antibiotic use to a central point where it will be collated and analysed



# NOAH and IFAH Europe proposals

- Unexpected treatment failures in veterinary medicine - not widespread
- Industry sponsored research CEESA survey backs this view<sup>(1)</sup>
- Data needs to be gathered across EU in a harmonised manner, harmonised methodology etc.
- More surveillance needed across EU on both target pathogen resistance and resistance transmission pathways
- Proposals for EU surveillance now being developed by Heads of Medicines Agency Veterinary (HMAv) as per Commission paper
- (1) Ref-A. de Jong, V. Thomas, U. Klein, H. Marion, H. Moyaert, S. Simjee, M. Vallé. Pan-European resistance monitoring programmes encompassing food-borne bacteria and target pathogens of food-producing and companion animals. *International Journal of Antimicrobial Agents* 41 (2013) 403– 409.  
<http://ac.elscdn.com/S0924857912004372/dx.doi.org/10.1016/j.ijantimicag.2012.11.004>

# NOAH and IFAH Europe proposals

- Use new and existing classes strategically
- Treatment choices - guided by diagnostics, to minimise resistance development but mandatory use of diagnostics prior to use of Abs - may cause welfare issues – development of pen side tests needed
- Prevention better than cure- farm biosecurity, building design and the use of vaccines
- Ongoing importance of Responsible Use of Medicines in Agriculture Alliance (RUMA)- actively involved in responsible use initiatives and implementation of the UK AMR strategy (EPRUMA in EU)



# NOAH and IFAH Europe proposals

- Strict interpretation of ‘the cascade’ required, but critical to retain ‘the cascade’ for welfare reasons
- Without cascade, minor use and minor species (MUMs) treatment needs unlikely to be met
- Improved regulatory framework- more licensed authorisations will lead to less cascade use
- IFAH Europe proposal for a true single market for veterinary medicines - may reduce need to resort to the cascade
- Need to retain in feed as a route - a solution, not a problem- improves welfare, practicalities need to be considered





# Conclusions

- The use of antimicrobials in veterinary medicine will change following legislative review
- Need a full range of antimicrobials to remain available for use in veterinary medicine (responsible use)
- Essential that a range of routes of administration remain available e.g. in-feed
- Need to encourage innovation and investment in vet med sector
- Over zealous use of the ‘precautionary principle’ has potential to negatively impact innovation and animal health and welfare
- International dimension must be remembered - avoid ‘exporting food production’



# Communicating on animal medicines

## Excerpt from NOAH launch brochure, 1986



### NOAH and its task

SCIENCE AND TECHNOLOGY make massive contributions to everyday life and nowhere more so than in the production of the food we eat.

Modern livestock farming is now more efficient and safe than at any time in history, thanks to the use of vaccines and antibiotics. Huge investment in animal health research and development in the past thirty years has developed controls for all the most serious livestock diseases and stock can now be raised in a healthy and more productive way to the benefit of all.

The companies which make up the National Office of Animal Health (NOAH) are at the forefront of all these improvements for animals and not least in the important pets sector where owners can be confident that their pet can look forward to a healthy, disease-free life.

It is NOAH's chief task to inform and educate the public about animal health and the part played by the companies which produce the products that ensure freedom from disease. NOAH's role is all the more vital given the rise in consumer interest in how our food is produced.

Misunderstanding can occur among the public about the need for animal health products. NOAH welcomes informed and rational debate, but it will at all times support that which has been scientifically tested and approved against ill informed comment.

The main concern of animal health companies is to produce safe products for livestock and consumers. The development of new products requires huge financial investment, and many years' work. This investment could be lost at a stroke if the product fails to come to market because of political expediency or the manipulation of consumer fears. If this threat grew too great, companies could be deterred from entering into long term research and animals, farmers and consumers would suffer.

Through liaison with opinion formers, decision makers, government officials, the veterinary profession, distributors and farmers, NOAH will work to convince the public that animal health matters and that the wise use of modern aids actually assists consumer safety.

Nothing changes!



# What do we know about consumer concerns?

- NOAH commissioned studies through the IGD in 2006 and 2009 which helped us to understand what consumers understood, or perceived about animal medicines in the food chain,
- Following these surveys we updated briefing notes and produced our ‘myth busting’ document:
  - ‘Animal Medicines- What you should know’
- In March 2013, following a further study, again commissioned by IGD, we held a further food chain conference, on working together to dispel the myths of livestock production

## What did we learn?

- Early surveys showed us that consumers had faith in UK farmers
- But some of the perceptions were disappointingly inaccurate – were they perpetuated by ill-informed media?
- Or mischievous lobby groups?
- Or was it because ‘we’ had not been proactive in our positive communications?

# Positive about farmers and independent checks

## 73%

British **farmers care** for the health and welfare of their animals



## 60%

Animal medicines are **assessed** and **checked** by independent scientists to ensure they are as safe for people



n.b. some thought there were NO checks



Source: IGD Shopper Insight





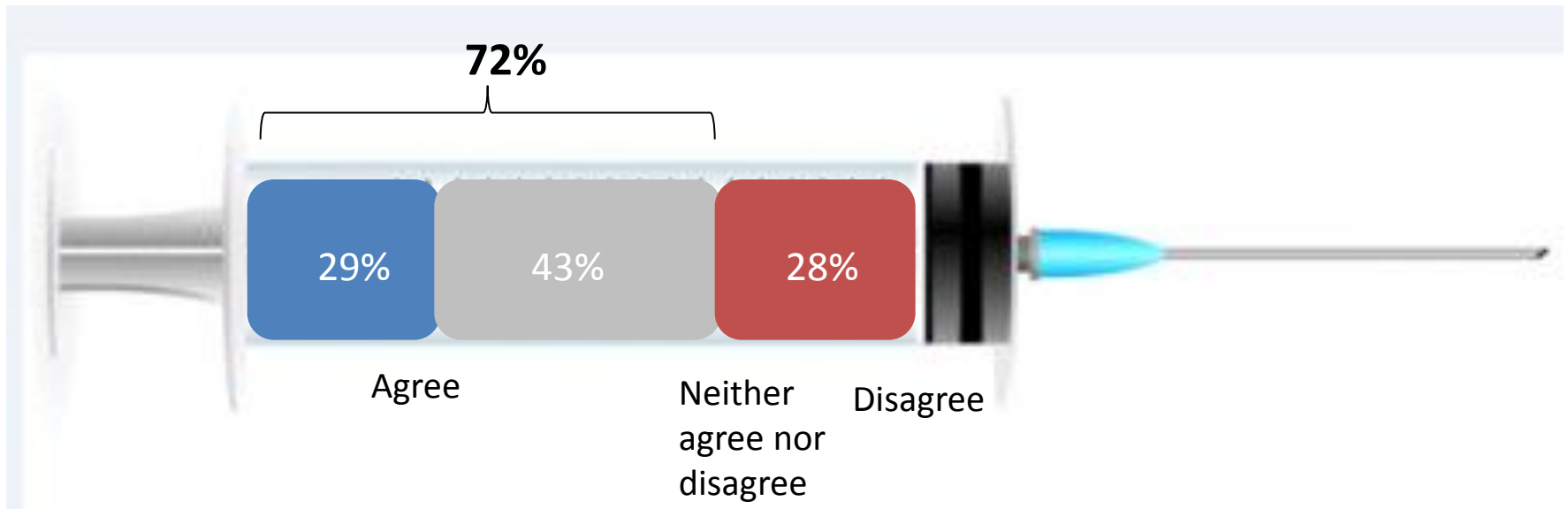
# Uncovering the myths

1. Medicines/vaccinations getting into **food chain**
2. **Growth hormones** used
3. Medicines more necessary in **intensive farming**
4. **Antibiotics** becoming **less effective** for people due to veterinary use



Source: IGD Shopper Insight

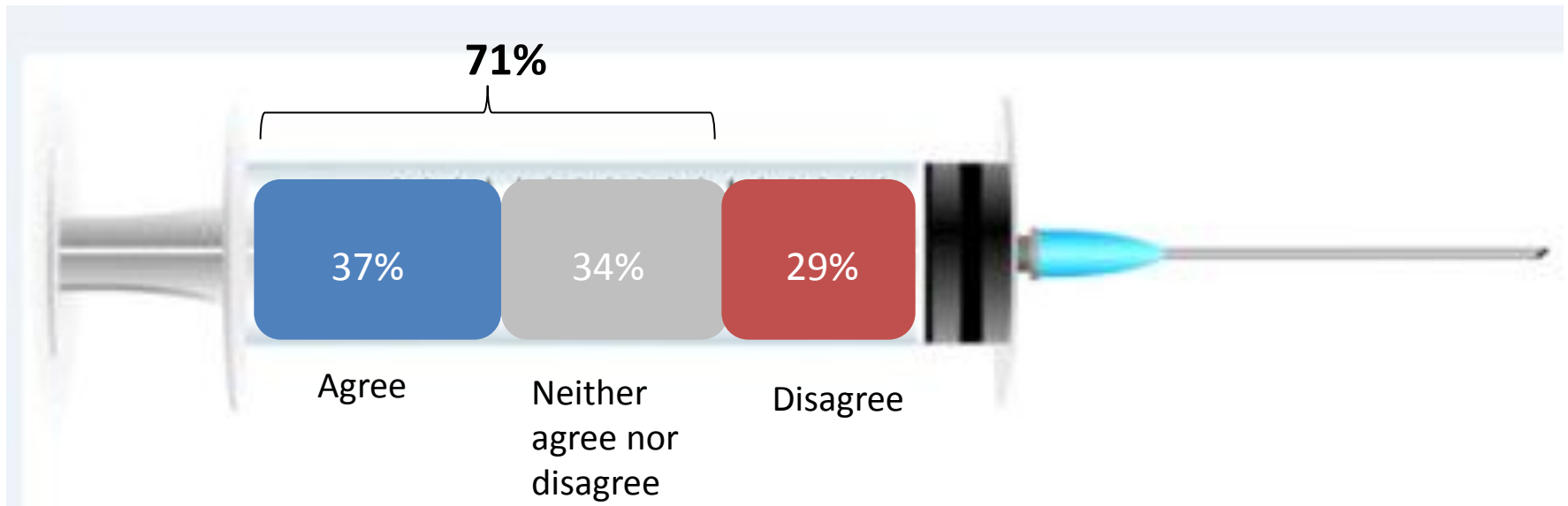
# Myth: medicines and vaccinations get into food chain



Source: IGD Shopper Insight



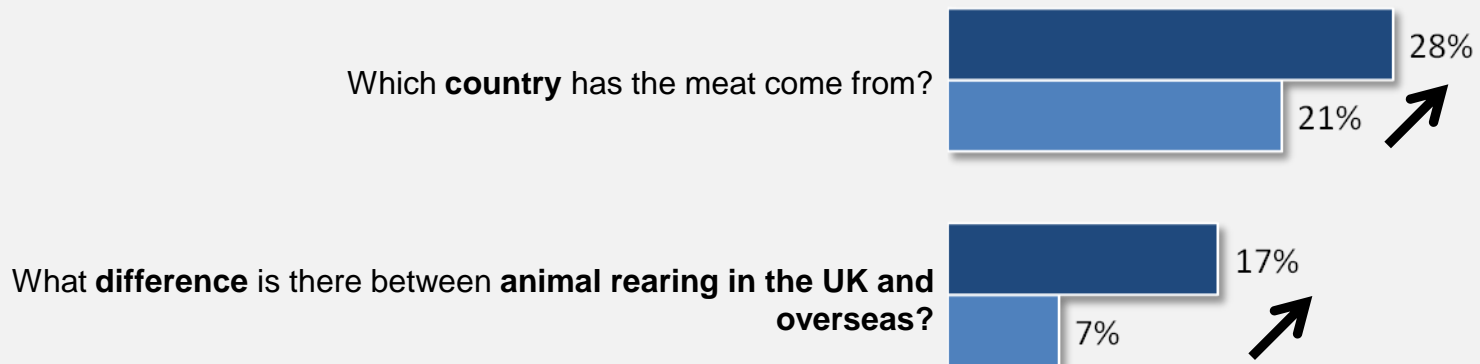
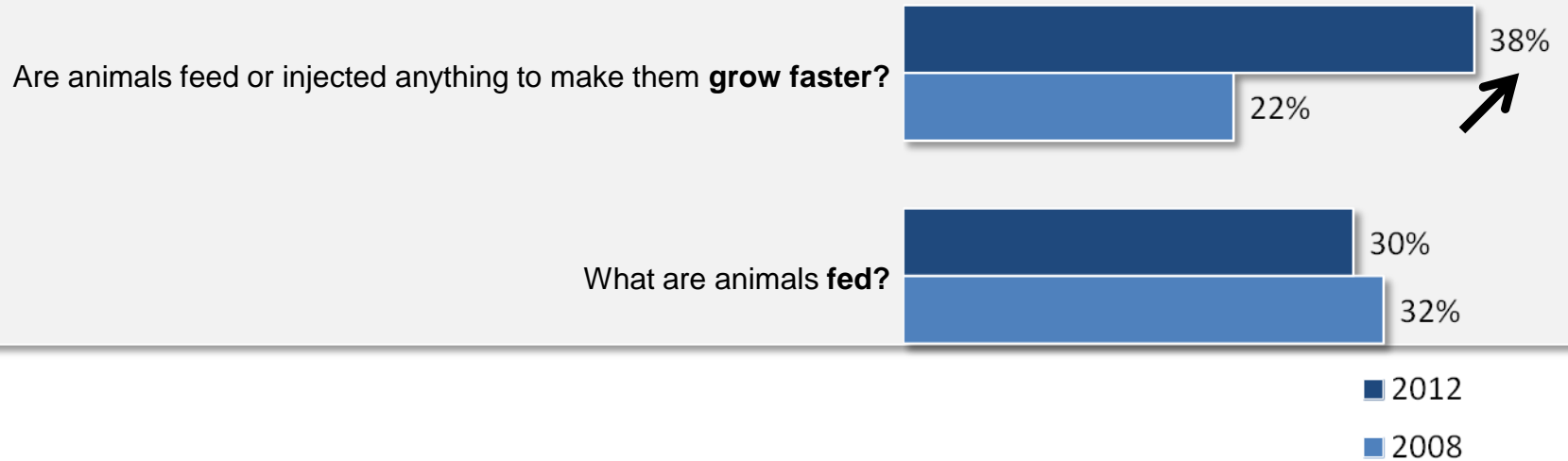
# Belief that growth hormones are used



Source: IGD Shopper Insight



# Increased demand for information on growth hormones



Source: IGD Shopper Insight

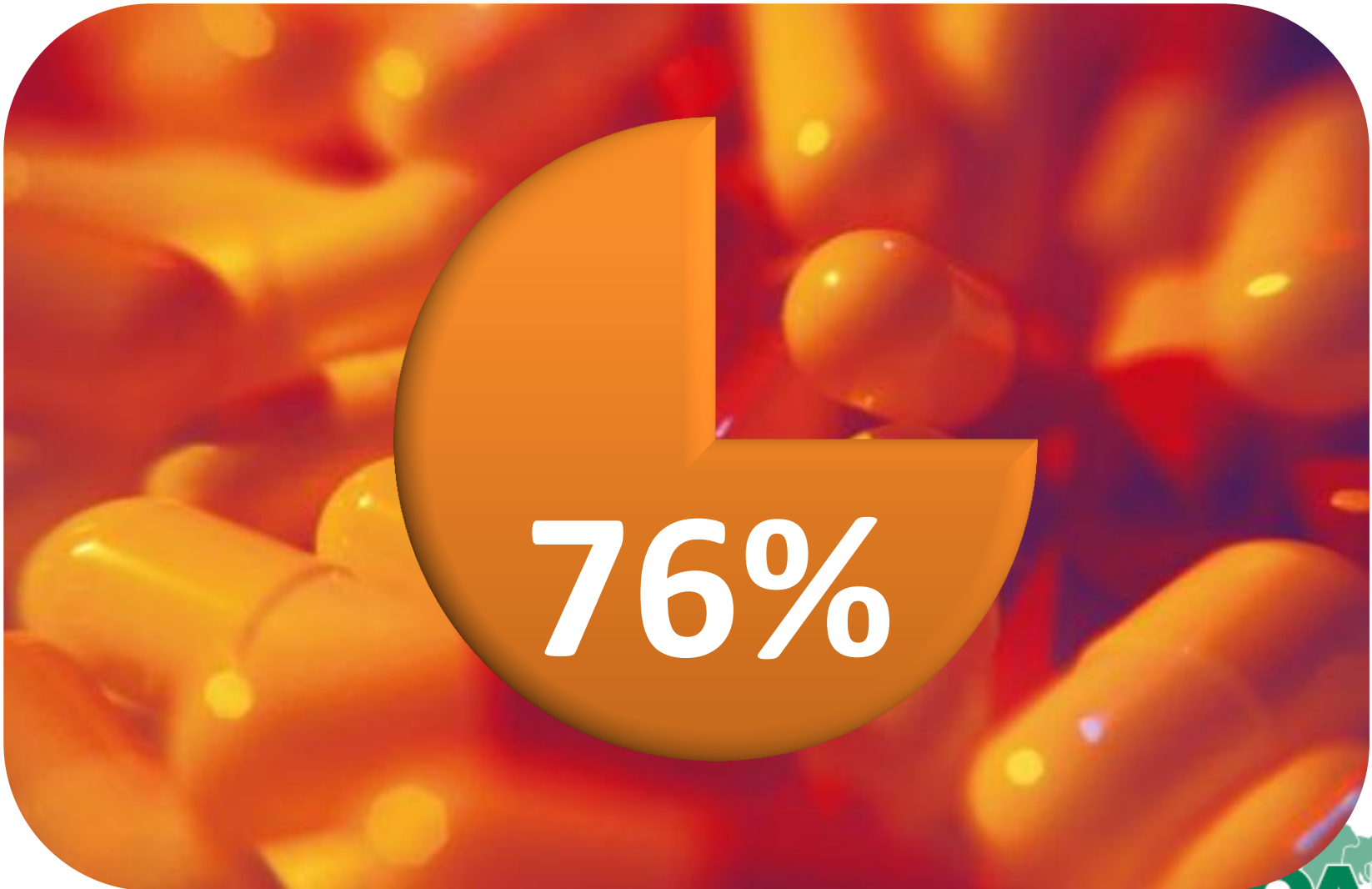
## Medicines more necessary in intensive farming



**90%**

Source: IGD Shopper Insight

# Antibiotics becoming less effective for people due to use in animals



Source: IGD Shopper Insight

Daily Mail, Tuesday, June 4, 2013

## Are farm animals to blame for the rise of superbugs?

It's normally pinned on doctors handing out antibiotics like sweeties. But there's another, very unsettling theory ...



Photo: Orlin Smith

in preventive veterinary medicine at the University of Cambridge Translational Microbiology unit.

The consequences of infection can be devastating. When a bug gets into your bloodstream — perhaps in childbirth, as a result of a bug from a serious urinary tract infection — the result can be fatal.

This is what Leticia Head suffered from, and it kills an estimated 37,000 Britons a year. The bug is greater with a superbug. A new resistant strain of E.coli can cause cystitis and make you three times more likely to die if you develop sepsis.

### The warnings that went ignored

**CONCERN** about superbugs has led to a battle about antibiotic use. Doctors want to reserve newer, more powerful antibiotics to save people in an emergency. But farmers want to use them on animals.

Ten years ago, a parliamentary committee warned that too many antibiotics were being used on farms, but the same quantities are still being used.

Furthermore, though hospital use of two of the best-known types of broad spectrum drugs (cephalosporins and the fluoroquinolones), which are effective against

different bacteria, has been cut by a third, on farms their use has risen by 68 per cent and 70 per cent respectively since 2001.

The trouble with broad spectrum drugs is that by killing off lots of different strains of bacteria, it's more likely that some of them will develop resistance.

### Why farmers say they're not to blame

**FAHMING** bodies claim resistant bugs found in farms rarely get into humans. They're backed up by the Department for Environment, Food and Rural Affairs (Defra).

"There is increasing scientific evidence that the use of antibiotics in animals is not a significant cause of resistance in bacteria that affect humans," says a spokesperson. "The clinical problems in humans are primarily the result of antibiotics used to treat human illnesses."

But others disagree, including Dr Daniela and Dr Frank Albrestrup, head of the microbial genomics and antimicrobial resistance unit at the Danish Technical University in Copenhagen.

His campaign has cut antibiotic use on Denmark's farms by 80 per cent since the mid-1980s. "Anyone still opposing the link between antibiotic use in food and

animal production and its direct impact on human health does so for other reasons beside health," he told The Lancet recently.

EU countries that have banned key farm antibiotics have lower levels of resistance to those drugs.

A type of antibiotic common on British poultry farms isn't used to treat campylobacter infections in birds in Finland. Just 1 per cent of campylobacter infections in Finnish humans are resistant to antibiotics.

However, in Hungary and Spain, where the drugs is used heavily, 90 per cent of human infections are caused by drug-resistant forms of the campylobacter.

And, according to a report from the World Health Organisation in 2011, drug-resistant salmonella in humans is linked to farm animals — and, if you are infected, your risk of dying within two years doubles.

Reducing the use of antibiotics by doctors is recognised as vital for stopping the spread of resistant strains. But if animal use isn't cut as well, farms can act as a reservoir of drug-resistant bacteria. Farmers view with alarm attempts to impose controls on

their freedom to use antibiotics. Owen Jones is a dairy farmer in West Sussex with a herd of 360 Friesian dairy cows that produce 7,000 litres of milk a day.

"We check every cow for any sign of mastitis before each milking," says Jones. "If it shows up, they get one of a standard antibiotic, double to the one used to treat breast-feeding mothers injected into the teat once a day for four days."

Though mastitis must be treated, he has no interest in using more antibiotics than necessary because they are expensive and, while the cow is being treated, its milk can't be used.

"You can't have the sort of drop in drug use that Denmark claims unless there has been serious over-use beforehand," he says. "Healthy conditions are the key to keeping down antibiotic use."

"We can control the situation much better than doctors — we don't have cows demanding three for a sniffle, and we have to pay for these expensive drugs. We can

make sure our patients finish the dose. Doctors can't do that. We don't have sick cows that need a lot of antibiotic treatments. They get culled. GPs can't do that."

### How vets cash in by doling out drugs

**HOWEVER**, not all dairy farmers are as conscientious as Owen.

Dairy calves are known to harbour a high level of antibiotic resistant E.coli bugs. A report has suggested this could be because farmers are feeding them on milk laced with antibiotics that should have been thrown away because it comes from cows being treated for mastitis.

Pigs and poultry account for nearly 90 per cent of the farm use of these drugs. The vast majority of piglets and chicks get put on antibiotics from birth because the conditions they are reared in puts them at raised risk of infection.

"Governments have routinely ignored the link between antibiotic resistance and the excessive use of drugs on factory farms," says Tracy MP Zac Goldsmith. "It's time there was a ban on routine use of antibiotics for prevention in poultry flocks."

Dr Mark Holmes, a former vet and now a senior lecturer in veterinary medicine at Cambridge, discovered the two new MRSA strains in unpasteurised milk. He has a lot of sympathy for good farmers such as Owen Jones, but stresses that many other countries accept resistant bugs from animals can create problems for humans.

"He is also worried there is an incentive for vets to prescribe drugs because they also sell them."

He also points out that "when you're faced with infected animals and you know the farmer is under financial pressure, you are going to use the antibiotics that will be most effective at getting the animals producing again, even if it is one that's vital for saving human lives."

It is unfair for the regulatory authorities to expect vets and farmers to take the long view when selecting antibiotics.

### How do we solve the problem?

**SO COULD** removing the payment incentive cut prescribing? Dr Aarweng thinks so.

Writing about the Danish scheme in science journal Nature, he said: "Preventing vets from profiting from drug sales had a huge impact on the overuse of antibiotics."

But the vets didn't lose money — they were paid to monitor the level of antibiotic use by farmers.

The data they provided allowed the Danish Agriculture Ministry to start issuing yellow cards in 2010 to farmers using high levels of antibiotics. The result was a reduction of 20 per cent in two years.

Something similar should happen here, says the Alliance to Save Our Antibiotics, a campaigning group formed by three charities critical of factory farming.

"The problem is that the industry 'don't even communicate to outline back on drugs," says Richard Young, who is livestock expert with the Soil Association, one of the charities involved.

For instance, Britain is the only country in the EU that allows drug companies to advertise antibiotics for animals. "This can only have the effect of increasing sales," says Young. "Under pressure from the vets' association last year."

In Denmark, there is a system to monitor antibiotic use and resistance in animals and humans.

It allowed us to see who was using too much and who was using the most dangerous class of drugs," says Dr Aarweng.

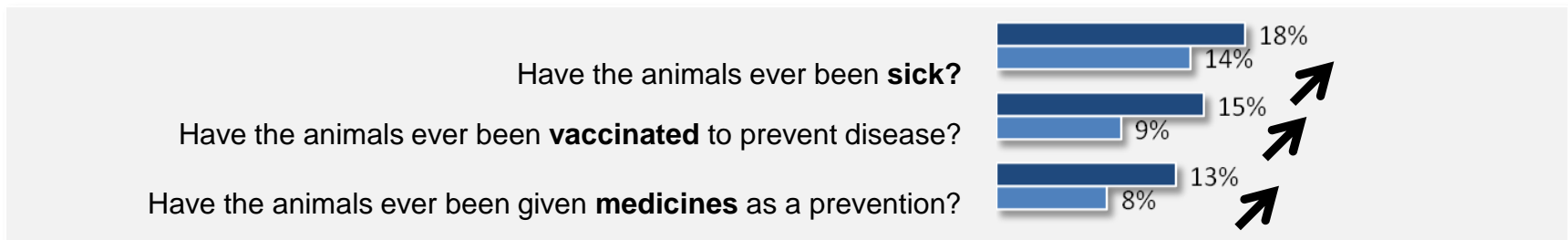
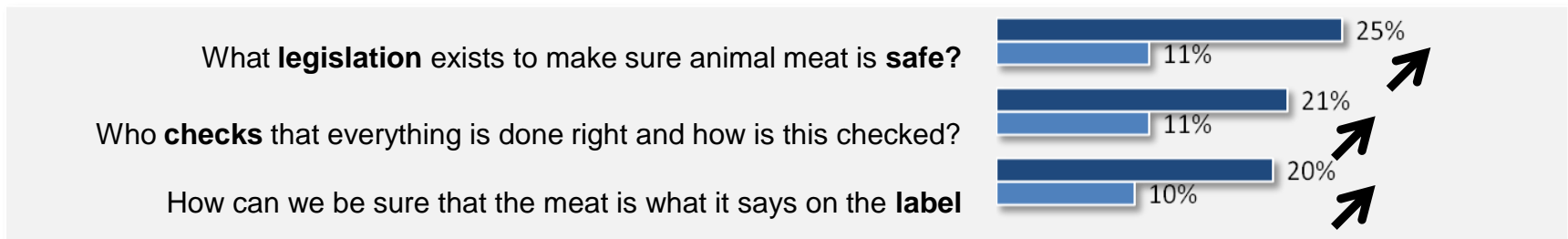
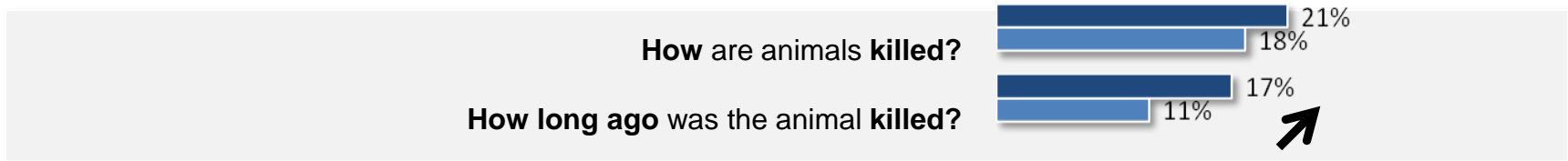
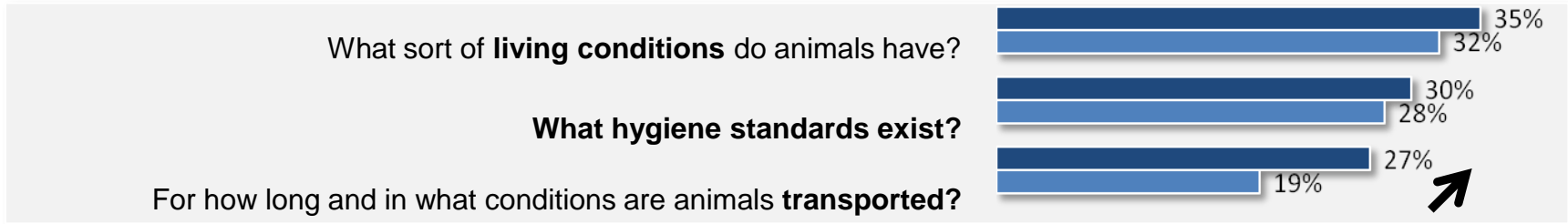
But the budget of Britain's industry regulator, the Veterinary Medicines Directorate, for monitoring resistance is being slashed.

Dr Daniels is in no doubt about the drug use that Denmark claims unless there has been serious over-use beforehand," he says. "Healthy conditions are the key to keeping down antibiotic use."

"We can control the situation much better than doctors — we don't have cows demanding three for a sniffle, and we have to pay for these expensive drugs. We can



# More consumers are demanding information



■ 2012  
■ 2008





## Two new NOAH videos:

- **Consumer Film - Animal Medicines in Food Production – Challenging Consumer Myths**
- <http://youtu.be/1qluroDR8Ak>
- **Industry Film - Animal Medicines in Food Production – The Food Industry Perspective**
- <http://youtu.be/UWihGoyJgBI>



# Questions?

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