THE USE OF ANTIMICROBIALS IN AGRICULTURE

A SOIL ASSOCIATION PERSPECTIVE

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UK Government's view

'There is scientific consensus that the use of antimicrobials in human medicine is the main driving force for antimicrobial-resistant human infections.'

'There is no conclusive scientific evidence that food-producing animals form a reservoir of infection in the United Kingdom'.

'Food is not considered to be a major source of infections resistant to antibiotics.'

Anna Soubry MP, Parliamentary Under-Secretary for Health, Hansard 9 January 2013

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Over prescribing by doctors

- A UK study found that up to 9 out of 10 prescriptions for antibiotics were unnecessary.
- UK doctors prescribe twice as many antibiotics per patient as Dutch doctors.
- Almost half the population believes antibiotics are effective against viruses; one third - coughs and colds.
- Not all patients complete a course of treatment.
- Some GPs prescribe antibiotics unnecessarily, as a placebo or because they don't want to upset the patient, or spoil their relationship with them.

JAC 2007; 60(suppl 1):i43-7 *Bekkers et al 2010, and other sources*

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‘Spread of antibiotic resistance through the food chain a growing public health problem and concern’

Leads to:

- Increased number of infections
- Increased frequency of treatment failures
- Increased severity of infections
- Prolonged duration of illness
- Increased frequency of bloodstream infections - Increased hospitalisation - increased mortality
- Increased costs to society

Prof John Threlfall HPA, BVA Congress 2012

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‘The global resistance problem’

- New antibiotic classes much harder and more expensive to develop.
- Only 3 new classes developed in last 30 years.
- Only 3 major drug companies developing new antibiotics – more profitable to develop drugs for chronic conditions.
- Most ‘new’ antibiotics are analogues, cross-resistant with existing drugs.
- Particularly critical for Gram-negative infections, like E. coli, Klebsiella and Acinetobacter. No new drugs in the pipeline.

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Lower use usually means lower levels of resistance

- Countries with low levels of use of farm antibiotics generally have much lower levels of resistance in zoonotic bacteria in animals, meat and humans (E. coli, Salmonella, Campylobacter, Enterococci). Examples: Sweden, Denmark, Norway, Finland.
- Animal species with lower levels of use have lower levels of resistance: Defra showed that 92.1% of E. coli from pigs were resistant, but just 5.7% from cattle and 3% from sheep (poultry not included). Approximately 95% of farm antibiotic use in the UK is in pigs and poultry.

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Lower resistance levels on organic farms

- Defra research compared 12 organic pig or poultry farms with 13 non-organic farms.
- Per kg of meat produced, non-organic pig farms used between 13 and 330 times more antibiotics than highest-consuming organic farm.
- Median number of resistance genes in E. coli from non-organic poultry five times higher than organic.
- SAC research also found much lower levels of resistance in E. coli from organic pigs compared with non-organic pigs.

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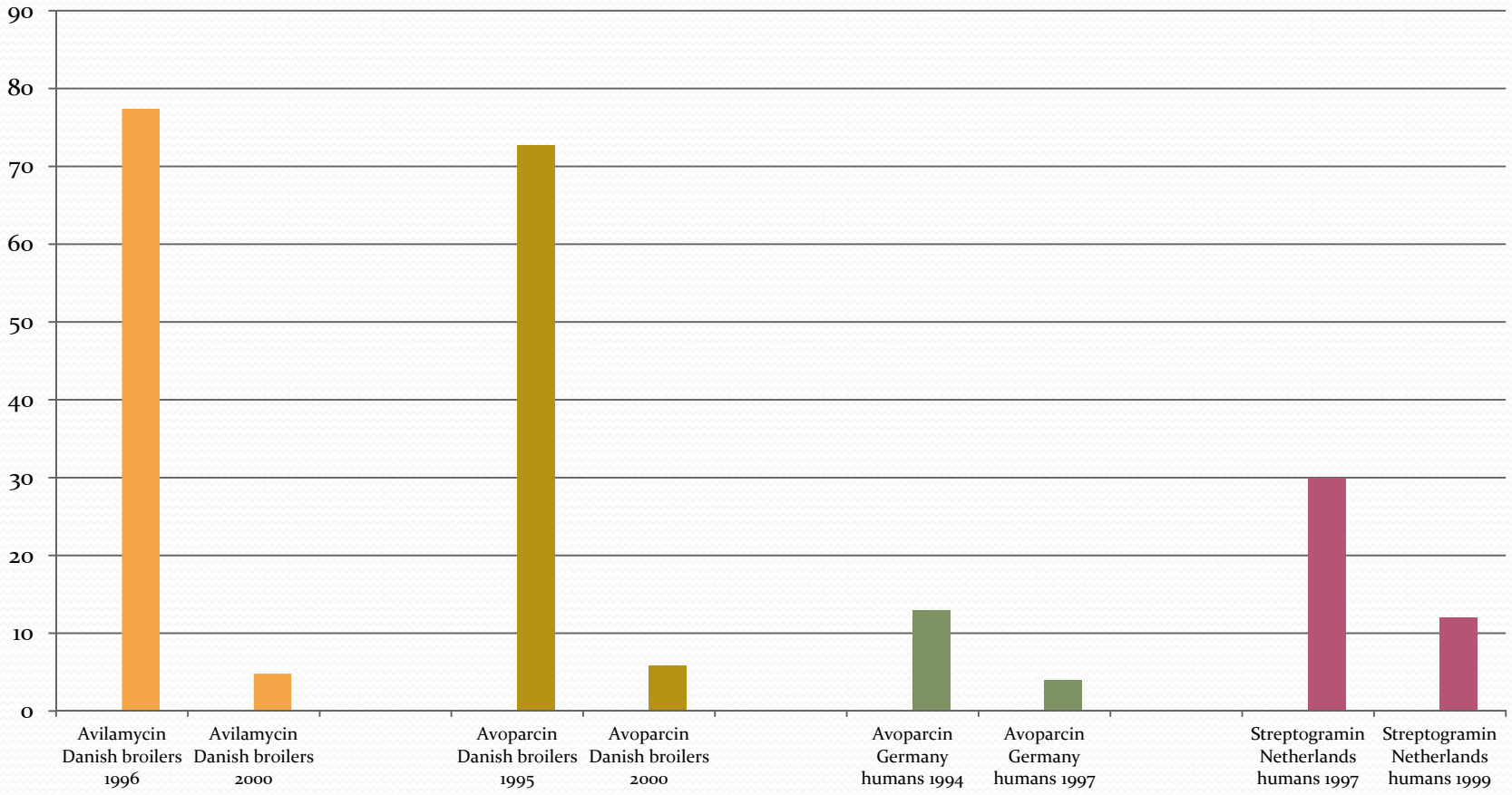
Resistance also an issue for farmers

- Very few antibiotics licensed for veterinary use.
- Vets very unlikely to get any genuinely new antibiotics for many years, if ever.
- Some cases of swine dysentery in UK already resistant to all licensed veterinary antimicrobials.
- Resistance to tetracyclines, macrolides, ampicillin sulphonamides and other in farm infections due to past overuse, causing treatment problems and encouraging use of critically important antibiotics.

Resistance to growth promoters fell after bans



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Resistance can spread to humans: Campylobacter I

- EFSA says 'Resistant Salmonella and Campylobacter involved in human disease are mostly spread through foods.'
- Before fluoroquinolones were introduced to farming in 1990s, no human cases of Campylobacter were resistant unless a patient had prior exposure to fluoroquinolones. By 2007, 46% resistant.
- DoH advisory committee said increase in human resistance 'followed the extensive use of enrofloxacin, a ciprofloxacin analogue, by the poultry industry'.

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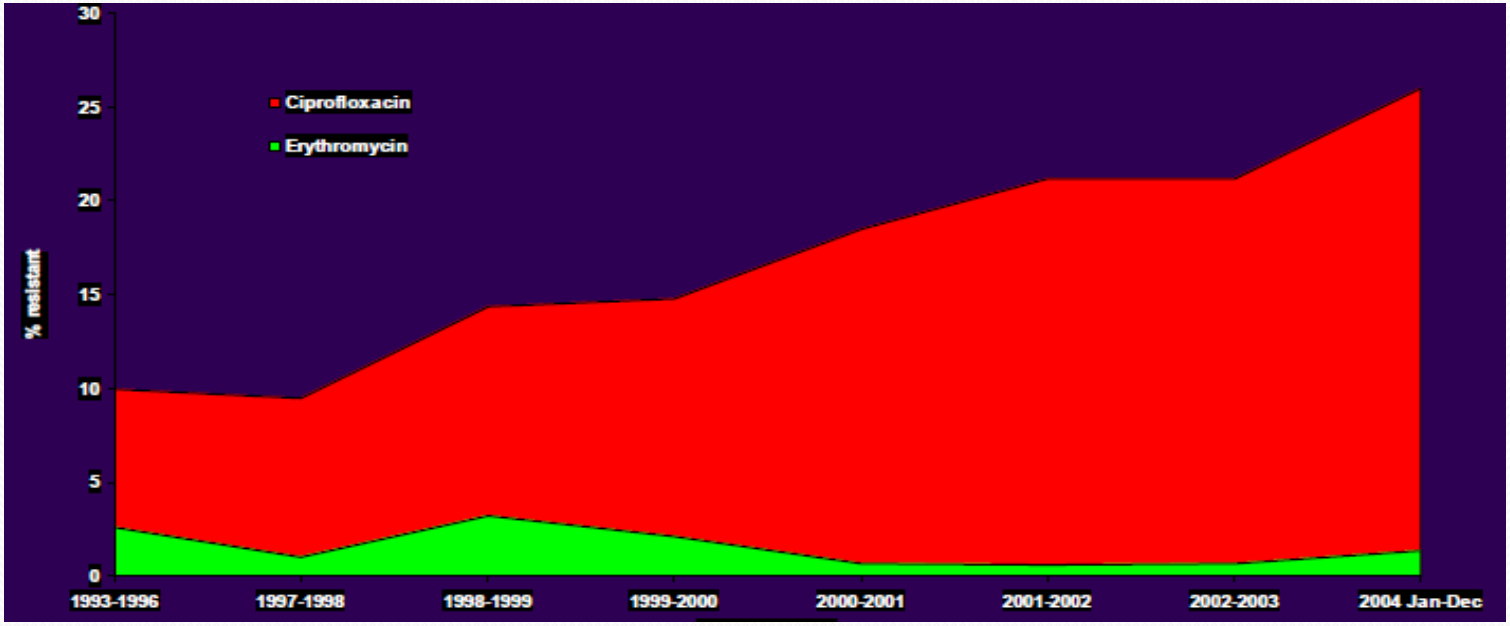
Campylobacter jejuni in humans, UK



Source: HPA

This graph of C. jejuni resistance in humans shows much higher levels of resistance to fluoroquinolones than macrolides. In 2007, 54% of human C. coli were macrolide resistant. C. jejuni associated with poultry, C. coli with pigs.

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Resistance can spread to humans: Salmonella

- A new epidemic multi-drug resistant strain of Salmonella - monophasic Salmonella typhimurium, has emerged in Europe.
- HPA and VLA and other scientists say pigs are 'the likely reservoir of infection', but also now in cattle.
- Imported beef has also caused major outbreak in four schools in France.
- EFSA estimated (2012) that 56.8 of all salmonella infections now originate from pigs.

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Resistance can spread to humans: E. coli I

- Tracing the spread of resistance from E. coli is more difficult than with Salmonella because we each have an average of 4 resident E. coli strains in our gut.
- EFSA says that it is 'highly likely' that resistance genes spread from E. coli on food to E. coli in our intestines.
- Example - A streptothricin antibiotic was used in pigs in East Germany but no equivalent then used in humans. Resistance was first found in porcine E. coli, then human E. coli, then human Salmonella and Shigella (dysentery).
- A French study found that feeding volunteers sterile diet led to large falls in resistant E. coli but insignificant falls in sensitive E. coli.

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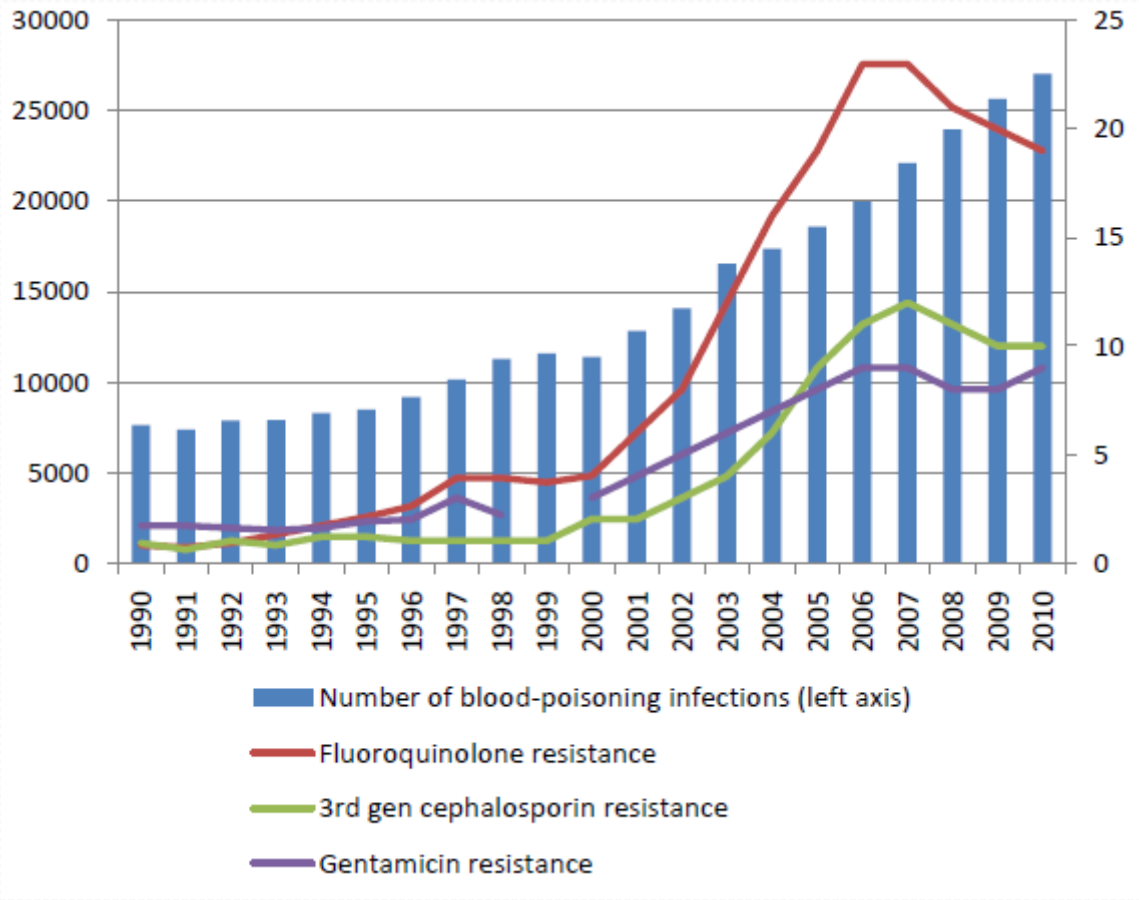
Rise of E. coli blood poisoning and antibiotic resistance UK 1990-2010



Source: Soil Association, 2012. E. coli superbugs in farm animals and food

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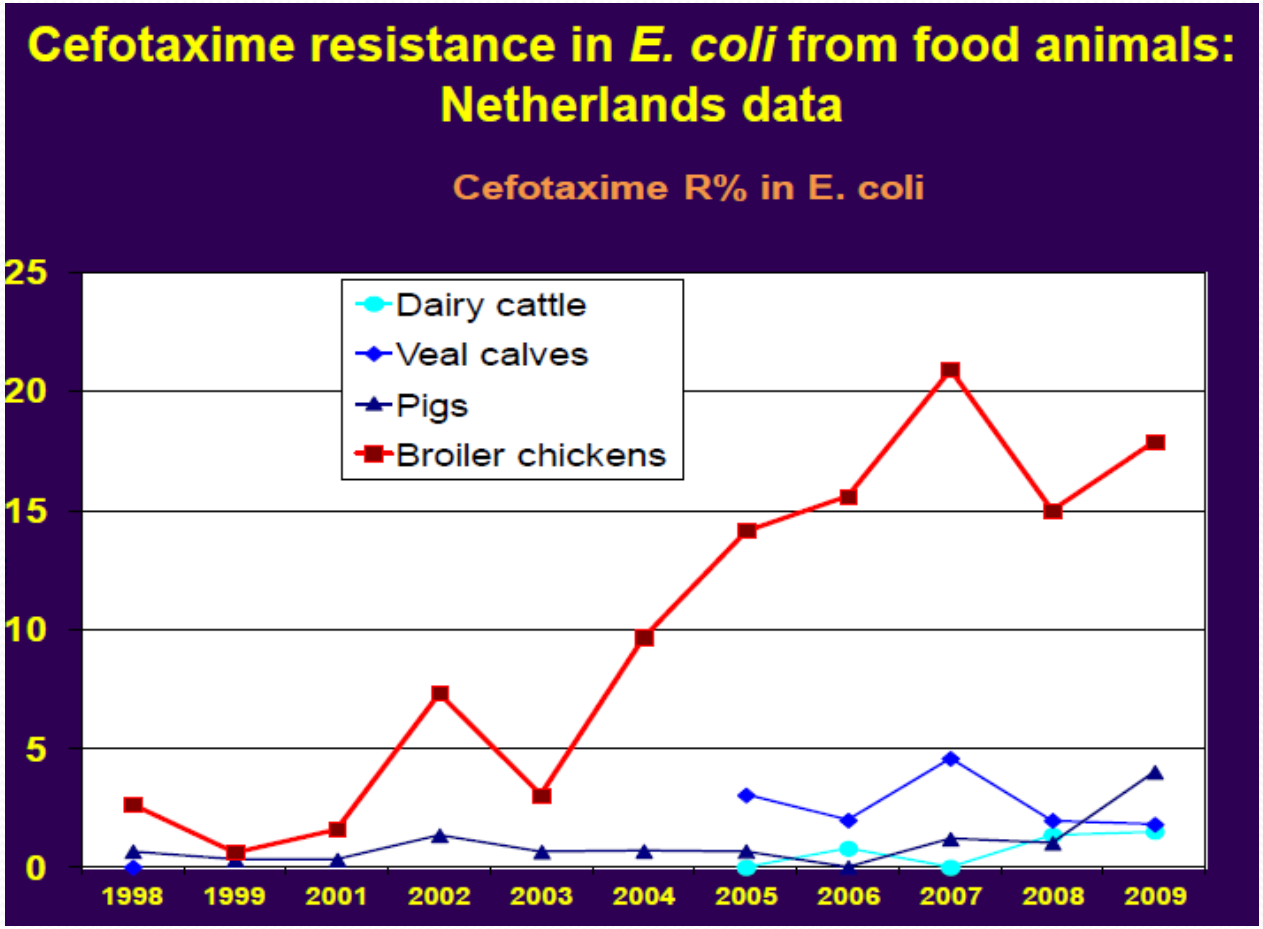
Resistance can spread to humans: E. coli IV

- Spanish and US studies have compared E. coli from humans and poultry for resistance to fluoroquinolones and cephalosporins.
- They found that resistant and sensitive poultry isolates were genetically similar. Human and poultry resistant isolates were also similar, but resistant and sensitive human isolates were different.
- They concluded: 'Many drug-resistant human fecal E. coli isolates may originate from poultry'.

ESBL resistance trends in farm animal E. Coli - Netherlands



Source: Dik Mavius, used in HPA presentation

Resistance can spread to humans: E. coli VI

- Dutch research has found that poultry are a significant source of human ESBL E. coli infections. Dutch and Danish studies have shown that farmers are much more likely to carry ESBL E. coli than the general population.
- In UK, little population research but high level of ESBL carriage in people in the community (11.3%) found in one study), despite modern cephalosporins not normally being prescribed by GPs. This ‘may point towards the foodchain being a source’ (HPA).

ESBL E. coli - UK farm animals

- 18 of 48 (37.5%) cattle farms (said by Defra to have fallen in 2012).
- 12 of 23 (52%) chicken slaughterhouses
- 3.6% individual chickens (said by Defra in 2012 to be increasing).
- 7 out of 7 pig farms (6 part of the same network)
- 438 of 504 (86.9%) pigs.
- Boot swabs from 18 of 337 (5.3%) turkey farms.
- These are small snapshots, not surveys, and give no indication national levels or trends over time.

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Resistance can spread to humans: enterococci

- Like E. coli, enterococci are normal inhabitants of human gut, but can sometimes cause serious infections.
- Experiments have shown that farm-animal enterococci can transfer resistance genes to human enterococci in the human gut.
- EFSA says: 'the reservoir of VRE [Vancomycin-resistant enterococci] in food-producing animals presents a definite risk of resistance genes being transferred to virulent human strains through food and other routes'.

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Resistance can spread to humans: MRSA

- In the UK, MRSA is still primarily a 'hospital superbug'.
- Two different types of MRSA (ST398 and mecC) have been found in a small proportion of UK milk samples.
- Both types of MRSA can cause serious infections in humans and have done so in the UK. Evidence suggests that ST398 came from humans, acquired methicillin and other resistance in farm animals, and then transferred back to humans (and on to other farm animals).
- Abroad, many new types of MRSA now being found in farm animals, including some epidemic in humans: ST1, ST5, ST8, ST9, etc. Some scientists concerned about huge size of MRSA reservoir (ST398 particularly). Developing situation – PVL virulence gene has now been found in MRSA ST398 in pigs. MRSA with PVL genes can cause very serious infections and are more common in the community.

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Waste milk: an ESBL E. coli and MRSA resistance reservoir?

- Waste milk produced during withdrawal period is fed to calves on 70% of farms. Organic regulations ban this use during statutory period, but allow during extended organic withdrawal.
- Until recently VMD allowed routine off-label use of chlortetracycline in calf milk, against EU regulations.
- Defra found cefquinome, a modern cephalosporin, in 21% of waste-milk samples. Older cephalosporins also found. Cefquinome widely used for lactating-cow and promoted for dry-cow therapy.
- Defra found ESBL bacteria, including E. coli, in 6% of waste-milk samples, including CTX-M14, CTX-M-15, common in humans, and CTX-M-1, less common.
- Defra scientists: 'feeding untreated waste milk to calves can lead to exposure to antibiotic resistant bacteria, including bacteria containing CTX-M enzymes'.

Acknowledgements

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References and further information can be provided on request

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http://www.soilassociation.org/antibiotics

The Soil Association is a founder member of the Save Our Antibiotics Alliance