The Use and Misuse of Antibiotics in UK Agriculture

Part 1: Current Usage

by John Harvey and Liz Mason
with a preface by Peter Luff MP

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PREFACE

by Peter Luff, MP for Mid Worcestershire and Chairman of the Commons Agriculture Committee

Perhaps we are too free in our use of antibiotics when treating human ailments. But antibiotic use in livestock production is also of concern, both to farmers and consumers.

Clearly farmers must be able to treat animals if they become ill. Consumers also need to be sure that the use of antibiotics on farms does not pose a threat to human health.

The distinction between the use of antibiotics for growth promotion and therapy has seemed a simple one, but in fact the issue is more complex since some growth promoting antibiotics afford a degree of disease protection. At a time when there is growing public pressure for tighter controls on the use of antibiotics in livestock production it is in everyone's interest that there should be a fuller understanding of the ways in which they are used and why.

This Soil Association report is a welcome attempt to provide that hard evidence.

More needs to be done to monitor the development and spread of antibiotic resistance in farm animals. We also need to gather statistics on antibiotic use so that we can establish whether changing trends in their use are reflected in the type and spread of resistance.

This report publishes estimates from NOAH (the National Office of Animal Health Ltd) and UKASTA (the United Kingdom Agricultural Supply Trade Association) on the total volume of antibiotics used in the UK and compares these with their use in human medicine. Interestingly it also compares use today with that thirty years ago, by reprinting data from the report of the Swann Committee.

Many would argue that this information should be collected centrally on an annual basis. I hope this report will both stimulate and inform the debates on this important issue.

REPORT SUMMARY

This report is part of the Soil Association's continuing campaign against the excessive use of antibiotics in agriculture. It aims to provide an overview of the scale and nature of antibiotic usage on UK farms in order to inform the debate on the extent to which this may be contributing to the problem of drug-resistant disease in the human population. It exposes a number of failures in the regulatory system and through the publication of the first detailed statistics for thirty years on the tonnage of antibiotics used on farms, highlights the extent to which antibiotics use in intensive livestock production has continued to rise despite all previous attempts to curtail it.

Key findings of the report are:

- Tetracycline use has increased by 1500% in 30 years, when it was supposed to fall
- Penicillin type drug use has increased by 600% over the same period
- Comparing industry estimates with published figures from the DOH suggest that about 1225 tonnes of antibiotics are used annually in the UK in the following proportions: Farm animals 37%, Pets and horses 25%, Medical use 38%
- Inclusion of the ionophores, a major class of in-feed antibiotics, which the industry leaves out of its tables on a technicality, would give a considerably higher percentage figure for farm use
- The Ministry of Agriculture Fisheries and Food does not collect data on antibiotic use on farms, despite this being a recommendation of several independent committees
- As many as 10,000 farmers in the UK may be illegally top dressing livestock feed with antibiotics
- There is a major disagreement between the British Veterinary Association and the pharmaceutical industry over the advertising of Prescription Only Medicines direct to farmers
- Virtually all growing pigs and broiler chickens receive antibiotics in their feed throughout their lives up to and including the day of slaughter
- Most intensively reared cattle are fed antibiotics routinely in replacement milk powders, compounded feed and feed blocks
- Banning individual antibiotics will not stop the problem continuing to get worse. A complete change in the way in which animals are reared is required

THE SOIL ASSOCIATION'S RECOMMENDATIONS

The Soil Association is calling for:

- A ban on all non-medical use of antibiotics in agriculture
- The prophylactic use of therapeutic antibiotics to be restricted to cases of genuine need and only made available as part of a planned disease reduction programme involving changes in housing, feeding and management practice
- Coordination of all government departments, agencies and other bodies with a statutory involvement in the regulation of antibiotic use on farms to be undertaken by the proposed Food Standards Agency
- Responsibility for the safety evaluation of veterinary medicines to pass to the proposed Food Standards Agency, as suggested in the Green Paper
- The establishment by government of a surveillance system for antimicrobial resistance, comparable with that for antimicrobial residues
- The central, annual collection of data on the use of antimicrobial agents on farms, in order to monitor trends in usage
- Livestock products imported into the European Union to be subject to routine surveillance for bacteria carrying antibiotic resistance and subject to the same controls in relation to permitted antibiotics as those produced within the EU.
- A ban on the advertising of antibiotics directly to farmers.

The Soil Association further recommends that:

- Veterinary surgeons should charge directly for advice and recoup a smaller proportion of their income from the sale of drugs.
- Veterinary and agricultural colleges should place greater emphasis on the teaching of drug-free preventative medicine

INTRODUCTION AND ANALYSIS

by Richard Young, Soil Association Policy and Campaigns Coordinator

Franz Fischler, the EU Agriculture and Rural Affairs Commissioner, has recently proposed a ban on four of the eight antibiotics currently licensed for growth promotion in farm animals throughout the EU. Because Britain permits the use of olaquindox, one growth promoting antibiotic not used elsewhere in Europe, such a ban would leave five antibiotics licensed for use in the UK without a veterinary prescription.

The move to introduce a ban on virginiamycin, tylosin phosphate, spiramycin and zinc bacitracin follows concern that their routine use may be a significant factor in the increasing incidence of drug-resistant disease in the human population. At first glance it may appear that the implementation of such a ban would resolve the problem in one easy step. However, while the Soil Association wants to see a ban on these antibiotics, it believes this is essentially a political gesture. Closer analysis reveals that banning a handful of drugs is an easier route for politicians than tackling the root cause of a problem, which is likely to continue getting worse despite the proposed ban, unless a more structured approach is adopted.

Concern about the way in which antibiotics are used on farms has been voiced by microbiologists for several decades, but action has only been precipitated recently by increasing, though as yet scientifically inconclusive evidence, that this legalised 'misuse' of antibiotics on intensive livestock farms is directly linked to the rise of untreatable infections in people. Bringing this to a head at the present time is the accession of Sweden and Finland to the European Union. These two countries already had bans in place on some or all growth promoting antibiotics before they applied to join the EU. In the interest of free trade within the community they were given only a limited period in which either to allow their use, or to persuade other member states that an EU-wide ban was appropriate. In the case of Sweden that period of grace is due to run out at the end of the year.

In the UK we are currently awaiting a report, now expected in January 1999, from the Advisory Committee on the Microbiological Safety of Food (ACMSF), which has had a working party investigating the spread of resistance through the food chain for the last two years. We are also expecting a reply from government to the recommendations made last April by the House of Lords Science and Technology sub-committee. In Europe growth promoting antibiotics are being considered one by one by the Scientific Committee for Animal Nutrition, the Standing Committee on Animal Feedingstuffs and a Multi-disciplinary Working Party under DG24.

This report was commissioned by the Soil Association to establish the extent of antibiotic use on UK farms, something we believe the government should be doing on an annual basis. We feel this task is important for two reasons. Firstly, without detailed information on antibiotic use it is difficult to establish precisely the extent

to which the use of antibiotics on farms is contributing to the problem of antibiotic resistance. Secondly, we believe that the banning of individual antibiotics will not, on its own, be sufficient to resolve the problem of antibiotic resistant bacteria passing from farm animals to people. While production systems remain unchanged farmers will simply move to those growth promoting antibiotics still licensed and the evidence suggests that, in many situations, veterinary surgeons will also find themselves with little alternative but to prescribe increased quantities of therapeutic antibiotics, both for disease prevention and for treatment. This is because all the growth promoting antibiotics also afford some degree of disease control. Until now the industry has kept very quiet about this, since openly to admit the therapeutic value of growth promoting antibiotics would be to expose the lie behind the whole industry and blow wide open the delicate compromise which has allowed their use to continue for the last thirty years.

British and, to a large extent, EU legislation on the farm use of antibiotics is still heavily based on the recommendations of the Swann Committee in 1969. It is quite clear from the Swann report that the committee wanted to ban all non-medical use of antibiotics. However, in the end the committee bowed to industry pressure and accepted that

> *those antibiotics which have little or no application as therapeutic agents in man or animals could be used for growth promotion purposes.*

It is on this basis that the growth promoting antibiotics have been licensed. Now that bans are becoming a real possibility the industry is referring to these therapeutic properties in a desperate attempt to win a stay of execution.

A clear example of this is given by Paul McMullin, the Head of the British Poultry Veterinary Association in a letter printed in the *Veterinary Times* in September 1997.

> *We have already seen a substantial increase in mortality attributed to necrotic enteritis, and cholangiohepatitis, since the, still temporary, suspension of … avoparcin. The inevitable consequence of a ban on such products would be the increased use of therapeutic antimicrobials.*

In other words, not only are many of the growth promoting antibiotics causing cross-resistance with important related therapeutic drugs, but the therapeutic properties of these drugs are also providing a prophylactic effect, even at the low doses at which they are used.

The Soil Association therefore believes that the British government and the European Union must recognise that a more detailed agronomic approach is needed which will bring about changes in the way in which farm animals are kept, in order to reduce the primary need for medication. Bans on individual products should then be scheduled sufficiently far in advance to give the industry time to

make the necessary alterations to production methods.

For this to be achieved we need first to have a clearer understanding of how and why such large quantities of antibiotics are currently being used; we then need a ministerial acknowledgement of the real scale of the task before us. This report, by freelance agricultural journalists John Harvey and Liz Mason, aims to provide some of that information. It is our hope that it will help to move the debate from a simple review of the safety of individual drugs to a review of the safety of modern livestock production methods which make such dependence on antibiotics inevitable.

The report provides, for what we believe could be the first time in 30 years, detailed estimates of the total quantities of antibiotics used annually on UK farms. It also looks at the use of antibiotics for each farm animal species. The report also examines a range of regulatory issues and exposes the fact that:

- 10,000 farms may be top dressing animal feed with antibiotics illegally,
- there is a major rift between the pharmaceutical manufacturers and British Veterinary Association over the advertising of antibiotics to farmers.

At the request of the National Office of Animal Health Ltd (NOAH) and the United Kingdom Agricultural Supply Trade Association (UKASTA) who kindly provided some of the statistics published in this report, we have printed data comparing medical use with agricultural use. The information on farm use is far from complete. Critically, it has not been possible to provide data for all antibiotics or to break down the antibiotic growth promoters by type. Nevertheless, even in this incomplete form it is possible to note some significant details. On the basis of the information we have been able to obtain, total antibiotics use is about 1,225 tonnes annually. Of this, it is estimated that 38% is used in human medicine, 25% for pets and horses, and 37% in farm animals. However it is important to point out that the figures relating to farm animals notably exclude the ionophores. These are probably the most widely used antibiotic class of all, included as coccidiostats in the rations of virtually all poultry destined for the table, and used in most cattle and some pig feed specifically for growth promotion. While we have been unable to obtain data on the quantities of ionophores used, indications are that their inclusion in the tables could double the total quantities listed as growth promoters. The Soil Association will show in a future report that the ionophores too pose serious potential health problems for the human population and also to some animal species.

Comparing medical and farm use of antibiotics, however, tells us only a limited amount. In addition we have therefore also reprinted some data for farm antibiotic use from 1966 so that an historical comparison can also be made. Many of the currently used growth promoting antibiotics and a small number of the therapeutic ones were either not available or not widely used in 1966. As a result it is not possible to make direct comparisons for all classes of antibiotics over this 30 year period.

However it is striking that the use of the penicillins and of the tetracyclines, the two classes of antibiotics which the Swann Committee banned for growth promotion on the grounds of the 'considerable evidence to show that their use as feed antibiotics has led to the emergence of bacterial strains with widespread resistance to them', have seen massive increases in use. Tetracycline use has in fact increased by 1500% over the last 30 years, and that of penicillin type drugs by 600% .

The mechanisms by which such use encourages the development of resistant bacteria are now well documented and understood, and it may be no coincidence that the incidence of multi-drug resistant salmonella resistant to tetracycline, has increased from about 15% in the early 1970s to over 80% today. However the theoretical possibility must also exist that such massive use of broad spectrum drugs like the tetracyclines, active as they are against the Gram negative food poisoning bacteria, may also have created, in ways perhaps not yet fully understood, a selection pressure for the development of entirely new food poisoning strains such as *E. Coli 0157* and *Salmonella Typhimurium DT104.*

It is ironic that not only did the Swann recommendations usher in a new range of growth promoting antibiotics, only now threatened with a partial ban, but it also completely failed to restrict the use of penicillin and tetracycline as it set out to do. It is in all our interests to ensure that we do not make the same mistake again.

Evidence in this report provides a testimony to the extent that farm animal production has become addicted to the routine use of antibiotics. We all know that such addictions cannot be cured simply by attempting to restrict the supply of drugs. Alongside the bans we must create a new climate for the production of inherently healthy animals from farm systems in which the animals are kept in more natural and less stressful conditions and routinely treated with respect rather than with antibiotics. This will require a concerted effort from MAFF, veterinary surgeons, agricultural advisers and farmers. Veterinary and agricultural colleges too will have to begin teaching the practices of sound farming methods and drug-free preventative medicine. Most of the information is already available, it has simply been overlooked in the years when drugs have been cheap, plentiful and poorly regulated.

Above all it will need support from consumers willing to pay a little more for meat over the counter and a little less for it through their taxes. It will also need confidence that such changes can be made. The Soil Association believes and hopes that the experience gained by organic farmers over the last few decades can help to provide such confidence and a number of inspirational models for more humane, safe and enlightened animal production in the future.

HISTORICAL PERSPECTIVE

A fuller understanding of how antibiotics came to be so widely used in agriculture is only possible by considering a brief history of their use.

In 1953, the British government passed the Therapeutic Substances (Prevention of Misuse) Bill. The name is somewhat misleading. The Bill extended the controls already in existence on the therapeutic use of penicillin, streptomycin and chlortetracycline to a range of new antibiotics coming on to the market at that time. However, just ten years after penicillin had first become widely available to save lives in a way never before possible, this bill made it legal for farmers and feed compounders to include penicillin and chlortetracycline (marketed as aureomycin) in the feed of pigs and poultry without veterinary prescription for the purpose of growth promotion.

The Bill had an easy passage through Parliament. Just one MP, Colonel Gomme-Duncan, spoke out strongly against it: 'May I ask whether we have all gone mad,' he said, 'to give penicillin to pigs to fatten them? Why not give them good food, as God meant them to have?' MPs were told that adding these two antibiotics to pig and poultry food would make animals grow faster and thereby increase the supply of cheap meat. With the food shortages of the war and post-war period still strong in the nation's mind it was an irresistible idea. A few MPs asked polite questions about possible residues and resistance, but received reassurances from Sir Thomas Dugdale, Minister of Agriculture, and Iain Macleod, Minister for Health, who said 'I am assured by the Medical Research Council […] that there will be no adverse effect whatever upon human beings'.

Three years of trials by the Agricultural Research Council had shown that about 75% of pigs and poultry given antibiotics on a daily basis showed increased growth rates and, more significantly since Britain imported large volumes of grain and other livestock feed, increased efficiency in converting food into meat. The greatest effect was found with aureomycin, but this was only manufactured in the USA. British drug companies were producing penicillin and, although paying royalties to the Americans who had managed to obtain international patents despite the pioneering development in Britain, it was still thought better for British industry and the balance of payments to promote penicillin alongside aureomycin.

By 1953 penicillin resistance in some bacteria had been frequently observed, however it was believed that this arose solely through mutation and the selective pressure of antibiotic use. However, in 1959 a Japanese scientist, T. S. Watanabe, discovered that antibiotic resistance could be infectious - that is that it could be transferred from one bacteria to another inside the alimentary system of human or animal. Suddenly there was a realisation that the continuous feeding of low doses of antibiotics to animals could after all pose a threat to human health. The government set up the Netherthorpe Committee in 1960 to examine the issue, but gave it

only limited terms of reference. In 1968 after serious outbreaks of multi-drug resistant salmonella food poisoning which were linked to the use of antibiotics in livestock production, government established the Swann Committee to examine the practice of feeding antibiotics to animals in relation to the issue of infectious drug resistance.

What was perhaps not counted on in 1953 was that the routine administration of antibiotics to farm animals for growth promotion also had a suppressing effect on the diseases to which animals are vulnerable. Animals in an antibiotic-induced state of artificial 'health' could be kept at a much higher density and savings made on space, labour and cost. As a result the use of antibiotics ostensibly only for growth promotion made possible the super-intensification of farm animals and also created a powerful lobby to resist any changes.

With insufficient hard evidence that the routine use of all antibiotics in livestock production really did pose a threat to human health the Swann Committee was forced into a compromise. Penicillin and the tetracyclines would be banned for unrestricted use as growth promoters, but vets would be allowed to prescribe them both prophylactically and therapeutically. Only antibiotics which would 'not impair the efficacy of a prescribed therapeutic antibiotic or antibiotics through the development of resistant strains of organisms' would be allowed as growth promoters.

This gave a green light for the development of antibiotics just for growth promotion but total antibiotic use did fall immediately post-Swann. By 1977, however, it was rising again on an annual basis, leading long-standing critics of government policy on antibiotics such as Professor Alan Linton, a member of the Veterinary Products Committee, to set out a detailed paper on 'Why Swann Has Failed'. Linton found that not only were we introducing a new range of growth promoting antibiotics, but the prophylactic use of therapeutic drugs was continuing to increase.

With increased intensification and specialisation being driven by agricultural policy and lucrative EEC capital grants, often conditional on increased intensification, there was an ever-increasing demand for the drugs that would make such stress and overcrowding possible. A few vets stood out against this, but simply saw their clients take their custom elsewhere. The vets of super-intensification tended to separate somewhat from the rest of the veterinary profession. Some were employed full-time by the large companies which came to dominate pig and poultry production. All were in the position where their monopoly 50% mark up on drugs provided the bulk of their income.

Watered down though the Swann Committee recommendations were, they were vigorously opposed by the industry which claimed, for example, that they would add threepence to a pound of bacon. The government was forced into a series of subtle back steps, much of it never fully reported. The Department of Health gave in to industry pressure and allowed tylosin to be used for both therapy and growth

promotion. Then in 1976 the use of growth promoting antibiotics was extended adult and breeding cattle, again totally against the Swann recommendations. By 1981 the Veterinary Products Committee (with little microbiological expertise, but strong industry representation) was falling out with a sub-committee of microbiologists set up to advise it. Exasperated, the sub-committee approached ministers direct for permission to review the safety of the very antibiotics under scrutiny and proposed for a ban today. Ministers refused to discuss the issue and simply sacked the sub-committee.

From that time until the establishment of a Working Group under the ACMSF there has not been an expert committee of microbiologists reviewing the safety of antibiotics in relation to the development of antibiotic resistance. Antibiotic use in agriculture has continued to increase and has broadened to include the widespread prophylactic use of important therapeutic drugs such as the fluroquinolones.

The Soil Association therefore awaits the ACMSF's report with interest.

1.1 The difficulty of obtaining data

Precise data on antibiotic use in animal and poultry husbandry in the UK is very difficult to obtain. This seems extraordinary in the context of the current debate about resistance and whether or not antibiotics should be more rigidly controlled. Even the Ministry of Agriculture has no data on annual use and the Veterinary Medicines Directorate (VMD), which licences antibiotics, is trying to improve the accuracy of the little information it has. The VMD has issued a tender for a survey to produce detailed information on antibiotic use in different animal species.

At the moment, there is no statutory requirement for the VMD to collect the data, and it is ironic that a detailed table of human antibiotic use in general practices and hospitals in the UK has just been published (SMAC, 1998). Ever since the report of the Swann Committee on the use of antibiotics in animal husbandry and veterinary medicine was published in 1969, eminent committees have been asking for statistics on annual use. In October last year, for example, a Ministry of Agriculture workshop in Birmingham reported that

> *Consumption figures for different countries in the European Union were presented and related to the overall presence of resistant bacteria. For the UK, this data was exceptionally difficult to obtain* (MAFF, 1998).

More recently, the same message came from a meeting organised by the Danish Ministries of Health and Agriculture in Copenhagen in September. Part of its recommendation states

> *Evaluation of the benefits and risks of antimicrobials depends on collecting detailed information about their consumption by animals and humans and their use in aquaculture and horticulture. Data should also be collected on antimicrobial agents used to treat animals (by species) and for growth promotion* (Ministry of Health, 1998).

In its tone, this is similar to a comment from the British Veterinary Association's antimicrobials working group:

> *Use of antimicrobials may lead to resistance patterns which could endanger human or animal health. […] The group would like to see a full benefit-risk analysis for all antimicrobial uses. Two such studies are in progress in Europe and the USA, and the data should be available before the end of 1998* (BVA, 1998).

Last year, the World Health Organisation organised a meeting in Berlin called 'The Medical Impact of the Use of Antimicrobials in Food Animals'. Under the heading 'risk assessment', the meeting concluded: 'No antimicrobial should be adminis-

tered to a food animal unless it has been evaluated and authorised by competent national authorities. This evaluation should include a thorough risk assessment which includes the development of resistance that may impact public health; and post-market monitoring programmes to detect emergence of resistance of public health significance' (WHO, 1997).

In another context, the working group of the Advisory Committee for the Microbiological Safety of Food (ACMSF) has also had a struggle to obtain data, as one of its members, Dr Norman Simmonds, explained to a House of Lords enquiry into antimicrobial resistance.

> *We had great difficulty finding out how much antibiotics are given to animals. I think that figures from NOAH [National Office of Animal Health Ltd, representing the drug companies], which are based on cost clearly do not tell you very much, and a lot of information is regarded as commercially sensitive. There is no central register of use. The records on farms are not that good even where they are meant to be good, and even on the best farms they are not perfect*
> (House of Lords, 1998, Evidence).

These statements show the importance of collecting usage data, and they are likely to be reflected in the report of the ACMSF on antibiotic resistance expected early next year. At about the same time, the Government will reply to the report by the House of Lords Select Committee on Science and Technology, entitled 'Resistance to Antibiotics'.

In response to the House of Commons agriculture select committee food safety report (House of Commons, I, 1998), which called for a ban on the use of antibiotics as growth promoters, the Government said it would act on the advice of its scientific committees, including the ACMSF and the Veterinary Products Committee (VPC). It reiterated the VPC's policy on the use of antibiotics as veterinary medicines: 'New antibiotics should not necessarily be precluded from therapeutic use in animals but their prophylactic use should be discouraged.' The VPC itself organised an open meeting on resistance in June, and is planning to offer advice to the health and agriculture ministers on the best ways of ensuring 'responsible use' of antibiotics by veterinary practices.

The phrase 'responsible use' crops up quite often, and is obviously seen by the farming industry as a way of preventing unilateral bans on specific antibiotics introduced by some EU member states. A National Farmers Union report on antibiotics is called 'Responsible Use of a Precious Resource' (NFU, 1998), and the NFU is now co-operating with other industry organisations to produce another report on 'responsible use' to coincide with the release of the ACMSF report.

1.2 Antibiotic use figures

In September, the *British Medical Journal* tried to establish usage. Mac Johnston, senior lecturer in veterinary public health at the Royal Veterinary College, said that in penicillin equivalents 'the veterinary use of antibiotics is just under 500,000 for all species compared with just over 760,000 for all medical use' (Johnston, 1998). Mr Johnston said a total of 1900 drugs is licensed for use in animals in the UK. Their market value in 1997 was £379 million, with 40% of sales for pets. Antimicrobial agents for farm and pet animals totalled about £80 million: of this, antibiotic growth promoters for foodstuffs were valued at £12 million.

NOAH claims the figures show that the market for animal medicines in the UK is small compared to the £6.6 billion spent in the UK on human medicines (about 30 times the farm animal expenditure). But when questioned by the House of Lords Select Committee on Science and Technology Roger Cook, NOAH director, conceded that a comparison between animal and human use on the basis of cost was not very realistic as a measurement of the amount of antibiotics used. Mr Cook told the Lords committee that NOAH had 'been trying to get information on the volumes of antibiotic usage in human medicine so we could present a proper comparative picture. Unfortunately it seems that nobody, not even the Department of Health, has those statistics'.

However, statistics have since been published in a report produced by the Department of Health's Standing Medical Advisory Committee (SMAC). NOAH agreed to provide comparative figures on animal usage for this report. The United Kingdom Agricultural Supply Trade Association (UKASTA) also provided figures on the annual use of antibiotics through veterinary use and in livestock feed. This is the first time these figures have been released or published in this form.

definitions:

ANTIBIOTICS active against bacteria and a few viruses. Originally fermented from natural microorganisms, they are now often produced synthetcally.

ANTIBACTERIALS active against bacteria. Includes all antibiotics and chemically synthesised drugs, such as sulphonamides.

ANTIMICROBIALS Includes all antibacterials and some other drugs active against other microorganisms such as fungi and protozoa.

TABLE 1 UK human and animal use of antibiotics (kg active ingredient)

	ANIMAL USAGE		HUMAN USAGE	
	1966 Swann Report	1996 NOAH survey[1]	1996 DoH[2]	1997/8 SMAC[3]
Cephalosporins, B-Lactams inc. Penicillins	16,825	121,603	195,841	314,498
Tetracyclines	19,635	323,151	38,130	47,500
Aminoglycocides	?	37,058	41	5,409
Macrolides	?	71,222	47,696	?
Metronidazoles	-	-	8,579	?
Fluoroquinolones inc. Nalidixic acid	-	1,437	8,970	14,547
Sulphonamide Trimethoprim	59,422	101,877	8,987	14,400
Antituberculous	-	-	2,174	?
Clindamycin Lincomycin	-	-	86	?
Urinary	-	-	1,332	?
Sectonomycin				
Fostomycin				
Rifampicin/Rifamycin	?	-	-	43
Fusicic acid	-	-	-	808
Glycopeptides	-	?	-	502
Chloramphenicol etc.	-	-	-	113
Nitrofurantoin	?	-	-	787
Others	?	283	287	-
Growth promoters	?	99,312	-	-
Total	**151,087**	**755,660**	**312,123**	**469,700**

NOTES

1 The 1996 NOAH survey involved all NOAH members supplying antibiotics products for farm and pet/horse use in the UK.

2 The 1996 DoH figures were taken from the DoH publication "Prescription Cost Analysis - England 1996". These figures exclude Wales, Scotland, Northern Ireland and hospitals (and private medicine).

3 These 1997/8 figures are from the report from the Standing Medicines Advisory Committee (SMAC) of the DoH entitled "The path of least resistance" published in September 1998 and covering the year to January/February 1998. The source of the data is given as "IMS Health, Maxims Database" year ended January/February 1998.

TABLE 2 Estimated annual usage of antibiotics in humans and animals in the EU in 1997 (tonnes active ingredient at 100% purity)		
Human use	5400	52%
Animal (therapeutic and prophylactic use)	3494	33%
Animal (growth promoters)	1599	15%
Total antibiotics	**10,493**	**100%**

NOTES

1 Currently FEDESA are doing an EU wide survey of antibiotic usage. As yet no detailed results are available, but this table gives the 'broad' result published at a meeting in Copenhagen in September.

2 Although this table appears to show that the usage of antibiotics by weight is slightly lower for farm animals than for human medical purposes, it is important to note that the ionophores, licensed for growth promotion and the control of coccidiosis, were not included in either the veterinary or the growth promoting categories. Since these are probably the most widely used in-feed antibiotics of all, their inclusion would have a significant effect on the figures.

TABLE 3 Quantity of active medicine incorporated into commercial compound feeds in the UK in 1996 (tonnes)	
Total output of commercial compound feeds	11,900,000
Total output of feed with VWD[1] (@ average 150 mg active medicine/kg feed)	750,000
Total active medicine incorporated under VWD[1]	110–120
Total output of feed with PML[2] (@ average 20 mg/kg feed)	5,500,000
Total active PML medicine used	105–115

SOURCE United Kingdom Agricultural Supply Trade Association Ltd (UKASTA).

NOTES

1 Veterinary written directions (VWDs) refers to the situation in 1996. The VWDs have now been replaced by medicated foodstuffs prescriptions (MFS) which are now required to incorporate 'Presciption Only Medicines' (POMs) into feed.

2 The 'Pharmacy and Merchants' List' (PML) (available without prescription) boxes would cover growth promoters.

TABLE 4 Tonnages of pig and poultry feed in 1995

	Total tonnage (thousand tonnes)	Total tonnage with VWD (%)	Total tonnage with PML (%)
PIGS			
Starter, Weaner	161.4	45-55	no data
Grower	580.1	35-45	no data
Finisher	941.1	15-25	no data
Breeder	698.4	10-15	no data
POULTRY			
Broiler starter	335.1	15-25	no data
Broiler grower Broiler finisher	1,340.3	less than 5	no data
Turkey starter Turkey grower Turkey finisher	766.1	less than 5	no data
Chicken starter Chicken grower	655.5	less than 5	no data
Layers for egg production	878.0	less than 1	no data
Breeder	5.3	5-10	no data

Source: UKASTA

1.3 TRENDS IN USE

NOAH says an increasing amount of antibiotics are being administered in water, although there are no figures on this. There are three reasons for adding antibiotics to water rather than feed on pig and poultry farms in particular:

- farmers can be much more precise about when treatment stops and starts by switching off a tap in the pig or poultry house
- animals or birds which are very sick are more likely to drink than eat, and water is an efficient way of treating them. 'If you have 3000 chickens, this is much better than chasing them around with a syringe', said NOAH's director, Roger Cook
- management of feed mills is made easier because there is less likelihood of cross-contamination.

Jim Reed, director-general of UKASTA, said that with reasonably healthy animals or birds, you can be pretty sure of the amount of antibiotic they will receive from a measured dose in feed. 'If you put the antibiotic in water, much the same applies. But there can be some conditions of livestock which cause them to drink excessively. If you apply it to them in any other form (than feed) which is all ad lib, you will have even less control.' After vaccines, feed was the most measured way to administer medicines, followed by water, Mr Reed said.

Figures are only of limited value without putting them into the context of the current debate about antibiotics. This is dealt with in the following section.

terminology:

The terminology with regard to medicinal feed additives can be confusing. European Union legislation which came into force in May 1998 has replaced 'Veterinary Written Direction' (VWD) with 'Medicated Feedingstuffs' prescription, and 'Prescription Only Medicines' (POMs) are now known as 'Medicated Feedingstuffs'. Antibiotic and chemical growth promoters and other antibiotics and medicinal additives which were known as 'Pharmacy and Merchants' List' (PML) products are now called 'Zootechnical Food Additives'.

PART 2 – Issues in the agricultural use of antibiotics

2.1 Controversial usage

Anitbiotics are used in farm animals for three reasons: to promote growth, to treat disease (therapeutic use) and to prevent disease (prophylactic use).

Following the Swann Committee report (House of Commons, 1969), legislation was introduced under the Medicines Act to divide antimicrobials into non prescription medicines (called Pharmacy and Merchants' List products or PMLs, for growth promotion and coccidiosis control) and prescription only (or POM products for disease control). Antibiotics used in human medicine, including penicillin, oxytetracycline and chlortetracycline were banned as growth promoters. However, no restrictions were made on the use of such antibiotics for prophylaxis or therapy in animal husbandry or veterinary medicine.

In 1992 the Expert Group on Animal Feedingstuffs (the Lamming Committee) recommended that:

> *Not only should antibiotics giving cross-resistance to those used in human medicine not be used as growth promoters but their prophylactic use in animals should be reconsidered (MAFF, 1992).*

In response the Government said it would seek advice from the Veterinary Products Committee (VPC) and the Committee on the Safety of Medicines. The VPC recommended in 1992 that new antibiotics should not necessarily be precluded from therapeutic use in animals but that their prophylactic use should be discouraged. In other words it was to do nothing about the prophylactic or growth promoting use of older, previously licensed antibiotics.

In November 1993, the VPC approved the use of enrofloxacin, a fluoroquinolone, in animals in the UK, despite evidence from the Netherlands demonstrating that the use of this antibiotic in poultry resulted in an upsurge of ciprofloxacin resistant campylobacter in poultry and humans. Enrofloxacin is used in broiler chickens in the first week of life to reduce vaccination damage, or in the third or fourth week to reduce respiratory difficulties caused by *E. coli*. Ciprofloxacin is the fluoroquinolone probably most used in humans in the UK (House of Lords, 1998, Evidence, p219-220).

Fluoroquinolones are not used as growth promoters, but according to a World Health Organisation press release this June they are currently used for treating animal disease in many countries and, in some regions, they are also used for disease prevention. However, according to WHO, 'the data available so far on their usage are scarce and are often the proprietary information of the drugs' manufacturers'. Some scientists say fluoroquinolones, which are only licensed to treat disease, are

being used for 'mass medication'. They are used in vaccine programmes and in very young animals, so although they are not used for growth promotion, mass treatment is causing concern (House of Lords, 1998, Evidence, p230).

Other antibiotics related to antibiotics used in man have been used, or continue to be used, as growth promoters or for widespread prophylaxis. The following are some of the most widespread:

- **avoparcin:** a member of the group of antibiotics called glycopeptides which also include vancomycin and teicoplanin. Vancomycin and teicoplanin are used in human medicine. (House of Lords, 1998, Evidence, p218-219). The use of avoparcin as a feed additive was suspended by the EU Commission from April 1, 1997 - only the UK voted against the ban. Between 1975 and 1996, avoparcin was used in feed for broiler chickens, turkeys, pigs, beef and dairy cattle, calves, sheep and goats. Depending on the livestock species, 4-50 milligrams per kg was added to animal feed.

- **virginiamycin:** used as a growth promoter in chickens, turkeys, pigs and cattle. Also used to prevent coccidioisis in chickens and turkeys, and in pigs to treat and control swine dysentery. Virginiamycin is a streptogramin antibiotic. Quinupristin/dalfopristin, another streptogramin mixture, has recently completed phase three clinical trials in the United States and Europe, and it was hoped that it would be suitable for the treatment of patients with GRE (glycopeptide-resistant enterococci) infections. But now there are doubts because virginiamycin use in animals may have already resulted in quinupristin/dalfopristin resistance. (House of Lords, 1998, Evidence, p.219).

- **tylosin phosphate:** the most popular growth promoting antibiotic in pig production. A member of the macrolide group of antibiotics and closely related to erythromycin, the drug of first choice for patients allergic to penicillin. Tylosin is also licensed as a therapeutic antibiotic. In 1969 the Swann Committee recommended that Tylosin should not be allowed for growth promotion, but the Department of Health eventually caved in to intense industry lobbying (McKinnon 1980). Tylosin has already been linked, along with virginiamycin, to the appearance of erythromycin-resistant campylobacter in humans.

- **zinc bacitracin:** a polypeptide widely used in pig and poultry production. It has so far not shown cross-resistance to therapeutic antibiotics. It is not used systematically since it is capable of causing kidney damage, but is used in a number of topical preparations.

- **avilamycin:** after not being used for a number of years avilamycin was relaunched by Elanco in April 1998 to exploit the market opportunity which arose from the ban on avoparcin. It is now widely used in poultry production. Although there is no evidence to show that avilamycin use compromises the effectiveness of any human drug used at present, it is known that bacteria resistant to it confer cross

resistance to a new and related antibiotic, Ziracin, currently being developed in the hope of treating vancomycin-resistant enterococcal infections in humans.

TABLE 5 Growth promoting antibiotics licensed for use in the UK

ANTIBIOTIC	PRODUCT NAME	COMPANY	USES
Avilamycin (oligosaccharide)	Maxus G200	Elanco Animal Health	Pigs, broiler chickens, turkeys (all growth)
Bambermycin (glycolipid)	Flavomycin 80	Hoechst	Pigs, cattle, domestic fowls, turkeys, rabbits (all growth)
Monensin (ionophore)	Romensin G100, Elancoban G200	Elanco Animal Health	Cattle except lactating dairy cows (growth), broiler and layer chickens (prophylactic)
Olaquindox (quinoxaline)	Enterodox 100 BMP	Nor-feed (UK)	Pigs up to four months of age (growth)
Salinomycin (ionophore)	Sacox 120, Kokcisan 120 G, Salocin 120, and others	Hoechst	Broiler chickens (prophylactic) pigs (growth)
Tylosin Phophate (macrolide)	Tylamix G100, Tylan G20, Tylasul G50 and others	Elanco Animal Health	Pigs, growth, prophylactic and therapeutic
Virginiamycin (streptogramin)	Stafac 500	Smithkline Beecham	Chicken, pigs, cattle (all growth)
Zinc Bacitracin (mixture of cyclic polypeptides)	Albac 150 granulated, Albac 100 lactodispersible	Alpharma	Growth promotion in pigs, poultry calves and lambs

SOURCE Soil Association.

2.2 Irresponsible usage

Many in the farming industry know that veterinary pharmacies in Ireland are currently sending UK farmers antibiotics through the post. This is acutely embarrassing because it undermines the industry's efforts to portray the use of antibiotics as responsible. Veterinary practices in England have discovered invoices from their farmer clients for Irish products sent through the post. The Veterinary Medicines Directorate says that since February 1 this year, farmers importing from Ireland are likely to have committed an offence. This is because since that date any product imported for administration to a farmer's own animals must be labelled for the UK market and carry the market authorisation number. So anything brought in without the label is illegal.

'Our main concern is that there could be a trade in products which are not POM

medicines in Ireland but which are POMs in England', said a VMD spokesman. Farmers could then administer an antibiotic without veterinary supervision which is an offence under the 1968 Medicines Act.

Roger Cook, director of NOAH, which represents companies making antibiotics, explains that some products (for example, dry-cow intramammaries) are the Irish equivalent of our PML products. In Ireland, farmers wouldn't need a prescription or have to be supervised by a vet to use these antibiotics. Irish VAT rules are different from England, which makes the imported antibiotics cheaper. 'Because they are being sold through the post by unscrupulous wholesalers, they are not incurring overheads such as veterinary advice' said Mr Cook. The VMD is co-operating with the Irish authorities to try to stop the trade.

2.3 Advertising

The agricultural trade press advertises antibiotics every week. Both NOAH and the VMD say this is allowed under the Medicines Act, but the British Veterinary Association (BVA) is more equivocal. In its latest code of practice on medicines the association says:

> *POM medicines should not be advertised or displayed to the public. Some commonly used medicines such as flea preparations are POM. Therefore, this restriction on advertising could limit education and provision of information to clients. The Royal College of Veterinary Surgeons has indicated that it is acceptable for members to display posters advertising POM medicines within the veterinary practice because this would constitute advertising to clients and not the general public (BVA, 1998).*

A VMD spokesman interpreted the advice as trying to persuade vets to treat animals on the basis of their own diagnosis and to discourage veterinary practices from 'promoting one product over another'.

NOAH seemed surprised by this advice, and Roger Cook said he would discuss the statement with the BVA. NOAH itself has a code of practice 'for the promotion of animal medicines' which is printed at the front of its *Compendium of Data Sheets for Veterinary Products* (NOAH, 1998). This says 'promotions shall be fair and shall not include exaggerated claims or inappropriately encourage the use of particular veterinary medicinal products'. A clause in the code covering journal and poster advertisements says such advertisements should contain the following information: the brand name of the product; the approved or other non-proprietary names of the active ingredients; a form of words which indicates clearly that further information is available on request; the company name and address; and, when promoting a POM medicine to the business or lay user, a form of words which indicates clearly that advice should be sought from a vet.

In its current guide to professional conduct, the RCVS states:

> *All advertising must be legal, decent and truthful. It must be fair, responsible and always in the interests of the animal actually or potentially under the care of the veterinarian. It must not endanger the good name and reputation of the profession (RCVS, 1996).*

In spite of all this careful wording, there is a difference of opinion between the BVA and NOAH about advertising POMs.

Chrissy Nicholls, head of veterinary services at the BVA, said: 'It is still our belief that advertising POMs in the farming press in particular should not happen because the veterinarian is pressurised to use a particular product - even if it is not one that he might wish to use'. Ms Nicholls added that there had been a cut-back in advertising POMs in the weekly veterinary press in favour of the weekly farming press because the manufacturers knew their advertisements had an impact on farmers. Bob Stevenson, a former BVA president, said his 'gut feeling' was that POMs should be promoted and carefully detailed to the veterinarian but not the farmer. 'I think advertising in a journal such as *Farmers Weekly* is inappropriate because it puts a lot of pressure on the farmer to approach his vet - and he doesn't understand why the vet might then say this product is not right for you.' Mr Stevenson added there was a danger that young vets trying to make their reputation would be leaned on by farmers saying that they would go somewhere else unless the product was made available. 'A very overt push of a potent POM without a very large slice of responsibility is totally unacceptable in my view', he added.

2.4 Overseas use and the question of imports

There seems little point in restricting antibiotic use in the UK if over-use in other countries encourages the build-up of bacteria resistant to antibiotics. Poultry imported from other EU countries for example may carry fluoroquinolone resistant campylobacter (House of Lords, 1998, Evidence, p220). This raises the issue of monitoring, including monitoring for antibiotic residues and monitoring of livestock and/or meat imports to see if they contain antibiotic-resistant bacteria. In evidence to the House of Commons agriculture select committee on food safety, the Public Health Laboratory Service (PHLS) said the following amounts of food were imported into the UK between January and October 1996 from non-EU countries (House of Commons, II, 1998):

(figures in tonnes)

feeding stuff for animals (excluding unmilled cereals)	**2,897,957**
fish (not marine animals), crustaceans, and molluscs	**339,953**
live animals	**717**
meat and meat preparations	**239,629**

Countries which export meat and other animal products into the UK are supposed to deposit their own residue surveillance plans with the European Commission. The Commission then has the right to carry out inspections in third countries. In addition, under the relevant veterinary checks directive, member states can inspect up to a 1% sample of what is being imported. The VMD is not currently doing any import monitoring. A VMD spokesman said: 'We are currently talking to our European colleagues about whether we can give them any help on the residues programme'.

The Copenhagen meeting organised by the Danish Ministries of Health and Agriculture said European surveillance of resistance should be started. This should 'collect data on trends in resistance in bacteria of human and animal origin'. Dr David Livermore, head of the Public Health Laboratory Service's antibiotic reference unit, said this kind of surveillance had not started yet, but 'it's moving further up the agenda, particularly with publication of the ACMSF working group report'.

Concern over antibiotic resistance has prompted EU animal health companies to set up a surveillance programme covering six EU countries, the UK, Spain, Sweden, Denmark, France and Holland. Strains of the bacterium *Enterococcus faecium* will be taken from pigs and poultry and tested for their sensitivity or resistance to antibiotics. Final results are expected early in the year 2000, according to NOAH, in their submission to the Advisory Committee on the Microbiological Safety of Food Working Group.

On the animal feed side, Jim Reed, director-general of the United Kingdom Agricultural Supply Trade Association (UKASTA), which represents companies which mix antibiotics into livestock and poultry feed, said there were no medicated feeds coming into the UK from non-EU countries. 'There may be some trade in specialist products such as vitamins and minerals, but trade in medicated feed across the English Channel scarcely happens at all.'

However, the Royal Pharmaceutical Society of Great Britain (RPSGB) says active ingredients for antibiotics and growth promoters are manufactured in Holland, Sweden and Norway and imported into the UK. POMs are also imported and distributed through agents. Figures on this are confidential. The RPSGB says medicated feed is also imported: for example Denkavit, a subsidiary of Dalgety, has a warehouse in Poole for importing milk replacers. This makes up a 'substantial proportion' of what is used in the UK, and is manufactured within the European Union.

2.5 Loopholes in regulation

In May this year new controls on additives and medicines in animal feeds were announced by the Ministry of Agriculture. These new controls, including the Feedingstuffs (Zootechnical Products) Regulations 1998 and the Medicated Feedingstuffs Regulations 1998, were introduced to fully implement an EU Directive. Before the new regulations the Medicines Act 1968 regulated all animal medicines, including growth promoters and other feed additives such as coccidiostats. But under European law growth promoters and coccidiostats are not considered to be medicines but zootechnical feed additives.

Announcing the new rules Junior Farm Minister, Jeff Rooker said:

> *These measures form an important part of the safeguards on the production and use of animal feedingstuffs. At all stages of the food chain it is essential that there are proper controls in place.*

But even such 'proper controls' can be avoided.

The Medicated Feedingstuffs Regulations apply to anyone incorporating a prescription only medicine (POM) into animal feed, including feed compounders and farmers who mix their own feed, the so-called home mixers. All feed compounders and on-farm mixers are required to be registered with the Royal Pharmaceutical Society of Great Britain (RPSGB) or the Department of Agriculture in Northern Ireland. But the BVA code of practice on medicines, published this year, states that the Medicated Feedingstuffs Regulations do not apply to farmers 'top-dressing' feed or medicating via the drinking water.

'Top-dressing' is literally sprinking product on feed, for example in a trough. Ten years ago, 17,000 home mixers, mostly farmers, asked for application forms to be registered so that they could be inspected under the old regulations by the RPSGB. But only 7000 forms were returned. The RPSGB says today that it cannot know how many of those remaining 10,000 units are still 'top dressing' with growth promoters and may have exploited the loophole which allowed 'top-dressers' to escape registration. The loophole arose because home mixers could claim that 'top dressing' was not incorporating. It is also interesting that the RPSGB expects just 3000 on farm mixers to be registered under the new regulations - 4,000 less than returned their forms ten years ago. An RSPGB spokesman said that even the latest regulations were imperfect, and that the society would rely on court cases to test the new regime.

3.1 Cattle

Antimicrobial therapy in dairy and beef units begins with the calf. Antibiotics are used for the treatment of infection in the young calf. In older calves, they play an essential role in the control of calf pneumonia (NFU, 1998). Neonatal diarrhoea (in newborn calves) is still regarded as the most important disease of young calves in both dairy and beef herds, and mortality varies widely from 0-80%. Neonatal *E. coli* infections may be treated with antimicrobials, usually administered orally as boluses or by injection. Occasionally water medication will be given, but this is exceptional. Diarrhoea may occur later in the calf's life (MAFF, 1998).

Medicated milk replacers may also be used to treat calves. The main prescription only medicines (POMs) included in cattle feed are prescribed mainly for young calves and include chlortetracyclines and oxytetracyclines (House of Lords, 1998, Evidence, p.531). An example of an antibiotic additive containing chlortetracycline, and marketed for use to treat respiratory infections, is Aurofac 200 Milk Replacer Additive. This is a soluble powder added to dried milk or milk replacer powder and incorporated at the time of manufacture or on the farm. It can also be added to liquid milk or to a small quantity of liquid as a drench. Treatment is recommended for five to seven days or until signs of disease are no longer apparent (NOAH, 1998).

The NFU says that antibiotics (for example, virginiamycin) have been used effectively and safely in calves, and whilst not used widely they can prove to be valuable aids to cattle farming (NFU, 1998). But scientists are concerned that the prophylactic use of medicated calf feed has contributed to the rise of multi-resistant strains of salmonellae in cattle. A report for the Ministry of Agriculture cites a continuous outbreak of *S. typhimurium DT 204C* amongst calves, adult cattle and farm staff in the UK. 'The multi-resistance of this organism was considered to be a problem resulting from the use of chlortetracycline and furozolidone in calf feed as prospective prophylactic medication' (MAFF, 1998, p.66). The antibiotic resistant *S. typhimurium DT 204* organisms are spread from farm to farm by animal movement and historically by calf movement, particularly through dealers.

3.1.1 Beef production

Calves destined to be reared for beef may be given an antimicrobial feed additive to promote growth when they begin to ruminate. Now that avoparcin is no longer available, monensin is the main antimicrobial growth promoter used in beef and growing cattle receiving supplementary feed (MAFF, 1998). The main PML additives for cattle feed are monensin and virginamycin (House of Lords, 1998, Evidence, p531).

Monensin sodium is an ionophore and not included in data obtained from NOAH for this report. It is marketed for use in cattle under the trade name Romensin. It is described by the manufacturers as suitable for use for improved feed conversion efficiency and/or weight gain in cattle, except in lactating dairy cows. It may be mixed into complete feed for housed cattle at a rate of 100g-400g/tonne to provide 10-40mg monensin/kg (10-40ppm) of finished feed. In supplementary feeds, the maximum dose in the daily ration must not exceed 140mg monensin/day for an animal of 100kg liveweight. Romensin can also be incorporated into feed blocks to provide a maximum of 230mg monensin/head/day for animals over 250kg liveweight. Cattle from commencement of rumination to 250kg liveweight should receive no more than 125mg monensin/head/day (NOAH, 1998). Romensin has no withdrawal period which means animals given feed containing this additive can be slaughtered immediately for human consumption.

3.1.2 The dairy herd

Dairy cows are routinely given antibiotics to treat and prevent mastitis. Mastitis, which is an infection of the cow's udder, is a common disease in dairy cows. It can be subclinical, where cows show no obvious symptoms, or clinical which causes painful swellings in one or more quarters of the udder. Mastitis is commonly treated with antibiotics administered as intramammaries directly into the cow's teat. The NFU says antibiotic treatment is essential for mastitis (NFU, 1998, p.22). But some experts disagree. 'Where there are visible clots in the milk but cows are not ill, standard practice is to use antibiotics, but this may not be the best option - studies show that some of these cows would show a visible cure just as quickly without antibiotic treatment' says Helen Biggadike, researcher at ADAS Bridgets Farm, in a recent *Farmers Weekly* article.

There are various types of mastitis-causing organisms including staphylococci. Staphylococci are currently the third most commonly isolated organism from milk samples by the Veterinary Investigation Centres. Antibiotics used to treat *Staphylococcus aureus* mastitis include: penicillin, nafcillin, cloxacillin, ampicillin, cefquinone, cephalexin, cefoperazone, cefuroxime, cephatrile sodium, cephalonium, streptomycin, neomycin, erythromycin, tylosin, spiramycin, and novobiocin. These may be given alone or in combination where appropriate (penicillin and streptomycin, for example). Figures for *S. aureus* in the UK suggest that around 60% of strains are penicillin resistant (MAFF, 1998, p63).

Streptococcus uberis is the second most commonly isolated bacterium from milk and is particularly associated with straw bedding. The same range of antimicrobials is used as for staphylococci (see above). But penicillins are the drug of first choice, often mixed with streptomycin. These are significantly cheaper than many other treatments. *Streptococcus agaclactiae* in the UK is sensitive to penicillin and only occasional isolates resistant to it have been described in the UK. Other streptococci are

present in bovine mastitis (*S. dysgalactiae* and *S. uberis*) and are much more frequently resistant to antimicrobials (MAFF, 1998, p64).

Mastitis infection can be monitored in herds through cell counts in milk and farmers are financially penalised by dairy companies for high cell counts. Big penalties are also imposed for milk contaminated by antibiotic residues and milk from treated animals must be withheld from sale for the required withdrawal period. Consequently it makes sense to prevent infection. Good hygiene is vital and farmers are also advised to use so-called dry cow therapy (or long acting antibiotic dry cow intramammaries) during the cow's dry period. This form of preparation has the dual role of treatment and prevention and has been well recognised for its benefits to cattle for about 40 years, The dry period is ideal because it occurs when there is no removal of the antibiotic or economic loss from the disposal of milk with antibiotic residues.

All 120 dairy cows which make up to the herd at Greenmount College, Northern Ireland are given 'routine mastitis treatment appropriate for the length of the dry period'. The need to prevent summer mastitis, so called because disease peaks in late July/early August, through use is also stressed in the college's dairy management notes. 'The emphasis must be on prevention, including dry cow tubes used to prevent access of mastitis causing bacteria, use of insecticides and dry cow antibiotic tubes to discourage flies actually landing and resting on hind quarters/udders every fortnight.' The prevailing consensus is that summer mastitis has to be prevented because in almost every case following infection the quarter will be lost and inevitably will cause the cow or heifer to be culled (NOAH evidence to ACMSF working party).

Other common uses of antibiotics in the dairy herd are to treat infection after calving and to treat lameness. Results of surveys show lameness is widespread in UK dairy herds affecting about 25% of cows. Bad feeding of high yielding dairy cows can make them prone to lameness which can be incurable. Badly designed housing particularly cubicles and rough concrete floors can also cause lameness. The NFU says antibiotic treatment is essential (NFU, 1998).

3.2 Sheep

Of all farm animals sheep receive the least antimicrobial treatment. The NFU say a typical less favoured area unit of 1000 ewes and 50 suckler cows will use about 2-4 100cc bottles of a long acting penicillin-type antibiotic in the whole year across sheep and cows (NFU, 1998).

Sheep vets including Richard Rowland, secretary of the Sheep Veterinary Society, Eifion Evans, vice-president of the British Veterinary Association, and James Hindson, say antibiotics are not used as growth promoters in sheep husbandry, and monensin (which was used to treat coccidiosis and toxoplasmosis) is no longer

used. They agree that if a farmer helps with lambing by putting his hand into the ewe, he will often give a shot of penicillin to prevent the spread of infection in indoor flocks. Some experts advise farmers to keep antibiotics on hand during lambing. Greenmount College management notes recommend including an antibiotic injection and antibiotic drench in the first aid cupboard at lambing. This is the most difficult time for sheep farmers as 75% of ewe deaths and 70% of lamb deaths occur at or near lambing.

Sheep are often housed during the last part of their pregnancy. In some cases, this continues for a few months and can lead to a build-up of *E. coli* and other environmental contaminants causing problems post-lambing in newly-born lambs. Where the build-up of *E. Coli* leads to scouring in newly-born lambs, oral antibiotics are used. Because there are numerous strains of *E. coli,* laboratory analysis of lamb faecal samples will determine the most appropriate antibiotics for a particular strain.

In their first year of lambing, ewes have two injections of a combined clostridial and pasteurellosis vaccine. In each subsequent year, there will be one vaccine. But outbreaks of pasteurella and pneumonia can occur despite vaccination: where acute clinical cases occur, intravenous injections of crystalline penicillin can be effective in big outbreaks across farms. Where there are a lot of cases, the vet may have to re-vaccinate. The stress of gathering ewes for this operation may cause yet more pasteurella, so the vet may use a long-acting formulation of penicillin to prevent the pasteurella spreading even further.

For enzootic abortion in ewes, a range of different vaccines is available. But if a farmer has not had this condition before and is hit by an abortion storm, he is advised to use a long-acting preparation of oxytetracycline to keep chlamydia bacteria under control.

With foot rot, vets used to rely on a foot bath and foot paring. They now recognise the beneficial effect in virulent outbreaks of foot rot of an initial injection of penicillin or oxytetracycline.

Eifion Evans, whose practice has eight vets covering hill and lowland flocks in North Wales, said vets have seen more listeria in sheep in the last few years. There is no vaccine against listeria, and any decision on the use of antibiotics would depend on the degree of infection, how long it has been present and which route it has taken to the brain. Mr Evans has used very high doses of oxytetracycline. But to emphasise the unpredictability of listeria, Mr Evans said he knew of one flock of 2,500 ewes with five cases of listeria where four recovered; in another flock of 200 ewes, there were 20 cases of listeria, and all but three of these cases died.

According to the NFU report the main reasons for antibiotic treatment in sheep are: pneumonia (respiratory problems), some foot rots (foul), mastitis, following assisted births, bites and inflamed wounds (dogs, snakes), joint ill, watery mouth and *E. coli* (scour).

3.3 Pigs

Pigs reared in indoor, intensive systems will receive antibiotic treatment throughout their life until slaughter - usually at under 6 months old. The amount appears to depend on the health status of the herd. In high health pig herds antibiotic use may be restricted to injections and growth promoter use. However, in most conventional herds water and feed medication is also practised. Important periods of use are in the farrowing house, and in the weaner and growing phases. Growth promoters are widely used during the early stages of growth.

In a survey of pig farms in 1995, farms were found which used only penicillin and streptomycin and, perhaps, tetracycline for wounds. These were high health herds and were free of most of the diseases requiring treatment. Other herds were infected with a range of diseases had been prescribed up to ten antimicrobials (MAFF, 1998, p67).

The NFU say prophylactic antibiotics are given mostly in feed, sometimes in the water when pigs are judged by the veterinary surgeon to be likely to suffer from an outbreak of disease (NFU, 1998, p24). It appears from the evidence that pigs in intensive conventional systems are likely to suffer from an outbreak of disease at most stages in their life.

In most conventional herds antibiotic treatment starts soon after birth. Piglets will receive treatment for enteritis and for respiratory disease. In a typical herd there is use of neomycin, apramycin, amoxyclav, ampicillin, enrofloxacin or trimethroprim sulphonamide in the diarrhoeic piglets for *E. coli* enteritis (MAFF, 1998).

At weaning (usually 3 weeks) all piglets are gathered, mixed and then reared to finishing weights. From weaning pigs will receive feed medicated with a growth promoter. Virginiamycin, tylosin, salinimycin, avilamycin or bacitracin zinc are commonly used. Copper at 175 ppm will be present in all rations.

Weaners usually develop post weaning diarrhoea caused by *E. coli* which occurs on day 3 post weaning. At weaning pigs will receive medication to treat the post weaning *E. coli* diarrhoea and any oedema (swelling) disease which may be present. In 50% of herds the feed is medicated with zinc oxide at 3000 ppm to prevent this and is usually given for two weeks in the feed (MAFF, 1998).

This point has also been made by NOAH in their submission to the ACMSF working group. In most instances on farm, say NOAH, preventative medicine should be integrated with management changes such as disinfection and on-farm movement controls. In oral evidence to the House of Lords select committee, Peter Watson, NOAH chairman of technical affairs and registration and development manager with drug company Bayer, said it was known that 'two days after you wean the pigs they will develop diarrhoea, and some will become very ill. You include a therapeutic drug over that period to prevent that happening and that is what we understand

as prophylaxis' (House of Lords, 1998, Evidence, p.208).

Post-weaning diarrhoea is quickly followed by a range of other diseases. Glassers Disease *(Haemophilus parasuis)* occurs at 4 weeks, pleuropneumonia at 6-8 weeks, proliferative enteropathy from 6 weeks and spirochaetal diarrhoea and colitis at any time from 6 weeks onwards (MAFF 1998). So, from two weeks after weaning pig feed may contain antibiotics to treat these diseases. This feed usually contains a tetracycline and is often a combination of chlortetracycline, sulphadimidine and penicillin (MAFF, 1998). The MAFF review adds 'it is important to realise that although each pig may receive a treatment course of a week at most, medication on the farm is continuous, as new pigs enter that age group every week'.

At 8 weeks the pigs are termed growers and moved to another house. Here they will develop enzootic pneumonia, streptococcal meningitis *(Streptococcus suis)* and, possibly, swine dysentery. Respiratory disease may cause problems until slaughter (MAFF, 1998).

The main use of antimicrobials against streptococci in farm animals is for the treatment and control of S. suis infection in pigs. Most isolates of *S. suis* are extremely sensitive to penicillin but resistance has been identified. Treatment is by using penicillin in feed or water. Recently, amoxycillin or amoxyclav have taken over this role (MAFF, 1998).

Mycloplasma treatment is particularly frequent in the pig *(M. hyopneumoniae)* and is the reason for the use of significant amounts of antimicrobial (MAFF, 1998). Mycoplasma is an infective agent distinct from bacteria as well as viruses. The products used include: tetracyclines, tylosin, tilmicosmin erythromycin in the udder, tiamulin, lincomycin and enrofloxacin. Resistance has been identified to all these microbials with the exception of enrofloxacin. (MAFF, 1998).

From the grower accommodation, pigs will be moved to the finisher accommodation at about 60kg until slaughter at 95-105kg. Antibiotic treatment may be given to sows for metritis, mastitis and for specific diseases such as erysipelas or leptospirosis (MAFF, 1998).

3.3.1 Pig 'vices'

As well as disease challenges, pigs in confined, intensive systems face injury from each other as a result of so-called 'vices', including tailbiting, and ear and flank chewing. An important factor in the development of such 'vices' is greasy pig disease or exudative epidermitis. A skin infection or wet eczema begins on the tip of the tail or ears, often started by a combination of feed contaminating the skin and splitting of the skin caused by trauma. *Staphylococcus hyicus* then invades and causes infection. The pig is attracted to the lesion and eventually this leads to vice. The Greenmount College management notes state that 'this situation is particularly apparent when pigs are first weaned into flat decks or nurseries or when they are

moved into second stage accommodation particularly if mixing takes place. Other diseases such as pneumonia can result in disadvantaged pigs being traumatised by others'.

Treatment involves determining the antibiotic sensitivity of the *Staphylococcus hyicus* if this is part of the problem and medicating feed for 7-10 days, injecting traumatised pigs with long-acting antibiotics, management control and prevention. The notes add 'if *Staphylococcus hyicus* infection is part of the problem, there will usually be a very good response to in-feed medication with tetracyclines'.

3.3.2 Residues in pigmeat

Not surprisingly the widespread use of antibiotics in pigs has resulted in residue problems. In 1995 representatives of UKASTA, together with officials from the VMD, Central Veterinary Laboratory and State Veterinary Service were involved in investigations into the source of sulphonamide residues in pig meat. This happened after a large pig slaughterhouse had some consignments of pigmeat exported to the Far East rejected. UKASTA told the Lords select committee,

> *The conclusions of the investigations indicated that the sulphonamide residue problem could be due to a combination of factors including deficiencies in the safe handling and usage of veterinary medicines and medicated feedstuffs on farm; increased use of sulphonamide medicated feedstuffs due to the increased level of respiratory disease occurring in intensively reared pigs; low level cross-contamination in feedingstuffs; and cross-contamination between medicated and non-medicated pigs on farm, during transport and in a lairage at the abattoir* (House of Lords, 1998, Evidence, p530).

The authors of MAFF's review of antimicrobial resistance say that the main problems with pig farms are 'the amount of antimicrobial used, the use of tylosin in the farm which results in the presence of *Campylobacter coli* resistant to tylosin at slaughter and the contribution made to the antimicrobial resistance pool by gut flora'.

3.4 Use in poultry

The poultry industry is split into two parts: the broiler industry, which produces birds slaughtered at 6-7 weeks old for the table, and the egg-producing sector where layers are reared and placed in percheries, laying barns or battery cages at 16-18 weeks for one egg laying cycle and then killed (MAFF 1998).

3.4.1 Broiler production

Broilers are placed on the floors of their houses which have been cleaned and dis-

infected since the previous batch. According to MAFF, they may be given a probiotic and will receive antimicrobial growth promoters (virginamycin, zinc bacitracin, bambermycin, and formerly avoparcin) and coccidiostats which may include monensin and salinomycin in their heat-treated diet (MAFF 1998). According to UKASTA, the main POM medicines incorporated into feed for poultry are penicillins, chortetracyclins and sulphonamides, while the main PML feed additives, which include growth promoting antibiotics and a range of antibacterial coccidiostats, are: virginamycin, zinc bacitracin, lasalocid, nicarbazin, monensin, salinomycin, narasin, clopidol, methylbenzoquate, dimetridazole, and nifursol (House of Lords, 1998, Evidence, p531).

The NFU says that antibiotics such as virginiamycin and avilamycin help birds achieve maximum benefit from their food. 'It is important for the health and welfare of broilers that birds are as even as possible in size and weight. Such uniformity is vital to give equal opportunity of access to food and drink' says the NFU antimicrobial working party report. 'They also help to prevent diarrhoea and necrotic enteritis which occurs in poultry whether kept for meat or eggs, whether in houses or on free range. The only birds that do not suffer from this condition are those kept in cages because they are separated from their own faeces'.

The NFU and the British Poultry Meat Federation (BPMF) say that as well as assisting welfare, growth enhancers reduce the amount of waste excreted and allow more land to be available for food production. But for some scientists reducing the amount of poultry litter produced is not a justifiable reason for antibiotic use. 'Antibiotics are a fantastic gift. To waste them just to get smaller amounts of animal faeces seems to me to be a mistake', Dr Norman Simmons told the House of Lords.

The BPMF says the only antibiotics authorised as digestive enhancers are ones that are not used or related to those used in human medicine. That may the case at the moment but as previously mentioned virginiamycin is a member of the streptogramin group of antibiotics and there are fears that quinupristin/dalfopristin, another streptogramin mixture developed for use in humans may not be effective because virginiamycin use in animals may have already resulted in human resistance (House of Lords, 1998, Evidence, p219).

What's in a name?

Growth promoting antibiotics are often referred to by the industry as Performance Enhancers or Digestive Enhancers. Under European law they have now been reclassified as Zootechnical Feed Additves.

According to the British Poultry Meat Federation they are not appetite stimulants. 'They do not make the bird grow any bigger than it otherwise would, so it is misleading to refer to them as growth promoters. Digestive enhancers reduce the amount of feed nutrients used by the bird to maintain its intestinal flora, freeing more nutrients for absorption, thereby improving the efficiency of feed conversion.' (House of Lords, 1998, Evidence, p.338)

Treatment is required for any outbreak of necrotic enteritis, Colisepticaemia salmonellosis causing mortality, outbreak of mycoplasma infection or outbreak of necrotic dermatitis *(Staphylococcus aureus)*. The antimicrobials used for salmonella and *E. coli* may include enrofloxacin and, now that necrotic enteritis is no longer supressed by avoparcin, amoxycillin/amoxyclav is commonly fed to birds to treat it. Colisepticaemia is one of the most serious and intractable disease problems of the growing birds and the antimicrobials used in its treatment are similar to those used for salmonella (MAFF, 1998).

The poultry industry says prophylactic medication is only used in specific cases of predicted disease infection. Rather than wait for the birds to become clinically ill (and possibly unable to eat or drink properly) before being treated, they are medicated at the time when the infection is predicted to occur (House of Lords, 1998, Evidence, p387). However, the NFU Antimicrobial Working Party says that

> *Routine prophylactic use of antibiotics is not considered good practice, but there are occasions when prevention is better than cure. In a shed there may only be at any one time a small proportion of birds that are actually ill, but mass medication is necessary to protect the rest, so this is essentially a mix of prevention and therapy* (NFU, 1998).

But given the large number of birds, even on relatively small holdings, mass oral medication is the only practical method of treating birds in most cases. Therapeutic treatment is applied when birds in a flock are either clinically ill and/or dying as a result of a bacterial infection. It is standard practice to identify the bacteria involved and carry out an antibiotic sensitivity test on them prior to or concurrently with any treatment (House of Lords, 1998, Evidence, p387). Examples of water soluble therapeutic antibiotics are amoxycillin for mycoplasma and bacterial infections. Neomycin may be given in water or in feed.

In 1993 the fluoroquinolone enrofloxacin was licensed for use in broilers in the UK. The MAFF review of antibiotic resistance also mentions 'the practice of injecting eggs with enrofloxacin prior to hatching'. The licensing of enrofloxacin has caused controversy due to the emergence of antibiotic resistant bacteria and some scientists are concerned over 'mass medication'. This has promoted drug manufacturers to respond stressing the controls on use.

> *It is Bayer Animal Health's policy to market fluoroquinolones for therapeutic use in animals only if a number of requirements have been fulfilled. Specifically, drugs are to be given on prescription only and administered under the supervision of a veterinary surgeon. A diagnosis should be based, wherever possible, on bacterial culture and sensitivity testing. Extra-label[1] and prophylactic use are not promoted; advertising is only to veterinary surgeons* (Watson et al, 1998).

1. The extra-label use of veterinary drugs refers to their use for purposes and animals for which they are not licensed at the veterinary surgeon's own discretion.

Nonetheless, scientists from the PHLS have pointed out that since 1994 the incidence of isolates of multi drug-resistant *Salmonella typhimurium DT104* from humans which are resistant to ciprofloxacin, a powerful and much used fluoroquinolone used in man, 'has increased exponentially', with 14% of isolates resistant to this antimicrobial in 1996 (Threlfall et al, 1997).

3.4.2 Residues in eggs

Chicken and eggs are not subject to statutory residue surveillance requirements, but antimicrobial and antibiotic residues have been found in substantial proportions of the egg samples which are analysed each year on a non-statutory basis.

The figures are divided into statistics concerning free-range and 'other' eggs. In 1997, residues of the antibiotic coccidiostat nicarbazin were found in 6.8% of the samples of each type of egg tested, compared to 10.7% overall in the previous year. Residues of lasalocid, another antibiotic coccidiostat, were present in 2.3% of free-range and 1.4% of other eggs in 1997.

It has been recognised that contamination with these drugs seems at least partly attributable to deficiencies in the manufacturing process. In 1995, when attention focused on the isolation of lasalocid residues in eggs, the fine powdery nature of the product was blamed for holdups in the mill and therefore contamination of feed destined for laying hens. After the introduction of a new, more granular version, it became noticeable that residues dropped. More recently there has been concern for the same reason over nicarbazin residues. The VMD has said that whilst the concentrations being found are not considered a health risk to consumers, the substance is not licensed for use in laying hens. 'Discussions are being held between the egg industry, UKASTA and the VMD on these findings', UKASTA told the House of Lords.

Dimetridazole and ronidazole (DMZ/RNZ) are antimicrobials not licensed for use in laying birds and which should therefore not be present in eggs at all. Their residues are present in the form of a common metabolite, and are listed in a single combined figure. DMZ/RNZ residues were found in 5.9% of free range and 4.8% of other eggs tested in 1997 (from samples of 219 and 207 eggs respectively). The proportions in 1996 were 8.8% and 13% (VMD, 1998). These antimicrobials are listed by MAFF as 'antimicrobials used in agriculture which may affect the antimicrobial resistance status of food borne pathogens or contribute to the antimicrobial resistance pool in man' (MAFF, 1998).

In the case of nicarbazin and lasalocid residues, the VMD report says that 'toxicological advice has stated that these concentrations did not pose a risk to human health'. For DMZ/RMZ residues, no comparable assurance was made. No mention is made at all of possible resistance issues.

3.5 Use in fish

Data on the use in fish are contradictory. The SMAC report from the Department of Health seems satisfied that use in salmon farming is falling. In the late 1980s, the salmon farming industry 'used considerable amounts of tetracyclines and, later, of quinolones'. In Norway, says the report, this usage peaked at 47 tonnes of antibacterial agents in 1987, but decreased to 1.5 tonnes by 1994 'reflecting increased regulation, vaccination and the segregation of farmed fish by age'.

However, a report published in 1993 by the International Council for the Exploration of the Sea was not nearly so complacent.

> *The main [antibacterial] compounds licensed for [fish farming] include oxytetracycline, oxolonic acid and tribrissen […] Most of the antibiotics used are persistent in the environment and spread from the farms to surrounding areas where accumulation in sediments may occur. Residues of oxolonic acid have been found in wild fish, shellfish and crustaceans in close proximity to fish farms, and the concentrations may far exceed levels accepted for human consumption [which were then 0.01mg/kg in Norway]. Little is known of the effects of these antibiotics, which can also reach wild fish and can induce the development of resistant bacteria* (North Sea Task Force, 1993).

Those sentiments are still relevant in 1998: 'Oxytetracycline is used [in fish farming], although it is recognised as unsuitable: salmon absorb only seven% of the administered dose and carp 1%, so most of the drug is wasted for its intended purpose and escapes into the environment' (Dr. Alan Long, private communication, 1998).

The Ministry of Agriculture review points out that freshwater and seawater salmonoid farms are important sources of fish in the UK. Major bacterial diseases of these fish include rainbow trout fry syndrome, bacterial kidney disease, enteric redmouth and furunculosis which cause significant losses.

Vaccination has reduced the need for treatment in furunculosis and the risk of antimicrobial resistance spreading from fish is now lower than for some years.

As far as imports are concerned, antimicrobial use is largely uncontrolled in India and the Far East which are sources of freshwater prawns and other cultured shellfish and farmed fish. The waste from poultry and pig units are used to feed fish and the fish are treated with a wide variety of antimicrobials. Imports of catfish from the United States may carry similar levels of antimicrobial resistant bacteria (MAFF, 1998).

The information on antibiotic usage on UK farms detailed in this report raises questions about:

The extent to which this use is contributing to the development of drug-resistant disease in the human population.

Changes needed in legislation and strategies that should be developed to reduce the threat posed to human health.

These will be the subject of future reports in this series by the Soil Association.

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