



# Too Hard to Swallow

*the truth about  
drugs and poultry*

The Use and Misuse of Antibiotics  
in UK Agriculture – part 3

Residues of Dangerous Drugs  
in Intensively Produced Chicken Meat and Eggs

Richard Young and Alison Craig

**Soil Association**

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The Soil Association is a membership charity which was founded in 1946 by a group of farmers, scientists and nutritionists who were concerned about the way food was produced. It is at the forefront of campaigning for safe, healthy food, an unpolluted countryside and a sustainable farming policy in Britain and worldwide.

The organisation has now grown in scope and complexity but the core message is essentially simple: there are direct links between the health of the soil, plants, animals and humans, and organic agriculture is a sustainable system of food production which is based on these interconnections.

To achieve this end, the Soil Association is working in many different areas:

- Lobbying work, backed by careful research, to press for radical change in food and farming systems.
- Campaigning to help bring pressure to bear on policy makers through the media and through public protest. Current campaigns include demanding the elimination of GMOs from the food chain; promoting the responsible use of antibiotics in farming; and working in partnership with conservation agencies to protect wildlife and biodiversity.
- Setting organic standards to ensure the integrity of organic food and other products. Soil Association Certification Ltd, a subsidiary company, runs the certification scheme used by 70 per cent of licensed processors and 55 per cent of producers, and awards the Soil Association Symbol.
- Providing professional and technical support to farmers and growers with the aim of increasing the amount of land farmed organically and providing more jobs in the countryside.
- Promoting organic food so that people everywhere will have the opportunity to buy and eat organic, be it from a local market, a box scheme, a corner shop or a supermarket.

The Soil Association provides modern, practical solutions to the problems facing society today.

*The intensive poultry industry violates all the principles of sustainable agriculture. It could be argued this is the most extreme form of factory farming. The bulk of the poultry market is controlled by perhaps a dozen individuals within a handful of companies who deal directly with the major retailers. The industry is largely hidden from public view. It allows no link whatsoever between the consumer and the producer, between human and animal.*

*It should therefore be no surprise that this secretive, undemocratic structure allows the perpetuation of practices which are wholly unacceptable. It is in this framework that grossly irresponsible risk-taking is possible. In exposing it, the Soil Association is attempting to prevent the human costs of a long-term public health problem.*

*The recent outbreak of foot and mouth disease has prompted calls for fundamental changes in agriculture. The truth has emerged: we have a system in which livestock is produced in unsustainable numbers, many of which are susceptible to disease and which are routinely transported hundreds of miles around the country before slaughter. Many people have been shocked and repelled by this vision. But what is the alternative?*

*Sir Albert Howard was right in his observation that society in general and farmers in particular should come to regard pests, diseases and parasites as 'nature's professors of good husbandry'. He said that they could teach us better than anything else how to farm for positive health. The truth is that only fundamental changes in poultry production systems will enable producers to wean themselves off the dreadful dependency on a wide range of drugs which suppress the symptoms of ill health, which is in turn caused by bad management.*

*If we want a drug-free future for our chickens, there is only one approach possible: it involves smaller colony sizes, and genuine free range mobile units that provide access to fresh grass – in other words, poultry systems which are fully integrated into a mixed organic farming system.*

*Is this an unrealisable dream? That depends on whether the consuming public wants cheap industrially produced food from production systems that violate animal welfare and erode public health, or whether we are prepared to pay more for a better alternative. The choice is ours.*

*Patrick Holden*

*Director, Soil Association*

# CONTENTS

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<b>FOREWORD</b> .....	3	<b>LASALOCID</b> .....	35
<b>ABBREVIATIONS</b> .....	5	The toxicity of lasalocid .....	35
<b>EXECUTIVE SUMMARY</b> .....	6	Lasalocid contamination .....	36
<b>INTRODUCTION</b> .....	14	Case study: the potential for lasalocid poisoning of the elderly .....	37
<b>1 CHEAP CHICKEN FOR ALL</b> .....	16	<b>THE OTHER IONOPHORES</b> .....	37
The economics of the broiler industry .....	16	The toxicity of maduramicin .....	37
The largest intensive broiler producers in the UK ...	17	The toxicity of monensin .....	37
<b>2 WELFARE AND DISEASE</b> .....	18	The toxicity of narasin .....	38
The suffering of broiler chickens .....	18	Ionophores in the food chain .....	38
‘The extreme of artificialdom’ .....	19	The toxicity of salinomycin .....	39
The squalor of the broiler shed .....	19	Residues in imported chicken .....	39
Overcrowding .....	19	<b>DIMETRIDAZOLE</b> .....	40
The causes of coccidiosis .....	20	The toxicity of dimetridazole .....	40
Coccidiosis in different production systems .....	20	Dimetridazole contamination .....	41
Control of coccidiosis in intensive broiler production	20	DMZ: the regulatory wrangle .....	42
Vaccination .....	21	<b>6 USAGE: QUANTITIES AND CONTROL</b> .....	43
<b>4 THE POISON PROP</b> .....	22	Usage data .....	43
Drugs used for coccidiosis control .....	22	Veterinary control? .....	44
The faithful shadow of resistance .....	23	<b>7 THE ROLE OF THE FOOD STANDARDS AGENCY</b> .....	45
Shuttle, switch and rotation programmes .....	24	<b>8 REGULATORY STATUS: THE FUTURE?</b> .....	46
<b>5 THE DRUGS: RESIDUES AND TOXICITY</b> .....	25	<b>REFERENCES</b> .....	49
<b>NICARBAZIN</b> .....	25	<b>APPENDIX 1:</b> <b>COCCIDIOSIS, HISTOMONIASIS,</b> <b>AND NECROTIC ENTERITIS</b> .....	51
The toxicity of nicarbazin .....	25	<b>APPENDIX 2:</b> <b>PRODUCTS AUTHORISED IN THE EU</b> .....	53
The VMD suppresses expert toxicological advice ...	26	<b>APPENDIX 3:</b> <b>GLOSSARY</b> .....	54
Nicarbazin: contamination .....	28	<b>APPENDIX 4:</b> <b>EXECUTIVE SUMMARY: THE USE AND</b> <b>MISUSE OF ANTIBIOTICS IN UK AGRICULTURE 2</b> .....	55
Nicarbazin and the VMD .....	29	<b>APPENDIX 5:</b> <b>SOIL ASSOCIATION STANDARDS</b> <b>FOR ORGANIC EGG AND POULTRY PRODUCTION</b> .....	57
Lies, damn lies and statistics .....	29	<b>ACKNOWLEDGEMENTS</b> .....	64
The real reason for nicarbazin residues? .....	31		
Case study: the potential for nicarbazin poisoning of pregnant women and the foetus .....	31		
Why such high residues? .....	32		
<b>THE IONOPHORES</b> .....	32		
The toxicity of the ionophores .....	32		
Ionophore toxicity in turkeys .....	33		
Residues of ionophores in Christmas turkeys: the role of the AGVR .....	33		

## ABBREVIATIONS

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ADI	Acceptable Daily Intake: an estimate of the amount of a substance, assuming a body weight of 60 kg, that can be ingested daily over a lifetime in the practical certainty, on the basis of all known facts, that no harm will result
AGVR	Advisory Group on Veterinary Residues, replaced in 2001 by the Veterinary Residues Committee
BPMF	British Poultry Meat Federation
CVMP	Committee for Veterinary Medicinal Products: a committee of the EMEA
DAL	In the absence of Maximum Residue Limits, the VMD set Differential Action Levels
ELISA	enzyme-linked immunosorbent assay
EMEA	European Agency for the Evaluation of Medicinal Products
FSA	Food Standards Agency
JECFA	Joint FAO/WHO Expert Committee on Food Additives: the body which sets international ADIs and MRLs
JFSSG	Joint Food Safety and Standards Group (MAFF), now part of FSA
LD <sub>50</sub>	In laboratory animal experiments, the dose that is lethal to half the test animals
MRL	Maximum Residue Limit (or Level): the maximum legally permitted concentration of a drug residue in food
NFU	National Farmers' Union
NOAH	National Office of Animal Health Limited – the trade body for the farm drugs industry
NOEL	No Observed Effect Level of a substance tested on laboratory animals
PPM	parts per million
RPSGB	Royal Pharmaceutical Society of Great Britain
SVS	State Veterinary Service
UKASTA	United Kingdom Agricultural Supply Trade Association Limited
VMD	Veterinary Medicines Directorate, the executive agency of MAFF responsible for licensing veterinary medicines and for a programme of residue surveillance

For glossary of technical terms , see page 55

### Overview

This report examines the intensive poultry industry and the residues of dangerous drugs that find their way into chicken meat and eggs.

It reveals that because of intensive farming methods, and inadequate consumer protection by the Ministry of Agriculture, Fisheries and Food (MAFF) and the Food Standards Agency (FSA), British farming may be incubating yet another serious threat to human health in the form of cancers, birth deformities, drug cross-reactions, and heart failure. This problem however is not uniquely British. Frozen poultry is a globally-traded commodity.

This new threat concerns chemical drugs used to control single-celled protozoan parasites. The most significant of these is called 'coccidia'. This causes serious illness in chickens. The drugs are known as antimicrobials, rather than antibiotics. As with BSE, and so many other food safety problems, it has its roots in intensive farming methods. In this case, the specific problems are the unnatural feeding practices and unsanitary, overcrowded, moist, dark, confined conditions in which large numbers of chickens are kept – conditions under which most would undoubtedly perish without drugs to keep them alive until slaughter.

In the past, a number of relatively safe drugs were available to control coccidiosis, but excessive reliance on drugs rather than good animal husbandry has honed drug resistance and these have become ineffective on most poultry farms. As a result, the industry now relies on about a dozen drugs, which it uses in rotation to slow the development of resistant strains. Most of these are so toxic they could never be used in human medicine, but the effect of their residues in our food has never been scientifically evaluated.

Almost half of these drugs belong to one family, the ionophores. Warnings of the serious danger posed by ionophore food residues come from the deaths of horses from eating pig feed and turkeys from eating chicken feed containing recommended levels; from dogs and cats eating pet food containing residues, and from cattle and sheep eating feed containing chicken manure. Chickens have been paralysed by the slight accidental overdosing of their feed. Other licensed antimicrobials may cause cancer and birth defects but scientists disagree and the truth cannot be established because the necessary scientific trials have never been undertaken.

British consumers now eat more chicken and chicken products than ever before. On average we consume a third of our body weight in chicken each year. Chicken is cheap and available, but as our consumption of chicken has gone up so has the use of these toxic drugs. As a result, assumptions made in the past about their safety as contaminants in our food should be revisited. Everyone knows that intensive chicken is produced at a high cost to the welfare of the birds, but do poor welfare conditions also have implications for our own health?

Driven by consumer concerns and pressure from multiple retailers, there has been an effort to improve the poor image of the British broiler poultry industry in recent years. Some 85 per cent of production, it is claimed, is now linked to the 'Assured Poultry Production' scheme, where it is maintained that significant improvements have been made. The limited evidence available suggests things have improved far less than the industry would like us to believe. However, even in the show-

piece units where recommended practice is followed fully, there remains an intrinsic welfare problem in all broiler houses. Many commentators have drawn the link between this and some of the obvious signs of ill health in birds, such as lameness and blisters. This report suggests there is also a link with the less visible diseases that are normally controlled by the routine inclusion of drugs in feed.

Residues of these drugs turn up in chicken liver and eggs on a regular basis. They are also present in chicken flesh.

### Main Findings

#### This report finds that:

- 1** Until 1998 there had been no statutory testing for drug residues in poultry in the UK. The scale of the residue problem that has since emerged should alert us to a range of issues relating to food safety regulation, farming practices and consumer choice.
- 2** Government regulators have routinely provided misleading information in their public statements about the incidence of drug residues in chicken meat and eggs.
- 3** They maintain that 99 per cent of poultry meat and 97 per cent of eggs are free of detectable residues. However, detailed analysis of the data on which their summaries are based suggests the actual levels could be up to 2,000 per cent higher.
- 4** Nicarbazin, shown to cause birth defects and hormonal problems in animal studies, has never been carefully evaluated for safety in humans. In 1999, the last year for which full figures are available, 17.8 per cent of chicken livers tested had residues of nicarbazin in excess of the Maximum Residue Limit of 200 micrograms per kg., the highest being 10,500 micrograms per kg., over fifty times the legally permitted level. Since then 127 out of 700 (18 per cent) of tested chicken livers contained residues of nicarbazin. Studies show that where it is present in liver it will also be found in flesh at lower levels. In addition it is found in approximately 2 per cent of eggs, even though it is not licensed for laying hens.
- 5** Lasalocid is not licensed for laying hens either. It is a member of the potent cardio-toxic ionophore family of drugs that have never been properly evaluated as residues in food. No Maximum Residue Limit has been set. Yet in 1999, one in every dozen tested egg samples (8.5 per cent) contained residues of lasalocid above the arbitrarily-decided action level of 100 micrograms per kg. The highest of these was 5,400 micrograms per kg. 12 per cent of chicken muscle also tested positive. Most recent results suggest that half of all quail eggs and 30 per cent of all quail muscle on sale in the UK contains residues of lasalocid above 100 micrograms per kg.
- 6** Dimetridazole (DMZ) has never been properly evaluated for safety. Scientific committees disagree about its safety, but it is suspected of being able to induce both cancer and birth defects. It is also not licensed for laying hens or broilers, yet in 2000, 2.6 per cent of broiler feed tested contained DMZ. No tests were undertaken for laying hen feed but in 1998, 2 per cent, and in 1999, 0.5 per cent of eggs contained residues of DMZ.

- 7 The misleading nature of official government statements on drug residues in food are the result of statistical and presentational techniques used by the Veterinary Medicines Directorate (VMD) an executive agency of MAFF. Essentially residues have been expressed as a percentage of all tests for all substances in chicken meat and eggs (most of which are negative) rather than as a percentage of the tests for each individual drug residue. As a result, the general public has been given an entirely false account of the true level of drug residues in food.
- 8 British consumers eat almost 10 billion eggs each year, and so even contamination in a tiny fraction of one per cent of eggs suggests a very large number of contaminated eggs are being eaten each day, and a large number of individual consumers potentially put at risk. Despite this, just 525 samples of eggs are tested each year by government regulators – one test for every 18 million eggs consumed. Samples for individual drugs in eggs from different species (hen, quail etc.) in different production systems (battery, perchery, free-range, organic) can be very small and insufficient to reflect the national picture or reveal patterns between different production systems.
- 9 Ionophore drugs can react badly with some prescription medicines, yet doctors have not been notified of the possible presence of dietary ionophore residues and are therefore unable to take this into account when prescribing.

### Discussion

- In 1999 (the last year for which full figures are available) a total of 8,063 poultry samples were tested for all likely drugs and contaminants. Of these, 8,007 (99.3 per cent) were, as the VMD states, ‘free of detectable residues’. However, only 264 samples of poultry liver were tested for ncarbazine, of which 47 (17.8 per cent) contained residues above the MRL. This same statistical trick, of expressing residues of each drug as a total of all tests undertaken for all substances, rather than as a percentage of the tests for that drug, is used throughout the residue-testing programme for each of the drugs of concern, and is a false basis on which to found policy on antimicrobials. It may even give the poultry industry itself the impression that there is no real problem.
- The actual situation may be worse even than these figures suggest. There are indications that when residues are found, the VMD warns the producer and suspends testing while attempts are made to find out what went wrong. The group set up by the VMD to reduce residues of ncarbazine is the ‘VMD/Industry Initiative’. This entity is highly secretive. The VMD will not even disclose how many members it has, let alone who they are or what reports have been generated.
- The VMD also maintains that these residue problems are caused entirely by ‘contamination at the feedmills’. This has clearly contributed to the problem, especially with eggs (in 1998 an organic egg was found to contain low residues of ncarbazine). However, while the VMD maintains that the residue problems can be solved by technical improvements at mills and an industry education campaign, evidence suggests otherwise. Despite regulatory effort, residues of lasalocid in eggs rose sharply in 1999. In addition to the problem at mills, residues in both chicken meat and eggs result from many other factors. These include:

- Accidental mixing up of batches of differently medicated feed
  - Failure to empty bins completely before refilling, and failure to clean bins and automatic feeding equipment properly
  - The setting of inappropriately short withdrawal times for some drugs
  - The failure of some producers (either for financial reasons, or through concerns that disease will reappear) to observe drug withdrawal times fully, before sending birds to slaughter
  - The use of very high stocking levels and the associated practice of ‘thinning out’ some birds towards the end of a production cycle when space is most limited
  - The inevitable recycling of drug residues after medications are withdrawn as chickens peck their own excreta – something they cannot avoid in intensive broiler systems
  - The dropping in 1998, of the requirement that veterinarians must consider and list all antimicrobials included in feed, when prescribing veterinary medicines for simultaneous use. (Some veterinary drugs dramatically reduce the elimination of ionophores from the body of farm animals. In some situations this could account for residues still being present in birds at slaughter.)
- When eggs are tested a ‘sample’ is made up of a dozen eggs, which are broken and mixed before testing. But about 90 per cent of egg samples show no detectable residues, so this pooling of eggs has the potential to dilute the actual residue levels in individual eggs considerably, and could reduce levels of some samples below detection limits. The VMD maintains this is not significant, since all eggs from individual suppliers will carry similar levels of residues. If this is true, however, it suggests that the total number of eggs actually contaminated could be significantly higher than official results indicate, since there is no information on the proportion of eggs released on the market by producers whose samples turn out to be positive.
- Government also maintains that residues of these drugs pose no health risk. It claims, for example, that ‘Nicarbazin residues are not primarily a safety issue’. However, the former Department of Health’s senior toxicologist, Dr. Derek Renshaw, now with the Food Standards Agency, is known to be personally concerned that nicarbazin was never properly evaluated for mutagenicity. He has stated in a personal communication seen by the Soil Association: ‘I feel uncomfortable when asked to comment on the consumer health significance of any residues of nicarbazin found in foods.’
- The same picture emerges for several other drugs. Dimetridazole (DMZ) is banned throughout Europe, except in the UK, where it can be used only for turkeys, pheasants, other game birds and pigeons. Yet residues are found in chicken feed, and as a result, in eggs. EU Committees disagree about the dangers posed by DMZ. One, the CVMP, recognises that DMZ may be genotoxic and carcinogenic and that guidelines governing its use currently do not offer adequate safety guarantees. Another, SCAN, believes that

the weight of evidence indicates that DMZ should not be considered as a genotoxic compound in mammals. However, Germany wants to see DMZ banned entirely, and British toxicologists (Dr. Derek Renshaw and Professor Diana Anderson) state: 'We are concerned that dimetridazole may be genotoxic. The dimetridazole molecule contains a structural alert: the 5-nitro ring. Several other compounds with a 5-nitro ring have been convincingly shown to be genotoxic.'

- Another large family of drugs, the ionophores, is also used to control coccidiosis in poultry. Some ionophore drugs are currently included in chicken feed at up to half the lethal dose. Susceptibility to the drugs varies greatly between species, individual animals and between different ionophores. Given the size of the industry and its cut-throat competitive nature it is hardly surprising that the ionophore drugs sometimes get mixed up or used at the wrong dose.
- Every Christmas for the last several years, large numbers of turkeys have died from accidental poisoning with the wrong ionophore in their feed, yet no turkeys have been withdrawn from the market and (as far as the authors of this report have been able to establish) no monitoring is undertaken to check whether otherwise unexplained heart attacks in humans may be linked to residues of ionophores consumed in poultry products.
- Yet, the assumption of safety by officials is possible only because there are no studies evaluating toxicity in humans. Laboratory tests have, however, shown that the ionophore lasalocid has a strong effect on human heart muscle at low levels and monensin, another routinely used ionophore, has been found to have a similar cardio-vascular effect in dogs at levels as low as one millionth of a gram per kilogram. Many of the animals that have died from ionophore poisoning have died from heart failure.
- Extrapolating from the toxicological data in animal tests it seems reasonable to suggest that some groups within society and some individuals could be significantly more sensitive to the harmful effects of ionophore residues than others. They could be a particular danger to older people – and according to the National Food Survey, people aged 65 – 74 eat more eggs than any other group.
- The tragic aspect of this potential problem is that those at greatest risk are also likely to be the poorest members of society. They have the greatest incentive to buy the cheapest food available – and this may once again be putting their health, and even their lives, at greatest risk.
- Further the poultry industry, as it exists, is currently locked into a vicious cycle, with limited potential for restructuring.

### **Restructuring the poultry industry**

- Poultry production has long been a fiercely competitive business; economies of scale and new techniques mean everything. This competition now takes place at a global, rather than a national let alone local level. Pressure is intensifying rather than declining as

supermarkets squeeze margins. Chickens were the first species to be bent to the rigours of the production line, but now when producers anywhere on the planet find a new way of increasing efficiency in the chicken factory, most producers worldwide have little alternative but to follow suit. If they do not, within weeks they find themselves being undercut by others and the tiny profit per bird on which they rely becomes a loss. As a result most of the smaller producers have already gone.

- British poultry producers find themselves in a particularly difficult situation. Pushed by consumer concerns over welfare and food safety, most UK producers have accepted the need for a line to be drawn, beyond which stocking densities and other abuses cannot go. In general, standards on British poultry farms are among the best in the world, yet the conditions under which the birds are kept is still lower than most of us find acceptable, and implementation of the guidelines is merely voluntary. With tight margins it is tempting for some producers to cross that line, either occasionally or regularly.
- Stronger controls are placed on the use of drugs within the EU than in many other countries. An inspection by EU officials in one non-EU country from which we import poultry found that veterinary drugs are widely available without proper veterinary supervision. Also between 1997 and 1999 the three antibiotic growth promoters most widely used in chicken production: avoparcin, virginiamycin and zinc bacitracin were banned in the EU. Led by some supermarkets and one of Britain's largest chicken producers, Grampian, many producers have also now stopped using the two remaining licensed chicken antibiotic growth promoters, avilamycin and bambermycin.
- For society these have been important developments. As the Soil Association has shown in previous reports, the use of these drugs causes antibiotic resistance and in the case of both avoparcin and virginiamycin there is compelling evidence that the routine inclusion of these antibiotics in animal feed was the principal factor behind the development of new strains of two hospital superbugs.
- Yet, the use of these drugs in intensive conditions helped to control disease, make animals grow more quickly and increase the efficiency of feed conversion. Most are still permitted in many non-EU countries and this helps to keep their production costs as low as 39 pence per kilo, compared with 49 pence per kilo in the UK. Partly as a result, imports have risen dramatically over the last two years and now account for over 40 per cent of all chicken sold in the Britain. It is not hard to sympathise with the chicken producer who complains that he has been put at a commercial disadvantage while the public health problem has still not been fully addressed.
- Profit margins in the UK are between 7 and 20 pence per bird. Just changing to vaccines instead of antimicrobials would increase costs by 6.8 pence a bird. Consumers would surely be prepared to pay 7p per chicken more for the added safety it would bring, yet in the current world market place and with the rules of the World Trade Organisation as they are, it is not easy to suggest exactly how this might be brought about.

- Organic production offers an attractive alternative for increasing numbers of producers, but it is clearly unlikely to be the first choice for most of the largest producers with the heaviest capital investment in poultry houses and automated equipment.

### Recommendations

- 1 In future, summaries of drug residue testing should state honestly and openly the percentage of positive tests for each drug. An estimate should then be included of how representative such sampling was for the entire industry. Overall analysis should draw together data for all available schemes. Efforts should also be made to simplify the arrangement of tables in residue reports in order to set out in one section data for individual drugs tested under the statutory, non-statutory and other schemes in order to permit more meaningful understanding of the overall national picture for each drug where positive results are found.
- 2 The drugs lasalocid and dimetridazole should be suspended for use in food producing animals as a matter of urgency. While better regulation might reduce the incidence of their residues and metabolites in food, it will never prevent it completely and consumers will have no assurances that potentially dangerous levels of either drug will not turn up in individual samples of chicken meat and eggs from time to time.
- 3 The drug nicarbazin should be suspended for use in food producing animals pending the completion of further studies and thorough consideration by regulatory committees of its safety as a food residue.
- 4 The use of all ionophore antimicrobial drugs should be phased out as soon as possible in place of better systems (such as organic production) where possible, and of vaccination where not.
- 5 To make this possible consumers should be prepared to pay extra for poultry produced in this way. An initiative is needed to bring together consumer group representatives, multiple-retailers and the poultry industry to consider ways in which this might be achieved. Multiple retailers should avoid selling chicken as a 'loss-leader'.
- 6 Government should ensure that the issues surrounding intensive poultry production, including the residues of potentially dangerous drugs in chicken meat and eggs, are included in the fundamental review of agriculture already promised.
- 7 Government should re-examine the terms of reference of the Veterinary Medicines Directorate, its sources of funding, potential conflicts of interest, and also consider handing responsibility for residue testing to the Food Standards Agency.
- 8 Government should work with our EU partners towards ensuring that poultry imports match, in every respect, the requirements of EU legislation. Consideration should be given to including the testing of imported poultry products in the statutory scheme.

Consideration should be also given to the possibility that processed chicken products entering the UK from other EU member states, may contain meat from birds that were in fact produced outside the EU.

- 8 The Department of Health should consider providing guidance on possible health problems for people taking some medical drugs known to react badly with the ionophores. This might include advising some patients to avoid chicken and egg products while on the medication. The Chief Medical Officer should conduct a review as a matter of some urgency.
- 10 To achieve clarity of purpose and efficiency of operation the role of policing the use of antimicrobial feed additives should be undertaken by the same body that carries out residue testing. In practice, it is suggested that this role should be taken from the Royal Pharmaceutical Society of Great Britain.
- 11 The new Veterinary Residues Committee should consider changes to the design of the residue testing programme to include a proportion of non-randomised samples targeted at specific areas, where an understanding of the industry suggests problems are most likely. It should ensure data is given in full and that summary statements are not misleading.
- 12 Regulators should assume that all drug residues in food pose potential dangers to consumer health in the absence of solid evidence suggesting otherwise. They should apply the precautionary principle and also be prepared to prosecute more often to ensure compliance with legislation.
- 13 The European Commission Food and Veterinary Office should undertake an inquiry and conduct an independent audit of the UK situation.
- 14 The European Commission should ensure that both veterinary medicines and zootechnical food additives are included within the remit of the proposed new European Food Authority on the grounds that they can affect human health.
- 15 The UK Food Standards Agency should lobby government for a more central role in the surveillance and regulation of food residues.

### INTRODUCTION

This is the third report in the Soil Association's series on the use and misuse of antibiotics in UK agriculture. Previous reports have looked at the use of antibiotics in all sectors of the UK livestock industry and examined the extent to which their overuse continues to contribute to the serious problem of antibiotic resistance in human medicine.

This report takes a slightly different approach. It examines two sectors of the livestock industry - broiler (chicken meat) and egg production - in greater detail, whilst also broadening its focus to include, along with antibiotics, the use of a wider group of drugs known as antimicrobials.

Many of the drugs discussed in this report are highly toxic and could never be used in human medicine. The findings about their use and misuse have been startling and expose a different problem to that highlighted in previous reports.

Resistance develops in the antimicrobials in just the same way as in the antibiotics. However, since the drugs have no application in human medicine the development of resistant strains does not pose a direct threat to our health. The issue instead is the risk of toxic residues in chicken meat and eggs and the complacency of the regulatory authorities towards this risk.

The problem of resistance in the antimicrobials has caused major practical problems for intensive broiler and egg producers who rely very heavily on them to control certain parasites and diseases in their flocks. Consequently many of the relatively non-toxic drugs previously used in this way are now effectively useless. Producers have to rely on a number of older drugs, many of which were licensed before strict safety guidelines were introduced. These have to be used carefully in rotation, combination and succession to be effective and to limit the development of resistance.

To be effective some of the antimicrobials

also have to be used at high rates – up to half the lethal dose for chickens. The toxic effects of these drugs vary significantly between different animal species and different antimicrobials. For example, whilst chickens may tolerate a certain drug at particular levels in their feed, if the same feed is accidentally given to turkeys the birds can die.

When everything goes precisely according to plan it is possible to use these dangerous drugs in just the right amounts and sequence, and for exactly the right duration in order to produce a bird or an egg containing no detectable residues. However given the size of the industry, the very low margins on which it operates and the very high bird to labour ratio, it is hardly surprising that things often go wrong with the management of the birds. Mistakes are made; carefully planned procedures breakdown and significant residues in meat and eggs result with potentially serious implications for human health.

Given the fact that most of the drugs discussed in this report have been used in this way for several decades, it is surprising to learn that until 1998 there was no statutory testing in the UK for the residues of any drugs in poultry meat or eggs. There was only a non-statutory scheme which very occasionally tested a few samples for residues of a few drugs.

We now have statutory scheme, funded by industry, to test for drug residues in poultry products. It examines about 8,000 samples each year and has been expanded and improved annually since its inception with greater attention paid each year to the problems identified in previous ones. In addition the non-statutory scheme has been retained. It is funded by government and used to target specific areas the statutory scheme does not cover adequately.

As far as the surveillance scheme is concerned things have improved significantly in the last few years.

At first glance, the detailed annual reports from the Veterinary Medicines Directorate on the drug residue testing schemes appear to

contain little cause for concern. The same reassuring and unambiguous message to consumers from MAFF and the poultry industry is contained in a leaflet entitled, *The Facts About Veterinary Residues in Food*. It states that “99 per cent of poultry meat and 97 per cent of eggs are free of detectable residues”.

Unfortunately this is simply untrue. If the published data is scrutinised in more detail a rather more alarming picture emerges, suggesting that since 1998 the actual incidence of significant drug residues in poultry meat has been in the region of 20 per cent and that of eggs 10 per cent.

At the heart of this deception is a simple statistical trick which is used throughout the VMD reports on drug residue testing, namely that of expressing the number of positive samples as a percentage of all tests undertaken for all substances and sometimes even all species.

Many of these drugs have never had legally enforceable maximum residue limits (MRLs) set, however, even where they exist the VMD is remarkably reluctant to enforce them.

Since 1998 some of these drugs have been reclassified as zootechnical feed additives. As a result these are not governed by medicines legislation. While the VMD is responsible for detecting their residues it can pass the buck on their farm use to the RPSGB.

But why do the regulatory authorities feel the need to side with the industry and also deceive consumers about the true extent of drug residues? Do these residues pose a real threat to human health? And what should be done about the current unacceptable situation?

This report begins by examining the practices and economics of the poultry industry to understand why these drugs are used at all. It details the true incidence of drug residues in poultry meat and eggs and considers how dangerous these residues might be for our health. The authors challenge conventional thinking amongst MAFF and the poultry industry that these substances are almost totally benign and questions how assumptions of safety

can be made when the necessary toxicological studies have never been undertaken.

Extrapolating from the studies available, the report concludes that on-going assurances about the low risk of significant drug residues occurring in poultry meat and eggs are widely misplaced.

The relationship between MAFF and the poultry industry is also briefly examined. In his Green Paper for the Food Standards Agency (FSA), Professor Phillip James recommended that the work of the VMD should largely come under the control of the FSA. However, as the government acknowledged in the 1998 White Paper, *A Force for Change*, this provoked a major protest from the industry and the government caved into pressure and rejected Professor James' proposal.

A clear conclusion of this report is that radical restructuring is needed within the UK poultry industry. The regulatory pressure that might encourage this is largely lacking and the industry itself has neither the incentive nor the inclination to make major changes itself. Without intervention 'restructuring' is likely to mean the further consolidation of the industry into even fewer larger companies. That, however, would only serve to make the problems identified in this report even worse.

What is required is that the inherent problems of the intensive poultry industry become the subject of public scrutiny and that this previously neglected sector is considered along with that of the rest of agriculture in the forthcoming debate about the future of food production in this country.

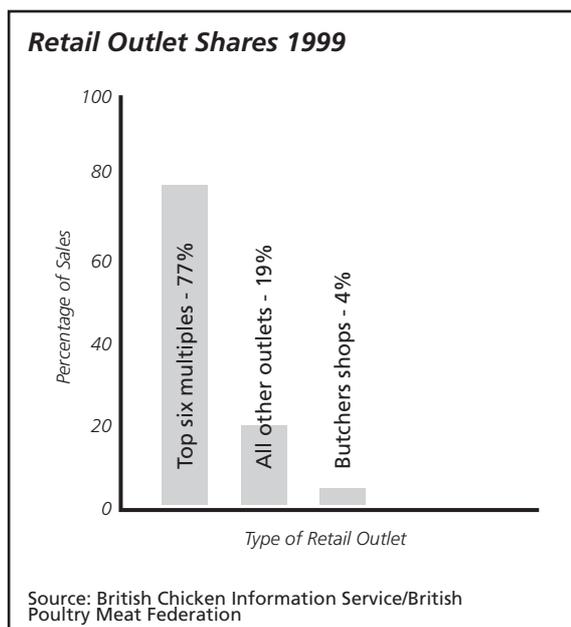
The drugs highlighted in this report are not permitted in the production of organic chicken or eggs in the EU. However, even in Britain, organic poultry standards vary considerably. The Soil Association maintains the highest poultry standards in the UK, but its producers have only a small share of the market. It is suggested that the findings of this report also have implications for the setting of minimum organic standards at a national level.

### 1. CHEAP CHICKEN FOR ALL

Foreign Secretary Robin Cook famously remarked that chicken tikka masala is now the national dish in the UK. Chicken, no longer a luxury, is cheap enough to be daily food for many: appearing as Sunday lunch, oven-ready meals, take away fast food, and high street sandwich bars. We now consume more chicken products than at any time in history, mainly because it is the cheapest form of meat available. Britons eat over 20 kilograms of chicken per person each year (British Chicken Information Service). Yet despite consuming up to a third of our own bodyweight in chicken, we know, or choose to know, very little about how it has been produced.

Concerns over Foot and Mouth have further increased sales of chicken: a MORI poll commissioned by Compassion in World Farming in the run up to Easter 2001 found that 14 per cent of us are eating more chicken.

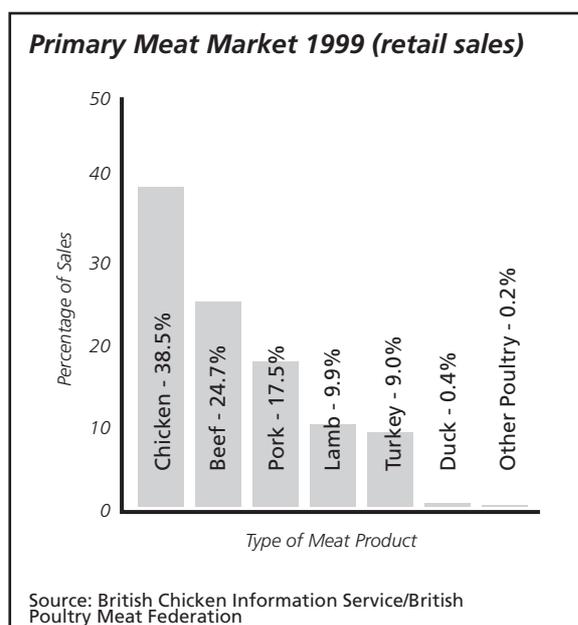
The vast majority (98 per cent) of this chicken is broilermeat from birds reared indoors in intensive highly-mechanised production systems (Sustain, 1999). Intensively reared turkeys, ducks and other species are reared in similar conditions. Their short, confined lives are often a continuous struggle against disease, overcrowding and suffering.



### The economics of the broiler industry

More than 750 million chickens are produced for eating each year in the UK: globally there are about 20 billion broilers at any one time, of which 25 per cent are in the USA, 14 per cent in the European Union, and nearly 19 per cent in China (CIWF/Turner, 2000). During the past five years, massive expansion in China and Brazil has increased world production of poultry meat by 20 per cent. EU production has risen 10 per cent, USA production by 21 per cent, Chinese production by 32 per cent in China, and Brazilian production by 30 per cent (Montobbio, 2000).

One of the main reasons production has been able to increase so rapidly is that selective breeding has allowed for shorter and shorter production times. The use of very high protein diets and growth promoting feed additives has also been significant. Since 1976 the length of time broiler chicks have taken to reach a slaughter weight of 2kg has been reducing by an average of 1 day every year. At the same time, the amount of feed needed to achieve this weight gain has been reduced by almost 40 per cent (CIWF/Turner, 2000). And in the global market computer programmes can source the 'Least Cost Formula' of available feedstuffs



(including such unlikely foods as coconut husks and banana skins) making feed even cheaper.

Intensive indoor housing for such relatively short lives allows for almost complete automation of the production system with minimal human labour required to 'tend' the birds. One stockman can be responsible for over 100,000 birds at a time. With automated lighting, ventilation, feed and water, one batch can be taken out and the next batch started in a continuous production operation. As a result, broilers are one of the cheapest forms of meat available to the consumer in the UK and consumption continues to rise.

Competing on price alone, producers work within tight financial margins with profit per bird estimated at between just 7 and 20 pence in the UK. A chick costing only 26 pence is grown for around 40 days before being sold for just over a pound sterling (Sustain, 1999). Profits are squeezed ever-tighter by even cheaper non-EU imports, principally from Brazil and Thailand, where production costs are about 25 per cent lower. Currently accounting for over 40 per cent of UK sales these have risen dramatically over the last two years, partly at the expense of the British industry which contracted by 3 per cent in 1999.

### The largest intensive broiler producers in the UK

Company	Number of intensive broilers produced/year	Approximate number of broilers to stockman
Bird, Frank	3,850,000	100,000; 'there is not a lot of physical work – 3 of our stockmen are women'
Bronte Foods	3 million	40,000
Faccenda Chicken	104 million	360,000 unit done by 2 men (180,000 each), with support
Grampian Country Food Group	188 million	80,000 to 100,000
Lloyd Maunder	20,800,000	'Depends on degree of automation'
GW Padley Poultry	would not disclose; more than 40 million	'On our larger farms we have 2 stockmen; on our smaller farms one' (plus support)
2 Sisters (includes Buxted, Devon Crest, Premier, Hermanns)	122 million	70,000
Sun Valley Foods	would not disclose; more than 40 million	55,000 to 150,000

From Mother Earth, the journal of the Soil Association, April 1958:

#### Broiler factories

Dr R F Gordon, Director of the Houghton Poultry Research Station, maintained that the hen was being exploited to an even greater extent than the pig. 'The extreme of artificialdom', with its accompanying environmental stress, was to be found, he said 'in the broiler industry', now said to be turning out 50 million carcasses a year. Mentioning that disease now costs the poultry industry from £15 to £20 million a year, with new diseases constantly appearing and some of them egg-borne from generation to generation, he asked what was the point of using so much ingenuity to save labour, which represents 10 per cent of production costs, when losses from disease might run as high as 25 per cent of production costs.

The UK now produces over 750 million carcasses a year. Disease (coccidiosis alone) is estimated to cost £38 million a year (Williams, 1999). Labour accounts for no more than 5 per cent of production costs (Parker, 2001).

### 2 WELFARE AND DISEASE

Welfare conditions in intensive poultry systems have been criticised by many concerned organisations and individuals. Visibly obvious health problems, such as lameness and blisters arising from poor welfare conditions have also been noted. Less attention has been paid to the consequences for bird health that arise from aspects of the intensive approach, where specific diseases are kept under control by the routine inclusion of feed additives.

Conscious of public concerns and under pressure from multiple retailers, British poultry producers have made efforts in recent years to introduce minimum production guidelines and improve the image of the industry. In a recent telephone conversation, Peter Bradnock of the British Poultry Meat Federation, said that 85

per cent of producers are now registered with the Assured Chicken Production scheme. British producers generally are also keen to stress that welfare standards in the UK are higher than in most of the countries from which we import large quantities of chicken.

While this may be true, and the Assured Chicken Production Scheme recommends the government guideline maximum stocking density of 34 kgs/sq.m., it still permits densities of 38 kgs/sq.m. It also allows lighting as low as 10 lux, half the bare minimum recommended by the Farm Animal Welfare Council in 1992. (Normal office lighting is between 300 and 500 lux).

It is a contention of this report that certain drugs used as feed additives to control disease, especially in broiler systems, pose a threat to

#### The suffering of broiler chickens

- Selective breeding for ever faster growth rate and feed conversion efficiency has caused most of the welfare problems broilers suffer from today. Broiler chickens have a mortality rate of one per cent a week, seven times the rate of laying hens of the same age.
- Because they grow too fast, millions and possibly tens of millions of UK broiler chickens a year may suffer from painful lameness due to abnormal skeletal development or bone disease, so that many have difficulty in walking or even standing. Lame broilers spend up to 86 per cent of their time lying down ...
- As a result of selective breeding, broiler chickens' hearts and lungs often cannot keep up with their bodies' fast growth rate. They frequently suffer from heart failure when they are only a few weeks old. Acute heart failure known as Sudden Death Syndrome kills 0.1 per cent to 3 per cent of broilers in European countries. In the UK at least 0.8 per cent of broilers die from Sudden Death Syndrome, amounting to over 6 million birds a year. A second form of heart failure known as ascites affects nearly 5 per cent of broilers worldwide. Ascites kills at least 1.4 per cent of broilers in the UK, amounting to nearly 11 million birds a year.

- High stocking density in broiler sheds restricts the broiler chickens' behaviour and causes health problems. High stocking density leads to increases in leg problems, breast blisters, chronic dermatitis, hock burns and infections. Crowded sheds lead to wet litter, increased air pollution from ammonia and dust particles and worse temperature and humidity control, all of which damage the broilers' health and welfare.
- The stocking density must be no higher than 25 kg per square metre (12.5 birds per square metre) 'for major welfare problems to be largely avoided'. Above 30 kg/square metre (15 birds per square metre) there is a 'steep rise in the frequency of serious problems'. The UK government's current guideline for stocking density (34 kg per square metre, or 17 birds per square metre) is well above the SCAHAW Committee's recommendation.
- Broilers that are allowed to grow to adulthood to be used for breeding are restricted to between one quarter and one half of the amount of food they want to eat during their growing period and 'appear to be chronically hungry, frustrated and stressed'.

Compassion in World Farming Trust/Turner, J 2000 The Welfare of Broiler Chickens – an analysis of the European Scientific Committee on Animal Health and Welfare (SCAHAW) report of March 2000.

human health. It is therefore necessary to detail some of the intrinsic welfare problems of broiler systems and explore the links between these and disease.

### 'The extreme of artificialdom'

An average broiler shed holds 30,000 to 40,000 birds; around six 'crops' per year are produced per shed. There are no windows and the birds do not see daylight. As a result synthetic vitamins have to be added to rations to keep the birds alive. Lighting, temperature, and air movement are artificially controlled.

Ammonia, dust, carbon dioxide, and carbon monoxide build up rapidly in broiler houses, and a shortage of oxygen can also contribute to disease. Ventilation systems are supposed to supply clean air at a steady temperature throughout the house, and to remove stale air and germs, but these systems are susceptible to mechanical failure. Eminent poultry veterinarian David Sainsbury records the results:

*.. the author has frequently been distressed by heavy mortality occurring in mechanically ventilated poultry houses after sudden rises in the ambient temperature and humidity (Sainsbury, 2000).*

### The squalor of the broiler shed

The birds are never cleaned out. As chicks they are placed on a thin layer of wood shavings, chopped straw, shredded paper or 'old' litter from previous crops which has been stacked and dried out, over concrete (Sainsbury, 2000). The birds are left in their own manure until slaughter. The sheds are then emptied and fumigated, usually with formaldehyde, in readiness for the next crop.

David Sainsbury also makes clear that it commonly gets wet in broiler houses (Sainsbury, 2001).

*It is frightening to see broilers, layers and breeders maintained throughout the winter months on accumulations of their own droppings, and in some*

*cases it is possible to have one's boots sucked off in the quagmire – it has happened to me! ...*

*Probably the most serious consequences of all are in breeder houses, where broiler chicks are bred. Here wet litter can have a calamitous effect on the feet of the cocks, causing accumulations of infected litter on the feet. (Sainsbury, 2000)*

### Overcrowding

It is routine practice to stock the birds as densely as possible. Towards slaughter weight, typically the space allowed per bird is no greater than an A4 sheet of paper. This restricts their movement, creating painful leg disorders and other health problems.

'The UK government's guideline for maximum stocking density is 34 kg of bird per square metre (around 17 birds at typical slaughter weight per square metre), although the range of stocking densities in Europe as a whole is between about 22 and 42 kilograms per square metre (11 to 25 birds per square metre). In Europe, only Sweden and Switzerland have legal limits on stocking density, while the UK and Germany have only recommended limits (CIWF/Turner, 2000).'

It is not surprising that birds in these large units are highly susceptible to disease. But what is not so widely realised, except by the industry, is that they are actually suffering from sub-clinical disease throughout their brief lives.

*There is now abundant evidence that the productivity of poultry may fall as the size of the unit increases and when there is no apparent difference in management between sites. In a survey carried out by the author [David Sainsbury], broilers showed a variation in finishing weight at the same age from 2.1 kg in groups of 20 to 1.4 kg in groups of 30,000, with an almost pro rata relationship with groups of between 50, 100, 500 and 10,000. These differences occurred with birds from the same genetic material, eating similar food... The decline in weight was almost certainly due to the increased incidence of disease ... (Sainsbury, 2000)*

There are many diseases in broilers, but this

report focuses on coccidiosis, 'undoubtedly the most important parasitic disease of poultry'. To understand the current problem with drug residues fully, however, some knowledge of two other diseases is also required. These are necrotic enteritis, which affects intensively managed poultry and histomoniasis, a disease of overstocked game birds and intensive free-range poultry. Further details are provided in Appendix 1.

### **The causes of coccidiosis**

Coccidiosis is an infectious disease caused by a microscopic protazoan parasite which damages the intestinal tract of the bird (or other animal host), causing illness and sometimes death.

The frequency and severity of coccidiosis outbreak is directly related to the unnatural cramped conditions imposed on intensively farmed livestock, most commonly the indoor reared broiler chicken. If coccidiosis is an indicator of stress, then the broiler shed is the most miserable place imaginable.

Wherever large numbers of animals are crowded together in overstocked, warm, moist, unchanging conditions, outbreaks of coccidiosis start to occur. In nature, the reproduction of the parasite is inhibited by daylight, cold, and a dynamic environment.

*The intensive rearing of large numbers of chickens in enormous houses creates conditions which are favourable to rapid multiplication of parasites which have short, direct life cycles (McDougald 1982).*

As coccidiosis affects all types of livestock kept in an intensive environment, it has now been recorded in farmed rabbits, cattle in feedlots, pigs, sheep, caged mink (Fayer and Reid, 1982), game birds and even fish.

### **Coccidiosis in different production systems**

Although coccidiosis does occur in chickens in natural conditions, outbreaks are rare. 'Chickens reared in traditional, low stocking density units,

such as free range backyard flocks seldom develop clinical coccidiosis as the number of oocysts in the environment will be comparatively low and immunity develops rapidly.' (Commission on Antimicrobial Feed Additives, 1997)

Coccidiosis has increasingly become a problem as systems have become more intensive and as the slaughter age has declined. Birds easily develop natural immunity to coccidia; however at 42 days, the age at which broilers are now generally slaughtered, their immune systems are still not fully developed. To acquire natural immunity to coccidia young birds ideally need to come into contact with low levels of several strains of the parasite.

This has traditionally been achieved in organic poultry systems through relatively low stocking rates, rotation of pasture, and periods when houses are kept empty. It may also be possible to achieve in the best free-range systems, but information is limited. It is, however possible that the higher stocking rates of up to 2500 birds per hectare now being deployed in some organic systems may make coccidiosis more difficult to control naturally. In organic production, the prophylactic use of coccidiostats is not permitted. Therapeutic use, which is strictly controlled, is permitted where a need can be demonstrated, and extended drug withdrawal periods are mandatory. A few organic producers are already using either vaccines or herbal preparations as part of their control procedures.

### **Control of coccidiosis in intensive broiler production**

Daily preventative drug treatment in feed is used against coccidiosis in intensive houses; breeder birds may be vaccinated. All intensively reared broilers and turkeys, and laying hens before egg production begins, routinely receive prophylactic anticoccidial drugs in their feed.

This preventative approach is taken because it is not economic to treat birds once they actually have the illness, and because the

withdrawal period of the necessary drugs is sometimes longer than the lifespan of the bird itself (Knott). Because of the massive levels of infective 'challenge' the birds face in the broiler house, and their short lives, they are unable to develop a natural immunity against the disease.

A 'withdrawal period' for these drugs, five to nine days before slaughter, is intended to prevent residues entering the food chain - as this report describes, it is often failing to do so. When the drugs are withdrawn, the disease can take hold with drastic results (Williams 1999). This is one reason why producers may be tempted to ignore withdrawal periods, if they feel they can get away with it.

### Vaccination

Schering Plough is the first company to have produced a vaccine against coccidiosis in the UK: Paracox and Paracox-5. Competitor companies have similar products in the pipeline. The vaccine is used by broiler breeder producers, and some organic producers, but uptake by commercial intensive broiler producers is negligible (Johnson, 2000).

There are a number of disadvantages with the vaccine for intensive broiler producers. Firstly, the cost – in a recent telephone call David Schofield of Intervet said:

*The vaccine is six to ten times more expensive [than anticoccidials], and at the moment the market is static. There is no pressure to use it, but if the supermarkets insist, this will change. The retailers aren't yet over-concerned, they aren't yet ready to start banning things. The feed industry may welcome the increased use of vaccines because it saves them fiddling around.*

Sufficient vaccine for 1000 birds currently costs £68. A second problem with the vaccine is that it may be killed if feed is contaminated with anticoccidial drugs, which, as this report describes, it commonly is.

Perhaps most significantly, the vaccine does not protect against necrotic enteritis (see

Appendix 1). Jeremy Johnson of Schering Plough, in a letter of 18th December 2000, denied that the vaccine actually *increases* incidence:

*Whilst we occasionally see necrotic enteritis in vaccinated birds, and whilst we believe there is a link between necrotic enteritis and clinical coccidiosis, we are not convinced that there is an increased risk of necrotic enteritis in vaccines from what we ourselves have seen.*

However, studies elsewhere have found that anticoccidial drugs not only control coccidiosis, but also protect birds against necrotic enteritis, in much the same way as the growth promoting antibiotics. In fact the increased use of some anticoccidial drugs may be partly due to the ban on some growth promoting antibiotics. Three ionophore anticoccidials, maduramicin, narasin and monensin, all reduce the bacterium *Clostridium perfringens* that causes necrotic enteritis, and increase chickens' growth rate. Two of these drugs, monensin and salinomycin are also still licensed for growth promotion in cattle and pigs respectively, and it perhaps is hardly surprising that they have a similar effect in chickens. Lasalocid has also been shown to have this effect (Commission on Antimicrobial Feed Additives, 1997);

As Jeremy Johnson explained (in a telephone conversation of 27 October 2000):

*The industry has a problem with necrotic enteritis. It is one of a suite of diseases which were well controlled by the growth promoter avoparcin. Since the withdrawal of the 'traditional' antibiotic growth promoters [avoparcin, banned in the European Union 1 April 1997, bacitracin zinc, spiramycin and virginiamycin, banned 30 June 1999] we understand that the incidence of necrotic enteritis has increased. The industry are using it as an excuse not to stop using the ionophore anticoccidials.*

Asked how the industry *could* reduce the disease, Jeremy Johnson said among other things it needs to 'look at stocking density, and improve nutrition and ventilation'.

### 3 THE POISON PROP

It is no exaggeration to say that the intensive broiler industry could not have developed without, and is entirely dependent on, antimicrobial drugs. By far the largest group of these are those used to control coccidiosis, known as anticoccidials or coccidiostats.

*It is an undisputed fact that the world's poultry industry could not exist without some means of controlling coccidiosis, a debilitating, sometimes fatal disease complex in chickens ... Since the 1940s, anticoccidial drugs of many different chemical types have been developed for commercial use. However, although successive improvements in their efficacy have been made over the years, resistance has developed to all of the anticoccidial drugs so far (Williams et al, 1999).*

#### Drugs used for coccidiosis control

DECADE	DRUG	CHEMICAL CLASS	FIRST AUTHORISED IN EU under 70/524/EEC
	sulphur	sulphonamides	
1940	sulphanilamide	sulphonamides	
	sulphaguanidine	sulphonamides	
	sulphadimidine	sulphonamides	
	roxarsone	arsenicals	
1950	nitrofurazone	nitrofurans	
	nitrophenide	nitrophenide	
	nicarbazine	carbanalide	1956
	furazolidone	nitrofurans	
1960	nitromide	dinitrobenzoyl chloride	
	buquinolate	quinolone	
	clopidol	pyridinol	1974
1970	monensin	polyether ionophore	1976
	amprolium	thiamine analogue	1970
	dinitolmide (DOT)	dinitrotoluamide	1970
	decoquinate	quinolone	1976
	robenidine	guanidine	1976
	arprinocid	nitrofurans	1983
	lasalocid	polyether ionophore	1983
	halofuginone	quinazolinone	1984
	salinomycin	polyether ionophore	1984
1980	narasin	polyether ionophore	1984
	maduramicin	polyether ionophore	1992
	diclazuril	benzene-acetonitrile	1993
1990	semduramicin	polyether ionophore	

- Adapted from Commission on Antimicrobial Feed Additives, Stockholm SOU 1997

Anticoccidial drugs have been used in far greater numbers, and quantity, on broilers than for any other farm animal. By 1979, over 30 drugs had been used for the prevention of coccidiosis in chickens, whereas only a few have been used on other species (Long, 1982).

Anticoccidials are not prescribed by a vet: they are sold direct to producers by pharmaceutical companies and agricultural feed merchants. The drugs are given in feed and no prescription is needed. Until the Medicated Feedingstuffs (MFS) Regulations were introduced in 1998, vets had to list all the other drugs being used, including anticoccidials, when prescribing therapeutic drugs. But the MFS regulations, in classifying the anticoccidials as harmless-sounding 'zootechnical feed additives', exempt them from vets' records.

Over the years since the discovery by Levine, in 1939, that the sulphonamides controlled coccidiosis, the poultry industry has moved on from one suite of chemical drugs to the next, as resistance appeared. In the 1970s, these were gradually succeeded by the ionophores; but now resistance to these is a problem. Coccidia have, so far, developed resistance to all coccidiostats used (Commission on Antimicrobial Feed Additives, 1997).

The coccidiostats have attracted little scientific – or public – attention. They have been used in greater quantities than any other class of drug. Serious deficiencies in risk control, at the feedmill and in the broiler house, are a particular characteristic of anticoccidial use.

The history of warfare against coccidiosis has seen few clean strikes. As world expert Larry McDougald remarks, it has been a series of hit-and-miss chemical bodging, with each new drug eventually defeated by resistance:

*Lest the reader be impressed by the long list of drugs and the evidence for their effectiveness, we must caution that none of these drugs can be accepted at face value. The 'faithful shadow' of drug resistance*

*has rendered some drugs useless; others have undesirable side effects* (Long, 1982).

As we shall see, the drugs described in this report, despite their widespread continuing use, have both of these problems.

In broad terms, the chemical drugs used from the 1940s have, as the parasite developed resistance to them, increasingly given way to the polyether ionophores, which are much more toxic, but to which the parasite is now developing multiple resistance. According to NOAH, the National Office of Animal Health Ltd, an association representing the veterinary pharmaceutical companies: 'The ionophores are unique in that they permit a small 'leakage' of coccidia to enable the bird to develop a certain level of immunity' ([www.noah.co.uk](http://www.noah.co.uk)).

### **The faithful shadow of resistance**

*The quotation from Schnitzer and Grunberg (1957) – "drug resistance has accompanied the development of chemotherapy like a faithful shadow and the history of chemotherapy is also a history of drug resistance – is nowhere more true than in the poultry industry" (Long, 1982)".*

When an anticoccidial is effective, it can act as a coccidiocide, that is, it kills the protozoa, or as a coccidiostat, when exposure arrests the protozoa, so that on the drug's withdrawal it is capable of continuing its life cycle. Only if, in the presence of a drug, the parasite can complete the process, and produce infective oocysts, can it be regarded as resistant.

Since 1955 experiments have been carried out to test for the development of resistance in the different strains of *Eimeria* (the protozoa which causes coccidiosis) to the various anticoccidial drugs. In developing the necessary experiments it was discovered to be advantageous, in producing the drug-resistant mutants that were needed, to have as great a number of coccidial oocysts as possible (Long, 1982).

What this signifies is a direct relationship between numbers of birds and the speed at which anticoccidial drug resistance develops.

The use of drugs at subtherapeutic doses also accelerates the emergence of resistant strains (Long, 1982), and, although studies of cross-resistance between the ionophores have been contradictory, the scientific consensus is that resistance to one leads to cross-resistance with all of them (Commission on Antimicrobial Feed Additives, 1997).

Although resistance of the parasite to the ionophores has developed more slowly than to some of the chemical drugs, it has steadily emerged throughout the 1990s. In 1994, a study of resistance found that the ionophores were actually less efficacious than the older, chemical drugs: tests found resistance to monensin in all samples, then in descending order: narasin, salinomycin, and maduramicin; lasalocid was found to be the most effective (Peeters et al, 1994).

Another study had similar findings, observing that although lasalocid was the most efficacious of the ionophores in controlling coccidiosis, most of the test isolates were, in fact, resistant to it (Chapman and Hacker, 1994). A recent German study found widespread resistance of *Eimeria* (the genus to which coccidia belong) to anticoccidials, mostly multiple resistances. Partial or complete resistance to maduramicin was found in seven isolates, to monensin in six, to salinomycin in five, and to nicarbazin in eight. Multiple resistance had developed in ten out of eleven of the resistant strains and cross resistance between maduramicin, monensin and salinomycin was observed (Stephan et al, 1997).

Most recently, a study found full cross resistance between the ionophores salinomycin and narasin; but no resistance to monensin and lasalocid was found. Resistance to ionophores was seen mainly among strains of poultry origin as opposed to those of pig origin (Buyaye et al, 2000).

At a recent conference on coccidiosis (Coccidiosis, 2000) the resistance problem was, as ever, on the agenda, and a recent trend was explored: the use of less 'effective' anticoccidials, so that the birds, exposed to greater challenge, have their immunity stimulated. But this strategy too seems doomed to failure: as we have seen, subtherapeutic doses actually accelerate the emergence of drug resistance.

### **Shuttle, switch and rotation programmes**

Although there is little scientific basis for the practice (McDougald, 1982), the industry uses a sequence of two or three different anticoccidials in an attempt, by limiting exposure, to reduce the problem of drug resistance. The theory is that any resistant parasites not eliminated by the first drug will be controlled by the second, and so on. But in practice coccidia are becoming multi-drug resistant.

The drug can be changed with the type of ration – starter, grower or finisher. Usually an 'efficient' drug, such as monensin, is employed from three weeks onwards, when exposure to coccidia is highest. Drugs with the shorter legally required withdrawal periods before slaughter can be used last in the sequence (Long, 1982).

A common shuttle is to use nicarbazin up to 15 days old, with a change to monensin up to 3 days prior to slaughter. Different drugs are used for summer and winter: nicarbazin is avoided in the summer months because of the heat-stress mortality it can cause.

The resistance problem is a routine consideration in the design of an anticoccidial programme. The producer, in conjunction with his vet and a drug company representative, will usually carry out lesion scoring of perhaps 20 birds, to assess the incidence of coccidiosis. Then a selection of drugs, which can be switched or rotated between batches, is chosen. The most common regime is a chemical drug followed by an ionophore, or ionophores are used throughout (Knott).

### 4 THE DRUGS: RESIDUES AND TOXICITY

Most of the drugs used in livestock production are not highly toxic. No one likes the idea of consuming any antibiotic residues, but many people take courses of antibiotics without harmful side effects and unless residues are present in food on a regular basis the consensus of scientific opinion is that only a very small proportion of people are likely to experience what is known as an 'Adverse Reaction' to occasionally encountered residues of medical antibiotics in food.

The situation with the drugs detailed in this report is very different. These drugs are so toxic that they could never be used in human medicine. They are also used in poultry feed at high concentrations, sometimes at between a third and half the lethal dose.

For a number of reasons residues of several of these drugs regularly turn up in eggs and other poultry products. British regulators state that these do not pose a threat to health. However, most of these drugs were licensed a long time ago when the regulatory process for new drugs was significantly less rigorous than today. There are serious gaps in the scientific data and for some, Maximum Residue Limits have never even been set.

For two years, since the extent of the problem first became clear to regulators, the Veterinary Medicines Directorate has been working behind the scenes to make the poultry industry take the problem more seriously. This has had some success and the overall level of positive samples for some of the drugs has fallen. However, even where this is successful consumers are only protected from dangerous drug residues when everything in the industry goes precisely according to plan. The right drug must be chosen for each species. The drugs must be withdrawn from feed exactly the right number of days before slaughter. No birds must be thinned out early. No one must ever allow feed to get mixed up. Feedmills, bins and pipelines must be

thoroughly cleaned between batches and withdrawal periods set by regulators must be long enough to ensure that residues disperse before birds are slaughtered. Even then, residues can occur.

### NICARBAZIN

#### The toxicity of nicarbazin

Introduced in 1956, nicarbazin has been a contaminant in our food for a long time. Over the last two years residues of this drug many times over permitted levels have occurred in the livers of around 20 per cent of all broilers on sale in the UK. It is also commonly found in eggs, even though it is not licensed for use in laying hens.

Latest figures reveal that 17 per cent of broiler livers tested had residues in excess of the JECFA MRL of 200 micrograms per kg, the highest of which was 10,500 micrograms per kg (VMD Annual Report on Surveillance for Veterinary Residues, 1999).

It is not the drug of choice for coccidiosis control, but resistance develops less quickly than with many other coccidiostats and this may explain its current level of use. As Larry McDougald explained:

*Despite good anticoccidial activity, the drug was beset with problems from side effects. The first significant problem was toxicity to laying hens, especially those with brown-shelled eggs. The electrostatic properties of the drug caused contamination of layer feeds in feed mills, which was sufficient to damage production in laying flocks. In broiler chickens, the drug will sometimes depress growth slightly, with the effect measurable at any time from 1 to 8 weeks. The use of nicarbazin has been associated with excessive mortality from heat stress, especially in birds 4-8 weeks old (Long, 1982).*

These problems have limited the use of nicarbazin and are found whenever it is used. Its side effects are lethal heat stress – nicarbazin-fed birds start to die in heat of 38

degrees or more – egg shell bleaching, yolk mottling, decreased egg production and hatchability, and lower egg weights (Fowler 1995).

One of the hidden ‘benefits’ of nicarbazin is that it makes the birds’ skin appear a more healthy yellow colour, believed to indicate

quality to the consumer. Producers have known about this since the 1980s, and a 1988 US study by Kenneth Bafundo confirmed it. He concluded: ‘... as growth periods shorten, effective use of pigmenting agents [and nicarbazin has this effect] earlier in the life cycle may become more important (Bafundo, 1988)’.

### **The VMD suppresses expert toxicological advice**

Dr Derek Renshaw, senior toxicologist at the Food Standards Agency, is concerned about the sparse information on which decisions about nicarbazin have been made.

He wrote in a letter to the VMD, on 4 October 1999: ‘You may recall that on several occasions at the [VMD’s] Advisory Group on Veterinary Residues, I ... have asked for details of the toxicology of nicarbazin. On each occasion, Dr Lawrence has offered to supply the data, but to this date I have received nothing.’

Commenting on the JECFA evaluation of nicarbazin, Dr Renshaw said that what jumped out at him was the inadequacy of investigations for mutagenicity: only bacterial assays have been performed.

Noting that the reports of SCAN’s evaluation of the drug give insufficient detail (CEC, 1984), Dr Renshaw says that why SCAN set a different, lower, ADI than JECFA is not clear.

Dr Renshaw concluded, in his letter: ‘As there have been gaps identified in the toxicological data on nicarbazin and as there are inconsistencies between the decisions of the two committees that have seen these data, I feel uncomfortable when asked to comment on the consumer health significance of any residues of nicarbazin found in foods.

‘For this reason, I feel that the manufacturer (represented by Dr Lawrence) should provide us with all of the toxicological data on this substance. It may be best if this could be kept on an informal basis. As I understand the situation, nicarbazin is a feed additive that is not used as a veterinary medicine, so VMD do not have the powers to require the company to submit data.’

A copy of this letter, intended for Dorothy Craig, a VMD consumer representative, was inadvertently faxed to Alison Craig, co-author of this report. Dr Renshaw has since told us that, when the VMD were questioned about the letter, they and the Department of Health put intense pressure on him to withdraw the statements he had made. ‘Colin Penny was annoyed with me, Andrew Wadge was annoyed with me!’ [Colin Penny was head of the residues surveillance department, VMD, until July 2000; Andrew Wadge is now head of Chemical Safety and Toxicology Division, Food Standards Agency].

So, writing subsequently to Alison Craig on 7 October 1999, Dr Renshaw claimed to have had a head cold when he wrote the first letter, suggesting that, with regard to his repeated requests to Dr Lawrence for more toxicological data, he had mixed nicarbazin up with another substance. He has since admitted that his letter did, in fact, refer to nicarbazin. He said that the VMD were so angry with him for accidentally allowing these concerns to be seen by the wrong party that in his annual DoH staff review his manager recorded the incident as a disgrace on his part.

One of the oldest anticoccidial drugs around, nicarbazin is often presented as safe because it has been used for so long. Dr Keith Lawrence, Technical Manager at Elanco, who market the drug on behalf of the Israeli manufacturer, Koffolk, says: 'Nicarbazin is probably the safest product on the farm. You can eat it like a spice. It is not a product that anyone has any toxicological concerns about.'

Yet, mysteriously, the regulators insist on the longest withdrawal period of all the anticoccidials for nicarbazin: 9 days. It is evidently a substance which is highly persistent in biological organisms.

The truth about its toxicity may emerge during the current EU review due to report in October 2003, by the European Union's Scientific Committee for Animal Nutrition. In the meantime, the last official authoritative evaluation was JECFA's in 1998 (Joint FAO/WHO Expert Committee, 1999). JECFA set an MRL of 200 micrograms per kg (ADI of 24,000 micrograms), even though there were not enough toxicological studies to form a scientific basis for doing so:

*The Committee noted the absence of certain toxicological studies in support of an ADI for nicarbazin. However, the other data available provided sufficient information to overcome the majority of these deficiencies. It was noted that nicarbazin has been used in veterinary medicine in many countries for over 40 years. On the basis of this long history of use and because use is restricted to starter rations in boiler chickens, the Committee considered that an ADI could be established.*

The JECFA ADI includes an arbitrary safety factor of 500 – 'chosen to account for limitations in the available data'. However, toxicologists, including Dr Alastair Hay, at Leeds University, refute any suggestion that, just because a drug has been used for a long time, it means it is safe.

In fact Dr Renshaw may be right to question the tests for the mutagenic properties of

nicarbazin. When Dr Frank Sullivan, formerly a senior toxicological advisor to the Department of Health, and a former member of the government's Committee on Toxicity, now retired, was shown the JECFA 1998 evaluation, he remarked, 'What's clear is that the mutagenicity package [of tests] is too small.'

While expressing his belief that nicarbazin has low toxicity he also noted one finding in particular. In a study on developmental toxicity examined by JECFA, when rat dams were dosed with nicarbazin at 600 milligrams per kg, their pups were found to have lowered body weight, reduced ossification suggesting retarded foetal development, hydronephrosis, and hyperplastic and bent ribs.

In a subsequent telephone conversation, 15 October 1999, Dr. Sullivan said that finding bent ribs is common in such tests, and reduced ossification and hydronephrosis are not unexpected. But he said he had never seen 'hyperplastic' (meaning enlarged) ribs before.

*This is very unusual, and I would question it. Hypertrophy – when an organ is big – occurs either because the cells are bigger, or because there is more than the usual number of cells.*

Dr Vyvyan Howard, Foetal and Infant Toxicopathologist at Liverpool University, cannot rule out the possibility, from the studies analysed in the JECFA report, that nicarbazin is mutagenic in mammals. Also in a telephone conversation he expressed the opinion that,

*The developmental study results are likely to be the most sensitive end points, and the drug could be bioactive at low doses. We also need to know how long it lasts in the body.*

## Nicarbazin: contamination

### Summary of current nicarbazin contamination

Poultry meat 98	Eggs 98	Poultry meat 99	Eggs 99
<p><b>Statutory scheme:</b> 58 liver samples (249 tested) from 100 to 7,200 micrograms per kilo <b>23 percent</b></p> <p><b>Northern Ireland scheme:</b> 2 livers from 322.3 to 3,693 micrograms per kilo</p>	<p><b>Statutory scheme:</b> 7 eggs (175 tested), from 10 to 320 micrograms per kilo <b>4 percent</b></p> <p><b>Non-MAFF scheme:</b> 1 organic egg (of 3) at 15 micrograms per kilo</p>	<p><b>Statutory scheme:</b> 47 poultry liver (of 264) from 210 to 10,500 micrograms per kilo <b>17.8 percent</b></p> <p><b>Northern Ireland scheme:</b> 1 liver with 415 micrograms per kilo</p>	<p>Not found (see below).</p>

Source: Annual reports on Surveillance for Veterinary Residues, VMD  
The EU MRL for nicarbazin is 200 micrograms per kilo (JECFA). In 1998 the VMD AGVR set a 'Differential Action Level' of 100 micrograms per kilo as a guideline to determine follow-up action; in 1999, the VMD used the JECFA MRL of 200 micrograms per kilo.

Since July 1999: of 700 poultry livers tested, 127 (18 per cent) have residues of nicarbazin above the MRL (VMD Medicines Act Veterinary Information Service, 34 to 38). Nine eggs have also been found with residues.

The 'VMD/Industry initiative' to reduce the incidence of nicarbazin residues commenced in July 1999 (see below) since when reported positives have been lower.

Do nicarbazin residues in livers mean that the muscle of the bird, which is eaten much more commonly, is contaminated? According to 'depletion' data (when the metabolism and excretion of the drug is traced in different

organs and tissues) there is a known relationship: 'In chickens, raised with 125 micrograms per kilo feed of nicarbazin, a steady state residue level of 240 to 390 micrograms per kilo in liver, and 8 to 10 micrograms per kilo in muscle, is still found after three to four weeks withdrawal', according to the EU Scientific Committee on Animal Nutrition, 1991.

And Maggie Green, of the VMD, when questioned why livers are sampled for residues, rather than muscle, says: 'because there's likely to be a higher level than in muscle, [so] we're actually providing a much clearer picture of what's there than if we look at muscle'.

### Five forms of nicarbazin are authorised for use on broilers in the UK

Drug	Product	Form	Withdrawal period	Authorisation holder
Nicarbazin/Narasin	Maxiban	granular particles	5 days	Eli Lilly
Nicarbazin	Carbigran	free-flowing solid	9 days	Koffolk (marketed by Elanco)
Nicarbazin	Nicarmix	n/a	9 days	Eurotec Nutrition
Nicarbazin	Elancocin	n/a	9 days	Eli Lilly
Nicarbazin	Koffogran	n/a	9 days	Koffolk

Source: VMD, 9 November 2000  
n/a not available

## Nicarbazin and the VMD

### Lies, damned lies and statistics

**1998** 'Poultry – out of 8,155 samples of liver, kidney and feed tested: 8,055 (98.8 per cent) were free of detectable veterinary residues; 4 (0.05 per cent) contained concentrations of veterinary residues below the MRL or Action Level; 96 (1.2 per cent) contained concentrations of veterinary residues above the MRL or Action Level (or 'positive').

**Eggs** – 512 samples of battery, free range and perchery barn produced eggs (a sample is made up of a dozen eggs) were collected on which 1,212 analyses were carried out: 499 samples (96.5 per cent) were free of detectable residues; 13 samples (2.5 per cent) contained residues above the Action Level (or 'positive').

Annual report on Surveillance for Veterinary Residues, VMD, 1998

**1999** 'Poultry – Out of 8,063 samples of liver, kidney and feed tested: 8,007 (99.3 per cent) were free of detectable veterinary residues; 48 (0.6 per cent) contained concentrations of veterinary residues above the Action Level (or 'positive'); 8 (0.1 per cent) contained concentrations of veterinary residues below the Action Level.

**Eggs** – 525 samples of caged, free range and perchery barn produced eggs (a sample is made up of a dozen eggs) were collected on which 1,331 analyses were carried out: 509 samples (96.9 per cent) were free of detectable veterinary residues; 2 samples (0.4 per cent) contained concentrations of residues above the Action Level (or 'positive'); 14 samples (2.7 per cent) contained concentrations of residues below the Action Level'.

Annual report on Surveillance for Veterinary Residues, VMD, 1999

'Statutory surveillance was extended to poultry and eggs in 1998 and the 1999 results show that 99 per cent of poultry meat samples and 97 per cent of egg samples are free of detectable residues'. Facts About Veterinary Residues in Food, VMD

**'If that is what we said, that's what we mean, and I would very much hope it is correct'**  
**Eric Crutcher, head of residues surveillance department, VMD, 21 May 2001.**

Poultry and eggs were included for the first time in the VMD's residue surveillance scheme in 1998 (VMD Annual Report on Surveillance for Veterinary Residues, 1998) (to comply with European Union Directive 96/23/EC).

In their 1998 summary for poultry, the VMD declares that 98.8 per cent of samples tested were free of detectable veterinary residues.

This is to omit to mention that 23 per cent of chicken liver samples were contaminated with nicarbazin above the JECFA MRL of 200 micrograms per kg – one was, at 7,200 micrograms per kg, 36 times the permitted level.

Nicarbazin contamination of eggs – it is not licensed for use in laying hens – was 10.7 per

cent in 1996, 6.8 per cent in 1997 (of which 1.4 per cent was above the permitted level), and 4 per cent in 1998, of which 0.6 per cent was above the permitted level.

According to the VMD 'the likely cause of these residues is contamination at a feed mill, during transport and/or inadequate cleaning out of hoppers and lines between batches of feed at farms. We are taking this up with the industry and fully expect to see a significant reduction in the numbers of positive samples found in 1999 (VMD Annual Report on Surveillance for Veterinary Residues, 1998)'.

Yet in 1999, 18 per cent of poultry liver tested contained nicarbazin in excess of the JECFA MRL. This time the highest residue was

52 times the permitted level. But in the summary for poultry, the VMD claimed that 99.3 per cent of samples were free from detectable residues.

Asked why these levels have not been included in the summaries, David Lewsey of the VMD replied 'Nicarbazin is classed as a zootechnical feed additive, not a veterinary medicine'.

The VMD have known since 1995 that nicarbazin residues in eggs were very high. Colin Penny, formerly head of the residues surveillance department of the VMD, said, in 1999: 'Nicarbazin started to appear in eggs 3 to 4 years ago. There were persistent low levels of nicarbazin, then a gap, then high levels. 'The reason they occurred is the electrostatic properties of the drug in the feedmills. But the big ones aren't caused by that – feed lots are being muddled up. You could have dedicated mills, but cost effectiveness does come into it.'

The VMD have done nothing to inform consumers or the Food Standards Agency about this problem. Even Mrs Dorothy Craig, consumer representative on their Advisory Group on Veterinary Residues was kept in the dark: she was not invited to meetings held throughout 1999 with industry, including UKASTA, BPMF, NFU, NOAH, RPSGB and JFSSG.

Copies of the AGVR's minutes were requested for this report from the VMD, but so far they have not been disclosed.

The VMD have been working 'behind the scenes' with industry, attempting to bring levels down before they are noticed. Repeatedly claiming that the nicarbazin crisis is 'not a public health risk', they boast a 'campaign to prevent nicarbazin residues': exclusively a dialogue with industry partners.

The VMD have now even handed to industry the job of investigating and following up positive samples (VMD Annual Report on

Surveillance for Veterinary Residues, 1998). 'The VMD and SVS must provide more consistent and comprehensive information on positive findings to key industry personnel more quickly', they state. This group is highly secretive. When we asked the VMD how many members it has, how many companies are involved, and to see any reports it has generated, we were told that this was not 'the basis of the agreement'. Such an arrangement effectively means that no producer will ever be prosecuted for contaminating food with nicarbazin, however grossly high the residues.

A likely factor contributing to such high residues is a failure to observe the withdrawal period of the drug. But the poster the VMD have issued to industry simply includes the following guideline:

'Do not remove birds for early slaughter while they are consuming feed containing nicarbazin'. There is no indication that to do so is illegal.

We asked the VMD about their policy on prosecution, as they claim, in their leaflet *Facts About Veterinary Residues in Food*, that they will prosecute where there are 'serious shortcomings or deliberate misuse'.

Eric Crucher, head of the residues surveillance department, says: 'If we find a case where there's an MRL and it is substantially above the MRL we will try and prosecute and we will ask an investigation officer at MAFF's legal branch to conduct an investigation. But given resources and so on you're not going to go out and prosecute every single one, you're going to find one where you're fairly sure it's been deliberately being done, or where someone has been so careless you take a prosecution to avoid it happening again'.

But for nicarbazin residues, no-one has been prosecuted. Eric Crutcher, when we asked him about the possibility of such a prosecution said, 'Oh, nicarbazin. I don't think we actually ... we don't actually send the SVS out for nicarbazin,

### **The real reason for nicarbazin residues?**

Perhaps one cause of the problem lies in the broiler house itself. The natural behaviour of poultry is to peck at the ground, feeding on vegetation, insects and soil organisms, and using the beak as an exploratory tool. In the broiler house, these activities are denied the birds. There is nothing in their environment apart from feed, water, and the manure-covered litter on which they stand. Broilers are bred to grow to slaughter weight in the least possible time: they are continually hungry and seeking food. So in the broiler house they must peck at the floor, ingesting their own excreta.

Jeremy Johnson of Schering Plough points out that nicarbazin is, in effect, commonly recycled by floor-reared birds eating their own faeces, which contain high levels of the drug, and a German study confirms it (Friedrich et al, 1984).

The problem is also euphemistically described in a report by SCAN (the EU's Scientific Committee on Animal Nutrition) in 1991:

'In chickens, raised with 125 micrograms per kilo feed of nicarbazin, a steady state residue level of 240 to 390 micrograms per kilo in liver, and 8 to 10 micrograms per kilo in muscle, is still found after three to four weeks withdrawal, due to cross contamination from stable nicarbazin residues in the litter. Despite the low tissue residues and the absence of significant differences there is a trend to increasing residue levels in time.'

would we?' His colleague Maggie Green, however, said they do, claiming that every nicarbazin positive in 2000 was 'followed up one way or the other'.

The VMD insist that these nicarbazin residues are due to 'cross-contamination at feedmills'. Yet, when questioned about this, Maggie Green says that it is the Royal Pharmaceutical Society's remit to inspect the mills, not the VMD's.

An industry-wide campaign by the VMD claims to have successfully reduced residues of sulphonamide in pigs over a ten-year period from 12 per cent in 1988 to 0.4 per cent in 1998. On this basis, we should expect illegally high residues of nicarbazin in poultry and eggs until at least the year 2008.

Reviewing one of the first MAFF residue reports of analyses from 1979 to 1985 in the British Medical Journal, Professor Truswell noted an early dilemma: 'Choices have to be made between random sampling of the main abattoirs in proportion to their throughput and sampling tissues from special subgroups of

animals that seem particularly likely to have been given the drugs (Truswell, 1988).' Yet despite these residues, the VMD is not prioritising poultry muscle and eggs as such a 'special subgroup': the Annual Plan, 2000 (for non-statutory surveillance), does not include any such precautionary checks.

### **Case study: the potential for nicarbazin poisoning of pregnant women and the foetus**

The mutagenicity, and other toxic properties of nicarbazin, have not been properly established: the studies on which the current MRL has been set were inadequate. Nicarbazin is not licensed for use in laying hens because it creates hormonal imbalance (Luck, 1979) and seriously affects egg development.

According to the National Food Survey (National Food Survey, 1998/99), women aged between 25 and 34 ate an average of 67 eggs each in 1998 (excluding in processed foods). Nicarbazin contaminated 4 per cent of these at high levels.

They also ate an average of 9.41 kilos of poultry meat: nicarbazin contaminated 23 per

cent of the poultry livers tested. In 1999, they ate 9.04 kilos of poultry: nicarbazin contaminated 18 per cent of the poultry livers tested.

These vulnerable groups are also being exposed at regular intervals to dimetridazole in both poultry meat and eggs.

### Why such high residues?

Under the Feedingstuffs (Zotechnical Products) Regulations 1998, all mills manufacturing or distributing any feed additive, premixture or compound that contain them, had to apply for official registration with the Royal Pharmaceutical Society of Great Britain, which has since then 'enforced [the regulations] initially in an advisory manner (Royal Pharmaceutical Society of Great Britain)'.

RPSGB enforcement, however, appears to have had no effect in reducing nicarbazin residues. An interesting record which raises questions about its rigour appears in UKEPRA News (the newsletter of the United Kingdom Egg Producers' Association) of 10 December 1999, under Phone Calls Received:

*A phone call this week from Neville Kearsey of SCATS feed company, reminding readers of several points which ought to be second nature but which he finds frequently amiss as he goes round the farms.... Bulk bins: these should be run down every month. He often finds that they are never emptied beyond the 3 tonne remaining stage ... thorough knockdown is also essential.*

As far as feedmills are concerned, the industry and retailers now regard dedicated mills as the way forward, evidently because the task of maintaining hygienic separation of medicated and non-medicated feed is too difficult. Ironically, coccidiosis specialist Larry McDougald wrote, of coccidiosis control: 'Of extreme importance is the technical capability of feed mills to blend feeds with low concentrations of relatively toxic drugs' (Long, 1982).

## THE IONOPHORES

### THE TOXICITY OF THE IONOPHORES

The ionophores are produced naturally by fermentation and are technically antibiotics. Six of them are used for the control of coccidiosis and the group as a whole is known to be highly toxic. Lasalocid, maduramicin, monensin, narasin and salinomycin, have a narrow range of safety: their lethal dose is generally no higher than two to three times the recommended dose. There are many reports in the literature of accidental intoxications of target and non-target species, and ionophore poisoning is a well known problem in poultry (Commission on Antimicrobial Feed Additives).

These drugs possess potent cardiovascular properties: they act on the heart and skeletal muscles at very low levels. Lasalocid has even been shown to cause contraction of human heart muscle in the laboratory (Levy and Inesi, 1974). No studies have examined whether rates of human heart disease are higher in people who consume eggs containing residues of lasalocid.

Monensin is another drug which induces coronary vasodilation in dogs and rabbits at low concentrations. In dogs, the cardiovascular effects of monensin can be detected at doses as low as 1 microgram (one millionth of a gram) per kilo body weight (Pressman and Fahim, 1983).

Some ionophores are much more toxic than others to different species. It is well known that horses are extremely susceptible to all of them, and most products containing ionophores carry a warning to keep away from equines. But cats are also remarkably sensitive: an outbreak of feline illness in 1996 was linked to cat food containing traces of salinomycin (Wheeler, 1997). Which of the ionophores are most toxic to humans is not known because such comparative experiments can not be carried out.

A study in 1999 attempted to rank the ionophores according to their chronic toxicity to

different species. The scientists found considerable variation, but in general maduramicin, followed by lasalocid then narasin were the most toxic (Oehme and Pickrell, 1999).

There is some evidence that these drugs will remain in the body when in combination with other chemicals. In a laboratory study, the elimination of monensin in rat liver was reduced by sixty per cent when tiamulin was added (Meingassner et al, 1978). If accumulation occurs, the chances of intoxication are increased.

People taking antibiotics against infection should not be exposed to residues of the ionophores. Monensin, narasin and salinomycin can interact with antibiotics such as chloramphenicol, erythromycin and oleandomycin; lasalocid interacts with chloramphenicol and sulphadimethoxine; lasalocid and monensin with furaltadone and furazolidone; and monensin with sulphaquinoxaline, sulphamethazine and sulphadimethoxine (Commission on Antimicrobial Feed Additives, 1997).

As we have seen, the mixing of drugs at feedmills is far from an exact science and mistakes are made. Feed can become cross-contaminated – traces of anticoccidials have been found in pet food as a result (Wilson 1980, Wheeler, 1996) – or else the drugs can be poorly mixed in, creating uneven concentrations.

A drastic but typical result occurred in 1982 (The Veterinary Record, 1982), when three houses of young chickens all became paralysed; they were found to have eaten feed containing monensin at 530 parts per million compared to the recommended level of 100 to 120 ppm.

Mortality in the broiler house due to poisoning by ionophoric anticoccidials may occur much more frequently than reports in the scientific literature suggest. Intoxication by these drugs is not easy to diagnose. Symptoms in laboratory animals include anorexia, hypoactivity, leg weakness, ataxia, dyspnea, depression and diarrhoea. There is no blood test

to detect the drug, and 'significantly greater than recommended use levels of ionophores in the feed must be found for confirmatory diagnosis of ionophore toxicity' (Novilla, 1992).

This may be a factor underlying the extent of heart disease in broilers, which is well-recorded.

Leg weakness, commonly suffered by broilers, can also be caused by monensin-poisoning (Oehme and Pickrell, 1999).

### **Ionophore toxicity in turkeys**

Letter in The Veterinary Record, January 27, 2001, from Geoff Pritchard and Heather Ainsworth

'Sir – Each year, the rearing of turkey poults for the Christmas trade brings with it incidents of ionophore toxicity ... Ionophores, such as salinomycin, narasin, lasalocid and monensin, are used in varying concentration in poultry feed as anticoccidial agents ... Clinical signs [of toxicity], which can develop within 24 hours, comprise muscular weakness with collapse, gasping respiration (mouth breathing) and death. Morbidity and mortality are often very high. In a recent outbreak in East Anglia 178 (24 per cent) of 750 turkeys aged 12 to 18 weeks died or were euthanased during a period of a few days shortly before Christmas.

The main situations under which ionophore toxicity occurs in turkeys are: inadvertent use of broiler or other feed containing ionophore; continuing to feed rations containing ionophore to older birds (either accidentally or through lack of awareness); and the accidental inclusion of ionophore in feed due to contamination at the mill ...'

### **Residues of the ionophores in Christmas turkeys: the role of the AGVR**

Before the establishment of the Food Standards Agency, total responsibility for the surveillance of food for dangerous drug residues was taken by MAFF's Veterinary Medicines Directorate.

The supposedly independent group scrutinising this activity was the Advisory Group on Veterinary Residues (AGVR), comprising representatives from MAFF, industry and with one consumer representative, Mrs Dorothy Craig.

The AGVR was operating between 1995 and 2000. None of its minutes have been published. Eric Crutcher, head of the residues surveillance department, VMD, says that the AGVR was set up 'so that information could be swapped freely, and people could talk in confidence', like the current 'VMD/Industry initiative' group on nicarbazin residues.

This is somewhat at odds with the formal description of the AGVR, which 'ensures that the VMD's surveillance programmes are subject to independent scrutiny and advice' (VMD Annual Report on Surveillance for Veterinary Residues, 1999).

The AGVR has now been replaced by the Veterinary Residues Committee, as part of the government's attempts to be more open when dealing with food safety.

Dr Derek Renshaw, a Department of Health toxicologist, was a member of the AGVR, and an advisor to MAFF on toxicological issues since the 1980s. He said (18th May, personal communication): 'Almost every Christmas we would get high residues of ionophores in turkeys. Sometimes these ionophores were licensed for turkeys, sometimes they were illegal. We would be running around in a panic, wondering if we should pull the whole thing – get turkeys withdrawn from the supermarkets. But we never had to'.

Asked how he assessed the likely health effects of such residues, Dr Renshaw said he would compare the level with the drug's Acceptable Daily Intake (ADI) figures, published in whatever evaluations had been done. But in fact, very few of these evaluations exist: expert body JECFA have not evaluated any of them (lasalocid, maduramicin, narasin, monensin, salinomycin) (Herrman, 2000), and opinions of

the EU SCAN committee note numerous gaps in experimental data. None of these drugs have a Codex Maximum Residue Limit (Kennard, 2000).

Asked what toxicological information he had been given, during his period of service on the AGVR, he said 'Virtually none'.

Dr Renshaw expressed the view that the toxicity of the ionophores to humans is 'fairly low'. Why did he think this? 'Because people have been exposed to these high residues and not been affected.'

While there are many studies of these substances from tests performed on laboratory animals which indicate their toxicity, but there are none on humans, since it is clearly not possible to test their effects directly on people.

Professor Peter Sugden, Professor of Cellular Biochemistry at the National Heart and Lung Institute (Cardiac Medicine), however, observes:

*Certainly, ionophores such as monensin have cardiovascular effects. For example, low dose monensin increases coronary blood flow and reduces peripheral resistance in dogs (Saini et al, 1979). It also has direct effects on the heart at high concentrations, being positively inotropic and increasing cardiac output ... However, I rather suspect that the non-cardiovascular effects of ionophores such as monensin may cause a greater problem than the cardiovascular effects. No doubt they would have cardiovascular effects eventually, but it is more likely that you would detect neurotoxic effects first.*

*There seem to be an awful lot of toxicological studies of these compounds, and I am sure that the animal work here is more than adequate to support the postulate that these are potentially toxic in humans. I think one can extrapolate reasonably from animals in these cases: the processes of neuronal ion movements are not significantly different between species.*

*I have never seen any suggestion that these drugs are ever going to be used therapeutically, presumably because the risks of exposing people to high doses therapeutically outweigh the potential benefits.*

## LASALOCID

### The toxicity of lasalocid

Lasalocid is not authorised for use in laying hens, only broilers. But of the 27 million or so eggs a day eaten in the UK, at least one in every dozen is contaminated with this drug. Of the ionophores, lasalocid has by far the greatest potential for causing residues in eggs (Kennedy et al, 1998). In 1994 a team of scientists in Northern Ireland discovered that 66.5 per cent of the eggs they sampled contained residues of the drug. However, since 1983, when it was authorised in the EU, residue levels remained largely unknown elsewhere in the UK until eggs were included in the statutory surveillance programme in 1999.

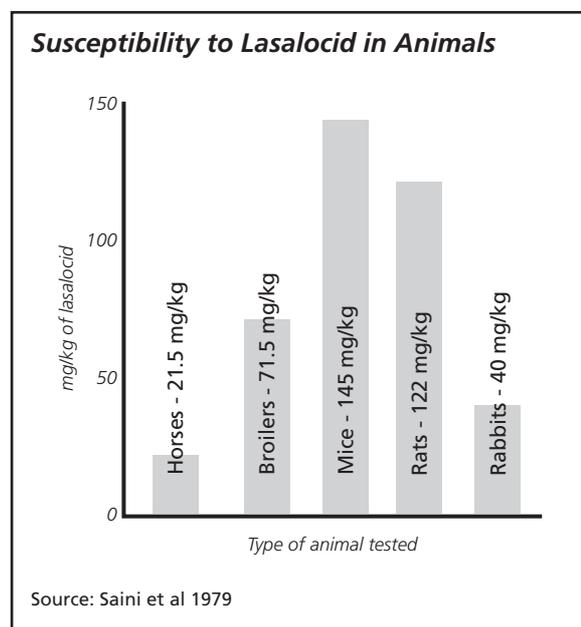
According to the VMD, the picture is less alarming: they record that 'the overall incidence of lasalocid in eggs has dropped from 10.7 per cent in 1994 to 1.1 per cent in 1998' (VMD Annual Report for Veterinary Residues, 1998), attributing the decrease to the introduction of a granular, instead of powder, formulation in 1996. The following year they had to revise this reassuring summary, having found that 8.5 per cent of eggs were still contaminated.

A sample is made up of a dozen eggs. However, since only some eggs are contaminated this pooling could dilute the residues in individual eggs below detection limits. The VMD maintains that all eggs from individual suppliers are likely to contain similar residue levels. Yet, if this is true, the actual percentage of contaminated eggs could be significantly higher than figures suggest as the contaminated eggs could be coming from the largest producers. There is no data on how representative sampling is of the industry structure.

The EU's Scientific Committee for Animal Nutrition has established an Acceptable Daily Intake for lasalocid of 5 micrograms per kilo bodyweight per day (July 1990); but whether this in reality protects consumers against the effects of this drug is questionable. The discovery in 1996 that lasalocid persists in eggs

for ten days after the withdrawal of medicated feed (Kennedy et al, 1996) suggests it could accumulate in humans exposed to traces on a daily basis.

Toxicological testing of lasalocid on animals has been carried out, indicating that there is wide variability in the susceptibility of different animals to the drug, and that it is highly toxic: the oral LD<sub>50</sub> – the lethal dose to 50 per cent of the test animals – is very low for most animals (Safran et al, 1993):



Cattle given 50 mg of lasalocid/kg had muscle tremors in the flank, anorexia, high respiratory and heart rate. Cardiomyopathy with congestive heart failure was also a common finding in cattle. A transient muscle weakness was observed in swine given 35 mg of lasalocid/kg, and death occurred when they were given 58 mg of lasalocid/kg at one time (Safran et al, 1993).

There is no EU MRL for lasalocid. In 1999 the VMD AGVR set a 'Differential Action Level' of 100 micrograms per kilo as a guideline to determine follow-up action.

**Lasalocid contamination, at extremely low levels, of dogfood, causes paralysis in dogs**

The severe effects of this drug at very low doses on dogs, accidentally poisoned by lasalocid-contaminated dogfood in Israel in 1993 (Safran et al, 1993), again raise the question of how toxic the drug is for humans.

The dogs suffered complete paralysis, including respiratory muscle paralysis in some cases, and took up to 50 days of treatment to recover. They suffered muscle weakness which progressed from the hind to the forelimbs, then paralysis of all limbs, difficulty breathing, and even cessation of breathing in the worst cases.

Laboratory tests revealed residues of lasalocid in the dogfood which the dogs had been fed, at 166 to 210 mg/kg of food. But the authors then experimented on dogs subsequently, to verify their diagnosis, and found

that the test dogs were susceptible to as little as 10 to 15 mg of lasalocid/kg of body weight, making them as sensitive as horses to this drug.

The authors, observing that there is a 'marked difference in the species susceptibility to lasalocid' and that 'the present state of our knowledge regarding the mechanism of action of ionophores as neurotoxins is scant ..', warn that 'the routine use of lasalocid as an anticoccidial agent in poultry feed also has the potential for leaving toxic residues of this substance in human food. This is especially important in the light of the unexpectedly low dose of lasalocid that caused clinical signs in the dogs. Although we do not have data on the concentrations of lasalocid that would cause clinical signs in human beings, we speculate that if the toxin has an accumulative effect, small residues in food for human consumption may potentially lead to subclinical effects in people'.

**Lasalocid: contamination**

**Summary of current lasalocid contamination. Lasalocid is not licensed for use in laying hens.**

Poultry meat 98	Eggs 98	Poultry meat 99	Eggs 99
<p><b>Statutory scheme:</b> 3 livers (237 tested), at 62, 63 and 140 micrograms per kilo <b>1.26 per cent</b></p>	<p><b>Statutory scheme:</b> 2 eggs (175 tested) at 43 and 60 micrograms per kilo <b>1.1 per cent</b> <b>Northern Ireland scheme:</b> 3 eggs at 9.7, 26 and 29.2 micrograms per kilo</p>	<p><b>Non-MAFF sources:</b> chicken muscle 5 samples (of 39): 7, 11, 20, 25, 52 micrograms per kilo <b>12 per cent</b></p>	<p><b>Statutory scheme:</b> 16 (of 188): <b>8.5 per cent</b>; 1.6 per cent above DAL <b>Non-MAFF sources:</b> not reported</p>

Source: Annual reports on Surveillance for Veterinary Residues, VMD

*Since July 1999:* 22 egg samples have had lasalocid residues above the DAL, 22 below; 5 samples of quails' eggs have had residues above the DAL at concentrations between 120 and 5,400 micrograms per kilo; 3 samples of quail muscle have been found to have lasalocid residues (VMD Medicines Act Veterinary Information Service, 34 to 38).

**Case study: the potential for lasalocid-poisoning of the elderly**

Lasalocid is a potent cardiotoxic drug, which is not licensed for use in laying hens.

According to the National Food Survey (National Food Survey, 1998/99), the people who eat the most eggs are from 65 to 74 years old. In 1998, they ate a minimum of 137 eggs each, 130 in 1999; excluding eggs in the processed foods. Lasalocid contamination of eggs occurred in 1.14 per cent of eggs in 1998, and 8.5 per cent of eggs in 1999.

Pensioners also ate an estimated 15.65 kilos of poultry meat each in 1998, of which 1.26 per cent was contaminated with lasalocid. In 1999, they ate 12.9 kilos of poultry meat; lasalocid contamination of five samples – 12 per cent – of chicken muscle was found.

### THE OTHER IONOPHORES

#### The toxicity of maduramicin

This drug was first authorised more recently than the others, in 1992. Its licence runs through to 2009 (Demade); currently only one anticoccidial containing it is permitted for use in Europe on broilers and turkeys.

The lethal effects of maduramicin at low doses can be seen in another intensive farming practice: feeding poultry litter – excreta – to cattle and other animals. This is done to bulk out feed and to reduce costs.

The use of faeces in feed was banned in Europe under the Feedingstuffs Regulations 1995. UKASTA deny that the practice, which was standard throughout the 1980s, continues in the UK. The regulations are enforced by Local Authority Trading Standards departments, but no test has been developed by public analysts to check for this contaminant in animal feed, and the Local Authorities Coordinating Body on Food and Trading Standards, LACOTS, are unable to say whether or not any contraventions have been detected or prosecuted (Du Val, 1998). Processors of byproducts for use in animal feeds are highly secretive about the ingredients they are currently using. These vary according to price fluctuations and availability (Mounsey).

A number of studies record the disastrous consequences of feeding cattle poultry waste containing residues of maduramicin. In one, fifteen outbreaks of toxic-waste induced heart failure in cattle and sheep in South Africa are recorded (Fourie et al, 1991). The unfortunate creatures were being fed poultry manure at up to 80 per cent of their ration. Within 20 to 40 days, up to 70 per cent of the herd or flock suddenly died. At post mortem the hearts of the animals were found to have cardiac dilation, or extensive hypertrophy and atrophy of the myocardial fibres. Remarkably, the drug was at very low doses: only 2.5 parts per million, or 6.1 parts per million.

A team of Israeli scientists also confirmed in 1992 that maduramicin is lethal to cattle (Perl et al, 1991). Sudden deaths were occurring at numerous farms throughout the beef-cattle-raising areas of Israel. Some of the cattle were eating more than 10 kilos of dried poultry manure per day, when the maximum amount stipulated was 3 kilos per head per day. Their subsequent analysis found that, even at the level of 4.8 parts per million, commonly found in the manure, maduramicin is cardiotoxic (Schlosberg et al, 1992).

#### The toxicity of monensin

First authorised for use in the EU in 1974, monensin has had massive market success. Larry McDougald wrote, in 1982: 'After its introduction in the US in 1971, monensin quickly became the product of choice for broiler chickens and has since set records for market penetration in most world markets. With over 80 per cent of the market in the US for several years, monensin has been fed to more chickens than any anticoccidial drug in history. The continuing success of this group of compounds is a result of 1) broad spectrum activity against six species of coccidia in chickens, and 2) lack of serious problems with drug resistance (Jeffers, 1978) (Long, 1982)'. But soon after this was written, resistance to monensin used in turkeys was noted (Jeffers and Bentley, 1980).

Monensin is popular for its 'feed-conversion-ratio' improvement effects, and during trials of anticoccidials carried out by Schering Plough, a 'feed-sparing' effect was also noted (Johnson), when birds on the drug consume less feed. Its toxic effects include an interference with feather growth in young chickens, and hyperexcitability (Kingston, 1977). Its toxicity at very low doses varies not only between species, but between breeds of chickens: White Rock hens were found to be more susceptible than Leghorn cross Rhode Island Reds in 1994 (Weisman et al). There is also a gender-specific effect: in LD<sub>50</sub> tests, the drug was tolerated less well by female rats and dogs, while the opposite

was observed in mice (de Sousa Spinosa et al, 1999).

Monensin toxicity was found to cause chicks to lose weight and go off their feed, even at the recommended dose for coccidiosis control, more markedly than salinomycin (Harms et al, 1988).

The drug is also cardiotoxic. 'At low concentrations, monensin increases coronary blood flow (Kabell et al 1979). In ischaemic areas of cardiac tissue, blood flow is already maximised in an attempt to maintain optimal perfusion of these areas. Induced dilation, by an ionophore, of normal coronary vessels would tend to further reduce the perfusion of an already compromised area, an effect known as coronary steal' (Kennedy et al, 1995).

Most disturbingly of all, the effects of monensin on the early development stage in life of organisms have been recorded. Indeed it is during the first few days in the growth of the *Eimeria* protozoa at which monensin is most

active (McDougald, 1982).

An experiment to see whether the offspring of rat mothers fed monensin were affected by the drug found that it has a 'notable adverse effect on growth with some limited effects on selective milestones of physical and functional development of the offspring during the postnatal period' (de Sousa Spinosa et al, 1999). The rat pups (whose mothers had been exposed to the drug) had decreased body weight, slower growth, and delayed incisor eruption. But *only the lower concentration of the drug* had the latter effect. The authors note that this has important implications for pregnant women.

### The toxicity of narasin

Authorised in the EU in 1984, narasin is considered safe to administer against coccidiosis at 60 to 80 parts per million (Jeffers et al, 1988).

### Ionophores in the food chain: the withdrawal period problem

In February 2001, a Warwickshire chicken farmer, Mohammed Yaseen, of Kalyal Poultry, was fined £3,000 with £3,000 costs for sending poultry to slaughter before withdrawal periods had expired on six separate occasions. Atherstones magistrates, in imposing the fine, described the matter as 'very, very serious'.

The farm was producing around 300,000 broilers a year. The contaminated carcasses had entered the food chain on at least five previous occasions: zinc bacitracin was in 12,408 of them, and salinomycin in 2,556.

A Warwickshire Trading Standards officer, on a routine visit to check medicine records at the farm, had suspected that the birds which had left that day for slaughter had not gone through a withdrawal period. A detailed analysis of feed delivery paperwork and abattoir/hauler information confirmed this was the case both on this, and on five previous, occasions.

Richard Brooks, Divisional Trading Standards Officer, Warwickshire, says: 'We were able to show that there were no withdrawal pellets [drug-free feed, to be given during the withdrawal period] on site, and none had been bought for some time'.

Asked if he thought that failing to observe withdrawal periods is common practice, Mr Brooks said he was fairly confident it was not. 'But the problem is if a slaughterhouse has a shortage, and gives a grower just a day's notice. Or if a buyer suddenly wants 4lb chickens instead of 5lb chickens. [Feed supply to broilers] is a very industrial process, which is carefully planned, and unexpected changes can cause problems.'

In a battery of toxicological tests on laboratory animals in 1994 (Novilla et al, 1994), narasin was also found to be highly cardiotoxic. It increased coronary blood flow in dogs at extremely low doses, from 0.0076 to 0.153 mg/kilo. Doses estimated to increase it by 100 per cent were as low as 0.04 mg/kilo. Experiments also found peripheral nerve damage in dogs.

Narasin is also highly toxic to turkeys, which are susceptible to all ionophores, though to a lesser extent monensin, affecting males worse than females (Salyi et al, 1988). Birds given just 40 to 50 mg/kilo of narasin suffer locomotor disorders, dyspnoea and diarrhoea, and at post mortem are found to have muscle damage that is visible to the naked eye.

### **The toxicity of salinomycin**

One of the more recently introduced ionophores, salinomycin has been authorised in the EU since 1984. It received a favourable review by the EU Scientific Committee for Animal Nutrition in September 1997. Used as a growth promoter in pigs, the drug has the same effect in broilers at 60 parts per million (Kassid, 1988). In anticipation of the inclusion of statutory random testing of poultry for veterinary residues, a team of scientists at the Department of Agriculture in Northern Ireland have relatively recently developed a test to detect salinomycin (Kennedy et al, 1995). They noted: ‘.. the cardiovascular properties of all the ionophores means that there is the potential for an adverse effect on human health’.

### **Residues in imported chicken**

A similar, and perhaps even worse problem with residues in poultry, may be found in Brazil, which is Britain’s main source of non-EU imported poultry. Annual British imports from Brazil are in the region of 30,000 tonnes.

A European Commission report, published in 1999, concerning the steps the Brazilian authorities had taken to control residues in

poultry exported to the EU, reached some alarming conclusions (European Commission, 1999). Sampling was found to be inadequate, both because sample sizes were too small and surveillance was not targeted. No surveillance was being undertaken for a number of products for which the EU requires exporters to carry out surveillance, and public laboratories where testing was carried out were found to have inadequately trained staff and outdated testing procedures. Furthermore, there are no formal procedures for taking legal action or imposing sanctions when excessive residues of veterinary medicines or environmental contaminants are found, and it is not clear that in such cases any action is being taken at all.

Perhaps most worrying of all was the lack of enforcement by Brazilian authorities of legislation relating to the distribution of veterinary medicines. Numerous outlets were found where many veterinary drugs including antibiotics were freely sold without prescription. While some drugs still required a prescription one outlet had a vet on the premises to write out prescriptions for birds he would never see. Although it is now illegal in Brazil to sell chloramphenicol and furazolidone as veterinary medicines both these drugs were found still to be available as ingredients in various veterinary products.

A similar visit by EU inspectors to Thailand, (EU, 1999) the second largest non-EU poultry supplier to Britain, in 1999, found major infringements in abattoir hygiene and document falsification, but did not consider the issue of drug residues in poultry products.

Despite this, a small number of samples of imported chicken meat tested under the UK non-statutory scheme, found no residues of antimicrobials or antibiotics in imported chicken during 2000. It is not clear whether this reflects the real situation or whether any distinction is made between EU source or non-EU source when samples are collected.

## DIMETRIDAZOLE

### The toxicity of dimetridazole

DMZ is a drug which is strongly suspected to be carcinogenic and genotoxic. It is not an ionophore, or an anticoccidial drug: it is fed to treat the diseases histomoniasis and trichomoniasis in game birds, turkeys and pigeons. DMZ is getting into poultry feed, and therefore eggs.

Those who have to handle it know that DMZ is a high-risk substance, but, unwarned consumers are also ingesting it on a regular basis, through contaminated poultry feed which leaves residues in eggs.

DMZ, first authorised in the EU in 1974, was withdrawn as a 'veterinary medicine' in 1996, but the UK is the only country in Europe to have a derogation permitting its continued use under prescription; according to Dai Thomas of the Royal Pharmaceutical Society of Great Britain: 'We have taken it upon ourselves to retain it because the House of Lords with their pheasants wouldn't contemplate its withdrawal'.

It is also authorised as a 'zootechnical feed additive' (under Directive 70/524/EEC) and is licensed as follows:

In 1998, the VMD discovered DMZ in 3 per cent of poultry feed (for species in which DMZ is unlicensed) (VMD Annual Report on Surveillance for Veterinary Residues, 1998). They were concurrently finding DMZ in eggs despite the fact that the drug is not permitted for use in laying birds: in 1998 DMZ was in four of the eggs tested. They explained: 'MAFF lawyers have advised that under the Feedingstuffs (Zootechnical Products) Regulations 1998, a method of manufacture which results in the incorporation of DMZ as an additive in feedingstuffs for animals other than turkeys and guinea-fowl cannot be permitted to continue. We have, with the RPSGB, taken this up with the feed manufacturers involved and have insisted they change their mill practice. If positive samples are found under the 1999 programme they may become the subject of prosecution action'.

They added: 'DMZ is unlikely to continue to be used as an additive. It is not being defended under the transitional arrangements for feed additives and therefore will not be authorised, probably from 1 October 1999'.

The following year, DMZ in feed for animals in which it is unlicensed appeared to have gone down: it was in just one sample of broiler feed at 3,000 micrograms per kg. This is 300 times the provisional MRL set by CVMP (which

Drug	Product	Species	Form	Treats (disease)	Authorisation Holder
DMZ	Emtryl Premix	Game birds	buff powder	Histomoniasis (hexamitiasis, trichomoniasis)	Merial
DMZ	Emtryl Pure	Game birds	yellow powder	Histomoniasis (hexamitiasis, trichomoniasis)	Merial
DMZ	Emtryl Soluble	Game birds	yellow powder	Histomoniasis (hexamitiasis, trichomoniasis)	Merial
DMZ	Emtryl Soluble	Pigeons	n/a	Trichomoniasis	Merial
DMZ	Harkanker	Pigeons	n/a	Trichomoniasis	Harkers
DMZ	Sintodim 200	Turkeys	granulated	Histomoniasis	Merial

Source: Annual reports on Surveillance for Veterinary Residues, VMD  
DMZ was added to Annex 4 of EU Regulation 2377/90 in July 1995. This means that no safe dose is recognised: it could have health effects at extremely low doses. As the 'no effect level' cannot be defined, neither can an MRL.  
n/a not available

expired in January 1995).

The VMD noted: ‘JFSSG toxicologists have advised that the possibility of the residue adversely affecting the health of a consumer cannot be ruled out. There may be a mutagenic/carcinogenic hazard to people handling such feed or consuming produce from animals treated with it’. But no prosecution was brought.

In the latest results (October 2000), DMZ in feed is up to around 2.5 per cent, with residues ranging from 100 to 350 times the old provisional MRL.

A vivid picture of the reckless use of DMZ in intensive pheasant rearing was painted by game consultant Mr John Robert Dalton (The Veterinary Record, 2000).

*The vast majority [of pheasant poults up to six days old] have no access to the outside world during this brief period. The disease syndrome for which [DMZ] is prescribed is generally described as protozoal diarrhoea, enteritis or, a misnomer, dysentery.*

*This syndrome is truly a disease of poor management, often a consequence of overstocking, poor hygiene and, sadly, the repopulation of a rearing hut that has already had one batch of poults through it in the season. Whatever happened to the adage that the most dangerous animal in the world to the young*

*of one species is a member of the same species just a little older?*

*..... I simply do not understand why most of the rations described by millers up and down the country are listed as containing dimetridazole as a standard inclusion. The ‘standard’ inclusion of it to treat a disease to which the ‘patients’ should not be exposed is simply more ammunition supplied to those who would have the product removed from our treatments list.*

The pressure on DMZ, evident in Mr Dalton’s letter, is echoed in a fact sheet recently issued by Mr Peter Cargill, Avian Business Manager at DMZ manufacturer, Merial Animal Health.

A stern reminder that the use of the products in species of bird other than those for which they are licensed is prohibited in all circumstances, it concludes:

‘The responsible use of DMZ in game birds will lead to the continuing availability of the product. Irresponsible use will ultimately lead to the withdrawal of the drug and seriously affect the viability of the UK game bird industry.

‘We are fortunate that the UK authorities have taken this approach and it is important that **everyone** involved in the use of this product is aware that **their** actions will influence the continued availability of DMZ’.

## Dimetridazole: contamination

**Summary of current DMZ contamination: DMZ is not licensed for broilers.**

Eggs 98	Poultry feed 98	Eggs 99	Poultry feed 99
<b>Statutory scheme:</b> 4 from 8 to 77 micrograms per kilo (of 194 samples); <b>2 per cent</b> <b>Non-MAFF sources:</b> 7 (of 13) at up to 13 micrograms per kilo <b>53 per cent</b>	<b>Statutory scheme:</b> 29 poultry feed (of 168), from 100 to 6,100 micrograms per kilo <b>17 per cent</b> <b>Northern Ireland scheme:</b> 1 at 500 micrograms per kilo	<b>Statutory scheme:</b> 1 (of 124); <b>Northern Ireland scheme:</b> 1 egg at 20 micrograms per kilo	<b>Statutory scheme:</b> 1 (of 233 samples) at 3,000 micrograms per kilo

Source: Annual reports on Surveillance for Veterinary Residues, VMD  
 There is no EU MRL for DMZ (although the CVMP allowed a provisional MRL of 10 micrograms per kilo which expired in January 1995) because no safe limit is recognised.

*Since July 99:* 2.5 per cent of broiler feed samples have been found to be contaminated with DMZ at high levels: of 804 samples tested, 20 were contaminated with DMZ at concentrations between 1,000 and 3,500 micrograms per kilo; 5 samples of quails eggs have also been found with DMZ residues (VMD Medicines Act Veterinary Information Service, 34 to 38).

### **DMZ: the regulatory wrangle**

Far from being withdrawn as a feed additive as the VMD has predicted, DMZ has recently been re-evaluated by the EU Scientific Committee for Animal Nutrition and declared of no risk to consumer health (EU, 2000).

Germany had recommended to the EC that DMZ should be suspended from the market, expressing doubts about its safety, and in particular, drawing attention to new scientific evidence indicating that a closely related substance, metronidazole, has been found to be genotoxic. Whereas DMZ causes an increase only in benign tumours in rats – no other carcinogenicity studies have been undertaken. Other nitroimidazoles, the group of closely related drugs which includes DMZ, cause malignant tumours.

'It is suspected that DMZ is genotoxic and carcinogenic and the conditions governing its use currently in force do not offer adequate safety guarantees, since, despite earlier findings, it has now been established that residues persist beyond the legally required withdrawal period; the exact length of the period for which they persist cannot be established' (EU, 2000).

Sweden went further, banning it as an additive in April 1999.

SCAN, however, concluded that as results in studies showing mutagenicity and genotoxicity are inconsistent, 'the weight of evidence indicates that DMZ should not be considered as a genotoxic compound in mammals'. However, the two British scientists on SCAN demurred. In their Minority Opinion, dissenting from the SCAN conclusion, they say:

*We are concerned that dimetridazole may be genotoxic. The dimetridazole molecule contains a structural alert: the 5-nitro ring. Several other compounds with a 5-nitro ring have been convincingly shown to be genotoxic in vivo. The results of genotoxicity testing of dimetridazole suggest two possible mechanisms by which dimetridazole may be genotoxic:*

*In some assays in bacteria and yeast, dimetridazole was nitroreduced to a reactive substance that caused gene mutations. Such nitroreduction may also occur in gut bacteria and in some mammalian tissues.*

The results of the in vitro comet assay show that dimetridazole, under certain conditions, can damage the DNA in mammalian cells by a mechanism involving production of active oxygen species. We cannot exclude the possibility that dimetridazole may have similar genotoxicity in vivo.

We expect that the exposure of human consumers to dimetridazole will be very low, but we can not identify a safe level of exposure.'

Even cooking does not reduce the risk: a recent study has found that although it reduces residue concentrations in eggs by between 14 per cent and 32 per cent of the original concentration, the process does not destroy DMZ (Rose et al, 1999). There is also evidence that the drug is excreted preferentially into the yolk (about 57 per cent of the total) (Posyniak et al, 1996).

## 6 USAGE: QUANTITIES AND CONTROL

**Usage Data****Sales of antibiotics/antimicrobials (tonnes active ingredient) in the UK 1993-1999 Source: VMD**

	1993	1994	1995	1996	1997	1998	1999
Total farm antibiotics/antimicrobials	475	533	608	629	564	522	411
Coccidiostats and growth promoters	114	139	124	113	121	103	66
Annual increase/decrease in coccidiostats sold		22%	-11%	-9%	7%	-15%	-36%

Source: Annual reports on Surveillance for Veterinary Residues, VMD

Between a quarter and a fifth of all antimicrobials sold for use in food animals are coccidiostats. According to VMD figures, coccidiostat sales as a proportion of other antimicrobials were highest in 1994, and formed around 20 per cent of these sales in 1998.

The VMD caution that the figures in this table are not complete. 'It has not been possible to obtain the full data, and whilst the total sales can not be estimated, it is expected to be higher than 66 tonnes' (VMD, 1999).

Roger Cook, of the National Office of Animal Health Ltd, the association representing veterinary pharmaceutical companies, declined

to provide any figures on sales of anticoccidials for this report, apart from one: their market value at the end of 1999 was £6 million.

NOAH's European equivalent, FEDESA, the European Federation of Animal Health, have called for a surveillance system to be instituted: 'The European Union and member states need to collect data on the supply and consumption of antimicrobial agents' (FEDESA, 1998). They also point to the need for a European surveillance system for antimicrobial resistance.

In 1997, some estimates were produced by UKASTA for the Science and Technology Committee of the House of Lords:

Feed	Total tonnage	Percentage containing anticoccidials/antiblackhead
Broiler starter	349.7	100
Broiler grower	1,399.0	100
Broiler finisher*		
Turkey starter		
Turkey grower	746.7	100
Turkey finisher*		
Chicken starter	145.2	Circa 80
Other poultry (eg duck, geese & game)	324.5	Circa 50
Layers for egg production	932.3	0
Breeder/rearer	384.3	Circa 70

\*There are withdrawal feeds made available which do not contain anticoccidials or antiblackhead additives but may contain growth promoters for which the withdrawal period is nil.  
Source: UKASTA

UKASTA claims that their Feed Assurance Scheme (UFAS) 'will certainly serve to reduce the risks of cross-contamination which might otherwise result in medicinal residues occurring in the 'wrong' feedingstuffs. We believe that UFAS presently covers at least 90 per cent of the commercially manufactured feedingstuffs sold in the UK' (Reed, 2000).

The VMD's figures on antimicrobials, published in May 2000 in response to recommendations made by the Advisory Committee on the Microbiological Safety of Food, are sparse. Minister of State for Agriculture, Baroness Hayman, said: '... we recognise that we need better information on how antibiotics and other antimicrobial products are used by farmers and I am pleased that information on sales is now publicly available' (MAFF, 2000).

Swedish consumption statistics are somewhat more thoroughly collected, and a more rigorous approach is notable (Commission on Antimicrobial Feed Additives, 1997). Their Board of Agriculture requires feed mills to report sales of medicated feed. Coccidiostats are controlled under veterinary prescription. When, in 1995, the figures did not match, the authorities knew that one or more feedmills had been supplying coccidiostats illegally, without prescription, and set about identifying which in order to take legal action.

There are also suggestions from vets and elsewhere in the UK of a large black market in some antimicrobials such as DMZ, but no reliable information is available.

### **Veterinary control?**

In practice, veterinary control over these substances is limited, even though, according to RUMA, 'under UK legislation most antimicrobial use in poultry is under the direct responsibility of veterinary surgeons' (Responsible Use of Medicines in Agriculture Alliance, 1999). The spurious nature of this role

is starkly evident in their subsequent remark:

*In general, a veterinary surgeon is expected to see the affected animal prior to prescribing medication. However, in poultry medicine, best practice in the control of infectious disease (biosecurity rules) often dictates alternative approaches.*

It is the farmer who controls anticoccidial administration.

The British Veterinary Poultry Association, in its 1998 guidelines on antimicrobials, which address the issue of resistance, pays lip service to clinical principles while supporting the agenda of the intensive poultry industry. On the one hand, they discourage vets from chemical prophylaxis: 'The use of therapeutic antimicrobial products in the absence of clinical disease or specific pathogenic infections and, in particular, long-term administration to prevent disease should not be practised without a clear justification' (British Veterinary Poultry Association, 1998).

But they then concede ground to the anticoccidials: 'It is recognised that prophylactic medication may be appropriate in certain precisely defined circumstances. Each practice should develop a written policy or protocol covering the circumstances in which this is considered appropriate'.

The British Veterinary Association has also produced recommendations. They barely refer to the anticoccidials, except to say that: 'Detailed preventive medicine programmes should be documented for all companies and/or farms. These should include all routine medications such as anticoccidials ....'

Until the Medicated Feedingstuffs Regulations were introduced in 1998, vets had to list all the other drugs being used, including anticoccidials, when prescribing therapeutic drugs. But the MFS regulations, in classifying the anticoccidials as harmless sounding 'zootechnical feed additives' in effect exempted them from vets' records. It is vital that such data-collection is reinstated on a mandatory basis.

### 7 THE ROLE OF THE FOOD STANDARDS AGENCY

The vision for the Food Standards Agency, expressed by government advisor Professor Philip James, was that its remit should cover the whole food chain 'from plough to plate' (James, 1997), and that food-safety related work, currently performed by MAFF agencies (the VMD and Pesticides Safety Directorate), should be removed from them and given instead to the FSA. MAFF, however, received 600 letters of protest from industry over the proposal to move the VMD from MAFF to the FSA (British Government White Paper), and, as a result, the government backed down.

Professor James emphasised that 'Great care is needed to ensure that food safety is not compromised by the transitional arrangements.'

His misgivings are justified. Over a year after vesting day, the FSA are still struggling with institutional procedures, and in particular, with the intransigence of the VMD. It reviewed its powers in pesticides and veterinary medicines work in December:

'Working Agreements are being drawn up between the FSA and PSD and VMD to ensure that these powers can be translated into actions. They set out how officials from the Agencies will interact and what the parties can expect from each other. PSD and VMD have very different cultures and their responses to the new arrangements reflect this' (Food Standards Agency, 2000).

Under pressure from the FSA (Atkins), the VMD were persuaded to replace the Advisory Committee on Veterinary Residues with a new, more independent committee, the Veterinary Residues Committee, which has met once.

Toxicologist and environmental health expert Dr Paul Brantom is the FSA nominee on this committee. So far he has not been an effective watchdog. Asked about residues in poultry meat and eggs, he reiterates the VMD

line that 99 per cent, and 97 per cent, respectively, are clear of detectable residues, and says that 'lasalocid has shown up in one or two eggs'. Dr Brantom has not yet seen the toxicological evaluations for these drugs.

Mrs Dorothy Craig is the consumer representative on the Veterinary Residues Committee. She says that, when the problem of nicarbazin residues in poultry meat was discussed at the inaugural meeting of the VRC, actual levels were not discussed, or given by the VMD. She too states that they are in order of one or two per cent.

An indication of the obstructiveness with which the FSA has to contend is in this response from Julie Norman, who leads on veterinary medicines within its Chemical Safety and Toxicology Division, when asked what concerns the FSA have about which veterinary residues.

'We have plans to tell people what input the FSA has made into ACP [Advisory Committee on Pesticides] and VPC [Veterinary Products Committee, the body which authorises new or renewed licenses]. This is more difficult with the VPC because VMD always cite the restraints of Section 118 of the Medicines Act as a reason for not giving out any information about what products are actually discussed at VPC meetings. FSA contributions are obviously recorded in the minutes but I can't give these to you without the VPC's agreement and they won't give it. Malachite green [an industrial chemical, unlicensed as a veterinary product, residues of which are being detected in trout] has circumvented the system because we specifically took it out of the VMD's ambit into ours where we could make our concerns etc public. You can therefore conclude that if we were really concerned about anything else we would have found a way to get round VMD's secrecy!' (Norman, 20 November 2000)

### 8 REGULATORY STATUS: THE FUTURE?

The anticoccidials have until now been the least regulated frequent-use drugs on the market. Classified anomalously as 'zootechnical feed additives' they have been exempted from the rigorous testing to which veterinary medicines have been subjected throughout the 1980s and 90s. They are simple formulation drugs, used on billions of broilers, and on other species, every day. They have entirely escaped the legislation on Maximum Residue Levels.

They are regulated in the European Union under a Directive, 70/524/EEC, which goes back to 1970. The Directive stated that: '... certain purely medicinal substances such as coccidiostats should, during a first stage, be regarded in relation to feeding-stuffs as additives, since most member states have been using them for collective prophylaxis, principally in poultry farming; whereas, however, they will be examined further if a directive on medicinal feeding stuffs is drawn up'.

However, they have never moved beyond that first stage. In 1981, when the Directive on veterinary medicines was drawn up, a system requiring products to meet strict criteria of safety, quality and efficacy, and to have an MRL, was instituted. But it was only applied to the veterinary medicines, not the coccidiostats.

Even in 1990, when a further Directive to regulate 'Medicated Feedingstuffs', all of which are required to have MRLs, was drawn up by the CVMP, the coccidiostats were specifically excluded.

So for thirty years a blind eye has been turned by legislators to these drugs. Why were they considered different? Fabia Dyer, Veterinary Assessor for the VMD, suggests an answer. Before residue detection techniques improved, the coccidiostats were thought not to leave the intestinal tract at all, and therefore were not considered medicines, capable of leaving potentially hazardous residues.

However, although this belief may have prevailed in 1970, by 1984 the science of residue analysis was very well advanced, as recorded in the report of an expert (joint committee of the Food and Agriculture Organisation/World Health Organisation (United Nations Food and Agriculture Organisation/World Health Organisation, 1984). Critically, it had been realised that: 'the presence or absence of residues following the administration of any animal drug is basically a semantic question; it depends upon the sensitivity of the analytical method used'.

Interestingly, in the latter report, the divide between veterinary drugs and anticoccidials is not recognised. 'The Consultation was particularly concerned that the lack of available information for accurately assessing the safety of residues in foods of many of the 'older' drugs (particularly those whose patents have expired) would prevent their evaluation, and it stressed the need for obtaining the necessary data...Access to proprietary data that support the safe and effective use of drugs may be necessary in arriving at appropriate Maximum Residue Limits (MRLs).

'...It is necessary to obtain further data for safety evaluation on the use of veterinary drugs, in particular those pertaining to the nature and quantities of residues likely to be present in foods of animal origin. This is of special concern when drugs are used during egg and milk production.'

All this, theoretically, is about to change. The anticoccidials are up for review under a new regime linking the product with the person placing it on the market. Since October 1999, each specific product must be tested and approved ('brand-specific approval'). The coccidiostats which were licensed before 1988 have been chosen to go first, and will be re-evaluated by October 2003.

JECFA only got round to evaluating nicarbazin in 1998. It found in its evaluation of

dimetridazole in 1989 that neither an ADI nor MRLs could be established. Neither of these is scheduled for re-evaluation by JECFA.

According to Dr John Herrman of JECFA (Herrman, 2000) 'The reason that lasalocid, maduramicin and narasin have not been evaluated is that no governments have asked us to evaluate them and no companies have made a commitment to provide the necessary data. Monensin and salinomycin were placed on the priority list at the Twelfth Session of the Codex Committee on Residues of Veterinary Drugs in Foods that was held in March 2000, but no sponsors willing to provide the necessary data were identified.'

Although it has taken thirty years to reach this point, it is likely that this schedule will slip. Manufacturers had to submit dossiers to SCAN by October 2000, and for all six anticoccidials in this report, dossiers were received by the deadline. But whether there is enough data in them to enable regulators to formulate MRLs is a different matter. Most of the toxicological studies on which the original authorisation was given are very old and out of date.

Schering Plough have developed a vaccine against coccidiosis with which these old drugs compete. They have a keen interest in their fate. They see it as unfair that whereas the veterinary products they market are subjected to rigorous testing, and are required to have an MRL, the coccidiostats are made to jump a much lower regulatory hurdle. 'Medicinal products for minor species, for example, are much less likely to create residue problems in food, or to create a public health concern, because they are used rarely', says Jeremy Johnson. 'But the coccidiostats are frequent-use drugs, and their residues are always turning up in chicken meat.'

Schering Plough have repeatedly asked the VMD when these coccidiostats are likely to be withdrawn, but are always referred to the EC. 'In their eyes this is just a European legislation

problem', says Jeremy Johnson. They have asked the Commission when, if the dossiers do not include enough information to formulate an MRL, the products will be taken off the market, but again have received no answer.

The regulatory black hole into which the anticoccidials have fallen has meant that even the VMD are not sure which ones are authorised, and which are not. Anticoccidial legal classification and use conditions are such a muddle of complexity, it is not altogether surprising that the VMD loses track of the status of some products. The legislation itself does not help: only the active ingredients are listed in the Directive, not the trade names. According to Fabia Dyer, nowhere in the Directive does it stipulate that companies must notify the competent authority of the country in which they are marketing the product – the VMD in the UK – that they are doing so. 'It means that we can't say for sure what is being marketed in the UK', she says.

There is a further dispute which is likely to cause a delay. A wrangle has broken out between the Commission and the European Parliament about the new authorisation process. The issue was raised by the Agriculture and Rural Development Committee in the Parliament, and has been bandied between them and the Commission since February 2000.

According to the VMD, who are involved in the negotiations, the wording of the new legislation is discriminatory, and will allow monopolies to emerge. It would favour the originators of the drug (the person responsible for the dossier upon which the original authorisation for the active ingredient was granted; or, if they have sold it, to their legal successor), at the expense of the 'generic' manufacturers (those who are not responsible for the dossier, and who manufacture the different products containing the active ingredient). This is the argument pursued by the VMD.

Fabia Dyer admits that the new organised system of evaluation would impose better safety controls, and that it would drastically cut down the number of products authorised. The acute conflict of interest at the heart of the VMD, already described by the Soil Association (Young et al, 1999), is allowing them to consider the economic advantages of their drug company 'stakeholders' instead of the advantages to public health of a meaningful central system of rigorous safety testing.

There is in fact provision under 70/524 whereby the coccidiostats could be withdrawn. Under the Directive (as amended in 96/51/EC, Article 3a), 'Community authorisation of an additive shall be given only if ... it does not adversely affect human or animal health or the environment.'

## PART THREE - RESIDUES OF DANGEROUS DRUGS IN POULTRY

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### REFERENCES

- Technical Bulletin of the American Soybean Association, PO36, 1997
- Arakawa, A., Fukata, T., Baba, E., McDougald, L. R., Bailey, J. S. and Blankenship, I. C., 1992, 'Influence of coccidiosis on salmonella colonisation in broiler chickens under floor-pen conditions', *Poultry Science* 71- pages 59-63
- David Atkins, Food Standards Agency, pers. comm.
- Bafundo, K. W., 1988, 'Effect of nicarbazin and narasin-nicarbazin combinations on broiler pigmentation', *Poultry Science* 68, pages 374-9
- British Chicken Information Service/British Poultry Meat Federation
- British Government White Paper, The Food Standards Agency: A Force for Change
- British Veterinary Poultry Association, 1998, Antimicrobials Guidelines
- Buyaye, P., Devriese, L. A., and Haesebrouck, F., 2000, 'Incomplete cross resistance against ionophores in *Enterococcus faecium* and *Enterococcus faecalis* strains from pigs and poultry', *Microbial Drug Resistance* 6, :1, pages 59-61
- CEC, 1984, Reports of SCAN, 4th Series, EUR 8769; Report of SCAN 10 July 1991; Report of SCAN 10 July 1996
- Coccidiosis 2000, Positive Action Publications
- Chapman, H. D., Hacker, A. B., 1994, 'Sensitivity of field isolates of *Eimeria* from two broiler complexes to anticoccidial drugs in the chicken', *Poultry Science* 73, pages 1404-8
- Commission on Antimicrobial Feed Additives, Stockholm SOU 1997
- Compassion in World Farming Trust/Turner, J., 2000, The Welfare of Broiler Chickens – an analysis of the European Scientific Committee report of March 2000
- email from Isabelle Demade, Principal Administrator, Scientific Committee on Animal Nutrition
- de Souza Spinosa, H., Nicolau, A. A., Maruo, V. M., Bernardi, M. M., 1999, 'Effects of monensin feeding during development on female rats and their offspring', *Neurotoxicology and Teratology* 21:4, pages 467-70
- Elwinger, K., Berndtson, E., Engstrom, B., Fossum, O., and Waldenstedt, L., 1998, 'Effect of antibiotic growth promoters and anticoccidials on growth of *Clostridium perfringens* in the caeca and on performance of broiler chickens', *Acta Vet Scand* 39, pages 433-41
- EU, 1999. Veterinary Inspection visit to Thailand, 31 Jan to 12 Feb. MAFF website
- EU, Opinion of the Scientific Committee for Animal Nutrition on the use of Dimetridazole in animal feedingstuffs expressed on 12 September 2000
- European Commission, 1999, Final report on a routine mission to Brazil on animal and public health
- European Commission, 1999, Rapport d'une mission réalisée au Brésil du 15 au 25 Mars 1999 concernant le contrôle des résidues dans les animaux vivants et leur produits
- European Commission, 2000, Final report of a mission carried in Brazil from 28 November to 6 December 2000 to evaluate the operation of control over meat products (Council Directives 72/462/EEC, 94/65/EC and 92/118/EEC) and to gather background situation on the animal health situation (FMD)
- Fayer, R. and Reid, W. M., in Long, P. L., 1982 *The Biology of the Coccidia*, page 467
- FEDESA, Press release, 10 September 1998
- Friedrich, A., Hafez, H. M., Woernle, H., 1984, 'Studies on the excretion of nicarbazin in eggs and faeces of cage and deep litter birds', *Tierarztl Umschau* 39, pages 764-72
- Food Standards Agency, 'The Agency's approach to pesticides and veterinary medicine residues in food', Agenda item 6, Board meeting 14 December 2000
- Fourie, N., Bastianello, S. S., Prozesky, L., Ne/J P. W., Kellerman, T. S., 1991, 'Cardiomyopathy of ruminants induced by the litter of poultry fed on rations containing the ionophore antibiotic, maduramcin', *Onderstepoort J Vet Res* 58, pages 291-6
- Fowler, N. G., 1995, *Anticoccidial Compendium*, Janssen Pharmaceutica
- Grumbles, L. C., 1965, *A Manual of Poultry Diseases*
- Harms, R. H., Ruiz, N., Buresh, R. E., 1988, 'Influence of monensin and salinomycin on the performance of broiler chicks', *Poultry Science* 68, pages 86-8
- email from Dr John Herrman, JECFA, 11 December 2000
- James, W. P. T., 1997, Food Standards Agency: an interim proposal, Cabinet Office, London
- Jeffers, T., Bentley, E. J., 1980, 'Monensin sensitivity of recent field isolates of turkey coccidia', *Poultry Science* 59, pages 1722-30
- Jeffers, T. K., Tonkinson, L. V., Camp, L. J., Murphy, C. N., Schlegel, B. F., Snyder, D. L., Young, D. C., 1988, 'Field experience trials comparing narasin and monensin', *Poultry Science* 67, pages 1058-61
- Jeremy Johnson, Schering Plough, letter of 10 November 2000
- Jeremy Johnson, Schering Plough, pers. comm.
- Joint FAO/WHO Expert Committee on Food Additives, 1999, 'Evaluation of Certain Drug Residues in Food', WHO Technical Report Series 888
- Kassid, J. F. H., Majeid, L. A., Juma, F. T., 1988, 'Effect of dietary salinomycin on growth performance of broilers', *Iraqi Journal of Agriculture* 6, pages 7-19
- email from Edith Kennard, Staff Officer, Codex Office, 20 November 2000
- Kennedy, D. G., Blanchflower, W. J., O'Dornan, C., 1995, 'Development of an ELISA for salinomycin and depletion kinetics of salinomycin residues in poultry', *Food Additives and Contaminants* 12:1
- Kingston, D. J., 1977, 'The influence of monensin sodium upon feather development of male chickens', *Australian Veterinary Journal* 53, pages 251-2
- Dr Claire Knott, Crowshall Veterinary Services, pers. comm.
- Levy and Inesi, 1974, in Commission on Antimicrobial Feed Additives, Stockholm SOU 1997, page 175
- Long, P. L., 1982 *The Biology of the Coccidia*
- Luck, M., R., 1979, The adverse effects of nicarbazin on reproductive activity in the hen, *British Poultry Society*, Nov 20:605-7
- McDougald, L. R., in Long, P. L., 1982 *The Biology of the Coccidia*
- MAFF, Press release, 8 May 2000
- Manuel Ribas Montobbio, General Assembly of a.v.e.c., *Poultry World*, December 2000
- Meingassner et al, 1978, in Commission on Antimicrobial Feed Additives, Stockholm SOU 1997, page 174

## PART THREE - RESIDUES OF DANGEROUS DRUGS IN POULTRY

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- Simon Mounsey, HGM Publications, pers. comm.
- National Food Survey 1998/1999, MAFF, The Stationery Office
- email from Julie Norman, Food Standards Agency, 20 November 2000
- Novilla, M. N., Owen, N. V., Todd, G. C., 1994, 'The comparative toxicology of narasin in laboratory animals', *Vet Human Toxicol* 36:4
- Mike Parker, former Poultry World journalist, pers. comm., 21 May 2001
- Oehme, F. W., Pickrell, J. A., 1999, 'An analysis of the chronic oral toxicity of polyether ionophore antibiotics in animals' *Vet Human Toxicol* 41:4, pages 251-7
- Peeters, J. E., Derijcke, J., Verlinden, M., Wyffels, R., 1994, 'Sensitivity of avian *Eimeria* spp to seven chemical and five ionophore anticoccidials in five Belgian integrated broiler operations', *Avian Diseases* 38, pages 483-93
- Perl, S., Schlosberg, A., Hoida, G., Davidson, M., Jakobson, B., Orgad, U., 1991, 'Cardiac failure in beef cattle fed dried poultry litter', *The Veterinary Record*, July 13th, 1991
- Posyniak, A., Semeniuk, S., Zmudzki, J., Niedzielska, J., Biernacki, B., 1996, 'Residues of dimetridazole in eggs after treatment of laying hens', *Veterinary Research Communications* 20, pages 167-74
- Pressman and Fahim, 1983, cited in Kennedy, D. G., Hughes, P. J., Blanchflower, W. J., 1998, 'Ionophore residues in eggs in Northern Ireland: incidence and cause', *Food Additives and Contaminants* 15: 5, pages 535-41
- email from Jim Reed, Chief Executive UKASTA, 20 November 2000
- Responsible Use of Medicines in Agriculture Alliance, 1999, *Responsible Use of Antimicrobials in Poultry*
- Rose, M. D., Bygrave, J., Sharman, M. 1999, 'Effect of cooking on veterinary drug residues in food: part 9 – nitroimidazoles', *Analyst* 124, pages 289-94
- Royal Pharmaceutical Society of Great Britain, *Changes to Animal Feedingstuffs Regulations – a guide for on-farm mixers*
- Safran, N., Aizenberg, D. V. M., Bark, H., 1993, 'Paralytic syndrome attributed to lasalocid residues in a commercial ration fed to dogs', *JAVMA* 202:8
- Saini et al, 1979, *Journal of Cardiovascular Pharmacology* 1, pages 123-38
- David Sainsbury, pers. comm., 21 May 2001
- Sainsbury, David, 2000, *Poultry Health and Management*, page 12
- Salyi, G., Szabo, E., Bago, G., Banhidi, G., Szilagyi, M. 1988, 'Narasin poisoning in turkeys', *Acta Veterinaria Hungarica* 36, pages 1-2
- Schlosberg, A., Harmelin, A., Perl, S., Pano, G., Davidson M., Orgad, U., Kali U., Bor, A., Van Ham, M., Hoida G., Yakobson, B., Avidar, Y., Israeli, B. A. and Bogin, E., 1992, 'Cardiomyopathy in cattle induced by residues of the coccidiostat maduramicin in poultry litter given as a feedstuff', *Veterinary Research Communications* 16, pages 45-58
- Stephan, B., Rommel, M., Dausgies, A., Haberkorn, A., 1997, 'Studies of resistance to anticoccidials in *Eimeria* field isolates and pure *Eimeria* strains', *Veterinary Parasitology* 69, pages 19-29
- Sustain, 1999, *Food Facts 9: Fowl Deeds*
- Truswell, A. S., 1988, 'Veterinary medicines in animal foods' *British Medical Journal*, 12 November 1988
- United Nations Food and Agriculture Organisation/World Health Organisation 1984, 'Residues of veterinary drugs in foods – report of a Joint FAO/WHO Expert Consultation, Rome 29 October to 5 November 1984' *FAO Food Nutrition Paper*
- Mark Du Val, Assistant Director, Local Authorities Coordinating Body on Food and Trading Standards, letter of 1 June 1998
- The Veterinary Record, 25 September, 1982
- Vissiennon, T, Kroger, H., Kohler, T, and Kliche, R., 2000, 'Effect of avilamycin, tylosin and ionophore anticoccidials on *Clostridium perfringens* enterotoxaemia in chickens', *Berl. Munch. Tierarztl Wschr*, pages 113 9-13
- VMD Annual Report on Surveillance for Veterinary Residues 1998
- VMD Annual Report on Surveillance for Veterinary Residues 1999
- VMD Medicines Act Veterinary Information Service 34 to 38
- VMD, 'Sales of antimicrobial products used as veterinary medicines or growth promoters in the UK in 1999'
- Weisman, Y., Wax, E., Bartov, I., 'Monensin toxicity in two breeds of laying hens', *Avian Pathology* 23, pages 575-78
- Wheeler, in Commission on Antimicrobial Feed Additives, Stockholm SOU 1997, page 174
- Williams 1999, cited in 7th International Poultry Health Conference, November 2000, Positive Action Conferences, page 2
- Williams, 1999, cited in 7th International Poultry Health Conference, November 2000 Positive Action Conferences, page 3
- Williams, R. B., Carlyle, W., Bond, D., Brown, I., 1999, 'The efficacy and economic benefits of Paracox, a live attenuated anticoccidial vaccine, in commercial trials with standard broiler chickens in the United Kingdom', *International Journal for Parasitology*, pages 29 341-55
- Wilson, 1980; Wheeler, 1996, in Commission on Antimicrobial Feed Additives, Stockholm SOU 1997, page 171
- [www.noah.co.uk](http://www.noah.co.uk) 'Anticoccidials'
- Young, R., Cowe, A., Nunan, C., Harvey, J., Mason, L., *The Use and Misuse of Antibiotics in UK Agriculture Part 2*, 1999, page 43

APPENDIX 1: COCCIDIOSIS, HISTOMONIASIS AND NECROTIC ENTERITIS

**Coccidiosis**

Coccidiosis is a parasitic disease caused by a unicellular protozoa, the smallest members of the animal kingdom. The organisms belong to the Eimeria genus in the class Sporozoa.

Coccidiosis is transmitted by direct or indirect contact with the droppings of infected birds. When the coccidia oocysts are ingested, they invade the bird's intestinal tract lining where they cause tissue damage, leading to sickness and often death.

So great is the reproductive potential that a single organism may produce about a million descendants (Grumbles, 1965). The oocysts become infectious after sporulation, 24 to 72 hours after they are shed in droppings. They thrive in warm and damp litter, but are also extremely hardy, and can survive for long periods outside the birds' bodies, spread between sites on dirty boots and equipment.

There are a number of species of coccidia, all of which produce a distinct disease process. If the birds acquire immunity to one, it does

not protect them from the others. The species of coccidia affecting chickens and turkeys are:

Coccidiosis occurs in growing birds and young adults. It is seldom seen in birds under three weeks old, unless they are brooded on contaminated litter. Old birds are usually immune, because exposure during early life is difficult to avoid (Grumbles, 1965).

The severity of the birds' illness depends on how many oocysts they have ingested, but typically the whole flock is affected. Birds go off their feed and water; they become pale and droopy, and often have diarrhoea. Weight gain is reduced and the birds may become emaciated. In the acute stages of coccidiosis, mortality is high.

Some species of Eimeria cause damage mainly in the intestine, and others in the caecum. Post mortem examinations reveal lesions that vary according to the Eimeria species present, the severity of the infection, and the stage of the disease.

Subclinical infection with coccidiosis predisposes the birds to intestinal clostridial overgrowth, and the interaction of coccidiosis with other avian diseases has been described (Commission on Antimicrobial Feed Additives, 1997).

CHICKENS	TURKEYS
Eimeria tenella*	Eimeria adenoides*
Eimeria necatrix*	Eimeria meleagrimitis*
Eimeria acervulina*	Eimeria gallopavonis*
Eimeria brunetti*	Eimeria meleagridis
Eimeria maxima*	Eimeria dispersa
Eimeria mivati*	Eimeria innocua
Eimeria mitis	Eimeria subrotunda

\*denotes the species considered to cause major outbreaks (Grumbles, 1965)

**Histomoniasis: blackhead**

Histomoniasis, also known as infectious enterohepatitis, or blackhead, is caused by another protozoa, Histomonas meleagridis. It is a critical disease in intensive turkey and game bird production.

Blackhead occurs in chickens as well, but they are less susceptible, and may be infected without becoming sick; the short growing period of broilers means that it is rarely diagnosed. Outbreaks in turkeys can often be traced to direct or indirect contact with

ranges, houses or equipment previously used by chickens (Grumbles, 1965).

The disease is transmitted by the ingestion of infected droppings. The parasite is often shed within the eggs of *Heterakis gallinae*, the caecal worm of chickens and turkeys, which allows it to survive for years outside the birds themselves.

As with coccidiosis, outbreaks of blackhead become more common and virulent wherever birds are kept in crowded, unchanging conditions. The land becomes contaminated with the parasite. It is recognised in the older standard texts on husbandry (for example, the 1965 classic *A Manual of Poultry Diseases*) that rotation is effective in its control. But where turkeys or game birds are kept in high numbers on the same area year after year, blackhead thrives and must be suppressed with drugs, most often dimetridazole.

Turkeys six to sixteen weeks old are most vulnerable to blackhead, especially those reared in open-sided sheds. They go off their feed, become thirsty, droopy, and have diarrhoea. The facial regions darken, hence the colloquial name of the disease. Mortality is variable but it can exceed 80 per cent in uncontrolled outbreaks. Post mortem examination reveals lesions in the caecum and liver.

### **Necrotic enteritis**

*Clostridium perfringens* is a normal part of the bacterial flora in the gut of broiler chickens, but under certain conditions (Elwinger et al, 1998), it can multiply and cause enteric disease.

*Clostridium perfringens* Type A is a cause of necrotic enteritis, a common disease in intensively produced broilers over two weeks old.

Poultry industry scientists claim that the causes of necrotic enteritis are not known, but they acknowledge that stress can be a triggering factor. As the American Soybean Association

(American Soybean Association, 1997) candidly describes:

‘Necrotic enteritis is often initiated by an alteration in the feeding program (commencing skip-a-day feeding or accidental starvation), environmental stress, overstocking, vaccination, movement or weighing of flocks, or saturation of litter’.

The disease was first described in 1961. Kohler et al observed an increase in the disease in 1977 as coccidia began to develop resistance to anticoccidials (Elwinger et al, 1998).

## PART THREE - RESIDUES OF DANGEROUS DRUGS IN POULTRY

### APPENDIX 2: PRODUCTS AUTHORISED IN THE EU

Drug	Product	Bird	Form	Legal status	Treats	Authorisation holder
Lasalocid sodium	Avatec 15% CC	Game birds	granular	MFS	Coccidiosis	Alpharma
Lasalocid sodium	Avatec 15% CC	Broilers, layers,	granular turkeys	ZFA	Coccidiosis 6 ch, 4 turk	Alpharma
DMZ	Emtryl Premix	Game birds	buff powder	MFS	Histomoniasis (hexamitiasis, trichomoniasis)	Merial
DMZ	Emtryl Pure	Game birds	yellow powder	MFS	ditto	Merial
DMZ	Emtryl Soluble	Game birds	yellow powder	MFS	ditto	Merial
DMZ	Emtryl Soluble	Pigeons	n/a	MFS	Trichomoniasis	Merial
DMZ	Harkanker	Pigeons	n/a	MFS	Trichomoniasis	Harkers
DMZ	Sintodim 200	Turkeys	granulated	ZFA	Histomoniasis	Merial
Nicarbazin/Narasin	Maxiban	Broilers	granular particles	ZFA	Coccidiosis 5	Eli Lilly
Nicarbazin	Carbigran	Broilers	free-flowing solid	ZFA	Coccidiosis 5	Koffolk
Nicarbazin	Nicarmix	Broilers	n/a	ZFA	Coccidiosis	Eurotec Nutrition
Nicarbazin	Elancocin	Broilers	n/a	ZFA	Coccidiosis	Eli Lilly
Nicarbazin	Koffogran	Broilers	n/a	ZFA	Coccidiosis	Koffolk
Narasin	Monteban	Broilers	granular meal	ZFA	Coccidiosis	Eli Lilly
Maduramicin ammonium	Cygro Premix	Broilers (turkeys 1%)	granules	ZFA	Coccidiosis 6 (turkeys 4)	Alpharma AS
Monensin sodium	Romensin	Cattle	granular	ZFA	Feed conversion	Eli Lilly
Monensin sodium	Ecox 200	Broilers, layers, turkey, cattle	powder (5 ch, 3 turk)	ZFA	Coccidiosis Feed conversion catt	Eco Animal Health
Monensin sodium	Elancoban	Broilers, layers, turkeys	granular meal	ZFA	Coccidiosis (5 ch, 3 turk)	Eli Lilly
Salinomycin	Kokcisan 120G	Broilers	n/a	ZFA	Coccidiosis	KRKA
Salinomycin sodium	Sacox 120	Broilers, layers, rabbits	powder	ZFA	Coccidiosis 6	Intervet Int bv
Salinomycin sodium	Bio-Cox 120G	Broilers	granular	ZFA	Coccidiosis 6	Alpharma AS
Salinomycin sodium	Sal-Eco 120	Broilers, pigs	powder	ZFA	Coccidiosis 6 Feed conv pigs	Eco Animal Health
Salinomycin sodium	Salocin 120	Piglets, pigs	granulate	ZFA	Feed conv pigs	Intervet Int bv

Sources: VMD; Noah; Handbook of Feed Additives 2001

MFS = Medicated Feedingstuff; ZFA = Zootechnical Feed Additive  
n/a not available

APPENDIX 3 GLOSSARY

ascites	oedema involving the abdomen; a very common complication of abdominal tuberculosis, of liver, kidney, or heart disease, as well as some parasitic infestations.
assay	test, trial
ataxia	inability to coordinate voluntary movements
broiler	chicken reared for meat
caecum	a sac with one opening: part of the intestine
challenge	a test for immunity
clinical	an instruction of medicine or surgery at the bedside of patients
comet assay	a rapid and very sensitive fluorescent microscopic method to examine DNA damage and repair at individual cell level
coronary vasodilation	expansion of a blood vessel in the heart
dyspnoea	difficulty in breathing
enteric	pertaining to the intestines; possessing an alimentary canal
genotoxic	describes a poisonous substance which harms an organism by damaging its DNA.
hydronephrosis	a condition in which the capsule of the kidney, or even the kidney itself, becomes greatly distended with urine which is unable to pass along the ureter into the urinary bladder owing to some obstruction in that channel
hyperplastic	the abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue
hypoactivity	hypo: defective, inadequate
in vitro	in the laboratory
in vivo	in life
ischaemic	deficiency of blood in a part of the body
isolate	a pure culture of bacteria
mutagenicity	quality of a substance that produces mutations
nitroreduce	reduction of nitration
oocysts	a cyst formed around a zygote (the first stage of an organism)
positive	a 'positive' sample is one in which residues of an unauthorised substance, or a substance above the MRL or DAL is confirmed
prophylaxis	preventive treatment against disease
protozoa	simple unicellular animal
schizogony	formation of 'daughter' cells by multiple fission
sporulation	the process of sporozoite formation: division of zygote producing an infective stage
subclinical	of a slightness not detectable by usual clinical methods
trichomoniasis	any infection caused by parasitic protozoa of the genus Trichomonas

### APPENDIX 4: EXECUTIVE SUMMARY: THE USE AND MISUSE OF ANTIBIOTICS IN UK AGRICULTURE 2

It is thirty years since the publication of the last independent advisory committee report into the problem of antibiotic resistance passing from farm animals to humans. The report, by the Swann Committee (Swann et al 1969), set out principles for the regulation and use of antibiotics in British agriculture and also influenced legislation worldwide.

In the UK, successive administrations have claimed to be guided by Swann, but closer examination reveals that in many respects this has not been the case.

The publication of this report from the Soil Association has been timed to coincide with the publication of a report from the Advisory Committee on the Microbial Safety of Food (ACMSF) - the first report from a government advisory committee specifically to look at this issue since Swann.

It is our hope that the committee will make far-sighted and prudent recommendations and that the concurrent publication of our report will help in a small way to draw attention to the subject and provoke wider public awareness and debate. Our principal findings are that:

- antibiotic-resistant bacteria in food pose a substantially greater risk to human health than antibiotic residues. In the UK we have a statutory residue surveillance programme, but no equivalent scheme to monitor resistance
- the threat to human health posed by antibiotic resistance transferring from farm animals is infinitely greater than that posed by BSE. The potential costs to the Treasury and the NHS are enormous and unquantifiable
- multiple-drug resistance is increasing at an alarming rate: in some salmonella from 5 per cent to 95 per cent in 20 years, in MRSA 2 per cent to 40 per cent in 10 years, but the supply of new antibiotics has slowed substantially and no genuinely new classes have been developed for over 20 years
- over-prescribing by veterinary surgeons caused the first multiple-drug resistance in the UK
- the agricultural contribution to the drug-resistance problem has consistently been underestimated

- previous attempts to reduce the use of antibiotics in agriculture have been unsuccessful. New products replace those banned and loopholes are always exploited. This process is continuing
- routine prophylaxis with therapeutic antibiotics poses as great a threat as the use of growth promoting antibiotics and a much greater threat than full therapeutic treatment for short periods
- despite the bans on several growth promoting antibiotics the overall threat they pose has not been reduced
- ways must be found to reduce the overall use of antibiotics in agriculture - ideally to less than half the present level
- deregulation, the introduction of the 'near market' research concept and the semi-commercialisation of the Veterinary Medicines Directorate during the 1980s have left the British government intellectually stranded. It has neither suitable research, surveillance data, nor genuinely independent advice to enable it to analyse, or deal adequately with, the problems caused by antibiotic use on farms
- over the last year the British government has allowed one previously little-used antibiotic growth promoter to come to be fed to virtually every broiler chicken in the country. The growth promoter, avilamycin, is almost identical to Ziracin, widely believed to be the best new life-saving medical drug we will see in the next decade. It is already on trial in British hospitals against three serious superbugs: VRE, MRSA and multiple-drug resistant strains of meningitis and pneumonia. The UK has carried out no research to see if this is safe, but research in Denmark has shown that the two antibiotics are totally cross-resistant and that avilamycin may also be selecting for resistance to vancomycin, currently still the most important antibiotic for treating superbugs. Day-old chicks, with a 42-day life expectancy, which were put on avilamycin following the ban on other growth promoters on 1 July, will be on sale in British shops within a few days of the publication of this report

- unlike some EU Member States, we have given no practical help or advice to our pig and poultry producers to enable them cope with recent antibiotic bans. As a result they have been put at a commercial disadvantage at a particularly difficult time for farming in general. Most are simply using more of the growth promoting and therapeutic antibiotics still permitted, instead of changing their methods of production, as has been the case in Sweden and Denmark

### Key recommendations:

#### bans and restrictions

- 1 the growth promoting antibiotic avilamycin should be banned immediately, with existing stocks destroyed and farmers compensated
- 2 an EU exemption should be sought for a limited period (up to a year) to allow the growth promoting antibiotic zinc bacitracin to be again added to broiler rations in order to facilitate an immediate ban on avilamycin. Zinc bacitracin should not, however, be relicensed as a therapeutic antibiotic because it too has a potential use in controlling epidemics of superbugs in hospitals
- 3 fluoroquinolone antibiotics should no longer be permitted for mass medication. Individual animals of all species should still be allowed to be treated in extreme situations. However, use in poultry production should effectively cease. Vets should record their reasons for selecting fluoroquinolones in the farm medicines book.
- 4 fluoroquinolones and third generation cephalosporins should not be permitted against enteric infections in any farm animals. This is to prevent the further development of resistant food poisoning strains

#### policy

- 5 EU agricultural policy should be further reformed to encourage livestock production methods with minimum dependency on antibiotics

- 6 practical and technical help should be given free of charge to producers to encourage them to alter production methods in order to reduce dependency on antibiotics
- 7 enteric salmonella in all farm animals should become a notifiable disease with a slaughter policy introduced for *S. typhimurium* DT104, rather than treatment with antibiotics
- 8 evidence to support the ban on antibiotic growth promoters is stronger than that for hormones. Britain should therefore push for the introduction of an immediate unilateral ban on the importation of any livestock products produced with drugs banned in the EU.
- 9 advertising of any prescription only veterinary medicines, except in the veterinary press, should become illegal

#### the veterinary profession

- 10 independent scrutiny of veterinary prescribing practice is needed to rebuild confidence and identify problem farms and practitioners. One single 'agency' should be given responsibility for all monitoring of antibiotic use on farms. Farms should receive annual visits and inspectors should prepare reports which are analysed by trained staff. Significant irregularities should be considered anonymously by independent vetting committees. Consistent over-use by farmers should trigger free advisory visits with producers required to implement recommendations. Poor prescribing by vets should lead to retraining, excessive prescribing should result in prosecution
- 11 veterinary surgeons should retain the right to dispense as well as prescribe veterinary medicines, but should no longer be responsible for checking farm records of these
- 12 Government should help establish a School of Preventative Veterinary Medicine to be run by vets and other specialists. It should research, collate and disseminate reliable information to farmers, vets and others

APPENDIX 5: SOIL ASSOCIATION STANDARDS FOR ORGANIC EGG AND POULTRY PRODUCTION

5.4.1 These Standards apply to all poultry, with specific requirements identified for individual species where appropriate. The husbandry of other poultry species not detailed will be assessed on the same principles, making alterations to any specific requirements as appropriate.

These Standards apply to all poultry, with specific requirements identified for individual species where appropriate. The husbandry of other poultry species not detailed will be assessed on the same principles.

**BREEDS AND ORIGIN OF STOCK**

**Principle**

5.4.2 Breeds chosen should be of a suitable disposition and physique to thrive under organic, free range conditions.

**Recommended Best Practice**

- 5.4.3 a) Purchase of stock from organic sources.
- b) The use of slow growing strains for meat production.

**Required**

Existing layers on a converting farm may start to produce organic eggs after a conversion period of 6 weeks, following the completion of the conversion of the land.

**Identification**

5.4.5 Identification of poultry should be per batch

Category	Details and Conversion Requirements
Birds for meat production	Non- Organic chicks can be purchased under 3 days of age and must undergo a 10 week conversion period. After 31st December 2003 organic chicks must be purchased.
Laying birds	Non – Organic birds can be purchased up to 18 weeks of age and must undergo a conversion period of six weeks. After 31st December 2003 organic chicks must be purchased.

Existing layers on a converting farm may start to produce organic eggs after a conversion period of 6 weeks, following the completion of the conversion of the land.

**Prohibited**

- 5.4.7 Purchase of stock from caged systems.

**GENERAL MANAGEMENT AND WELFARE**

**Required**

Poultry operations must be an integral part of the whole farm organic system or, failing that, of cooperating organic farms in the area, in terms of manure and rotational management and, where possible, also feed.

Poultry must have continuous and easy daytime access to pasture and / or range, except in adverse weather conditions.

- 5.4.10 Outside access is required for at least (proportion of life):

<b>Layers</b>	All laying life
<b>Broilers</b>	2/3 life
<b>Turkeys</b>	2/3 life
<b>Ducks</b>	2/3 life
<b>Geese</b>	2/3 life
<b>Guinea Fowl</b>	2/3 life

5.4.11 In addition to the veterinary and other records as detailed in section 2.3, records must also be kept of mortalities (and the cause of death), morbidity, hock damage and reject percentages (and the cause of rejection) as a means of evaluating the health and welfare status of the poultry operation. The Certification Body reserves the right to impose conditions of management on operations which fall short of expected levels of health and welfare.

### Prohibited

5.4.12 Organic and non-organic poultry of the same species may not be reared or kept on the same holding, unless this forms part of the conversion plan.

Such 'parallel production' should only take place during the time that non-organic batches established prior to the start of conversion are completing their production.

5.4.13 Poultry may not be permanently housed.

### Pasture and Range

#### Recommended

- 5.4.13 Grass/clover leys based on fescues and other grasses which tend towards tillering rather than leaf length.
- 5.4.14 Companion grazing with sheep for sward management.
- 5.4.15 Conditions that favour the development of natural dusting areas.

5.4.16 Access to woodland.

5.4.17 Poultry should have access to outside drinkers.

#### Required

- 5.4.18 *The land to which poultry have access must be well covered with suitable and properly managed vegetation.*
- 5.4.19 Pasture must be rested from poultry to allow vegetation to grow back, for health reasons and to enable built-up fertility to be used for:
- In the case of layers at least nine months after each batch.
  - In the case of birds for meat production at least two months per year and in addition for one year every three years.
- 5.4.16 These requirements shall not apply to small numbers of poultry which are not kept in runs and which are free to roam throughout the day.
- 5.4.17 Poultry must have access to feed and water at all times in daylight hours,

Small numbers means up to about 50 birds, but the exact number will depend on the system, to be agreed with SA Cert.

except just prior to transport and/or slaughter when feed may be withheld for a limited period.

- 5.4.18 Poultry must have access to shelter at all times and be provided with protection from predators (e.g. foxes).
- 5.4.19 Adequate cover, either natural (trees, shrubs, etc), or artificial (screens, trailers, etc) must be

provided in the free range areas to give the birds conditions akin to their native habitat, protection from overhead predators and shelter from extreme weather conditions.

- 5.4.20 Waterfowl must have access to a stream, pond or lake, whenever the weather conditions permit. Such water must be well maintained and managed to prevent the build-up of stagnant water and decaying vegetation, pollution and disease risk.

The water must be at least sufficient for the waterfowl to be able to dip their heads into it.

- 5.4.21 Maximum outdoor stocking rates:

<b>Layers</b>	1000b/ha
<b>Broilers</b>	2500b/ha
<b>Turkeys</b>	800b/ha
<b>Ducks</b>	2000b/ha
<b>Geese</b>	600b/ha
<b>Guinea Fowl</b>	2500b/ha

## Housing

### Recommended Best Practice

- 5.4.22 In the design of poultry enterprises, preference should be given to mobile houses, as these allow for greater flexibility of management and the ability to integrate the

poultry operation into the organic farming system.

### Required

- 5.4.23 Where housing units accommodate more than the normal social group size of the species (generally greater than 100 adult birds), then the number and distribution of feeders, drinkers and other facilities and/or provision of partitions, etc must be adequate to allow the development of social groups within the unit.

### Permitted

- 5.4.24 1) The following number of birds in a housing unit:

<b>Layers</b>	500 birds
<b>Broilers</b>	500 birds
<b>Turkeys</b>	250 birds
<b>Ducks</b>	500 birds
<b>Geese</b>	250 birds
<b>Guinea Fowl</b>	500 birds

### Restricted

- 5.4.25 1) Housing units containing more birds than those specified in 5.4.24 may be allowed by derogation, only where the following conditions are fully complied with:
- a) The maximum number of birds allowed in each housing unit will be assessed by a calculation of the area of pasture available to the birds within the designated ranging distance for the species, taking into account the following parameters:

the designated ranging distance:

<b>Layers</b>	100m
<b>Broilers</b>	50m
<b>Turkeys</b>	50m
<b>Ducks</b>	50m
<b>Geese</b>	100m
<b>Guinea Fowl</b>	100m

the maximum outside stocking density as in 6.419.

the exclusion of additional areas that are required for rotation/resting of the pasture (as per 6.414).

the exclusion of the area taken up by the house, access roads, concrete aprons, etc.

- b) A demonstrably high level of bird health and welfare.
- c) Good environmental conditions, both inside the house and externally on the range.

In any event, the housing unit size shall not exceed:

<b>Layers</b>	2000 birds
<b>Broilers</b>	1000 birds
<b>Turkeys</b>	1000 birds
<b>Ducks</b>	1000 birds
<b>Geese</b>	1000 birds
<b>Guinea Fowl</b>	1000 birds

A derogation to allow these larger housing unit sizes will only be given if it can be demonstrated that the conditions above are fully complied with and can be maintained. If breakdown occurs, SA Cert may require the housing unit size to be decreased.

5.4.26 Between batches of poultry, houses must be emptied of birds and cleaned and disinfected, preferably with steam, blowtorch, or lime, depending on the construction of the house. Houses must be left empty for sufficient time to break pest cycles.

See 4.6.17 for details of permitted disinfecting materials.

## PART THREE - RESIDUES OF DANGEROUS DRUGS IN POULTRY

The following shall apply to indoor housing and facilities:

	Layers	Broilers	Turkeys	Ducks	Geese	Guinea Fowl
Maximum stocking rates in fixed housing	6b/m <sup>2</sup>	10 b/ m <sup>2</sup> (21kg/m <sup>2</sup> )	2 b/m <sup>2</sup>	10 b/m <sup>2</sup>	2 b/m <sup>2</sup>	10b/m <sup>2</sup>
or stocking rates in mobile housing	6b/m <sup>2</sup>	16b/m <sup>2</sup> (30kg/m <sup>2</sup> )	3b/m <sup>2</sup>	16b/m <sup>2</sup>	3b/m <sup>2</sup>	-
Minimum perch space (cm/bird)	18 cm/ b	-	40 cm/ b	-	-	20 cm/b
Individual nest boxes (max no. birds/nest box)	6b/ nest	-	-	-	-	-
or communal nests (min cm <sup>2</sup> /bird)	120 cm <sup>2</sup> /b	-	-	-	-	-
Maximum slatted floor area (per cent of floor area)	50%	50%	50%	50%	50%	50%
Minimum exit/entry pop-holes (m length per 100m <sup>2</sup> floor area)	4m/ 100m <sup>2</sup>	4m/ 100m <sup>2</sup>	4m/ 100m <sup>2</sup>	4m/ 100m <sup>2</sup>	4m/ 100m <sup>2</sup>	4m/ 100m <sup>2</sup>
Maximum area of poultry houses per Unit (m <sup>2</sup> )	deleted	1,600 m <sup>2</sup>	1,600 m <sup>2</sup>	1,600 m <sup>2</sup>	1,600 m <sup>2</sup>	1,600 m <sup>2</sup>

The indoor stocking rates in buildings that were used for organic laying flocks up to 24th August 1999 may remain at 12 birds/m<sup>2</sup> until 24th August 2002, decreasing to 9 birds/m<sup>2</sup> until 24th August 2003, and to 6 birds/m<sup>2</sup> thereafter.

Where the house design incorporates a solid floor in one identified area then the ratio of solid floor to slats may be reduced to 1/3 solid floor: 2/3 slatted area.

5.4.28 Litter must be replenished regularly and kept in a dry and friable condition suitable for scratching and dust bathing.

5.4.29 Artificial lighting may only be used to prolong the day length up to a

total of 16 hours and the day must end with a dusk.

### Recommended Best Practice

- 5.4.30 a) Organic straw as litter material (preferably chopped).
- b) Pop-holes located on different sides of the house so as to be able to avoid adverse weather conditions affecting the environment inside the house.

### Permitted

- 5.4.30 a) Non-organic untreated straw as litter material (preferably chopped).
- b) Shavings/ bark from non-treated

timber as litter material.

**Prohibited**

5.4.31 Paper-based bedding material.

**DIETS**

**Required**

5.4.32 All poultry must have access to insoluble grit.

5.4.33 Poultry diets must contain a minimum of 65 per cent cereals or cereal by-products.

**Permitted**

5.4.34 Until 24th August 2005, where organic feeds are not available, non-organic feedstuffs as specified in paragraphs 5.617 to 5.619 may be fed up to a total of 20 per cent of the annual intake, with a maximum daily intake of 25 per cent (calculated as a percentage of total dry matter of the agricultural ingredients).

As a guide the following dry matter intakes can be used to calculate non-organic allowances. Please note that justification will be required in the management plan as to DMI used.

Bird Type	Av. Total Daily DMI
Layers	0.118
Table Birds	0.077
Turkeys	0.138
Geese	0.150
Ducks	0.150

**Prohibited**

5.4.35 Synthetic yolk colourants, in-feed medication and all other feed additives.

5.4.36 Forced feeding systems.

**BIRD HEALTH**

**Required**

5.4.36 Poultry must be checked three times daily by a suitably trained/experienced stockperson, who should pass within 3 metres of each bird.

**Prohibited**

- 5.4.37 a) Clipping primary flight feathers.
- b) Beak clipping and tipping, caponisation and all other mutilations.
- c) Brought-in poultry from conventional origin whose beaks have been clipped or tipped.

## Age at Slaughter

### Required

5.4.38 The minimum slaughter age, except where traditional or slow growing strains are used, must be:

<b>Layers</b>	-
<b>Broilers</b>	81 days
<b>Turkeys</b>	140 days
<b>Ducks</b>	49 peking 84 Muscovy 92 Mallard
<b>Geese</b>	140 days
<b>Guinea Fowl</b>	94 days

Where slow growing strains are used, the slaughter age is unrestricted (but note the conversion period of 10 weeks for non-organic 'day old' chicks). Where slow growing strains are not used, the minimum slaughter age is defined above. There is currently no specific list of slow growing strains and until one is developed, all but the modern fast growing Ross/Cobb type hybrids will be considered as included.

This report is part of the Soil Association's continuing campaign against the excessive use of antibiotics in livestock production. It is also part of its campaign to raise awareness about key issues that underpin organic farming standards and the Soil Association's commitment to maintaining their integrity.

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