APPENDIX D: LIVESTOCK AND THE USE OF ANTHELMINTICS

Introduction

Grazing livestock may suffer from the activities of many parasites, including gutworms, lungworms, tapeworms, liver fluke and a range of ectoparasitic arthropods including ticks, lice, warble flies and blood-sucking insects. They may seriously affect the health and growth of livestock, and hence the financial return to farmers.

Chemicals which control one or more endoparasitic worm group are called anthelmintics. Some also control ectoparasites as well.

Notes on specific chemical groups used as anthelmintics

Source: 'Farmers Weekly' April 12 1991. Mainly derived from Joint Nature Conservation Committee leaflet 'Chemical Alternatives to Treatment of Cattle with Ivermectin'. D. McCracken (Dept. Agric. & Env. Sci. The University, Newcastle), & E Bignal (JNCC)

Key to abbreviations used for parasite groups:

GTW= gutworms; LGW= lungworms; TPW= tapeworms;
LVRF= liver fluke; EP= ectoparasites (including larvae of some insects which penetrate the body)

BENZIMIDAZOLES Effective against GTW, LGW, TPW, and some control of LVRF. Given by mouth; Oxfendazole can also be injected into rumen or used in pulse-release devices ('Autoworm' or 'Synthanic Multidose'). Usually administered at start of grazing season. Also fenbendazole ('Panacur[R], Hoechst'). Alternative to avermectins.

IMIDAZOTHIAZOLES Effective against GTW, LGW only. Given by mouth, injection and pour-on. 'Levamisole[R]' preparations should not be given simultaneously with organophosphorous preparations, or for 14 days before or after treatment. Alternative to avermectins.

TETRAHYDROPYRIMIDINES Effective against GTW only. Morantel tartrate is currently sold as a slow-release device in cattle which is effective for 90 days ('Paratect[R] Flex Bolus'). It gives no protection against lungworms, so a vaccination programme is needed in conjunction with it. Alternative to avermectins.

SALICYLANILIDES & SUBSTITUTED PHENOLS Effective against LVRF, and partially protects against GTW, TPW and EP.

SYNTHETIC PYRETHROIDS Effective against EP only. Applied as sprays, impregnated in ear tags against flies, or as a pour-on. Persist well on coat or skin, but not in tissue. Valuable against skin parasites e.g. lice, ticks some mites and nuisance flies. Low mammalian toxicity, but very poisonous to fish and crustaceans.

ORGANOPHOSPHATES Effective against GTW and EP only. Some, e.g. 'Coumaphos^{R}', used as powders for use against lice and fleas. Others, e.g. 'Chlorpyrifos^{R}', are used as sprays for tick control. Some can act systemically, via mouth or as a pour-on, to control warble fly larvae, lice and mites causing sarcoptic and chorioptic mange of cattle. Short-lived in animal tissues but last a reasonable time in the coat. Dangerous to operators using them, so needs special protective measures. Residues of 'Dichlorvos^{R}' in horse dung can have an adverse effect upon dung beetle fauna, and magpies have died after feeding on the backs of cattle treated for warble fly.

AVERMECTINS (fungal fermentation products) Effective against GTW, LGW and some EP e.g. sucking lice and warble fly. Can be administered as drench (pour-on), oral paste, subcutaneous injection or bolus. Has serious impact on dung fauna life cycles, especially those of cyclorhaphous flies and dung beetles. Includes 'Ivomec^{R}, MSD Agvet', 'Ivomec^{R}, SR bolus, MSD Agvet', 'Avomec^{R}, MSD Agvet' and 'Doramectin^{R}, Pfizer'.

MILBEMYCINS (fungal fermentation products) Effective against GTW, LGW and EP. Recently developed by Cyanamid of USA. Moxidectin tested by Strong and Wall (1994) on cattle and shown not to be toxic to dung fauna larvae. Includes'Cydectin^{R} Cyanamid'.

NB Whichever chemical is used, it is important to read instructions carefully in relation to the pest type controlled; class of stock recommended; limitation as to use; dose rate and the withholding period. Farmers should consult a vet to develop a control strategy designed for the farm which preferably does not rely too heavily on stock chemical treatment.

AVERMECTINS

These are compounds belonging to a family derived by fermentation from a naturally-occurring soil actinomycete, *Streptomyces avermitilis*. They were discovered in the mid 1970's. Synthetic derivatives are now available, such as avermectin B1, which has two hologes, $B1_a$ and $B1_b$. Ivermectin is a mixture of the two homologes, and is marketed and sold for use in cattle as 'Ivomec^{R}, MSD'.

Control programmes for treatment using ivermectin were given in Part 2.

Control of infections in young animals may require several treatments, or use of a pulse-release bolus. This strategy allows young cattle to graze the same pasture early in the grazing season until pasture contamination with infective larvae becomes high. They are then treated with an anthelmintic to remove existing burdens and transferred to a parasitologically 'clean' pasture; the so-called 'dose and move' strategy.

Some farmers do not treat until a clinical problem occurs, and a therapeutic treatment is then required to prevent cattle losses. Whichever program is adopted, a strategic treatment at the end of the period of transmission is commonly recommended ro remove burdens acquired late in the grazing season. On some farms this may be the only treatment administered in a year. The avermectins and some of the benzimidazoles can be very valuable at this time because of their good efficacy against *Ostertagia ostertagi* adults and larvae. Avermectins also remove several potentially damaging ectoparasites, including lice, mange mites and warbles (Ryan & Guerro, 1987).

Treatment of second season animals may also be undertaken, but at reduced frequency. Adult dairy or beef cattle are rarely needed to be treated. In horses a bi-monthly treatment schedule during the period of risk has proved effective in helping prevent adverse effects of the main target parasites including large and small strongyles and stomach bots.

METHODS OF ADMINISTRATION OF IVERMECTIN TO LIVESTOCK

Ivermectin can be used to treat livestock in four possible formulations. These are listed in the following table, with details of the livestock concerned, and the nature of the ivermectin medium used.

Table 1: Source Steel, 1993

Ivermectin formulations for livestock; dose rate is 200 μg/kg except where indicated

Admin. route	Species	Ivermectin. conc. (%, w.v)	Formulation
Subcutaneous	Cattle,Sheep	1	non-aqu. soln.
Oral Drench	Cattle	0.4	"
	Sheep,Goats	0.08	Aqu. micelle
	Horses	1	"
Oral Paste	Cattle	0.15	N/A
	Horses	1.87	
Topical (pour-on) 500 ug/kg	Cattle	0.5	N/A
Intrarum. bolus 40 ug/kg/day for 120 days	Cattle	0.5	Osmotic pump

Ctle = cattle
Topical (pour-on) = 500 μg/kg
Intraruminal bolus for cattle uses an osmotic pump (lasts 120 days).
Non-aqueous solution = 60% propylene glycol: 40% glycerol formal (v/v) for cattle injections & 100% propylene glycol for cattle oral drenches. For sheep, goats and horses the oral drench is an aqueous micellar solution of ivermectin which is formed with a surface-active agent, polyoxyethylene sorbitan monooleate, and cosolvents, glycerol formal and benzyl alcohol.

Does the formulation used and its method of administration matter?

Steel (1993) states that the biological half-life of ivermectin in plasma is similar in cattle (2.8 days) and sheep (2.7 days), but because of a larger volume of distribution, plasma clearance is more rapid in sheep. However, injection of a (tritium labelled) subcutaneous formulation of ivermectin prolongs plasma residence time and persistence of residues in liver and fat. Increasing the organic solvent content of subcutaneous formulations slows the release of drug from the injection site and thereby prolongs its presence in the bloodstream. (Lo et al, 1985: half life 2.0 days with aqueous micelle; 3.7 days in mixed aqueous micelle/glycerol formal 50:50 v/v; 8.3 days non-aqueous propylene glycol-glycerol formal 60:40 v/v.) Because ivermectin and its metabolites are mainly excreted in bile, residues continue to appear in faeces for substantially longer after subcutaneous injection compared with oral dosing. At least 98% of the ivermectin dose is excreted via the dung no matter what administration route is used (Halley et al., 1989; Chiu et al., 1990).

Pour-on applications and aqueous based injectable formulations in cattle may therefore reduce the impact of ivermectin treatment on dung fauna (Sommer *et al.*, 1992) compared with organic solvent-based ones. Binding of avermectins to digesta particulates during gut transit may potentially lower drug bioavailability and also contribute to faecal residues. Further research on formulation and dosage strategies is advocated to increase bioavailability at the gastrointestinal site of action, so that both dose rate and faecal residues can be reduced.

REPORT OF THE UNITED STATES DRUG ADMINISTRATION (Bloom and Matheson, 1993; small part only.)

Chemicals introduced into the environment tend to distribute within and between environmental compartments (air, water, soil, and biota). This distribution pattern will, in large part, determine whether or not organisms present in a compartment will be exposed to levels of chemicals sufficient to cause adverse effects.

Certain physical or chemical properties can be used to predict a chemical's potential for distribution among compartments. Ivermectin's very low vapour pressure indicates that it is unlikely to enter the atmosphere. It has low water solubility (<4 mg/l), but the K_{ow} value indicates a moderate affinity for lipid-like material.

Tests to find the ability of ivermectin to distribute between soil and water were conducted. A soil sorption/desorption test, a soil column leaching test and a soil thin-layer chromatography test all confirmed that avermectin compounds appear to bind very strongly to a wide variety of soil types. The distribution adsorption coefficient, expressed on the basis of organic carbon in the soil (K_{oc}) for ivermectin has been reported to be between 12600 & 15700. These values show very strong binding to soil. Ivermectin appears to be very immobile and would not be expected to readily transfer into the aquatic environment from animal-waste contaminated soils. Ivermectin in aquatic systems would be expected to bind tightly to sediment or particulates.

ACTUAL EFFECTS OF IVERMECTIN INTRODUCED TO THE ENVIRONMENT

Halley *et al.* (1993) gave the following summary of abamectin B1 and ivermectin effects following research in the Merck Laboratories in New Jersey. Numerous environmental fate and effects studies have been carried out and reviewed. Both are immobile in soil, rapidly photodegraded in water (half-life 0.5 dys in summer) and as thin films on surfaces (half-life <1 dy), and aerobically degraded in soil (ivermectin in soil/faeces mixture = 7-14 dys half-life; avermectin B1a = 2-8 weeks) to less bioactive compounds. Abamectin is not taken up from the soil by plants, nor is it concentrated by fish. *Daphnia magna* is the fresh water species found to be most sensitive to ivermectin & avermectin (LC50 values of 0.025 & 0.34 ppb respectively). fish (e.g. rainbow trout) are less sensitive (LC50 values of 3.0 & 3.2 ppb respectively). In the presence of sediments, toxicity towards *Daphnia* is significantly reduced. Neither chemical has any significant antibacterial or antifungal activity. They display little toxicity to earthworms (LC50 values of 315 ppm & 28 ppm in soil for iverm. & abamect. resp.) or avians (abamamectin dietary LC50 values for bobwhite quail & mallard of 3102 ppm & 383 ppm resp.) and no phytotoxicity. Residues of the avermectins in faeces of livestock affect some dung-associated insects, especially their larval forms. This does not delay degradation of naturally formed cattle pats under field conditions, however, in some cases, delays have been observed with artificially formed pats. Based on usage patterns, the availability of residue-free dung and insect mobility, overall effects on dung-associated insects will be limited. As they undergo rapid degradation in light and soil, and bind tightly to soil and sediment, they will not accumulate and will not undergo translocation in the environment, minimising any environmental impact on non-target organisms resulting from their use.

DUNG DEGRADATION

Wall & Strong (1987) & Strong & Wall (1988), using data from cattle dosed at 40 ug/day with continuous intraruminal dosing, concluded that degradation of manure pats was prolonged and populations of dung-degrading insects in pats were decreased. The sustained release formulation was estimated (Strong and Wall, 1988) to lead to concentrations of 400 or 500 ug/kg ivermectin in the faeces. This compares with a peak of 80 ug/kg between day 3-7 post dose with pour-on; decreasing to 13 ug/kg at day 42. Also treatments with pour-on or injections are a maximum three times per year, compared with 120 days for bolus.

Ivermectin is therefore not likely to be a problem in the wider environment. It is its failure to degrade within dung, and its impact on the dung fauna which are causes for ecological concern, especially with the use of a bolus.

AVERMECTINS AND THEIR EFFECTS ON DUNG INSECT FAUNA

1) VIEW OF A. B. FORBES, 1993, REPRESENTING MERCK SHARP AND DOHME.

How much avermectin is used world-wide?

The answer to this question is pertinant since the amount used will influence the levels of possible environmental damage worldwide.

Forbes used these figures: 1.3 billion cattle world-wide; An average cow treated is about 200 kg mass (allowing for the smaller size of those actually treated); assumed all avermectin sold in 1991 was used, and that each cow was treated once, then 15% of the world's cattle were treated. The figure falls if some were treated more than once in the year. In North America. where about 111 million cattle exist, about half receive no anthelmintic treatments at all. Just over half of the remainder (about 25%) were treated with avermectins, with an average dose rate of 1-1.3 per animal/year. Younger cattle are treated more often than adults. If seasonal sales reflect usage, 40% of the sales of avermectins occur in the fourth quarter of the year, coinciding with large intakes into feedlots, calf weaning, and movement to winter grazing. World-wide the sales show a similar pattern; a peak in 4th quarter; a secondary peak in the second quarter. The secondary peak not only reflects sales in the southern hemisphere, but also use in young stock in the early grazing season, particularly in Europe.

Forbes consideration of the ecological impact of avermectins

Daily faecal production by cattle is about 6% of body mass (Marsh & Campling, 1970). Forbes estimates for a typical herd: young stock contribute about 20% to total dung deposited by a beef herd, and <5% by a dairy herd. Treatment of young animals would result in only a small proportion of their faeces containing residues, thus further reducing the potential for any effects. Seasonal treatment patterns show that many ivermectin treatments occur when the insect dung fauna are reduced and inactive e.g. during temperate winters and subtropical dry seasons. This would further reduce the potential of avermectin residues to affect local pasture ecology (Ridsdill-Smith, 1988). Grazing milking herds provide further sources of dung free of faecal residues of avermectins.

Many members of the insect dung fauna colonise dung from species other than cattle (Halffter & Matthews, 1966; Fincher et al, 1970; Skidmore, 1991), and hence the untreated other animals supply further food supplies. Treatments are rarely administered simultaneously to all cattle on the same farm, so alternatives exist. Adjacent farms are likely to be out of phase in their treatments.

Although the number of treatments of horses is potentially greater per year, the oral formulation of ivermectin used does not result in persistent excretion and faecal residues. Activity is not normally detected later than 72 hrs after administration (Ewert et al, 1990; Herd et al, 1990). Horses produce dung at a rate of 3% of body mass/day (Rossdale, 1976) ie a 600 kg horse would produce 18 kg dung/day or 6.57 tonne/year. If it were treated 3 times during a grazing season, no more than 5% would contain residues.

Forbes conclusions

Any potential ecological impact resulting from the use of avermectins in large animals world-wide should be limited by the dilution effects of untreated animals, lack of synchrony of treatments, the timing of treatments often not coinciding with the main dung insect breeding seasons, treatment of housed or penned animals and the limited period of time after treatment when sensitive dung feeding insects are at risk. Gross effects on dung degradation or pasture availability have not been observed following the use of avermectins under commercial conditions which have been in operation for 10 years or more, and on experimental farms for 15 years. Improved health and performance resulting from control programs utilising avermectins in cattle and horses could not be expected to be sustained if pasture ecology and quality were adversely affected by their use.

2) VIEW OF INDEPENDENT DUNG FAUNA ECOLOGISTS

Strong (1992) reviewed the available evidence on the impact of ivermectins on dung insects, and McCracken (1993) considered the potential of ivermectins to affect all types of wildlife.

STUDIES OF COLEOPTERA AND DIPTERA FEEDING ON DUNG

Toxicity to adult beetles entering contaminated dung appears to be low, but studies have shown effects do occur. The age of individuals may be important e.g. *Copris hispanus* and *Onitis belial* adults die if they are newly emerged in the dung of cows injected 1-5 days earlier, but can survive if they are a few days older (Wardhaugh & Rodriguez-Menendez, 1988; Houlding et al., 1991). Possibly permeability of the cuticle changes in early life result in this effect, but the full mechanism is not known.

Larval stages are much more sensitive, possibly due to their more permeable cuticle, e.g. *Onitis gazella* larvae cannot survive in dung deposited up to 21 days post-treatment (Roncalli, 1989), and it is about 8 weeks after treatment that larvae of *O. binodis* can develop normally. Larval *Copris hispanus* cannot complete development until 16 days after injection (Wardhaugh & Rodriguez-Menendez, 1988). Similarly *Aphodius* larvae die in dung collected 1-2 days after injection (Madsen et al., 1990). Numbers of *Aphodius* larvae were markedly depressed in dung voided by cattle fitted with a bolus releasing 40 μg/kg/day (Wall & Strong, 1987).

Ivermectin in cattle dung does not deter colonising insects (Strong and Wall, 1988, 1994), and may even be more attractive to burying beetles than control dung (Wardhaugh and Mahon, 1991, Holter *et al.*, 1993). Wardhaugh and Mahon also showed that adult departure rates from the treated dung were slower. These effects were noted for dung up to 25 days after injection. Similar effects were noted for sheep, but the attractive period was much reduced.

Diptera are also affected, but Cyclorrhapha much more than Nematocera. Annelid densities do not seem to be affected by avermectin treatment (e.g. Wall & Strong, 1987), possibly because soil contact accelerates degradation.

Larval insects treated with sub-lethal doses of avermectins often fail to grow at the normal rate; be unable to shed their skins, or metamorphose into a pupa. All of these events would be expected if there is an anti-feeding effect, or if neuromuscular paralysis occurred. A failure to pupate is not, however, entirely explained by an inability to feed and accumulate tissues and reserves. Some dipterous larvae will not pupate normally after ivermectin contact, even though they have ceased feeding before contact.

Studies in Australia by Wardhaugh *et al.* (1993) showed dung from ivermectin-drenched sheep caused significant mortality to newly-emerged larvae of the bushfly *Musca vetustissima* for up to 1 week after treatment. Those drenched with a mixture of levamisole and oxfendazole also resulted in larval mortality, but the effect was limited to the first 48 hrs after treatment. Flies reared to adult stage on dung collected up to 32 days post-drenching were tested for evidence of fluctuating asymmetry as an indication of developmental stress. None was found for either drench treatment, but ivermectin residues may directly affect wing size. In contrast Strong and James (1993) found very low levels of ivermectin exposure (0.0005 ppm) to larvae caused wing abnormalities in *Scatophaga stercoraria*, as well as larval mortality at higher levels. (EC50 values for 24 and 48h exposure of 0.051 ppm and 0.036 ppm (wet weight) respectively.) In addition to the significantly higher level of fluctuating asymmetry, 23% of the treated insects developed new veins and cells in their wings. They drew attention to the practice of failing to observe the full impact of sub lethal effects, which can be as serious as those of acute toxicity.

Wardhaugh *et al.* (1993) also found that the introduced dung beetle *Euoniticellus fulvus* was sensitive to ivermectin residues in sheep dung. In the first day after drenching, dung caused mortality among newly emerged beetles and delayed the reproductive development of survivors. However, beetles in which the reproductive development was impaired regained their capacity following transfer to non-toxic dung. Day 1 caused no mortality among sexually-mature adults, but there was a significant reduction in their fecundity. Dung collected 2-10 days post-drenching had no effects on either the survival or reproductive development of adult beetles, regardless of age. Residues in dung collected 1-2 days post-drenching caused 100% mortality in beetle larvae, but by day 5 there was no evidence of acute toxicity.

BALANCING THE CONFLICT OVER THE USE OF IVERMECTIN

Avermectins clearly are valuable broad-spectrum anthelmintics which can help veterinary practitioners and farmers to maintain healthy, profitable livestock. After drench and injection administration methods the dung initially produced by livestock is ecotoxic to the dung beetle and cyclorhaphous dipteran fauna by interferring with the adult beetle's capacity to reproduce, and the capacity of larvae of both groups to feed, grow and develop (Strong *et al.*, submitted), rather than by any obvious 'knockdown' effect. Such an effect would be more easily detected, and may have delayed or prevented licensing approval in various countries. After a maximum of about 10 days following drench and injection treatment, further dung excreted shows much lower ecotoxicity, though we cannot yet rule out further sub-lethal effects, such as minor deformities which may prove to have a genetic basis. Ecotoxicity may further be reduced if the drug was injected as aqueous micelles, rather than in organic solution.

As Forbes (1993) has argued, the percentage of cattle treated world-wide is probably less than 15%. With the asynchronous use which happens over much of the regions in which it is employed, it should be no surprise that its environmental impact has been limited so far. However, its use is likely to increase, especially in countries like Australia (Wardhaugh *et al.* 1993). Also, until recently approval has only been for drench, injection and paste formulations. We are now faced with a much more worrying trend. This is the use of sustained-release bolus formulations which are now being licensed.

SUSTAINED INTRARUMINAL RELEASE

An intraruminal sustained-release bolus for cattle utilising an osmotic pump has been in progress for several years and is now available. It is designed to deliver a minimum of 40 μg/kg/day over 120 days. Pope et al. (1985) showed that this delivery system achieved steady-state concentrations in plasma within 7-14 days and a systemic availability of 40%. From this study it was predicted that at 40 μg/kg/day mean steady state levels of approx. 20 ng ivermectin/ml plasma would result. However, in trials calves given this dose showed mean plasma levels of only <5.5 ng/ml plasma (Baggott et al., 1986). The reasons for the difference is not known, but may be due to the presence of a substantial mixed gastrointestinal nematode infection in the calves used. Abomasal parasitism may reduce the systemic availability of anthelmintics (Marriner et al., 1985), whereas intestinal parasitism appears to have no significant effect (McKellar et al., 1991). It may be that higher doses are therefore necessary to achieve parasite control, and even higher levels will be added to the environment.

Strong *et al.* (submitted) have recently tested the effects of ivermectin and fenbendazole sustained-release boluses on cattle. Their results, from blind tests using dung collected 21 days after dosing, showed that both types of treated dung, and control dung were equally attractive to adult *Aphodius* dung beetles, with a slight tendency towards treated dung being more attractive. Development of larval beetles was normal in both control and fenbendazole treated dung, but was prevented from progressing past the first instar by ivermectin. Dung degradation was also noticibly inhibited by ivermectin.

The pressure to switch from pour-on, paste or injection administration to bolus sustained release devices is likely to rise as it reduces the number of handling events of livestock needed. This saves manpower and therefore costs.

This suggests that total avermectin losses from livestock to the environment will rise in many countries in the near future. Since all dung from a bolus-treated animal is likely to be ecotoxic to dung fauna, and they last for 120 days, this could pose a serious threat to foods webs based on dung fauna. This is not the only problem which is likely to arise. Prolonged exposure to ivermectin is predicted to hasten the development of resistant worms and other parasites.

IMPROVED STRATEGIES IN THE USE OF ANTHELMINTICS

Herd (1993) agreed with the views of Waller (1993) that the total reliance on anthelmintics to control nematode parasites is no longer tenable. In the USA the situation is even less tenable because of trends for ivermectin over-use, a lack of effective monitoring of its effects on the host, parasite and the environment. There is an obvious need for better use of existing anthelmintics, and better dissemination of reliable information to vets. and livestock owners. The consequences of drug abuse and short-sighted sales tactics that make no effort to conserve anthelmintic efficacy have been seen already in the development of resistance to ivermectin by sheep and goat nematodes in the USA and other countries. Herd summarised a number of epidemialogic approaches to parasite control for horses, cattle and sheep in northern USA to control worms effectively.

The approaches reduced costs, labour and drug-related problems. They were explained in a series of papers published over more than a decade. They include strategies, such as pasture hygiene, which is designed to minimise resistance, encystment and ecotoxicity; others, such as spring treatments, may require some manipulation to avoid ecotoxicity. They have been used on a limited basis so far, but are urgently needed now.

Waller (1993) of CSIRO in Australia, summarised the future of livestock health practices in his abstract which is as follows.

Farmers world-wide have come to expect, and rely almost exclusively on, broad-spectrum anthelmintics to control nematode parasites among their livestock. However, the threats of resistance, residues and ecotoxicity are of increasing concern to the future of chemotherapy. It is imperative that sustainable parasite control schemes be developed and implemented which will integrate a range of techniques to minimise anthelmintic use and still maintain high levels of profitability of the farming enterprise. At present, these need to focus on the better use of existing drugs to maximise their effectiveness and minimise the selection for resistance and impact on the environment. New drugs should also be used according to these principles. In future it is expected that other non-chemotherapeutic options will become available, e.g. helminth vaccines, resistant hosts, biological control using fungi (e.g. Grønvold *et al.* 1993), and nematode growth regulators, which will revolutionise the current thinking on nematode parasite control of livestock.

REFERENCES FOR PARTS 1 TO 4 AND APPENDICES

BAGGOTT, D.G., BATTY, A.F. & ROSS, D.B. (1986) The control of mature nematode infections in cattle by sustained delivery of ivermectin. Proc. 14th World Congress on the Diseases of Cattle. August 1986, Dublin. World Association for Buiatrics, Dublin, pp. 160-165.

BAKER, R.R. (1969) The evolution of the migratory habit in butterflies. Journal of Animal Ecology 38, 703-746.

BAKER, R.R. (1978) *The Evolutionary Ecology of Animal Migration*. Hodder & Stoughton, London.

BAKER, R.R. (1984) The dilemma: when and how to go or stay. In: *The Biology of Butterflies*, (eds. R.I. Vane-Wright & P. Ackery). Academic Press, London.

BAKER, R.R. (1985) Moths: Population estimates, light-traps and migration. In: *Case studies in population biology*. (ed. L.M. Cook). Manchester University Press, Manchester. pp. 188-211.

BAKER, R.R. & SADOVY, Y. (1978) The distance and nature of the light-trap response of moths. Nature, London 276, 818-820.

BARNES, H.F. (1937) Methods of investigating the bionomics of the common crane-fly, *Tipula paludosa* Meigen, together with some results. Annals of Applied Biology 24, 356-68.

BLOOM, R. A. & MATHESON,III, J.C. (1993) Environmental assessment of avermectins by the US Food and Drug Administration. Veterinary Parasitology 48, 281-294.

BOWDEN, J. & MORRIS, M.S. (1975) The influence of moonlight on catches of insects in light-traps in Africa. III. The effective radius of a mercury-vapour light-trap and the analysis of catches using effective radius. Bulletin of Entomological Research 65, 303-348.

CAMBEFORT, Y (1991) Biogeography and evolution. pp 51-68. In: *Dung Beetle Ecology*. (eds. I. Hanski, & Y. Cambefort) Princeton University Press, Princeton, New Jersey.

CARTER, D.J. & HARGREAVES, B. (1986) *A field guide to the caterpillars of butterflies and moths in Britain and Europe*. Collins, London.

CHUI, S.H. L., GREEN, M.L., BAYLISS, F.P., ELINE, D., ROSEGAY, A., MERIWETHER, H. & JACOB, T.A. (1990) Absorption, tissue distribution, and excretion of tritium-labeled ivermectin in cattle, sheep and rat. Journal of Agricultural and Food Chemistry 38, 2072-2078.

COOK, L.M. & SARSAM, V. (1981) Polymorphism in the moth *Noctua pronuba* (L.) Heredity, London 46, 443-7.

COULSON, J.C. (1959) Observations on the Tipulidae (Diptera) of the Moor House Nature Rserve, Westmorland. Transactions of the Royal Entomological Society of London 111, 157-74.

COULSON, J.C. (1962) The biology of *Tipula subnodicornis* Zetterstedt, with comparative observations on *Tipula paludosa* Meigen. Journal of Animal Ecology 31, 1-21.

DENHOLM-YOUNG, P.H. 1978 Studies of decomposing cattle dung and its associated fauna. D. Phil. thesis. Univ. of Oxford, England.

EWERT, K.M., DIPIETRO, J.A., BERENBAUM, M.R. & TODD, K.S. (1990) *Musca domestica* bioassay for detection of larvicidal activity of ivermectin in horse feces. In: Proc. 71st Annual Meeting of the Conference of Research Workers in Animal Disease, 5-6 November, Chicago, Abstract 157, p. 27.

FINCHER, G.T., STEWART, T.B. & DAVIS, R. (1970) Attraction of coprophagous beetles to feces of various animals. Journal of Parasitology 56, 378-373.

FORBES, A.B. (1993) A review of regional and temporal use of avermectins in cattle and horses worldwide. Veterinary Parasitology 48, 19-28.

GREGG, P.C., FITT, G.P., COOMBS, M. & HENDERSON, G.S. (1993) Migrating moths collected in tower-mounted light-traps in northern New South Wales, Australia: species composition and seasonal abundance. Bulletin of Entomological Research 83, 563-568.

GREGG, P.C., FITT, G.P., COOMBS, M. & HENDERSON, G.S. (1994) Migrating moths collected in tower-mounted light traps in northern New South Wales, Australia: influence of local and synoptic weather. Bulletin of Entomological Research 84, 17-30.

GRØONVOLD, J., WOLSTROP, J., NANSEN, P., HENDRIKSEN, S.A., LARSEN, M. AND BRESCIANI, J. (1993) Biological control of nematode parasites in cattle with nematode-trapping fungi: a survey of Danish studies. Veterinary Parasitology 48, 311-325.

HALFFTER, G. & MATTHEWS, E.G. (1966) The natural history of dung beetles of the sub-family Scarabaeinae (Coleoptera: Scarabaeidae). Folia Entomolologica Mexicana 12-14, 1-312.

HALLEY, B.A., NESSEL, R.J. & LU, A.Y.H. (1989) Environmental aspects of ivermectin usage in livestock: general considerations. In: W.C. Campbell (Editor), *Ivermectin and Abamectin*. Springer, New York, pp. 162-172.

HALLEY, B.A., VANDENHEUVEL, J.A. & WISLOCKI, P.G. (1993) Environmental effects of the usage of avermectins in livestock. Veterinary Parasitology 48, 109-125.

HANSKI, I. (1979) The Community of Coprophagus Beetles. D. Phil. thesis, University of Oxford, England.

HANSKI, I. (1980a) Spatial patterns and movements in coprophagous beetles. Oikos 34, 293-310.

HANSKI, I. (1980b) Patterns of beetle succession in droppings. Ann. Zool. Fenn. 17, 17-25.

HANSKI, I (1986) Individual behaviour, population dynamics and community structure of *Aphodius* (Scarabaeidae) in Europe. Acta Oecol., Oecol. Gen. 7, 171-87.

HANSKI, I. & CAMBEFORT, Y. (1991) *Dung Beetle Ecology*. Princeton University Press, Princeton, New Jersey.

HARTSTACK, A.W., HOLLINGSWORTH, J.P. & LINDQUIST, D.A. (1968) A technique for measuring trapping efficiency of electric insect traps. Journal of Economic Entomology 61, 546-552.

HERD, R.P. (1993) Control strategies for ruminant and equine parasites to counter resistance, encystment, and ecotoxicity in the USA. Veterinary Parasitology 48, 327-336.

HERD, R.P., JERNIGAN, A.D., STINNER, B.R. & PURRINGTON, F.F. (1990) Ecotoxicity of anthelmintics. In: Proc. 35th Meeting of the American Association of Veterinary Parasitologists, 21-24 July 1990, San Antonio, No. 37.

HOESE, B. & SCHNEIDER, P. (1988) Der Fettgehalt bei Maikäfern, *Melolontha melolontha* L. und *M. hippocastani* F., während der postpupalen Diapause und im frühen Imaginalstadium. Zoologische Jahrbücher Physiologie 92, 471-485.

HOLTER, P. (1975) Energy budget of a natural population of *Aphodius rufipes* larvae (Scarabaeidae). Oikos 26, 177-86.

HOLTER, P. (1979) Abundance and reproductive strategy of the dung beetle *Aphodius rufipes* (L) (Scarabaeidae). Ecological Entomology 4, 317-26.

HOLTER, P. (1982) Resource utilization and local coexistence in a guild of scarabaeid dung beetles (*Aphodius* spp.) Oikos 9, 213-27.

HOLTER, P., SOMMER, C. & GRØNVOLD, J. (1993) Attractiveness of dung from ivermectin-treated cattle to Danish and afrotropical scarabaeid dung beetles. Veterinary Parasitology 48, 159-169.

HOULDING, B., RIDSDILL-SMITH, T.J. & BAILEY, W.J. (1991) Injectable abamectin causes a delay in scarabaeine dung beetle egg-laying in cattle dung. Australian Veterinary Journal 68, 185-186.

JONES, G. (1990) Prey selection by the greater horseshoe bat (*Rhinolophus ferrumequinum*): optimal foraging by echolocation? Journal of Animal Ecology 59, 587-602.

JONES, G. & MORTON, M. (1992) Radio-tracking studies on habitat use by greater horseshoe bats (*Rhinolophus ferrumequinum*). In: *Wildlife telemetry: remote monitoring and tracking of animals* (eds. I.G. Priede & S.M. Swift) 521-537 Ellis Horwood, New York, London etc.

JONES, G, & RAYNER, J.M.V. (1989) Foraging behaviour and echolocation of wild horseshoe bats *Rhinolophus ferrumequinum* and *R. hipposideros* (Chiroptera, Rhinolophidae). Behavioural Ecology and Sociobiology 25, 183-191.

JONES, G., DUVERGÉ, P.L. & RANSOME, R.D. (1995) Conservation biology of an endangered species: field studies of greater horseshoe bats. Symposium of the Zoological Society of London No. 67, 309-324.

LANDIN, B-O. (1961) Ecological studies on dung-beetles (Col. Scarabaeidae). Opusc. Ent. Suppl.XIX. - Lund.

LANDIN, B-O. (1968) The diel flight activity of dung-beetles (Col. Scarabaeidae). Opusc. Ent. Suppl. XXXIII. - Lund.

LAURENCE, B.R. (1956) The larval inhabitants of cow pats. Journal of Animal Ecology 23, 234-60.

LEWIS, T (1969a) The distribution of flying insects near a low hedgerow. Journal of Applied Ecology 6, 443-452.

LEWIS, T. (1969b) The diversity of the insect fauna in a hedgerow and neighbouring fields. Journal of Applied Ecology 6, 453-458.

LEWIS, T. (1970) Patterns of distribution of insects near a windbreak of tall trees. Annals of Applied Biology 65, 213-220.

LINSSEN, E.F. (1959) *Beetles of the British Isles, Series II.* Warne, London and New York.

LO, P.-K.A., FINK, D.W., WILLIAMS, J.B. & BLODINGER, J.A. (1985) Pharmokinetic studies of ivermectin: effects of formulation. Veterinary Research Communications, 9, 251-268.

LUMARET, J.-P. & KIRK, A.A.(1991) South temperate dung beetles. pp 97-115. Dung Beetle Ecology. (eds. I. Hanski, & Y. Cambefort) Princeton University Press, Princeton, New Jersey.

MADLE, H. (1934) Zur Kenntnis der Morphologie, Ökologie und Physiologie von *Aphodius rufipes* Lin. und einigen verwandten Arten. Zool. Jahrb. Anat. Ont. 58. Jena.

MADSEN, M., OVERGAARD NIELSEN, B., HOLTER, P., PEDERSEN, O.C., BROCHNER JESPERSEN, J. VAGN JENSEN, K.-M., NANSEN, P. AND GRONVØLD, J. (1990) Treating cattle with ivermectin: effects on the fauna and decomposition of dung pats. Journal of Applied Ecology 27, 1-15.

MARRINER, S.E., EVANS, E.S. & BOGAN, J.A. (1985) Effect of parasitism with *Ostertagia circumcincta* on pharmokinetics of fenbendazole in sheep. Veterinary Parasitology, 17, 239-249.

MARSH, R. & CAMPLING, R.C. (1970) Fouling of pastures by dung. Commonw. Agric. Bur. Herbage Abstr. 40, 123-130.

MCANEY, C.M., SHIEL, C., SULLIVAN, C. & FAIRLEY J.S. (1991) *The Analysis of Bat Droppings.* Occasional Publication of the Mammal Society No. 14.

MCCRACKEN, D.I. (1993) The potential for avermectins to affect wildlife. Veterinary Parasitology 48, 273-280.

MCKELLAR, Q.A., JACKSON, F. COOP, R.L., JACKSON, E. & SCOTT, E. (1991) Effect of parasitism with *Nematodirus battus* on the pharmokinetics of levamisole, ivermectin and netobimin. Veterinary Parasitology 48, 123-136.

MERRITT, R.W. (1974) The Species Diversity and Abundance of Insects Inhabiting Cattle Droppings. Ph.D. dissertation University of California, Berkeley, USA.

MERRITT, R.W. & ANDERSON, J.R. (1977) The effects of different pasture and rangeland ecosystems on the animal dynamics of insects in cattle droppings. Hilgardia 45, 31-71.

MIKKOLA, K. (1972) Behavioural and electrophysiological responses of night-flying insects, especially Lepidoptera, to near-ultraviolet and visible light. Annales Zoologici Fennici 9, 225-54.

MOHR, C.O. (1943) Cattle droppings as ecological units. Ecological Monographs 13, 275-309.

MUIRHEAD-THOMSON, R.C. (1991) *Trap responses of flying insects.* Academic Press, London.

POPE, D.G., WILKINSON, P.K., EGERTON, J.R. & CONROY, J. (1985) Oral controlled-release delivery of ivermectin in cattle via an osmotic pump. J. of Pharm. Sci. 74, 1108-1110.

RANSOME, R.D. (1968) The distribution of the greater horseshoe bat, *Rhinolophus ferrumequinum*, during hibernation, in relation to environmental factors. Journal of Zoology, London 154, 77-112.

RANSOME R.D. (1971) The effect of ambient temperature on the arousal frequency of the hibernating greater horseshoe bat, *Rhinolophus ferrumequinum,* in relation to site selection and the hibernation state, Journal of Zoology, London 164, 357-371.

RANSOME, R.D. (1973) Factors affecting the timing of births of the Greater horseshoe bat, (*Rhinolophus ferrumequinum*), Periodicum Biologorum 75, 169-175.

RANSOME, R.D. (1978) Daily activity patterns of the Greater horseshoe bat, *Rhinolophus ferrumequinum*, from April to September. In Olembo RJ, Castelino JB, Mutere FA, eds. *Proceedings of the Fourth*

International Bat Research Conference, Kenya National Academy for Advancement of Arts and Science, Kenya Literature Bureau, Nairobi, 259-274.

RANSOME, R.D. (1989) Population changes of Greater horseshoe bats studied near Bristol over the past twenty-six years, Biological Journal of the Linnean Society 38, 71-82.

RANSOME, R.D. (1990) The natural history of hibernating bats. London: Christopher Helm.

RANSOME, R.D. (1995) Earlier breeding shortens life in female greater horseshoe bats, Philosophical Transactions of the Royal Society, Series B 350, 153-161.

RANSOME, R.D. (submitted) Climatic effects upon foraging success and population changes of female greater horseshoe bats.

RANSOME R.D. & MCOWAT, T.P. (1994) Birth timing and population changes in greater horseshoe bat colonies are synchronised by climatic temperature. Zoological Journal of the Linnean Society 112, 337-351.

RIDSDILL-SMITH, T.J. (1988) Survival and reproduction of *Musca vetustissima* Walker (Diptera: Muscidae) and a Scarabaeine dung beetle in dung of cattle treated with avermectin B1. Journal of Australian Entomological Society 27, 175-178.

RILEY, J.R., REYNOLDS, D.R. & FARMERY, M.J. (1983) Observation of the flight behaviour of the armyworm moth, *Spodoptera exempta*, at an emergence site using radar and infra-red optical techniques. Ecological Entomology A 8, 395-418.

ROBERTSON, A.G. (1939) The nocturnal activity of crane-flies (Tipulinae) as indicated by captures in a light trap at Rothamsted. Journal of Animal Ecology 8, 300-22.

RONCALLI, R.A. (1989) Environmental aspects of use of ivermectin and abamectin in livestock:effects on cattle dung fauna. In: W.C. Campbell (Editor), *Ivermectin and Abamectin*. Springer, New York, pp. 173-181.

ROSSDALE, P.D. (1976) *Inside the horse*. The California Thoroughbred Breeders Association, Arcadia, CA, USA.

RYAN, W.G. & GUERRERO, J. (1987) Effect of ivermectin on performance of cattle treated at housing. Agri-Practice 8, 34-36.

SCHAEFER, G.W. (1976) Radar observations of insect flight. In: *Insect Flight*. (ed. R.C. Rainey). Blackwell, London. pp. 157-97.

SCHMIDT, G. (1935) Beiträge zur Biologie der Aphodiinae (Coleoptera, Scarabaeidae). Stettin. ent. Ztg. 96, 2. Stettin.

SINGH, M.P. & KEVAN, D.K.McE. (1965) Notes on three common species of agrotid moth. Entomological Record and Journal of Variation 68, 233-5.

SKIDMORE, P. (1991) *Insects of the British cow-dung community*. Occasional Publications No. 21, Field Studies Council.

SOMMER, C., STEFFANSEN, B., OVERGAARD NIELSEN, B. GRØNVOLD, J. VAGN JENSEN, K.-M., BROCHNER JESPERSEN, J., SPRINGBORG, J. & NANSEN, P. (1992) Ivermectin excreted in cattle dung after subcutaneous injection or pour-on treatment: concentrations and impact on dung fauna. Bulletin of Entomological Research 82, 257-264.

SOTTIBANDHU, S. (1978) Behaviour of Moths in Relation to Light Traps. Ph.D. thesis, University of Manchester.

SOUTH, R. (1961) *The moths of the British Isles*. Warne, London & New York.

SPEAKMAN, J.R. (1990) The function of daylight flying in British bats. Journal of Zoology, London 220, 101-113.

SPEAKMAN, J.R. (1991) Why do insectivorous bats in Britain not fly in daylight more frequently? Funct. Ecol. 5, 518-524.

STEBBINGS, R.E. (1982) Radio tracking greater horseshoe bats with preliminary observations on flight patterns. Symposium of the Zoological Society of London No. 49, 161-173.

STEEL, J.W. (1993) Pharmokinetics and metabolism of avermectins in livestock. Veterinary Parasitology 48, 45-57.

STEVENSON, B.G. AND DINDAL, D.L. (1985) Growth and development of *Aphodius* beetles (Scarabaeidae) in laboratory microcosms of cow dung. Coleopt. Bull. 39, 215-20.

STRONG, L. (1992) Avermectins: a review of their impact on insects of cattle dung. Bulletin of Entomological Research 82, 265-274.

STRONG L. (1993) Overview: the impact of avermectins on pastureland ecology. Veterinary Parasitology 48, 3-17.

STRONG, L. & WALL, R. (1988) Ivermectin in cattle: non-specific effects on pastureland ecology. Aspects of Applied Biology 17, 231-238.

STRONG, L. & WALL, R. (1994) Effects of ivermectin and moxidectin on the insects of cattle dung. Bulletin of Entomological Research 84, 403-409.

STRONG, L., WALL, R., WOOLFORD, A. & DJEDDOUR, D. (submitted) The effects of ivermectin and fenbendazole administered by sustained-release bolus on the insect colonisation of cattle dung.

TAYLOR, L.R. (1963) Analysis of the effect of temperature on insects in flight. Journal of Animal Ecology 32, 99-117.

TAYLOR, L.R. & CARTER, C.I. (1961) The analysis of numbers and distribution in an aerial population of macrolepidoptera. Transactions of the Royal Society of London 113, 369-386.

TAYLOR, L.R., FRENCH, R.A. & WOIWOD, I.P. (1978) The Rothamsted insect survey and the urbanization of land in Great Britain. In: *Perspectives in Urban Entomology*. Academic Press, London & New York pp. 31-65.

TAYLOR, L.R. & WOIWOD, I.P. (1980) Temporal stability as a density-dependent species characteristic. Journal of Animal Ecology 49, 209-24.

WALL, R. & STRONG, L. (1987) Environmental consequences of treating cattle with the antiparasitic drug ivermectin. Nature 327, 418-421.

WALLER, P.J. (1993) Towards sustainable nematode parasite control of livestock. Veterinary Parasitology 48, 295-309.

WARDHAUGH, K.G. & MAHON, R.J. (1991) Avermectin residues in sheep and cattle dung and their effects on dung-beetle (Coleoptera: Scarabaeidae) colonization and dung burial. Bulletin of Entomological Research 81, 333-339.

WARDHAUGH, K.G. & RODRIGUEZ-MENENDEZ, H. (1988) The effects of the antiparasitic drug, ivermectin, on the development and survival of the dung-breeding fly, *Orthellia cornicina* (F.) and the scarabaeine dung beetles, *Copris hispanus* (L.) *Bubus bubalus* (Oliver) and *Onitis belial* (F.) Journal of Applied Entomology 106, 381-389.

WARDHAUGH, K.G., MAHON, R.J., AXELSEN, A., ROWLAND, M.W. & WANJURA, W. (1993) Effects of ivermectin residues in sheep dung on the development and survival of the bushfly, *Musca vetustissima* Walker and a scarabaeine dung beetle, *Euoniticallus fulvus* Goeze. Veterinary Parasitology 48, 139-157.

WARING, P.A. (1989) Comparison of ligh-trap catches in deciduous and coniferous woodland habitats. Entomologist's Record 101, 1-10.

WARNKE, G. (1931) Experimentelle Untersuchungen über der Geruchssinn von *Geotrupes silvaticus* Panz und *Geotrupes vernalis* Lin. Zugleich ein Beispiel zur problem der Orienterung der Tiere in Raum. Zeitschrift für vergleichende Physiologie 14 Berlin.

WARNKE, G (1934) Die Geruchsorgane der Lamellikornier. Zool. Anz. 108 Leipzig.

WHITAKER, J.O. (1988) Food habits of insectivorous bats. In: *Ecological and Behavioural Methods for the Study of Bats* (ed. T.H. Kunz). Smithsonian Institution Press, Washington.

WHITE, E. (1960) The natural history of some species of *Aphodius* (Col., Scarabaeidae) in the northern Pennines. Entomologists Monthly Magazine 66, 25-30.

WILLIAMS, C.B. (1958) *Insect Migration.* Collins, London.

YASUDA, H. (1987) Reproductive properties of two sympatric dung beetles, *Aphodius haroldianus* and *A. elegans* (Coleoptera: Scarabaidae) Res. Popul. Ecol. 29:179-87.