Flubenvet™

Dewormer for Poultry

JANSSEN ANIMAL HEALTH

Contents

1 The worm problem surfaces again in the poultry sector

One of the main reasons why laying hens were transferred to wire cages years ago was to prevent parasitic infections. In wire cages, contact with faecal material is rare and consequently there is only a limited risk of coccidiosis or worm infections. Today there is a strong trend towards putting laying hens back onto litter, with the inevitable consequences. In The Netherlands (in 1997), the Poultry Health Institute investigated the incidence of worm and lice infestations in layer flocks that were not kept in battery cages. The results show that 68% of the flocks were infested with worms and 50% with lice.

All poultry reared on litter or in free range systems are at risk from worm infections. Only in broiler chickens, when slaughtered before 50 days of age, is the risk small.
Litter provides the worms with a new opportunity. Indeed, worm eggs and their vectors, such as beetles and flies, thrive well on litter and soil. Depending on the worm species, the eggs may survive for months or sometimes for more than a year. Bringing the birds into contact with the litter will cause infection and re-infection.

The concentration of large numbers of poultry on farms has also increased the chances of survival for most worm species.

Once a worm infection is established in a flock, the whole environment will be heavily contaminated with infective worm eggs. Therefore a good prophylactic deworming programme should be a standard management procedure on any poultry farm.

Worm infections cause serious problems, particularly in flocks reared on litter.

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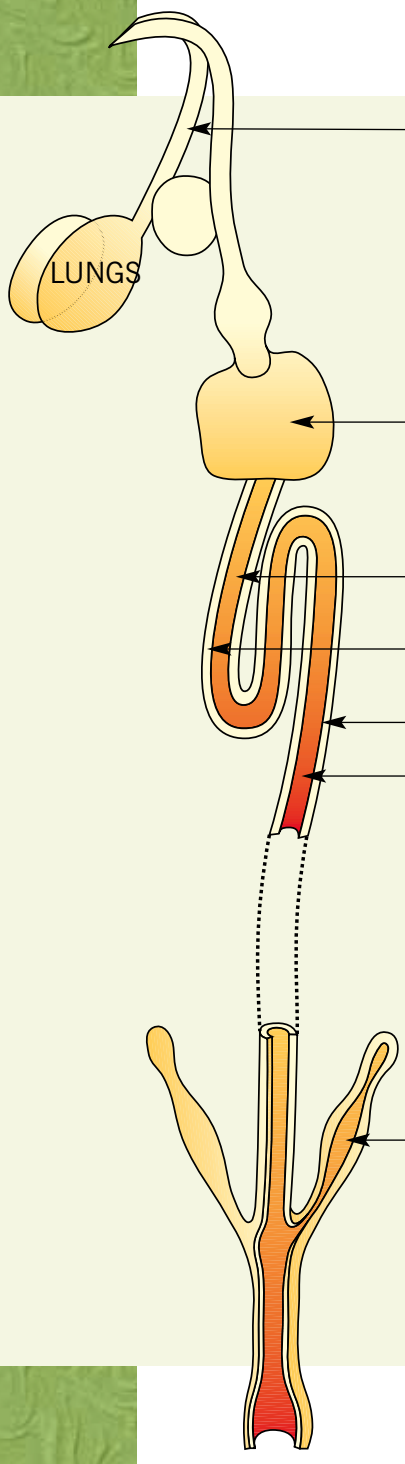
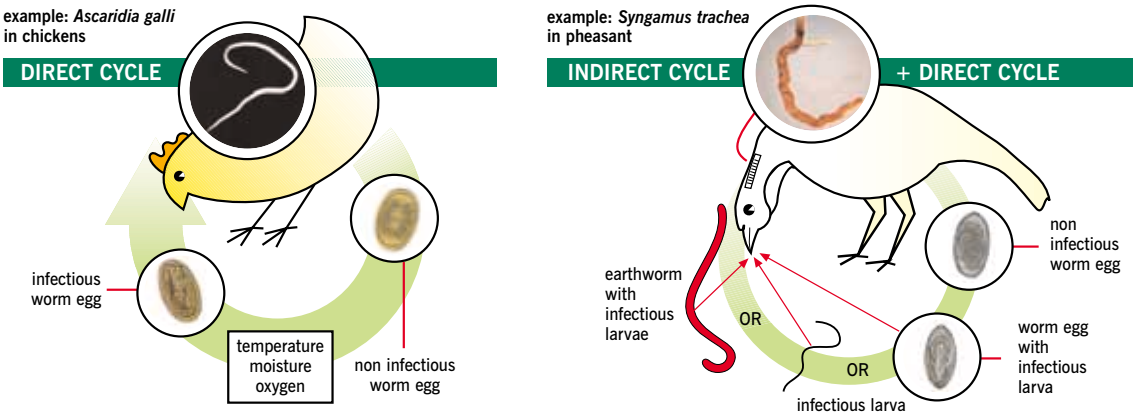
2 Poultry worms cause damage



TRACHEA	lumen	*Syngamus trachea* (gapeworm) (in turkeys and game birds)
STOMACH		*Amidostomum anseris* (stomach worm) (in geese and ducks)
DUODENUM	lumen	*Ascaridia galli* (large roundworm)
		Davainea proglottina (small tapeworm)
	wall	*Capillaria obsignata* (hairworm)
SMALL INTESTINE	wall	*Capillaria obsignata* (hairworm)
	lumen	*Raillietina* spp. (large tapeworm)
		Ascaridia galli (large roundworm)
CAECUM	lumen	*Heterakis gallinarum* (small roundworm)

3 Worms lay eggs, too

In order to survive, parasitic worms have to produce tremendous numbers of eggs. Those eggs are spread with the excreta in poultry houses, nests, on the ground, etc. They first have to "mature" or embryonate. That may happen in two ways: in a direct life cycle they embryonate in the environment and the host can actually ingest the egg or the egg can hatch on the ground and the host ingests an infective larvae; in an indirect life cycle this will happen in an intermediate host. Once the egg, larvae or intermediate host is ingested the larvae are released in the host and a new wave of parasites mature in the host to lay eggs again.



Route of infection:

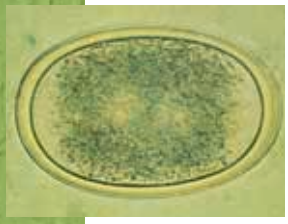
(1) Even when birds are placed on fresh litter, infection can be brought into the premises by larvae or worm eggs which adhered to staff clothing or footwear, materials, trucks, feed bags, insects, wild birds, cats, dogs, etc. A few grams of dung contaminated with worm eggs are sufficient to re-start a worm infection in a flock.

(2) Once the litter is contaminated with worm eggs, it is difficult to break the cycle of continuous re-infection of poultry. In the birds, the eggs or larvae develop into adult egg laying worms that, again, contaminate the litter with massive numbers of eggs.

In some worm species, the infection is transmitted by an intermediate host such as snail, fly or beetle. Birds that have an outside run will therefore more easily contract an infection than those that are kept inside. However, even when birds are kept in batteries infection cannot be completely avoided and is often due to transmission via flies and small meal worms.

Worm eggs are hard to eliminate

Worm eggs may remain infectious for months and sometimes for more than a year if circumstances in the litter are favourable. The egg wall is thick and thus resistant to most disinfectants. Worm eggs will even survive in, say, 0.1 N sulphuric acid or in 2% formalin.



worm eggs cannot "mature" or become infectious

- in a very dry atmosphere;
- at temperatures below 10°C to 15°C ;
- at very high temperatures (above 34°C);
- in the absence of oxygen.

worm eggs are destroyed by:

- drought;
- heat;
- prolonged and deep frost;
- direct sun light.

4 Diagnosis of worm infection

A. Diagnosing worm infection from the symptoms in birds is generally very difficult since worm infections are normally of a "chronic" nature and most of the symptoms are non-specific, occuring with other diseases such as coccidiosis. The occurrence of one or more of the following symptoms should give a warning to investigate further:

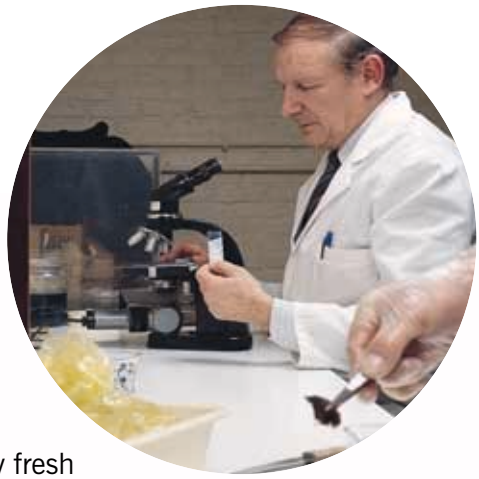
- higher mortality
- marked variability in size of the flock
- poor growth
- poor condition of the birds:
  rough feather coat, pale heads, anaemia, birds failing to thrive
- reduced laying rates, reduced egg weights
- reduced hatchability
- loose droppings

Pale and limp wattles and comb caused by parasitic anaemia

Young turkey in a poor condition due to parasitism

B. Faecal examination: Counting worm eggs in the faeces provides a good indication of the degree of infection in a poultry house, provided it is based on a representative number of samples from intestinal as well as caecal droppings. However, one should always bear in mind that during the prepatent phase of the infection, the birds can harbour large numbers of immature worms, without worm eggs being present in the faeces.

Sampling Technique:
When faecal samples are taken, ensure that only fresh faeces are collected and that the sample is representative. Thus for chickens the procedure is as follows: in the evening brown paper is laid under the perches (8 sheets of 1 by 0.5 m per 1000 birds) and randomly spread. In the morning small heaps of faeces are collected at random.



For flocks of up to 500 birds a minimum of 20 samples of faeces from the small intestine and 20 from the caecum are collected. For each additional 500 chickens that number is increased by 2x10 fresh samples, with a maximum of 2x50. Slimy and flat droppings should be taken. If no paper can be spread under the perches, the faecal samples are taken directly from the litter or from the perches. They should be really fresh and not mixed with litter. When a henhouse is divided into several sections, samples are taken from each section. Pending microscopic examination, the droppings should be kept in small plastic bags or in specially designed small pots.

C. Post-mortem examination can provide additional information once a worm infection is diagnosed by positive EPG* counts. A representative number of birds from different places on the farm should be examined.

Large and small ascarids and also adult stages of the large tapeworms are easily recognised in the intestines.

Hairworms can be seen by mixing the intestinal scrapings with water in a petri dish. The thin white threads, when put on a dark background, are visible with the naked eye. These scrapings can also be pressed between glass slides and held up to the light for inspection.

***EPG: number of worm eggs per gram of faeces**

5 Worms – don't watch them wriggle

A veterinary perspective

The worm problem!

Worm infections cause damage to the birds' gut. This may result in a variety of problems including:

- Loss of shell colour and strength, yolk colour and egg size.
- Poor body weight gain leading to different sized or sick birds. Affected birds may be dull and show pale combs.
- Poor feed conversion.
- Increased cannibalism through vent pecking due to straining.
- Increased risk of egg peritonitis.
- Death: In very heavy infestations.

We all look forward to the advent of Spring with longer days and warmer weather. Unfortunately, so do the worms! It is usually thought that worms begin to thrive on pasture and in our birds once the ambient temperature stays consistently over 10ºC. Increasingly, worms are more of an all year round phenomenon, but the 'Spring rise' is an added torment. So this is a good time to be thinking about your long term worming strategy.

There are three main worms that may cause problems in free range birds:

1) Roundworms (*Ascaridia galli*)

These are the biggest and most common. They are white, up to two inches long and may be visible in droppings in heavy infestation.

2) Hairworms (*Capillaria*)

These are much smaller (hair-like) and are barely visible with the naked eye but can cause significant damage even in only moderate infestations.

3) Caecal worms (*Hetarakis gallinarum*)

As their name suggests, these worms spend most of their time in the lower end of the gut, the caecae. Frequently they cause no obvious harm in themselves but can carry another parasite *(Histomonas)* into the bird. *Histomonas* is the cause of Blackhead and hence control of one parasite can help to control another. With the increasing incidence of histomoniasis for which there is currently no licensed treatment, the role of regular worming is even more important.

Birds become infected by picking up worm eggs from grass, soil or faeces. The worm eggs need warm, moist conditions to develop outside the bird which is why problems are frequently worse in the Spring and Summer, especially following a wet Spring.

If the situation was as clear cut as this preamble suggests, then why does worm control tend to be so hit and miss?

The answer probably lies in the fact that we don't spend enough time thinking about how the problem affects specific sites.

Surprisingly, despite the fact that worms are not a new phenomenon in free range poultry, surveys and investigations on the incidence and control of these parasites are few and far between – especially those related to the types of farming and management practices in place today.

A survey to obtain better information about the pattern and prevalence of worms in free range flocks, was recently undertaken by The Scottish Agricultural College, Auchincruive. The results give an interesting insight into the problem and yield some useful suggestions for control strategies.

The survey looked in detail at 27 sites around the country and involved taking faecal samples on four separate occasions from 20 weeks of age, accompanied by the detailed history of worming strategies before, during and after sampling.

What did the survey show? Firstly, 26 of the 27 flocks had evidence of a worm burden at some time during the survey confirming what we already knew – worms are common! The 27th flock was interesting. It was a flock of 6,000 birds wormed at housing with flubendazole in the feed (the licensed wormer, Flubenvet, Janssen Animal Health), housed on deep litter/slats with a droppings pit, with birds having access to rotation paddocks not used by poultry in the preceding two years.

Worming before coming into lay.
20 of the 27 flocks were wormed before coming into lay. All 13 flocks that had been wormed with Flubenvet before coming into lay tested negative for worms at 20 weeks of age. Of the 7 flocks wormed with an unlicensed or unknown worming product, 5 were still positive for worms at 20 weeks.

and squirm!

When were the worm eggs found?
As the flocks got older, they were more likely to be carrying worms and the peak number of worms in individual samples occurred at around the time of peak production.

Does worming in lay help?
15 flocks were wormed with Flubenvet in lay after a positive worm egg count was obtained. 9 of these were negative on subsequent testing and a further 3 had their count reduced by over 90% at the next sampling. The remaining 3 flocks saw their worm burden reduced by between 50% and 90%.

So what does all this tell us?

1) Worms are common and almost inevitable in laying flocks unless birds are effectively wormed before the move to laying accommodation and have the luxury of moving to 'clean' pasture.

2) Worming prior to the onset of lay with the only licensed wormer means that you should at least start production with a clean slate.

3) Worms can build up quickly on the laying site and can peak at a time when birds are trying to reach peak egg production.

4) Worming in lay can remove or greatly reduce the offending worm burden.

5) Worming only once during lay may not prevent worms from the pasture re-infecting birds and building up to significant levels, suggesting repeated worming may be necessary.

So how does this affect my farm?
The answer is that you need to start looking.

Undoubtedly, some producers have been in business for many years and have never identified a problem. This may be due to the fact that your pullet rearer has delivered you a clean flock and either by your good management, pasture rotation, soil type and drainage or good old fashioned luck, your birds have not met a challenge during lay. Secondly, your birds may have met a moderate burden which has not had a significant effect on performance – or you just haven't noticed!

So where do I go from here?
Firstly, it is important to know your enemy before you can work out what you need to do about it. Worm burdens can be most easily identified by examination of droppings for the presence of visible roundworms. However this won't identify hairworms which can frequently be more severe in their damage to bird performance but are too small to see. Therefore, sending faeces samples to your veterinary surgeon gives a more informative answer – twenty fresh samples taken off the slats will give you a good idea of what worm burden is present.

The most accurate diagnostic method is to submit ailing, thin or other culled birds to your vet for a routine post mortem and health screening, where visible and microscopic tests on the gut can be done, often picking up a burden before it becomes 'patent' ie when birds are pushing out large numbers of eggs that could be detected on a droppings sample.

When do I test?
It is a good idea to test your birds via their droppings soon after arrival on site to check they are worm-free before they start to lay. After that, it is worth establishing a strategic programme with your vet. Clearly if you experience a drop in production, loss of egg size or shell colour, it is worth following this up with a faeces sample and ailing or recently dead birds.

If no specific problems are experienced, the survey discussed earlier suggested that peak worm egg output tends to coincide with peak egg production. So a sample taken then, proving negative, gives you a good comfort factor that nothing is really going wrong. A sample late in the life of the flock again gives you a benchmark for your worm control strategy and also lets you know the likely status of that paddock for the next flock in.

- Regular worming, on the basis of previous experience and discussion with your veterinary surgeon.
- Effective paddock rotation, to reduce worm build up and put off land becoming 'fowl sick'.
- Use good draining land or try to improve drainage.
- Avoid access to poached, muddy areas that encourage worms (and other nasties!).
- Use stones in the area close to popholes to help clean feet and allow droppings passed there to dry, be broken up and be exposed to ultra violet light which is lethal to worm eggs.
- Keep pasture cut short, especially close to the houses, again to allow UV sunlight access to droppings.
- Regular worm egg counts to monitor the success of your chosen strategy.
- Submit birds for post mortem at peak, mid and/or end of lay to check their worm burdens

Armed with all this information, you can develop a worming strategy and pasture management programme which suits your specific enterprise, and helps to avoid problems before they affect your birds and your pocket!

JAH would like to thank the 'Ranger', the magazine of the British Free Range Egg Producers Association, for allowing us to include this article, written by Crowshall Veterinary Services, in our brochure. www.bfrepa.co.uk

6 Damage done by worms

In young chickens (replacement pullets or broilers)

Young chickens are very susceptible to roundworm infections. *Ascaridia* and especially *Capillaria* infections will cause depressed growth and undermine the general health status of flocks. This in turn can jeopardise vaccination schemes.

The massive impact of ascarids was shown in a study[6] with broiler chickens each artificially infected with 500 ascarid eggs. This single infection caused serious clinical signs 6 weeks later. The chickens showed emaciation, loss of comb colour, leg colour and plumage brightness, diarrhoea, drooping wings, ruffled feathers and a gradual loss of strength manifested by leg weakness. At autopsy, the small intestine showed external macroscopic lesions of haemorrhage and congestion.

In laying hens and breeder birds

Significant drops in egg production are apparent in infected breeders or layers because of ascarid infections. An additional concern of ascarid infection in laying hens is that occasional worms may undergo an aberrant migration and become incorporated into an egg. This will be very unappealing to the consumer.

The large roundworm damages the chicken's intestinal mucosa. Massive ascarid infection may cause intestinal blockage and possible rupture, loss of blood and nutrients.

A hairworm *(Capillaria)* infection can produce severe clinical signs. Affected birds appear pale and depressed, they become emaciated, develop diarrhoea and may die. Hens with capillariasis may develop a secondary vitamin A deficiency which, on top of the decreased laying rates, will cause reduced hatchability in breeders and pale yolks in layers. Gapeworms *(Syngamus trachea)* are a serious threat to farms with a free range management system. The gapeworm life cycle may involve the earthworm. In the earthworm, infections can persist for many years and over a period of time soil can become heavily infected. Moreover, wild birds will provide reservoirs of infection for domestic birds like turkeys, pheasants and ducks.

Turkeys

Recent studies confirm that worm infections in turkeys are very common and cause considerable losses. The turkey roundworm - *Ascaridia dissimilis* - is a serious threat. Primarily, the larval stages give cause for concern[14].

The intestines of turkeys often contain only a few adult worms, whereas the larval population can be significant. These larvae cause 2 phenomena not known to most turkey breeders. First they cause a necrotic-like enteritis, most severe in the jejunum, often with additional *E. coli* and/or *C. perfringens* infection, resulting in low market weights[17] or even mortality[13]. Secondly the migrating ascarid larvae[12, 15, 16] may cause 'white spots' on the liver. These visible areas of damage may cause livers to be rejected at slaughter.

In young turkeys heavy infections with the caecal worm, *Heterakis gallinarum*, may cause serious damage such as thickening of the caecal mucosa and small haemorrhages. This worm is also the transmitter of the flagellate *Histomonas meleagridis*. In the liver and the caecum it causes infections and diarrhoea resulting in many rejections ("blackhead"). In breeder turkeys, the tiny hairworms in the stomach (*Capillaria* spp.) can cause severe loses. Young turkeys are also very susceptible to gapeworm infections (*Syngamus trachea*).

Adult gapeworms frequently obstruct the trachea, so that the bird is literally choked by the worms.
The picture shows a young turkey which has died from 'gapes', in a typical 'choked' pose.

Opened windpipes of pheasants with gapeworms

Game birds (pheasants and partridges)

Wild birds are naturally fairly resistant to parasitic infections, but when confined in small areas, they may become severely infected. In particular, younger birds are susceptible to a vast number of parasitic infections which cause serious disease and high mortality. *Syngamus trachea* infection needs to be tightly controlled, but *Capillaria* and *Ascaridia* infections are also quite common and can cause significant direct and indirect losses.

7 Blackhead

Comparison of a healthy chicken liver (left) and one darkened and damaged by Blackhead. The white blotches are areas damaged by the disease.

Young turkeys with Blackhead symptoms. Plumage becomes fluffed, they show signs of dehydration and often have dark head appendages. Blackheads are hardly ever observed. First symptoms appear after about day 3 of infection. By day 9 infected birds are usually dead.

A closer look at the damage caused to a chicken liver by Blackhead. The moon-like craters in the liver are dead areas.

Veterinarian Peter van Beek is a poultry health specialist. He worked for the Poultry Department of the Animal Health Service in the Netherlands for many years before setting up his own consultancy service, Poultry Consulting International. In this article he examines a disease which, he says, could seriously affect European poultry industries.

Blackhead is a serious threat to the productivity and profitability of poultry farming in the UK and elsewhere in Europe – particularly where there is a move to free-range and deep litter production systems. Turkey enterprises can be severely affected by the disease, with mortality rates of 50-90 per cent where there are no effective preventive measures. With chickens, mortality rates of up to 20 per cent can occur.

The disease generally strikes young birds, but those of all ages are susceptible. Re-infections in flocks can occur due to lack of immunity build-up.

The very common small roundworm, *Heterakis*, is the link in infecting chickens and turkeys with *Histomonas meleagridis*, the pathogen that is the causal organism of blackhead. However earthworms, fleas and other insects can play a role in the spread of infected worm eggs.

All poultry susceptible

In the past this disease occurred mainly in free-range poultry and in particular when chickens were housed with turkeys or peacocks, partridges and pheasants. From the age of about two weeks, all poultry are susceptible and the disease can become chronic. At present there is only one preventive agent for turkeys, available as a feed additive. But in the event of an outbreak there is no medication to treat the disease. Consequently, it is very important to know the factors involved in the cause and course of the disease. Through regular deworming it is probably possible to gain better control over two disease factors at once: roundworm and *Histomonas*. Deep litter housing and free-range production increase the risk posed by both factors. Additional efforts to combat blackhead must focus on prevention.

Historical sketch

The causal organism *(Histomonas meleagridis)* of blackhead was first described in 1895. However, actual blackheads are rarely observed and when present they may be due to other conditions. In about 1920 Tyzzer, who played a very important role in the description of many pathogens in poultry, gave a more accurate characterisation.

However, it was not until 1962 to 1974 that the disease was studied in detail, when it was discovered the infection could occur by a number of routes. It was found that in addition to *Histomonas*, small roundworms *(Heterakis)* play an important part and that earthworms can also transmit the infection. Certain bacteria in the caecum were also found to be necessary for the development of the condition.

In 1997 an alarming number of severe *Histomonas* infections were observed in chickens reared for meat in several American states. Mortality rates at times reached 20 per cent. With Europe about to practice deep litter housing again on a large scale there will be new opportunities for *Histomonas*. Recently in 2004 in Germany, France and the Netherlands several cases of Blackhead were seen in grandparent and breeder turkey flocks, but also some cases in finishing flocks. In chicken flocks an increased number of cases in many European countries were also seen.

Pathogen and its life cycle

Histomonas meleagridis is a protozoan and occurs in many forms. The free-living form is a rather fragile amoeba — a microscopically small, unicellular organism with a whip-like appendage and sometimes pseudopodia (little feet). But it is very clever at using various intermediate and carrier hosts to survive and spread. The main intermediate hosts are small roundworms and earthworms.

Heterakis (small roundworm) occurs in all poultry and is found primarily in the caecum. Earthworms can ingest many roundworm eggs. Since earthworms and roundworm eggs are very common and are almost impossible to eradicate, *Histomonas* can spend years waiting for a victim to ingest it. When birds are housed in deep-litter systems, and in particular when they have an outdoor run, there is a greater risk of *Histomonas* infection – mainly because roundworm infections and earthworms are so common in these conditions.

Routes of infection

1. Direct transmission: the amoebae that have proliferated in chickens, turkeys or pheasants, or any other poultry species, are excreted via droppings and can be ingested immediately by other chickens or turkeys. This route of infection is probably less important for spreading the disease between different flocks or locations as amoebae are quite susceptible to dehydration. But within a flock, direct transmission can be very important. In fact after introduction of a single infected *Heterakis* egg, the infection may spread among the rest of the flock by direct transmission.

Health specialists can then be frustrated in finding Blackhead while failing to demonstrate the presence of *Heterakis* in that flock. This is reported to be a frequent occurence by Professor Larry McDougald of the University of Georgia.

2. Intermediate host: a chicken or turkey is infected with small roundworms (*Heterakis*). *Heterakis* eggs are infected with the amoeba in the chicken or turkey gut. These infected worm eggs are excreted via droppings and are ingested by another chicken or turkey. The amoeba is then released into the digestive tract of the new host. Worm eggs can remain infective for months and perhaps for years.

3. Both carrier and intermediate host: the course of events is the same as described in 2, but the *Heterakis* eggs infected with *Histomonas* are now ingested by earthworms (or their larvae). The *Heterakis* larva and the *Histomonas* amoeba are then released into the earthworm. The *Histomonas* amoeba can survive here for three years and possibly longer. When the earthworm is ingested, the chicken or turkey becomes infected. Although there are few findings on this subject, many different insects (flies, beetles and even cicadas) can act as carrier hosts for *Heterakis* eggs.

It is clear there are many opportunities for transmission of *Histomonas* infection. The amoeba also has enormous potential to survive outside the host chicken, turkey or any other poultry species.

Clinical picture

All poultry species are susceptible, but some are more so than others. Turkeys, partridges and peacocks are particularly susceptible and often die a few days after infection. Chickens, guinea fowl, quails and pheasants are slightly less susceptible and acute mortality rates are lower, but they may develop a chronic infection. The speed at which the disease develops also depends on the infection pressure – the greater the number of pathogens ingested, the more severe the symptoms.

There are no characteristic symptoms, only characteristic post mortem findings. For this reason, clinical symptoms and post mortem findings are described together in Table 1.

Laboratory diagnosis in chickens is not always simple and a culture method has been developed in the United States to enable better diagnosis. In turkeys the hepatic alterations are far more characteristic. Turkeys, peacocks and partridges are extremely susceptible to *Histomonas* and rapidly become severely ill. Without effective measures the mortality rate is about 50-90 per cent.

In chickens too, mortality of up to 20 per cent can occur. Birds of all ages are susceptible, but the disease generally occurs in the young. The ubiquitous small roundworm, of course, plays an important role in the disease process. The risk of *Histomonas* infection is greater for free-range birds due to the accumulation of roundworm eggs in the environment as well as the ingestion of infected earthworms, which also act as a reservoir for *Histomonas*.

In the USA several severe cases were seen in broiler parent flocks, especially when so-called skip-a-day feeding was used. Possibly changes in acidity in the digestive tract result in increased sensitivity to infection.

Table 1. Clinical symptoms and post mortem findings of Blackhead

Days after infection	Symptoms and findings
About 3	The birds present the initial mild symptoms of general disease. At this point a few small haemorrhages are visible in the caecum that may strongly resemble caecal coccidiosis in chicken (*Eimeria tenella*).
4	The haemorrhages in the caecal mucosa become greatly extended and the disease spreads via the circulation, reaching the liver and other tissues.
6	Caseous inflammation of the caeca and initial hepatic lesions are visible as small dot-shaped foci, but these are not yet typical.
7 to 8	The caecal wall has thickened and casts can be found in the caecal lumen. When the hepatic lesions become larger and enclose necrotic centres, the characteristic foci become visible. The birds are now severely ill, their plumage is fluffed and they show signs of dehydration and often have dark head appendages. Blackheads are hardly ever observed.
9	Turkeys sometimes produce sulphur-coloured, foul-smelling droppings and have a greatly enlarged liver. The birds generally die soon afterwards due to dehydration and general malaise. Chickens do not produce sulphur-coloured droppings, but may present a bloody caecal discharge. In chickens, the clinical picture is generally less severe than in turkeys. However, since the disease may become chronic and is then associated with loss of weight and production, infections in chickens can be very harmful long-term.

Disease prevention

For decades the industry was able to use preventive and curative agents like ronidazole, dimetridazole and nifursol. These were approved in the form of animal feed additives.

Drugs for the treatment of birds infected with *Histomonas* were discontinued a few years ago. This fact in itself is surely a disgrace as far as drug policy throughout Europe is concerned, particularly since *Histomonas* is about to become a bigger threat.

Some resistance (immunity) develops after a *Histomonas* infection, but that is not always enough to prevent re-infection. Attempts at vaccination have not been successful either. The option the industry has left is to focus on prevention by controlling the intermediate host and the immediate environment of chickens and turkeys.

Main weapon

Consequently, the main weapon against *Histomonas* seems to be regular deworming.

In poultry farming, particularly free-range and in deep litter systems, a well-considered deworming program is critical, particularly since the number of available agents is very limited.

On turkey farms too, it is advisable to check regularly for the presence of *Heterakis* so that timely measures can be taken.

The control of vermin, blood lice, insects and so on is also important. The risk in free-range birds is so great that the control of worm infections and *Heterakis* is hardly feasible.

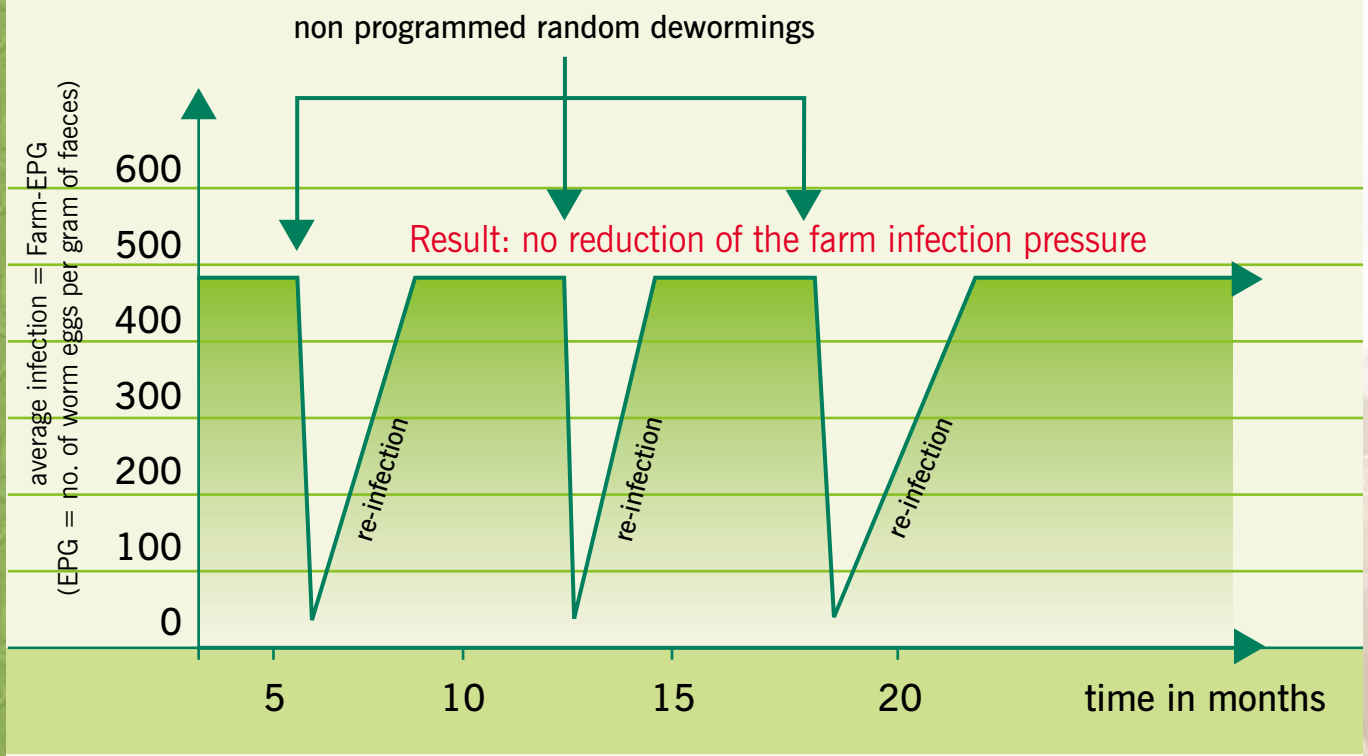
Organic and free-range farms in particular should be especially mindful of this fact.

Keeping chickens together with turkeys, peacocks, partridges or guinea fowl is also inadvisable in the extreme.

8 Prevention rather than cure

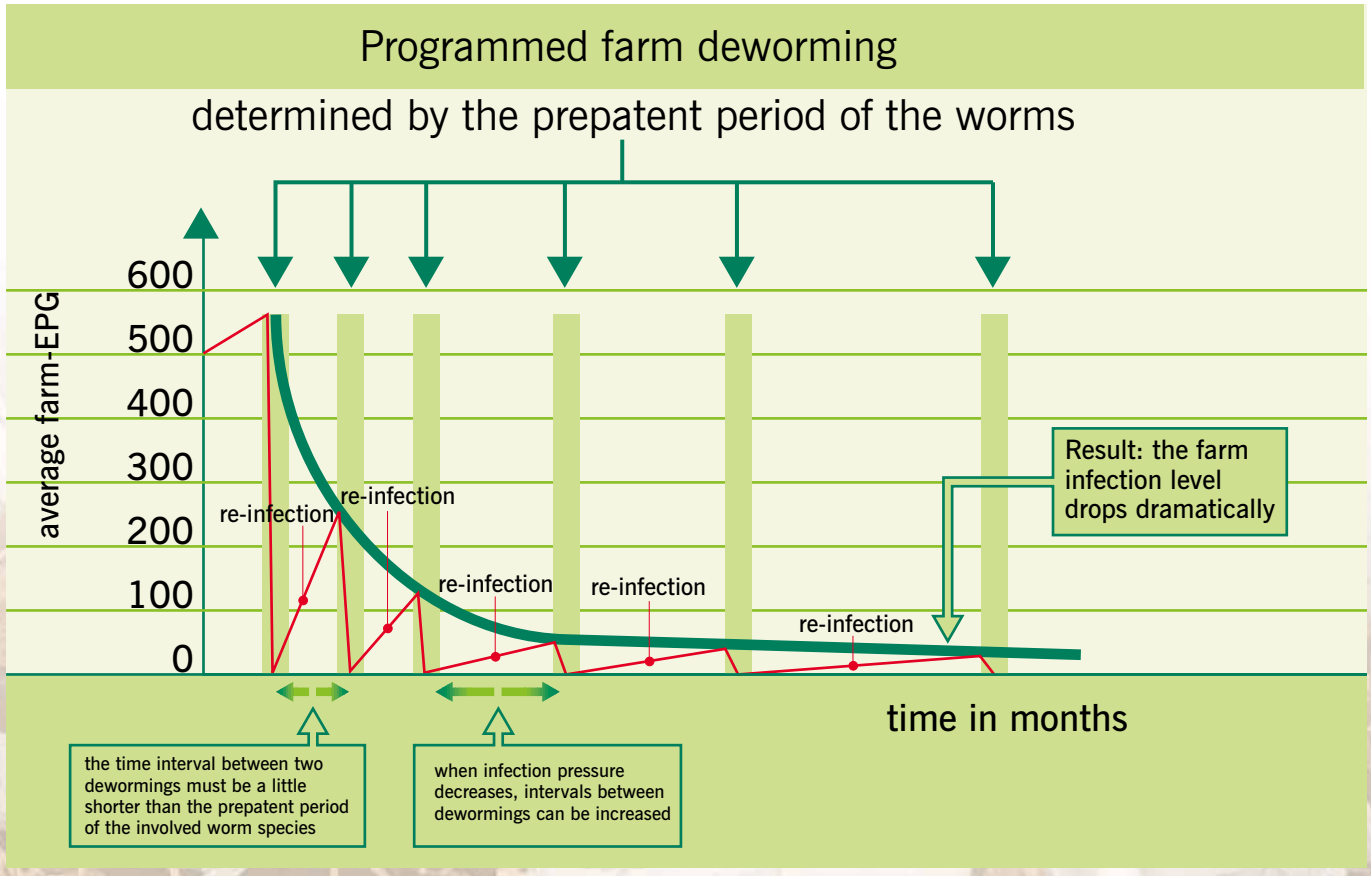
The source of a worm infection is through litter or faecal material contaminated with worm eggs, or through intermediate hosts such as flies, beetles and earthworms. Even after deworming all birds, the soil or litter bedding will remain contaminated with high numbers of worm eggs and continuous re-infection of the flock will take place. Occasional deworming treatments are not effective. The use of anthelmintics has to be programmed with the aim of keeping the infection pressure on the farm as low as possible. Such a programme will take into account the life cycle of the worms. A potent anthelmintic, fully effective against mature and immature stages of the worms, must be used. Even if only a low percentage of worms or larvae remain present in the birds after treatment, they would continue to produce large numbers of eggs and quickly re-contaminate the environment.

Conventional deworming of poultry: **not effective**



A strategic deworming programme

A strategic deworming programme has to be targeted at the entire farm. Correctly implemented, it will result in a dramatic reduction of the worm infection pressure within a defined time period. After a number of treatments, the farm infection pressure will be reduced to a level that can be maintained with an increased interval between treatments. The treatment intervals are determined by the prepatent* period of the worm(s) concerned. The objective is to keep all birds free of adult, egg laying worms. When this is maintained for a sufficiently long period, the infection pressure will gradually decrease or, where this was low already, will certainly not have the chance to increase.



*Time interval from when the worm egg or larvae is ingested by the bird until worm eggs appear in the faeces

THE PREPATENT PERIOD OF THE IMPORTANT POULTRY ROUNDWORMS

Nematodes:		
Ascaridia galli	young birds	35-42 days
	adult poultry	50-56 days
Syngamus trachea		18-20 days
Capillaria obsignata		20-26 days
Heterakis gallinarum		24-30 days
Capillaria contorta		30-60 days
Amidostomum anseris	in geese	14-22 days
	in ducks	35-49 days
Trichostrongylus tenuis		8-10 days

To limit the chances for re-infection from the environment:

- regularly replace litter, keep it dry, prevent excessive build-up of faeces;
- never feed on the floor or on litter;
- develop good hygiene practice and prevent infections from being imported onto the farm;
- control flies, beetles, snails, earthworms;
- use a deworming programme that helps to minimise the excessive shedding of worm eggs.

9 Efficacy of Flubenvet

Flubenvet is highly effective against all important roundworms that occur in poultry.

Flubenvet has been tested extensively in 48 clinical trials in 10 different countries, involving 134,069 chickens, 17,957 pheasants, 4,921 turkeys, 6,249 geese and 1,042 partridges. In all clinical studies, the activity of flubendazole (the active ingredient in Flubenvet) was evaluated either by critical tests or by control tests. In the **critical tests**, each bird serves as its own control as the number of parasites expelled after treatment is evaluated against the number of parasites retained after treatment. In the **control tests**, either EPG values before and after treatment are compared (called 'control EPG' test) or the residual worm burden after treatment is evaluated in a number of randomly selected birds from each treatment group and compared with the worm burden of the untreated group (called 'control worm' test).

Flubendazole proved to be a highly efficacious anthelmintic against the various parasite species of poultry.

In **chickens** fed *ad libitum* at 30 ppm for 7 days, it provides a 97% – 100% activity against *Ascaridia*, *Heterakis* and *Capillaria* infections.

In **turkeys** fed *ad libitum*, 20 ppm flubendazole in the feed for 7 days is completely effective against *Ascaridia*, *Capillaria* and *Syngamus*.

In **geese** fed *ad libitum,* 30 ppm flubendazole for 7 days is highly efficacious. Complete efficacy is obtained against *Capillaria, Syngamus, Trichostrongylus* and the stomach worm *Amidostomum anseris*.

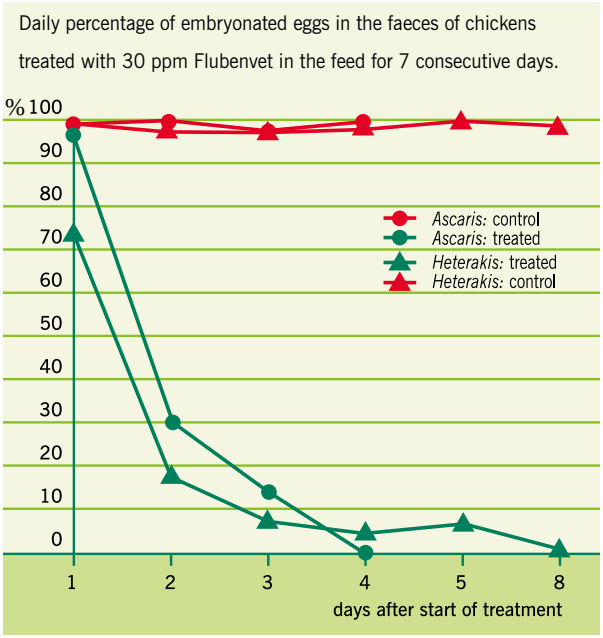
In **pheasants and partridges,** the dose of 60 ppm for 7 days provides very high activity against *Capillaria, Syngamus, Heterakis* and *Ascaridia* infections.

Summary of the clinical trials with Flubenvet in chickens

Treatment (ppm)	Number of birds treated	Evaluation	% Efficacy		
			A. galli	*H. gallinarum*	*Capillaria* spp.
30 ppm for 7 days	18	critical	100	100	
	9	control EPG	100	100	
	12	control worm	100	100	100
	25	control EPG	100	100	
	25	control worm	100	100	
	8	critical	100	100	
	17,141	control EPG	100	100	100
	2,200	control worm	97	97	100
	360	critical EPG	100		
	22,000	control	100		100
	12	EPG/worm			

Summary of the clinical trials with Flubenvet in turkeys, geese, pheasants and partridges

Treatment (ppm)	Number treated	Evaluation Test	% Efficacy					
			A. galli	*H. gallinarum*	*Capillaria* spp.	*S. trachea*	*A. anseris*	*T. tenuis*
Turkeys								
20 ppm for 7 days	5	control EPG	100		100			
20 ppm for 7 days	4	control worm				100		
20 ppm for 7 days	10	control worm			100			
Geese								
30 ppm for 7 days	5,000	control EPG					99.7	100
30 ppm for 7 days	1,200	control worm			100	100	99.8	
Pheasants								
60 ppm for 7 days	1,000	control worm			100	100		
60 ppm for 7 days	2,500	critical EPG		100	100	100		
60 ppm for 7 days	11,000	critical EPG	100	100	100	100		
60 ppm for 7 days	1,515	critical EPG			100	100		
Partridges								
60 ppm for 7 days	1,000	control worm				100		
60 ppm for 7 days	12	control worm	100	100	92	100		



Worm eggs are killed by Flubenvet

A number of chickens, artificially infected with *Ascaris* and *Heterakis*, were divided into 2 groups: one group was treated with the therapeutic dose of 30 ppm Flubenvet in the feed for 7 consecutive days. The other group remained untreated and served as controls. The treatment resulted in a complete elimination of the worm burden 2 to 3 days after the start of treatment. From the second day of treatment, the ovicidal effect of the Flubenvet treatment could be observed, because of the strong reduction in embryonation rates.

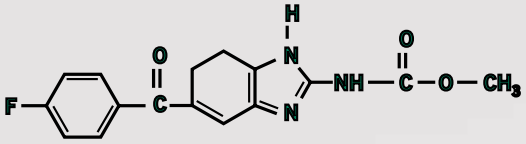
Summary of the efficacy spectrum of Flubenvet

Poultry species	Worm species	Treatment schedule	Anthelmintic efficacy
Chickens	ascarids, hairworms *(Ascaridia galli, Heterakis gallinarum, Capillaria* spp,	30 ppm, 7 days	**97-100%**
Turkeys	ascarids, hairworms, gapeworms *(Ascaridia galli, Capillaria obsignata, Syngamus trachea)*	20 ppm, 7 days	**100%**
Geese	hairworms, gapeworms, stomach worms *(Capillaria anseris, Syngamus trachea, Trichostrongylus tenuis, Amidostomum anseris)*	30 ppm, 7days	**99-100%**
Pheasants, partridges	ascarids, hairworms, gapeworms *(Ascaridia galli, Heterakis gallinarum, Capillaria* spp*., Syngamus trachea)*	60 ppm, 7 days	**100%**

10 Flubenvet: safety profile

Pharmacodynamics of flubendazole

Flubendazole belongs to the chemical group of the benzimidazole carbamates. It has the following chemical structure:



Flubendazole is very poorly soluble in aqueous systems, such as the gastro-intestinal tract, which results in a low dissolution rate and a low absorption. This is reflected by the high faecal excretion of unchanged parent drug. The small fraction that is absorbed is extensively metabolised by first-pass metabolism in the liver. The biotransformation products are excreted quickly with the bile and the urine.

Flubendazole acts by binding to tubulin, the dimeric subunit protein of the microtubules. It inhibits microtubular assembly in absorptive cells, i.e. of the intestinal cells of nematodes or the tegumental cells of cestodes. Flubendazole also inhibits the microtubule-dependent processes in the embryonation phase of the worm egg (ovicidal effect).

Because of its low solubility in aqueous systems, flubendazole has a very good safety profile.

Safety profile of flubendazole

Acute studies

The acute oral toxicity was evaluated in rats, mice, guinea pigs, chickens and guinea fowl. No mortalities occurred and the LD_{50} values were >10 000 mg/kg in rats and mice, >5000 mg/kg in guinea-pigs, >640 mg/kg in chickens and >400 mg/kg in guinea fowls.

Repeated dose studies

The subchronic toxicity of flubendazole has been studied after daily oral administration to rats (up to 160 mg/kg BW) and dogs (up to 40 mg/kg BW) for 3 months.
No adverse effects were observed.

Reproduction studies

Rats, mice and rabbits received flubendazole in their feed during the period of pregnancy. No drug-induced embryotoxic or teratogenic effects were evidenced at doses up to 60 mg/kg BW.

Mutagenicity studies

In a series of mutagenicity studies including bacterial, yeast, insect and rodent systems, flubendazole was devoid of any mutagenic potential.

Tolerance in the target animal species

Broilers

Different groups of broiler chickens received doses of 30, 60, 120 and 180 ppm for 7 consecutive days in their feed. Even at the highest dose, no side effects were observed and body weight gain remained normal.

Laying hens

A single dose of 640 mg/kg body weight did not affect clinical behaviour or body weight. During a laboratory trial, Hisex layers were treated with doses of 30, 60, 120 and 180 ppm flubendazole for 7 consecutive days. No negative effect was seen on clinical behaviour and egg production. In addition large scale field studies were organised to confirm the safety of Flubenvet in laying hens. The first trial comprised 22,000 birds treated for 7 consecutive days at 30 ppm flubendazole. In a second trial 24,000 birds were treated for 5 days at 30 ppm flubendazole. No effects on egg laying rates, egg weight or egg quality were seen.

Breeder hens

A laboratory trial[3] was conducted at the R.V.K. Institute in Merelbeke, Belgium. 400 females and 40 males of the Ross 208 breeder strain, 40 weeks old, were treated with 60 ppm flubendazole in either mash or pelleted feed. Laying rates, egg weights, fertility, hatchability, embryonic mortality and chick quality were carefully measured before, during and after treatment. None of these parameters were affected by the Flubenvet treatment (see table).

Effect of Flubenvet in either meal or pelleted feeds for broiler breeders on laying rates, hatchability and weight of settable eggs.

Week	Feed-Treatment	Lay (%)*	Egg weight (g) (settable) *	% Hatchability
38	meal (control)	68.4^{a} (± 1.5)	---	-
	pellet (control)	62.6^{b} (± 0.83)	---	-
39	meal (control)	71.3^{a} (± 1.4)	60.4^{a} (± 0.27)	91.5
	pellet (control)	62.8^{b} (± 1)	59.3^{a} (± 0.3)	90.7
40	meal (Flubenvet)	70.1^{a} (± 0.71)	60.6^{a} (± 0.18)	89.2
	pellet (Flubenvet)	64.1^{a} (± 1.17)	59.5^{a} (± 0.27)	89.7
41	meal (control)	60.60^{a} (± 1.20)	60.1^{a} (± 0.42)	89.9
	pellet (control)	63.10^{a} (± 2.50)	59.4^{a} (± 0.15)	91.9

*Averages followed by the same letter are not significantly different from each other (p> 0.05).

Pheasants and pheasant breeders

Flubendazole at 60 ppm in feed does not adversely affect egg production or hatching results. In a field trial performed with pheasant breeders in France, Flubenvet was incorporated in the feed at 60 ppm and given for 7 days. The parameters studied were percentage of egg lay, fertility and hatchability. There was no negative effect on any of these parameters[4].

In another field study performed in the United Kingdom, Flubenvet was incorporated in a pelleted pheasant feed. The treatment with 60 ppm of Flubenvet did not have any adverse effect on the number of eggs laid, egg fertility or hatchability[5].

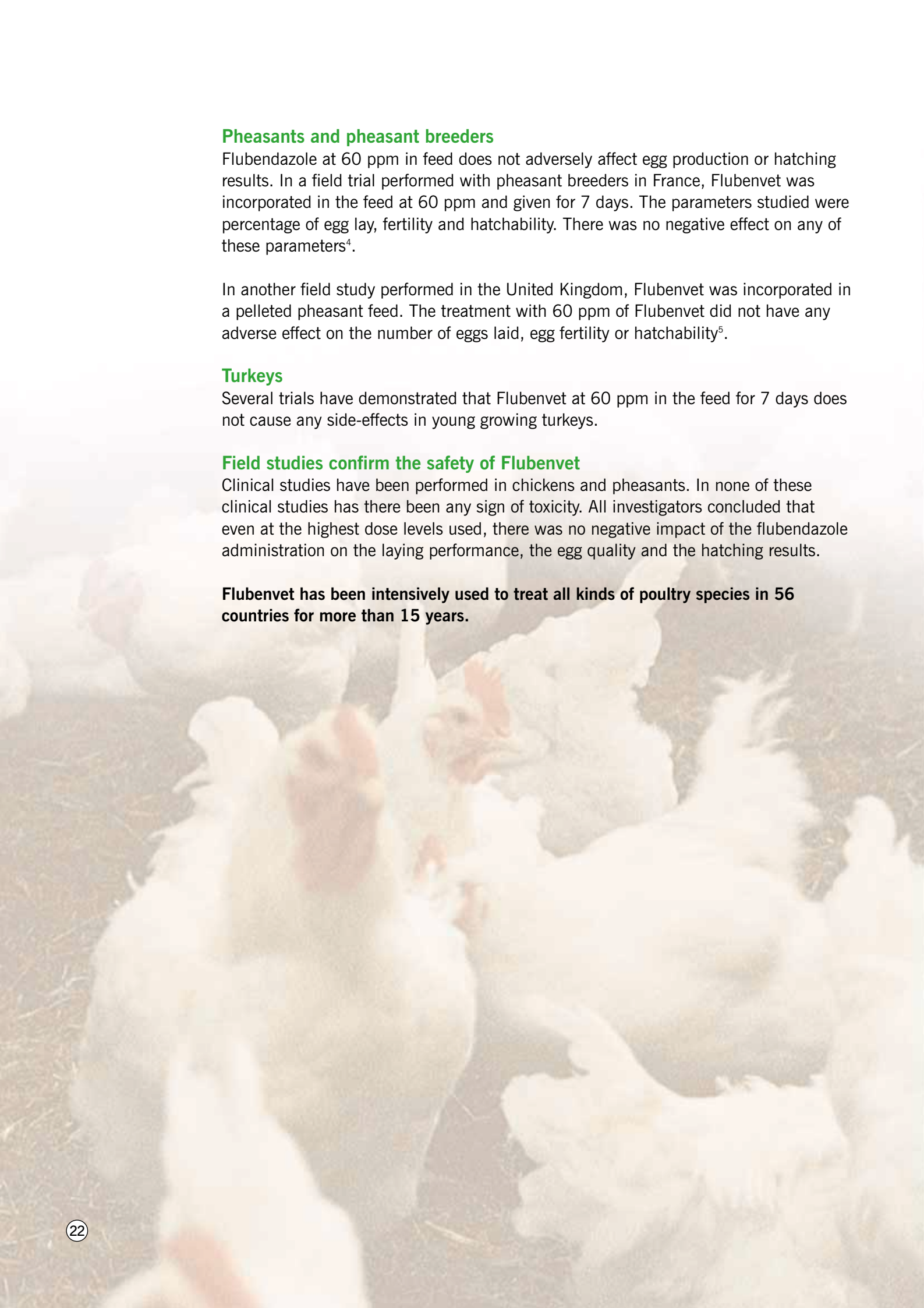
Turkeys

Several trials have demonstrated that Flubenvet at 60 ppm in the feed for 7 days does not cause any side-effects in young growing turkeys.

Field studies confirm the safety of Flubenvet

Clinical studies have been performed in chickens and pheasants. In none of these clinical studies has there been any sign of toxicity. All investigators concluded that even at the highest dose levels used, there was no negative impact of the flubendazole administration on the laying performance, the egg quality and the hatching results.

Flubenvet has been intensively used to treat all kinds of poultry species in 56 countries for more than 15 years.



Number of birds treated and monitored	Treatment schedule	Observations
chickens		
10,085 Hybro and Ross broiler breeder hens	flubendazole at 4 ppm for 62 days	no negative influence upon reproduction parameters
5,093 Hubbard broiler breeder hens	flubendazole at 10 ppm for 7 days	no negative influence on egg-laying performance and hatchability during or after treatment
33,000 hens of various breeds	flubendazole at 30 ppm for 7 days	no side effects during or after treatment
17,141 Ross broiler breeders	flubendazole at 30 ppm for 7 days	no side effects during or after treatment
23,500 heavy breeders (breed not specified)	flubendazole at 30 ppm for 7 days repeated every 3 weeks	no negative effects on laying performance and fertility
5,950 Hubbard broiler breeders	flubendazole at 60 ppm for 7 days	no changes in egg production or reproductive performance
24 Hisex hens	flubendazole at 30, 60 or 120 ppm for 7 days compared with untreated controls	no adverse effects on body weight, food consumption and egg production; no side effects
220 Arbor Acres	flubendazole at 60, 120 or 180 ppm for 7 days compared with untreated controls	no drug or dose-related effects on mortality, clinical behaviour, egg production, egg weight and egg quality, hatching results, offspring performance
pheasants		
80	flubendazole at 60 ppm for 7 days	no drug-related effects on egg production or egg hatching; no side effects
1,100	flubendazole at 60 ppm for 7 days	no side effects

Safety aspects for feed mill operators and poultry farmers

- In the toxicity studies dermal application to or inhalation by laboratory animals did not induce drug related effects.
- A primary eye irritation study conducted in rabbits revealed minimal ocular irritation. This indicated that flubendazole premix is devoid of irritating potential after accidental exposure of the mucous membranes.
- As a precaution, staff are advised to wear protective clothing and a dust mask during the production or handling of Flubenvet premix.

Consumer safety

In accordance with Council Regulation (EEC) No. 2377/90, the regulatory authorities have examined flubendazole with the aim of establishing Maximum Residue Limits (MRLs).
These MRLs indicate the maximum levels of residues that can be present in edible tissues without posing a health risk for the consumer.

The following MRLs for flubendazole were adopted in Commission Regulation (EC) No. 100/98 of 13 May 1998 (Official Journal of the European Communities):

Marker residue	Animal species	MRLs	Target tissues
Sum of flubendazole and its main metabolites	Pigs, chickens, turkeys (*), game birds	50 µg/kg 50 µg/kg 400 µg/kg 300 µg/kg	Muscle Skin + Fat Liver Kidney
Flubendazole	Chickens	400 µg/kg	Eggs

(*) MRL for flubendazole in turkeys adopted in the Commission Regulation (EC) No. 2385/1999 of 10 Nov 1999.

Flubenvet withdrawal periods (UK)

Poultry species	Withdrawal time in days
Broiler chickens (meat)	7
Laying hens (eggs)	0
Growing turkeys (meat)	7
Geese (meat)	7
(eggs)	7
Game birds (meat)	7

On the basis of residue depletion studies, it can be measured how quickly the drug residues are excreted and removed from different parts of the body. These studies allow us to predict how soon after treatment the tissue residues have dropped below the MRL levels .

Safe for other animal species

Specific studies have shown that flubendazole is very well tolerated in cats, dogs, pigs, cattle, small ruminants and rabbits. Accidental feeding of Flubenvet or Flubenvet supplemented feed to any of these animals does not pose any health risk. However all reasonable precautions must be taken to prevent this.

Safe for use in combination with other poultry feed additives

Until now no incompatibilities have been reported with other feed additives or therapeutics.

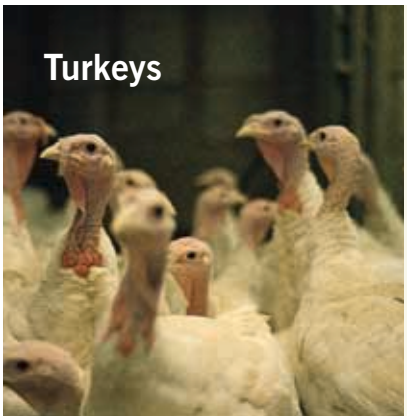
In broilers, the concurrent use of flubendazole (60 ppm for 7 days) with the anticoccidial diclazuril at 1 ppm had no negative influence on behaviour, general health, weight gain and feed conversion.

In a trial with pheasants, the combination of flubendazole with anticoccidials meticlorpindol and the combination meticlorpindol - methylbenzoquate, the anti-blackhead drug dimetridazole and the antimicrobial furoxone was shown to cause no adverse effects.

In partridges, the combined use of flubendazole at 60 ppm with diclazuril at 4 ppm for 7 days in the feed had no negative influence on behaviour, general health, weight gain or feed conversion ratios. In turkeys, the combination of flubendazole at 20 ppm with diclazuril at 1 ppm for 7 days had no negative influence on body weights, feed consumption or feed conversion. Side effects were never observed.

11 Suggested Flubenvet deworming programmes

 Replacement pullets reared on litter	Treat at week 5, week 10 and week 15 of age. Thoroughly deworm before putting into batteries.	30 ppm Flubenvet mixed into the feed for 7 days.
 Laying hens	Thoroughly deworm before putting into batteries. On litter bedding: treat at 4 week intervals in case of high infection pressure. Otherwise the intervals can be extended to 6 or 8 weeks.	30 ppm Flubenvet mixed into the feed for 7 days. 30 ppm Flubenvet mixed into the feed for 7 days.
 Broiler breeders	Treat at 4 week intervals in case of high infection pressure. Otherwise the intervals can be extended to 6 or 8 weeks.	30 ppm Flubenvet mixed into the feed for 7 days.



Deworm at week 5, week 10 and week 15 (depending on the slaughter age).

In case of gapeworm infection, the interval between treatments should be reduced to 18 days.

20 ppm Flubenvet mixed into the feed for 7 days.

Deworm at week 3, week 7, week 11 (maximum interval of 3 weeks between treatments in case of gapeworm threat).

Pheasants and partridges:
60 ppm Flubenvet for 7 days.

Deworm regularly
(see table page 16: prepatent period of important worm species).

30 ppm Flubenvet mixed into the feed for 7 days.

12 Flubenvet™: practical data

1. Composition
Active ingredient : 25 g flubendazole per kg Flubenvet™ 2.5% authorised intermediate product.

2. Product characteristics
Aspect: beige powder, completely tasteless and odourless.
Flowability: freeflowing.

3. Mixability
Mixability tests[21, 8] at TNO in The Netherlands and at the German IFF confirm that the mixing uniformity of flubendazole at normal concentrations in animal feed is excellent. With different types of mixers and in various types of feed the coefficient of variation (C.V.) was always below 5%.

4. Stability
The German Forschungsinstitut Futtermitteltechnik (Braunschweig) performed tests with complete broiler feed supplemented with flubendazole. After use of a pressure conditioner - (feed temperatures of 116°C at the head of the conditioner) - with subsequent pelleting, the flubendazole concentration did not significantly decrease[8]. This value did not deteriorate after two months storage of the pellets. Mixing uniformity was excellent.

In a stability experiment[21] performed at the TNO Institute of The Netherlands, flubendazole was mixed and pelleted into a representative feed at 15 ppm. It was evident that after pelleting and expanding, with a maximum product temperature of slightly over 100°C, flubendazole remained stable.
Storage stability of flubendazole in pelleted feed proved to be excellent for at least 12 weeks under ambient conditions. Up to 12 weeks, the flubendazole quantity recovered from stored feed was over 90% of the initial value.

In a comparative experiment[3], done at the Belgian Research Station for Small Stock Husbandry at Merelbeke, the influence of heat during pellet processing upon the flubendazole concentration was evaluated. It was concluded that the steam pelleting process (temperature of 85°C) did not significantly alter the flubendazole content in the pellets when compared to the concentrations in meal.

Analytical tests[9] showed that the increase of pressure, necessary for the production of pellets, has no effect on the stability of flubendazole.

Up to a temperature of 100°C, flubendazole is completely stable. Flubendazole remained stable after 15 days at 17,000 Lux.

5. Shelf life
In its original packaging under normal storage conditions, Flubenvet™ intermediate remains stable for 4 years.

Flubenvet™ in prepared feeds has a shelf life of 2 months.

6. Withdrawal periods

Poultry species	Withdrawal time in days
Broiler chickens (meat)	7
Laying hens (eggs)	0
Growing turkeys (meat)	7
Geese (meat)	7
(eggs)	7
Game birds (meat)	7

Flubenvet: technical information

Presentation:
Flubenvet™ Intermediate is a beige medicinal intermediate containing 60g flubendazole in 2.4kg bags. (2.5% w/w flubendazole) Flubenvet™ Intermediate Gamekeeper Pack is a beige powder containing 6g flubendazole in a 240g tub (2.5% w/w flubendazole). Flubendazole is a broad spectrum anthelmintic for oral administration, active against mature and immature stages and eggs of the following nematodes of the gastrointestinal and respiratory tract: *Ascaridia galli* (large roundworm), *Syngamus trachea* (gapeworm), *Heterakis gallinarum* (caecal worm), *Capillaria* spp. (hair worm), *Amidostomum anseris* (gizzard worm), and *Trichostrongylus tenuis*.

Flubendazole has no adverse effect on egg laying or hatchability.

Incorporation: Flubenvet™ Intermediate – add required amount of Flubenvet™ Intermediate to at least 5kg of one of the feed ingredients and mix well. Thoroughly mix this premix with the remaining ingredients making in all one tonne of medicated feed, which can be fed as pellets, mini-pellets, starter pellets or crumbs. Flubenvet™ Intermediate Gamekeeper Pack – each 240g tub of Flubenvet™ medicates 100kg/220lb of finished pheasant feed or 200kg/440lb of chicken feed.

Dosage:
a) Pheasants and partridges – 2.4kg Flubenvet™ Intermediate per tonne of feed.
Dosage equivalent to 60g of flubendazole per tonne of feed (60ppm).
240g of Flubenvet™ Intermediate Gamekeeper Pack per 100kg of feed (60ppm). Treat for 7 consecutive days.
b) Chickens and geese – 1.2kg Flubenvet™ Intermediate per tonne of feed.
Dosage equivalent to 30g flubendazole per tonne of feed (30ppm).
240g of Flubenvet™ Intermediate Gamekeeper Pack per 200kg of feed (30ppm). Treat for 7 consecutive days.
c) Turkeys – 800g Flubenvet™ Intermediate per tonne of feed. Dosage equivalent to 20g flubendazole per tonne of feed (20ppm). 240g of Flubenvet™ Intermediate Gamekeeper Pack per 300kg of feed (20ppm). Treat for 7 consecutive days.

Treatment frequency:
On infected premises, treatment at 3 weekly intervals may be necessary to control worm infestations.

Precautions:
Birds must not be slaughtered for human consumption during treatment. Chickens, turkeys, geese, pheasants and partridges may be slaughtered for human consumption only from 7 days from the end of treatment.

Turkeys, geese, pheasants and partridges
Eggs must not be presented for human consumption during treatment. Eggs may be presented for human consumption only after 7 days from the end of treatment.

Chickens
Eggs may be presented for human consumption during and after treatment when dosed at the rate of 30ppm in feed i.e. 1.2kg Flubenvet™ Intermediate per tonne of feed or 240g per 200kg of feed.

FOR ANIMAL TREATMENT ONLY. KEEP OUT OF REACH OF CHILDREN.

Pharmaceutical Precautions:
Flubenvet™ Intermediate & Flubenvet™ Intermediate Gamekeeper Pack should be stored in tightly closed original container below 25°C. The product will remain stable in finished feed for 2 months.

Package Quantities:
Flubenvet™ Intermediate is available in 2.4kg bags and Flubenvet™ Intermediate Gamekeeper Pack in 6 x 240g tubs.

Further Information:
Flubenvet™ Intermediate is an approved intermediate product manufactured in the UK from flubendazole 5% w/w.
Marketing Authorisation Number: VM 00242/4056.

Flubenvet™ Intermediate may only be incorporated by approved manufacturers at the above incorporation rates.

For further information please contact:
Janssen Animal Health, a division of Janssen-Cilag Ltd, Saunderton, High Wycombe, Bucks HP14 4HJ, UK.
Tel: 01494 567555 Fax: 01494 567556 e-mail: ahealth@jacgb.jnj.com

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