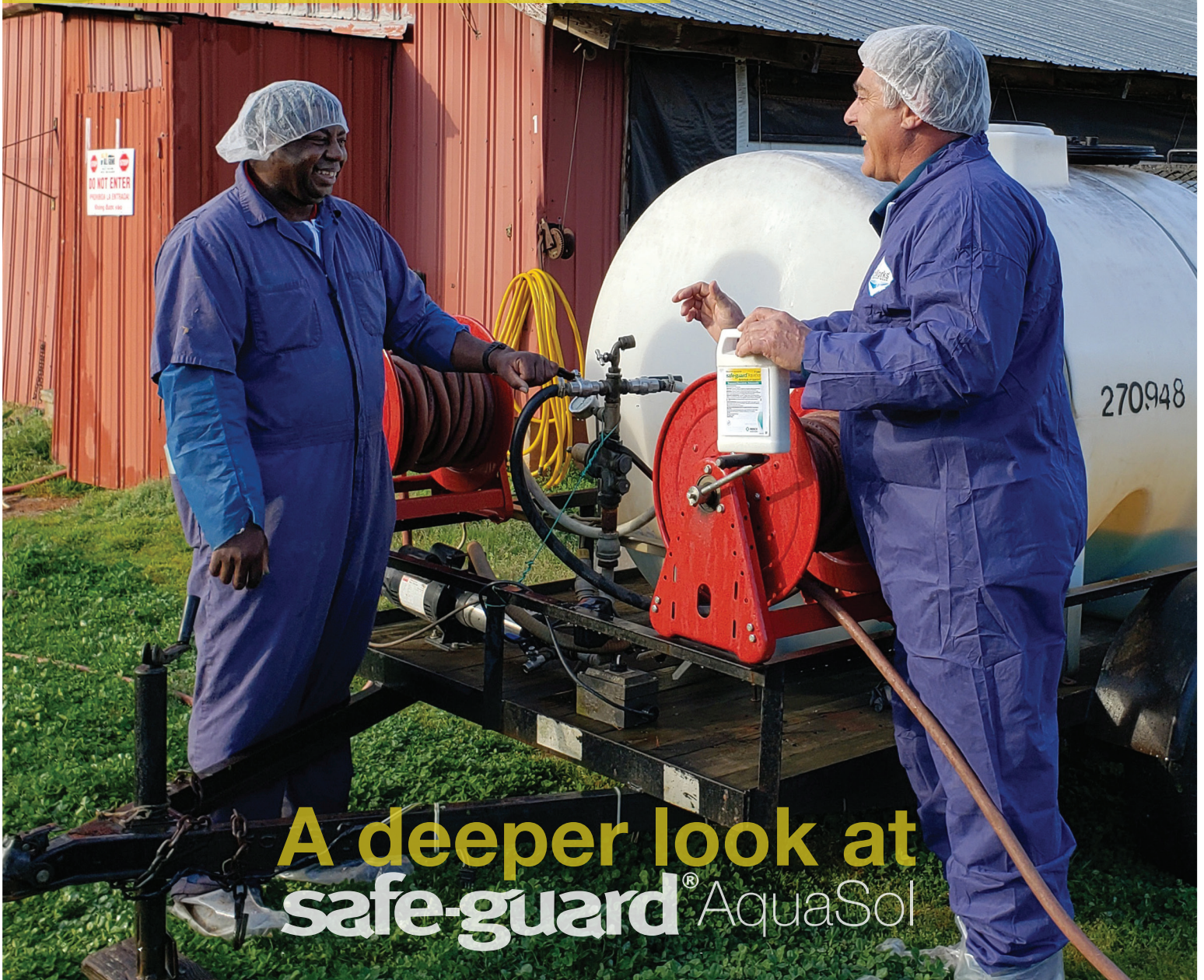


HATCHING INNOVATIONS

The stories behind the science.



A deeper look at
safe-guard[®] AquaSol

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Safe-Guard[®] AquaSol

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Myth vs. Fact – Safe-Guard® AquaSol

Myth: Safe-Guard AquaSol (fenbendazole oral solution) and Safe-Guard® (fenbendazole) Dewormer for Beef & Dairy Cattle and Goats Suspension 10% – are the same product.

Fact: The Safe-Guard ruminant drench product, a dewormer used safely for decades in many species (Safe-Guard Suspension 10%), is vastly different from the Safe-Guard AquaSol dewormer labeled for use in poultry. While both dewormers use the same active ingredient (fenbendazole), a novel process employed to produce Safe-Guard AquaSol yields particle sizes 10 to 100 times smaller than Safe-Guard Suspension 10%. These microparticles are then able to remain in suspension for up to 24 hours without agitation. This unique feature of Safe-Guard AquaSol prevents settling in water lines and damage to dosing equipment. Additionally, Safe-Guard AquaSol is a 20% suspension - two times more concentrated than the Safe-Guard Suspension 10% product, an essential factor to consider when calculating cost.

Myth: The cost of Safe-Guard AquaSol is significantly more expensive than other dewormers currently available.

Fact: When calculating the cost of deworming a flock, it is important to remember that Safe-Guard AquaSol is more concentrated than other anthelmintics on the market. As a 20% suspension, Safe-Guard AquaSol contains 200 milligrams (mg) of fenbendazole per milliliter (ml) of solution. When calculating the required dose for your flocks, one ml of Safe-Guard AquaSol will treat more than 440 pounds of live weight. At the labeled dose of one mg per kilogram (kg) per day for five consecutive days, one gallon of Safe-Guard AquaSol will treat 333,800 pounds of live weight. To calculate a daily dose of Safe-Guard AquaSol, estimate live bird weight (in pounds) and multiply by a factor of 0.00227. This calculation will generate the dose in milliliters necessary for one day of treatment and should be administered for five consecutive days. Finally, it is important to remember, when administered at the labeled dose, Safe-Guard

AquaSol is extremely effective against round (*Ascaridia galli*) and cecal (*Heterakis gallinarum*) worms, while other off-label dewormers on the market require increased dosing levels to accomplish similar reductions in parasite burden. A simple cost comparison (see table below - prices as of March 2021), shows Safe-Guard AquaSol is a better value than other products used off-label.

Dewormer	1 L – Lbs. treated	Cost per Liter	Cost/1000 lbs. BW
Safe-Guard AquaSol	88,105	\$200	\$2.27
oxfendazole	72,000	\$255	\$3.54
albendazole	25,000	\$81	\$3.24
levamisole	6,500/pk	\$16.55/pk	\$2.55

Myth: Safe-Guard AquaSol treats the protozoan (*Histomonas meleagridis*) responsible for blackhead disease.

Fact: Safe-Guard AquaSol is NOT labeled for the treatment of blackhead disease, as no claims are made regarding its ability to affect the protozoa *Histomonas meleagridis* or blackhead disease. However, Safe-Guard



Birds drinking Safe-Guard AquaSol.

AquaSol can effectively control the primary vector responsible for transmitting blackhead disease – the cecal worm (*Heterakis gallinarum*)¹. Treating flocks early and often with Safe-Guard AquaSol can reduce or eliminate cecal worm infestation resulting in reduced incidence and severity of blackhead disease in flocks.

Myth: Safe-Guard AquaSol is not shelf-stable for three years.

Fact: When stored according to the label, Safe-Guard Aquasol and its active ingredient, fenbendazole, can be safely stored for three years after the manufacturing date with no loss of effectiveness.

Myth: Safe-Guard AquaSol does not remain suspended in solution significantly longer than other dewormers.

Fact: Safe-Guard AquaSol employs a novel manufacturing process, which creates a smaller and more homogenous fenbendazole particle size. This process, referred to as ‘wet milling,’ reduces fenbendazole by approximately 10 to 100 times when compared to other Safe-Guard products. The resulting fenbendazole microparticles can remain in suspension for significantly longer (24 hours) eliminating the need for agitation, while also preventing the product from settling in water lines or damaging equipment.²

Myth: Duration of Safe-Guard AquaSol treatment has no impact on efficacy.

Fact: Safety and efficacy data produced in commercial poultry flocks by Merck Animal Health clearly show parasitic worm populations are more effectively eliminated with extended exposure to fenbendazole. When Safe-Guard AquaSol is administered over the course of five consecutive days per the labeled dose, the product demonstrated that it is highly efficacious against the labeled parasites³. Shortening the duration of treatment reduces efficacy.

Safe-Guard Suspension 10% is labeled for single-day treatment in a variety of ruminant species, as their unique physiology allows for significant recycling of fenbendazole and its active metabolites. Whereas recycling of fenbendazole is limited in monogastrics



(single stomached animals) and is further compromised by extremely short (four hours) feed passage times in poultry. As such, the best efficacy was found with a treatment duration of five days.

Myth: Safe-Guard AquaSol cannot be used practically in broiler breeder pullets on skip-a-day feeding.

Fact: Dosing of Safe-Guard AquaSol is solely dependent on the weight of the flock being treated and not feed or water consumption. During feed restriction, water consumption will be significantly less than on standard feed days. However, birds will still be consuming water, thus allowing for deworming of the flock. Deworming on days of restricted feed is encouraged, as feed passage times are slowed, and uptake of the fenbendazole is increased.

With the use of a water meter, this reduction of water consumption can be measured, and a historical baseline developed for your location. This water consumption history can then be used to determine the volume of stock solution necessary to deliver Safe-Guard AquaSol in a timely manner. To ensure all the stock solution is consumed by the flock, Merck Animal Health suggests creating the stock solution based on 50% of the daily water consumption. See calculation example on page 4:

Historical water consumption at 18 weeks = 2500 gallons (gal)

2500-gal x 50% = 1250 gal ÷ 128 = 9.8 gallons of stock solution

In the example above, a 10 gallon stock solution, based on 50% daily water consumption, delivers the dewormer in the ideal 6-8 hour range.

Myth: The final concentration of Safe-Guard AquaSol in the drinking water is important to ensure a successful deworming.

Fact: The daily dose of Safe-Guard Aquasol administered is based on the live weight of the flock to be treated. This is calculated as milligrams per pound (0.00227 mg) or milligrams per kilogram (0.005 mg) based on each milliliter of Safe-Guard AquaSol containing 200 mg of fenbendazole (20% suspension). So, when calculating the dose of Safe-Guard AquaSol to deworm a flock with 10,000 pounds of chicken live weight, use the example below:

10,000 lbs. x 0.00227 mg =

**22.7 ml of Safe-Guard AquaSol per day for five consecutive days
[or, when using kilograms, 4,545 kg x 0.005 mg = 22.7 ml]**

**Total Safe-Guard AquaSol = 22.7 ml X 200 mg/ml =
4540 mg / day (fenbendazole)**

In the example above the flock of 10,000 chickens would receive a dose containing 4,540 mg of fenbendazole each day for 5 consecutive days. Administration of Safe-Guard AquaSol occurs via the drinking water with the most common method of introducing Safe-Guard AquaSol into the drinking water system is through a medicator pump.

The standard inclusion rate of these pumps is one ounce of product to one gallon of water (1:128). The product injected into the water supply is pumped from a concentrated stock solution. In the example above, if the 10,000-bird flock was consuming 1,200 gallons of water per day, and we wanted to treat all 1,200 gallons, approximately 9.4 gallons of stock solution would be required ($1200 \text{ gal} \div 128 \text{ oz/gal} = \sim 9.4 \text{ gal}$). As mentioned in the previous question (#7), to ensure all the Safe-Guard AquaSol is consumed, and every bird receives a full dose, it is good practice to medicate the flock at 50% of the flock's historical daily water consumption. So, in our 10,000 bird flock example above, the 22.7 ml daily dosage of Safe-Guard AquaSol would be mixed with

approximately five gallons of water (50% daily water consumption based on 9.4 gal) to form the stock solution. Once the five gallons of the stock solution has been consumed, the flock will be supplied with unmedicated water for the remainder of the day.

In this example, the final concentration of Safe-Guard AquaSol is not essential, as the water is simply a conduit to deliver the dewormer. This example would be analogous to someone who takes a daily aspirin. Their dose is one aspirin, and the amount of water consumed to swallow the aspirin is inconsequential.



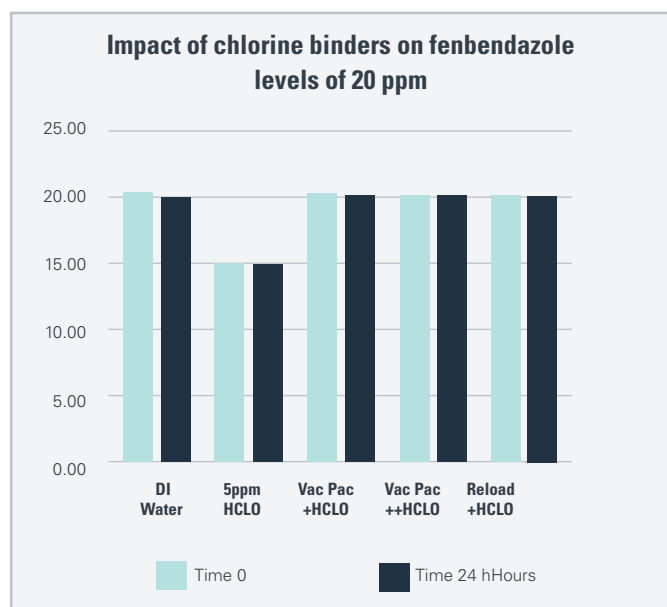
Good deworming begins with proper mixing of stock solution

“Safe-Guard AquaSol has proven efficacy in poultry against many types of parasitic worms, is exceptionally safe, and is stable, remaining in suspension for up to 24 hours without agitation.”

Myth: There is no risk to efficacy when Safe-Guard AquaSol is administered via municipal water or water that has been treated with a chlorine-based water sanitation system.

Fact: Safe-Guard AquaSol (fenbendazole) may be degraded by chlorine at levels of five ppm and greater. Some municipal water supplies may contain chlorine at levels that could negatively affect fenbendazole activity. Thus, if chlorinated water is used on the farm, it is good practice to add a chlorine stabilizer to the drinking water before the Safe-Guard AquaSol is administered. A study⁴ was performed to determine the impact of commonly used chlorine binders on fenbendazole, both in non-chlorinated water and chlorinated water. A Safe-Guard AquaSol solution of 20 ppm was made up in deionized water (positive control) and in water containing five ppm hypochlorous acid (negative control). The chlorine binders Vac-Pac® and Vac-Pac Plus® (Animal Science Products, Inc. Nacogdoches, TX) and Reload Pack (Boehringer Ingelheim Vetmedica, Inc. St. Joseph, MO) were mixed according to the label into water containing five ppm hypochlorous acid. After preparation of the chlorine binder solutions, Safe-Guard AquaSol was added to create the concentration of 20 ppm fenbendazole. The solution was tested for fenbendazole levels immediately after preparation and again at 24 hours. All solutions were prepared and tested in duplicate. The results of the study are depicted in Figure 1.

Figure 1.



It should also be noted that other products commonly added to poultry drinking water (organic acids, medications, iodine, etc.) have not been tested for compatibility with Safe-Guard AquaSol and mixing products for co-administration is discouraged.

Myth: Rotation of dewormers can be a good practice to avoid resistance and there are plenty of FDA approved products to rotate with Safe-Guard AquaSol.

Fact: Regardless of the species treated or product utilized, rotation of commonly used drugs can be an effective strategy to minimize the development of resistance. Safe-Guard AquaSol is an extraordinarily effective and safe dewormer for poultry, and when used according to the label, will reduce the likelihood of fenbendazole resistance within parasite populations. As mentioned above, best practices employed to prevent resistance often include rotation. However, for rotation to be effective, the mode of action of the new drug must be different than that of the previously used drug. Pharmacologically speaking, the new drug must be of a different drug-class than the previously utilized drug. Fenbendazole, the active ingredient of Safe-Guard AquaSol, is in the benzimidazole class of anthelmintics.

Producers must also keep in mind that it is often likely that other products will NOT be labeled for use in poultry, and the use of such products will constitute off-label use. In these cases, due to a lack of research in poultry, efficacy and safety data, dosage, and withdrawal times are unavailable. On the other hand, Safe-Guard AquaSol has proven efficacy in poultry against many types of parasitic worms, is exceptionally safe, and is stable, remaining in suspension for up to 24 hours without agitation.²

An Informational Outline of the Animal Medicinal Drug Use Clarification Act (AMDUCA) for off label drug use can be found using the following link: https://www.aasv.org/documents/extralabel_brochure.pdf

No withdrawal period is required when used according to the label. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

¹ McDougald, Larry. (2008). Histomoniasis (Blackhead) and other protozoan diseases of the intestinal tract. *Diseases of Poultry*. 1095-1105.

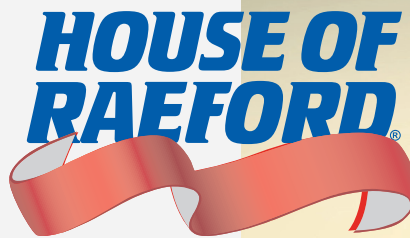
² Data on file, Merck Animal Health.

³ Freedom of Information Summary, NADA 141-449.

⁴ Data on file, Merck Animal Health.

Hefty cost of roundworms at big bird complex

Field trial¹ involving 1.4 million broilers revealed significant performance losses from roundworms and a cost-effective solution in Safe-Guard[®] AquaSol (fenbendazole oral suspension) poultry dewormer.



Today's fast-growing and high-yielding broiler breeds are susceptible to significant performance losses due to even a very low roundworm burden. A field trial involving 1.4 million big bird broilers at a US poultry integrator showed body weights were reduced and feed conversions rose when flocks went untreated for roundworms.

The trial in 30 broiler houses on six farms growing nine-pound (62 day) broilers over three grow-out cycles at House of Raeford's Louisiana complex resulted in an overall 2.4% weight gain and 5.5 points lower average feed conversion ratio (FCR) for broilers treated with Safe-Guard AquaSol.

Treatment benefits in all three grow-out cycles

Broiler performance was negatively impacted by worm burden in the untreated flocks during all three grow-out cycles in the trial. The performance improvement for treated broilers was greatest for the first cycle (when there was the heaviest worm burden) but continued for the treated birds in the second and third cycles.

- **Cycle 1** – 3.08% weight increase; 5.6 pts lower feed conversion
- **Cycle 2** – 1.75% weight increase; 5.8 pts lower feed conversion
- **Cycle 3** – 2.2% weight increase; 5.0 pts lower feed conversion

Does worm burden hurt broiler performance?

House of Raeford Corporate Veterinarian, Shannon Jennings, was asked about the results of the trial. He replied, "I was truly amazed with the results. In the first cycle of the trial, treated flocks gained about one third of a pound of liveweight more than untreated flocks. The treated flocks also improved 5 points on feed conversion. Before the trial, I was concerned that roundworms were affecting our broiler performance but was uncertain as to the possible extent of the problem. After the trial, I was able to quantify the amount that roundworm burden contributes to broiler performance and found it to be significant. Seeing the flock performance differences in the trial made me realize that we had more of an issue with roundworms hurting performance than I realized."

Even low roundworm burden hurts performance

Over the course of the trial, the roundworm burden in all houses began high (average adult worm burden => 40



House of Raeford big bird complex

worms per bird) in spring 2016 and naturally declined in the control houses during the summer months, while the treated houses dropped to zero after treatment. Even when the worm burden was low in untreated houses, weight gain and feed conversion were measurably worse than liveweights and feed conversion ratios in the houses treated with Safe-Guard AquaSol.

House of Raeford's treatment program

"It is nice to finally have an approved product that is effective." Dr. Jennings said. "Before now Piperazine was the only dewormer approved for chickens. Piperazine was what we used to initially treat birds, but later found that AquaSol did a better job. In the past, when posting sessions showed roundworms to be a problem, we would often spot treat with Piperazine or an extra-label application of another product. With the arrival of the next flock, we quickly noticed the problem reoccurred and proved our approach was a hit and miss. I now believe in treating all farms across the board for one full grow-out cycle is the key."

Treatment cost and return

Recommended total dosing (5 day treatment) of Safe-Guard AquaSol is 2.27 mg per pound of liveweight, which amounts to \$2.27 per 1,000 pounds of body weight.² One liter of the concentrated dewormer will treat 88,105 pounds of liveweight (one gallon treats 333,516 pounds of liveweight). "Our live production team looks closely at costs every day. Some have suggested that the product is too expensive and needs to be used sparingly; but when they saw the performance improvement through the trial work, they got on board with the program."



Dr. Shannon Jennings

“I was truly amazed with the results. In the first cycle of the trial, treated flocks gained about one third of a pound of liveweight more than untreated flocks.”



“After seeing the performance improvements that resulted from the deworming treatment at the Louisiana complex, we began using the same roundworm treatment in our Georgia and South Carolina complexes.”

“Every point of feed conversion means a significant savings in feed cost. By saving on feed cost, it will more than pay for the cost of treatment along with the benefits of the liveweight gain. The dollars in benefits outweigh the cost of the AquaSol treatment.” he said.

Experience in multiple complexes

“We were having a serious roundworm issue in three complexes. After seeing the performance improvements that resulted from the deworming treatment at the Louisiana complex, we began using the same roundworm treatment in our Georgia and South Carolina complexes. We found that once farms were treated with AquaSol the roundworm problem was cleaned up. Then it was just a matter of monitoring farms for worm loads. We do not treat every farm every year. We monitor farms, and if we see that worm populations are increasing in a complex, we retreat all farms across the board,” he said.

No withdrawal period is required when used according to the label. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

¹Data on file, Merck Animal Health.

²Cost to deworm 4 lb. bird = \$0.0091.

“Life is too short to be wormy”

Protecting poultry from enteric parasites

Today, the average broiler breeder house is home to about 14,000 birds¹ that start producing hatching eggs at 26 weeks of age. One breeder farm, consisting of two breeder houses, produces enough hatching eggs to supply chickens for eight, four-house broiler farms for a year. Ensuring a steady supply of hatching eggs for the 60 billion chickens produced globally each year, doesn't allow much room for breeder hens to be wormy.

The poultry industry uses a variety of deworming programs in breeders, but no monitoring is typically done to determine the efficacy of these deworming programs. Dr. Steve Fitz-Coy, Scientific Affairs Manager at Merck, just completed a two-year study to assess how the current enteric parasite prevention programs are working in the field.



Evidence of ever present cecal worm challenge

In this study², breeder birds from several broiler companies across the South Atlantic region were evaluated regularly for intestinal parasites from the summer of 2017 to the fall of 2019. The survey population included replacement pullets, slips and birds in production ranging in age from 3 to 60 weeks.

Three to five birds were submitted from each farm and routine health surveys were performed. Investigators evaluated the intestinal tract of each bird for *Eimeria*, a parasite causing coccidiosis in poultry, as well as helminths, including roundworms (*Ascaridia galli*, *Heterakis spp* and *Capillaria spp*) and tapeworms (*Raillietina spp*). The birds from the various farms were divided into four age groups: 10 weeks and less, 11-20 weeks, 21-40 weeks, and 41-60 weeks.

Summary of the data showed coccidia species significantly higher in the youngest group, with the level of overall coccidia declining significantly as birds got older. This data indicates coccidial control programs appear to work well with development of long-term immunity.



Original drawing by our own Jerry Reeves, Poultry Account Manager

For roundworms, the opposite was true, with the greatest population found in birds after placement in the breeder house between 21-60 weeks of age.

Age groups (weeks)	<i>Ascaridia galli</i>	<i>Heterakis spp</i>	<i>Capillaria spp</i>	Tapeworms
% birds with worms				
< 10	4.7	1.4	0.3	3.7
11-20	5.0	6.0	0.2	1.4
21-40	18.9	22.9	15.7	1.4
41-60	44.4	35.8	12.3	6.7

- All 3 species, (*Ascaridia*, *Heterakis*, *Capillaria*) were numerically higher as a percentage of birds evaluated after placement in the breeder house with significant differences noted for all species in the oldest time period of 41-60 weeks.
- Tapeworms were found less often but showed a numerical increase in the final 41-60-week age range.

The results of this survey revealed older breeder birds (21-60 weeks) harbored significantly more roundworms than the two younger groups (3-20 weeks), indicating a need to monitor breeder birds in the production phase more frequently and provide the appropriate deworming treatment as needed.

No withdrawal period is required when used according to the label. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

¹Based on current housing construction of a 42 X 600 ft broiler breeder house.

²Presented at the 2020 AAAP Symposium.