PROTOCOLS FOR PARASITE CONTROL PROGRAMS AND RESEARCH

Robert S. Rew, M.S., Sc.D.
Rewsearch Consulting
(edited/revised by Mark L. Pinkston, M.S.)

Summary
Research protocols aimed at developing effective parasite control programs must consider numerous factors that impact the validity and value of product/program assessments. Information regarding the particular parasites occurring in the production environment, their life cycles, the age of cattle and their grazing status/experience must all be considered in developing appropriate and effective research protocols. Appropriate assessments of parasite control products and programs require costly and labor-intensive methodologies (e.g., necropsy and worm counts) beyond those provided by simple fecal egg count reduction tests. Similarly, cost factors have so far impeded the conduct of valid scientific studies on the degree of parasite resistance in U.S. cattle populations. Research collaboration by industry stakeholders (regulatory, pharmaceutical, producer groups) will be required to generate meaningful, scientific understanding of resistance issues.

Key points
• The development of effective and strategic parasite control programs is a critical, ongoing effort to help ensure the economic impacts of parasitism for U.S. cattle producers are mitigated.

• Parasite control protocols must be defined by the parasite threats that are endemic in the production environment as well as the grazing status and age of host cattle.

• Simple assessment of post-treatment fecal egg count reduction alone does not provide adequate information for determining anthelmintic product efficacy.

• No valid scientific studies on the degree of anthelmintic resistance in U.S. cattle populations have been conducted, largely due to the immense costs involved.

• Implementation of treatment protocols recommended by Pfizer Animal Health can help ensure optimal benefits are derived from parasite control programs.
For years, parasitologists, veterinarians and pharmaceutical companies have invested heavily in researching and developing parasite control programs for the U.S. cattle industry. These efforts are critical for helping ensure the economic impacts of parasitism for cattle producers are mitigated.

Parasite control protocols for cattle are designed to effectively remove or limit helminth and arthropod parasites and, if possible, prevent reinfection. Four categories of parasites pose the greatest threats to the economic productivity of cattle:

- Roundworms/nematodes (19 species in U.S. cattle)
- Arachnids/ticks and mites
- Insects/flies and lice
- Flukes (both cattle and deer varieties)

Tapeworms and protozoa (e.g., coccidia, Babesia, Anaplasma, Sarcocystis) often are included in typical control programs, but adult tapeworms are not economically important, and protozoa (which are economically important) will not be addressed here.

**Parasite life cycles**

The design of effective parasite control protocols must consider the life cycles of the various target parasites. Roundworms, arachnids and insects have direct life cycles, meaning no intermediate hosts are required for their maturation and transmission. In contrast, flukes have an indirect life cycle that requires a snail intermediate host (where miracidial larvae mature to cercariae/metacercariae) to complete their life cycle. Control of flukes is more complicated because snail control also must be an element of any control program.

Ticks have two types of life cycles: single-host and multihost. Single-host ticks feed on only one host throughout all three life-cycle stages (larvae, nymph, adult). *Boophilus*, for example, is a single-host tick that will only infect and mature on cattle. The majority of tick species in the United States are multihost ticks (e.g., *Amblyomma*, *Rhipicephalus*, *Dermacentor*, *Ixodes*), which can mature and complete their life cycles on cattle as well as other common animals (deer, rabbits, groundhogs, mice, etc.). Thus, control of multihost ticks is exceedingly difficult because treatment of all hosts capable of harboring ticks is required to eliminate infection sources.

**Research protocols**

Deworming protocols for cattle must be defined by the parasite threats that are endemic in the production environment as well as the grazing status and age of the host cattle. Assessment of the protocol outcome will be defined differently for cows, pre-weaned calves, weaned calves (grazing stockers) and feedlot cattle.

**Protocol 1 — Grazing cows with calves**

A research protocol for grazing cows should first be defined by the desired outcomes, which may be to measure cow and calf weights at birth, calf weight at the time of treatment, calf weight three months post-treatment, and/or cow and calf weights at weaning. Additional weigh points also may be collected to reduce the statistical variation.

Cow/calf research studies may be approached in two ways. The first method is to treat all animals in a herd at the same time and compare their outcomes to an untreated herd (or a competitive product treatment). This design requires that the herds be maintained on separate pastures. Thus, “pasture” defines the degrees of freedom of the statistical analysis; multiple pastures are needed for each treatment group to achieve a powerful analysis of the data. The second method is to treat half of a herd on a single pasture and compare it with the other half of the herd that received no treatment (or a competitive product treatment). This approach allows the herd to be maintained on a single pasture, and the degrees of freedom of the analysis is defined by the number of animals in each treatment group.

Unfortunately, each protocol strategy has inherent weaknesses. If separate pastures are employed, they must be very similar throughout the trial, and multiple pastures are needed. Not only is this costly but also locating several similar pastures is usually difficult. However, if a single-pasture trial is conducted, study results may not actually address the questions that producers want answered because they have no intention of treating only half their herd (or treating with two products). When all cattle are maintained on the same pasture, treated animals will be penalized by the presence of untreated animals and untreated cattle will be benefited by the treated animals (treated animals will experience a much heavier challenge than if all animals were treated; and untreated cattle, in turn, will experience a much lighter challenge than if all animals were untreated).

The length of a cow/calf study usually is nine months to one year. Performance variables such as pregnancy rate, weight gain or loss, and body condition scores are usually measured, but other variables such as feed availability may overwhelm the effects of parasite treatment. Pregnancy rates may be impacted by severe parasite infections but are not reliable indicators of successful parasite control programs because too many other variables influence reproductive success. For calves, outcomes such as
birth weight and weaning weight are usually assessed, but again, nutrition is a very important variable (milk production by the cow is the major nutritional factor for early weight gain, while feed availability and quality impacts weight gain later in the study).

The timing of treatment is another difficult issue for cow/calf studies (and adding fluke control to the study further increases this difficulty). Cows need to be treated prior to calving to get them prepared for their most stressful period. In contrast, calves do not need to be treated until they are ingesting parasite larvae. Calf treatment in midsummer (pre-weaning) has shown to be very impactful for gain and immune competence. A cleanup dose for the cows at the beginning of autumn is beneficial in the South to remove inhibited Ostertagia. In the North, a lice treatment should be provided in midautumn. (For fluke treatment timing, see “Factors that Impact Product Efficacy” section.)

**Protocol 2 — Weaned calves (grazing stockers)**

Studies involving grazing stocker animals are easier to design and repeat/verify. A direct beneficial effect of worm reduction on the weaned calf can be assessed, rather than a mixture of both direct and indirect effects on a cow/calf pair. These studies also can be conducted for a much shorter duration (45 to 120 days), reducing variables typically encountered in longer cow/calf studies. In addition, stocker studies of more than 90 days can clearly demonstrate differences in average daily gain benefits provided by a short-acting product compared with a long-acting product. Treatment timing also is easier, focusing on the weaning-to-feeder period when grass is available.

**Protocol 3 — Feedlot cattle (nongrazing)**

Feedlot studies are the easiest and most reliable type of research to conduct because cattle are similar in weight and size, are not exposed to reinfection (short-acting and long-acting products are more equalized), and are consuming a defined diet. Animals can be housed in small pens, providing good statistical power to the analysis of treatment of all animals in a pen. Since cattle are weighed upon arrival at the feedlot, accurate dosing is not a problem, and treatment can be administered at entry to reduce handling expenses. Multiple data points can be easily collected because animals are weighed pretreatment, at reimplant and at slaughter — without increased animal handling. In addition, feed consumption, feed conversion and carcass-quality parameters can be added to the outcome measurements.

**Protocol types**

Specific Pfizer Animal Health guidelines have been developed for the following types of research protocols:

1. Discovery research — efficacy, safety, stability, toxicology, pharmacology, etc., studies to determine potential efficacy and safety of a product candidate
2. Development research — efficacy and safety trials conducted according to government regulatory standards for purposes of attaining registration of the product
3. Pre-approval technical research — clinical/field trials to test the efficacy and productivity vs. untreated controls
4. Post-approval marketing research — clinical/field trials to compare efficacy and productivity vs. controls treated with a competitive product
5. Testimonial research — supplying product to a veterinarian or producer to test with their own protocol

Protocol Types 2, 3 and 4 require inputs from the study investigator, monitor and biometrician so generated data permit appropriate statistical analyses. Data generated by Protocol Type 1 may or may not be statistically analyzed, while Protocol Type 5 data are not analyzed. Only statistically analyzed trials can be used in printed marketing materials.

**Efficacy assessment issues**

A significant problem for conducting any internal parasite study is the assessment of product efficacy by either fecal egg counts and/or actual parasite counts (the latter also applies to acarines and insects). Although parameters such as weight gain, body condition scores, feed conversion, carcass quality, etc., comprise the most important issues to producers and veterinarians, benefits must be correlated to the reduction of parasite burdens. If cattle harbor large numbers of inhibited/developing parasite larvae or if host immune responses have moderated fecal egg counts (but not actual nematode counts), measurement of fecal egg count reduction after treatment is not a reliable indicator of treatment efficacy. Notably, these conditions describe most animals greater than 2 years of age.

The only reliable measure of anthelmintic efficacy is to necropsy cattle two weeks after treatment, count the internal parasites (adults and larvae) and, thus,
directly quantify worm count reduction compared with untreated controls. However, the costs and labor involved in such an assessment are enormous. Research costs would be far more tolerable if test animals could somehow be euthanized, the worms counted, and then the animals returned to life and productivity. However, because every animal (both treated and untreated) must be purchased to determine product efficacy, great costs are involved and no live animals exist for examination of growth benefits. A compromise of performing necropsy on only 10 percent of the animals (both treated and untreated) is still very cost-restrictive in a commercial herd, and it introduces a correlation factor between sample data and whole-herd data that adds an additional error term in the analysis.

**Surveys for resistance**

An ongoing discussion in the parasitology community concerns how a survey for anthelmintic resistance in U.S. cattle might be accomplished. One survey attempt was conducted in 2009 by the National Animal Health Monitoring System (NAHMS) involving a questionnaire about anthelmintic use and a kit for testing fecal samples to assess post-treatment fecal egg count reduction. However, the survey did not monitor the accuracy of anthelmintic application nor did it sample the same cattle pre- and post-treatment. Pfizer Animal Health conducted a subsequent survey in 2010 using face-to-face interviews with producers and veterinarians and inquiring about anthelmintic use and opinions about anthelmintic resistance. Although these various techniques are relatively inexpensive, they simply report opinions; they do not provide scientific evidence of resistance or data that could help establish understanding of any resistance problems.

To scientifically detect and quantify anthelmintic resistance, fecal sample collections and post-treatment fecal egg count reduction tests would need to be conducted under very strict supervision. In addition, animal necropsies would be required to identify and count nematode burdens. Such protocols would need to be conducted in a representative number of animals grouped by weight/age, management systems and areas of the United States. The costs of such a program, designed to involve sufficient numbers of animals in each subgroup that would allow valid biostatistical analyses of the data, would be enormous. This most certainly will not transpire unless multiple stakeholders that could potentially benefit from the database collaborate to fund such an undertaking. Interested parties from the U.S. Department of Agriculture, Food and Drug Administration, pharmaceutical companies, veterinary associations (e.g., American Veterinary Medical Association; American Association of Veterinary Parasitologists), and cattle producer associations (state and national cattlemen groups) could generate protocols to assess how much anthelmintic resistance is present in U.S. cattle and which products are involved. If these data were generated, scientifically valid programs could be devised to help deal with existing resistance and/or help find new answers to solve future impacts of increasing resistance.

More often than not, instances of lessened anthelmintic efficacy (as well as parasitides in general) are impacted by factors other than resistance or drug activity failure. Simply put, proper use of anthelmintics, at the proper time of the season, is critical in ensuring effective parasite control. To assist in the ongoing battle against the performance-robbing impacts of parasitism, Pfizer Animal Health has developed the following brief set of treatment recommendations for helping ensure optimal benefits are derived from parasite control programs:

- Treat cattle with DECTOMAX® Injectable in the spring.
- Treat cattle with VALBAZEN® and/or DECTOMAX Pour-On in the fall.
- For producers in Gulf states, northwestern Oregon, Washington or California, treat cattle with VALBAZEN and/or DECTOMAX Pour-On in the spring and DECTOMAX Injectable in the fall.
- Treat feedlot cattle with DURASECT® II Pour-On for lice breaks.

**DECTOMAX Important Safety Information:** DECTOMAX Injectable has a 35-day pre-slaughter withdrawal period. DECTOMAX Pour-On has a 45-day pre-slaughter withdrawal period. Do not use in dairy cows 20 months of age or older. DECTOMAX has been developed specifically for cattle and swine. Use in dogs may result in fatalities.

**VALBAZEN Important Safety Information:** Cattle must not be slaughtered within 27 days after the last treatment with VALBAZEN. Not for use in lactating dairy cattle. Do not administer to female cattle during the first 45 days of pregnancy or for 45 days after removal of bulls.