Volume 1 Issue 2

dvm business essentials

Aurora Pharmaceutical, LLC
Innovative Products Backed by Exceptional Service

aurora PHARMACEUTICAL®

BUSINESS ESSENTIALS - INSIDE

www.aurorapharmaceutical.com

Bringing Customers to the Veterinarians' Door Critical to All Our Success

Bob Rehurek,
Director of Sales and Marketing
Aurora Pharmaceutical, LLC

While traveling with various distribution partners and Aurora sales professionals the past few months, I was impressed with the level of uptake equine veterinarians have had with our FDA-approved **Equisul-SDT®** (sulfadiazine/trimethoprim) and **Altren®** (altrenogest) products. They kept telling me they appreciated Aurora's commitment to spending seven years and millions of dollars to obtain the FDA approval on Equisul-SDT. They also communicated how much they liked the packaging and apple flavor that helps customer therapy compliance. And they have totally adopted the new 150 mL bottle for the Altren product. They appreciate the safety (vs. pouring product from a bigger bottle into smaller dose containers) and ease of use and how simple it is to educate owners to manage the product effectively.

However, there was always one caveat to the conversation … the veterinarian was supporting and purchasing our new products, but they wanted help moving the product into the equine customer's hands. They asked Aurora to help them convince equine owners of the apparent safety, convenience and value of these two new drugs.

> *"We have always believed veterinary medications – dispensed through a veterinarian – assure clients they have the proper drug for their equine athletes or animal(s)."*

We listened, and we acted. The first thing we did was produce several advertising messages geared directly at equine owners and breeders highlighting the benefits of Altren for controlling estrus in performance mares. We also designed an aggressive educational and promotional advertising campaign directed to swine producers promoting **SwineMate®** (altrenogest). Additionally, we developed a series of ads touting the FDA-approved, veterinarian-supported therapeutic effectiveness of the new combination antimicrobial properties of Equisul-SDT. These ads have been placed in the mainstream equine press (see ads right) and are appearing throughout 2018. The ads focus on the major strengths, safety features, per-dose economics and proven research of each product. **ALL THE ADS** direct the equine owners to *contact their local veterinarian* for more information and product availability.

Second, we are developing educational and veterinarian-based articles stressing drug compliance, correct handling of products (especially any altrenogest product) and why supporting research-based, FDA-approved products makes sense. Our hope is that magazine editors will run these articles to support the veterinarians' commitment to use only FDA-approved products when one exists vs. using off-label, compounded, non-animal-tested medication labels.

This will endorse the veterinarians' message of therapy protocol compliance and using approved drugs specifically made and tested for each species. Again, all articles lead the reader directly back to their veterinarian for answers and product purchases.

All of our success begins and ends with the veterinarian. That commitment starts with Aurora's Sales and Technical Services teams providing all our distribution partners with the most up-to-date and complete data possible on all our products. It also includes a partnership commitment to bring all our products to the market at the same prices – regardless of the size of the clinic. And, of course, a dedicated, highly trained distribution network who work closely with the veterinarian.

AAEP President Stresses …

Mentoring is a Critical Step Toward Success of Next Generation Veterinarians

American Association of Equine Practitioners (AAEP) President, Margo Macpherson, DVM, MS, DACT, is a relentless, highly regarded clinician/scientist who has dedicated her professional career to combining both veterinary medicine and research.

Dr. Macpherson currently serves as a tenured professor at the University of Florida College of Veterinary Medicine and previously worked as a private practitioner in central Kentucky and served as a lecturer at the University of Pennsylvania. She received her veterinary degree from Michigan State University in 1990 and a master's degree from Texas A&M University in 1994.

Dr. Macpherson has worked in private practice at the backside of a racetrack, mixed animal practice and owned her own business. Through all that, she always knew she wanted to be in an academic research position.

"That drive allowed me to pursue a residency at Texas A&M and that proved to be the most pivotal move of my career," she recalls.

"Through some excellent mentors, it laid the groundwork for my career. I worked under Dr. Terry Blanchard and Dr. Dickson Varner. They promoted their young veterinarians by encouraging them to do graduate work. This move taught me about good clinical science and opened doors that have allowed me to be here today.

"I am a clinician first and a scientist second," Dr. Macpherson continues. "I enjoy finding things that improve equine health, particularly with regard to equine pregnancy. I also enjoy the fact that from each project that we conduct in our laboratory, everyone involved (students, residents and faculty members) learns new skills or gains clinical experiences that enhance our skills as veterinarians.

"I have devoted a significant portion of my professional career trying to unravel the complexities of equine placentitis," she states. "Work from our laboratory has helped direct treatment choices for mares with placentitis by providing information about efficacy of commonly used antimicrobial and anti-inflammatory treatments."

Dr. Macpherson's work has shown that some commonly used drugs do not cross the equine placenta. Importantly, they have shown drugs that have improved foal survival in mares affected with placentitis. More recently, they have adopted an evidence-based approach to identifying how effective drugs may work in placental infections. "That's how I became familiar with **Equisul-SDT®** (sulfadiazine/trimethoprim)," she continues. "We've worked with trimethoprim sulfa products for many years because it's a product that's readily available to the practitioner in the field. This product allows us a multi-pronged approach – an antimicrobial for the bacterial infection (with *Streptococcus equi zooepidemicus* being the primary bacteria or pathogen involved in placentitis), *E. coli*, pseudomonas and as an anti-inflammatory promoting uterine quiescence."

Margo Macpherson
DVM, MS, DACT
AAEP President

Dr. Macpherson has been studying human sulfamethoxazole since 2003. "I can't make a change in my research approach right now because all my work has been comparative with sulfamethoxazole," she states. "The flaw, however, is that the main pathogen, *Step zoo*, has developed about a 20% resistance rate to the drug. This has caused us to look at other antimicrobials, like Equisul-SDT, that may be useful for treating mares with placentitis.

The sulfadiazine/trimethoprim product has some distinct advantages. It certainly offers ease of use. It makes my life infinitely happier to dispense Equisul-SDT because it's so much easier to draw the liquid up and administer it to a horse vs. crushing tablets, mixing them up into a paste, assuring consistency, etc. I've been impressed with the product so far."

AAEP Role

Dr. Macpherson says her main role as President of the AAEP is to provide leadership on the important aspects facing all 9,000+ equine veterinarians.

Dr. Macpherson believes some veterinarians feel that the younger vets have a sense of entitlement. "Working with them every day, I can assure you they are extremely hard-working individuals who happen to see the world through a different template. They've seen their own parents working 80-90-hour work weeks and the impact it has on a family, such as missed events or failed marriages. Young veterinarians (and all professionals for that matter) are making lifestyle decisions to avoid the pitfalls their parents faced.

"On the other side of that," she continues, "young vets sometimes fail to understand how much a practice owner gives when building a practice. There is an emotional attachment to the practice that may not be evident to an associate. For many practice owners, the investment is more than just making money, it's an investment of a lifetime. We need to illuminate both sides so there is an honest discussion on how we can make this young group feel welcomed while acknowledging the contributions of those who built practices.

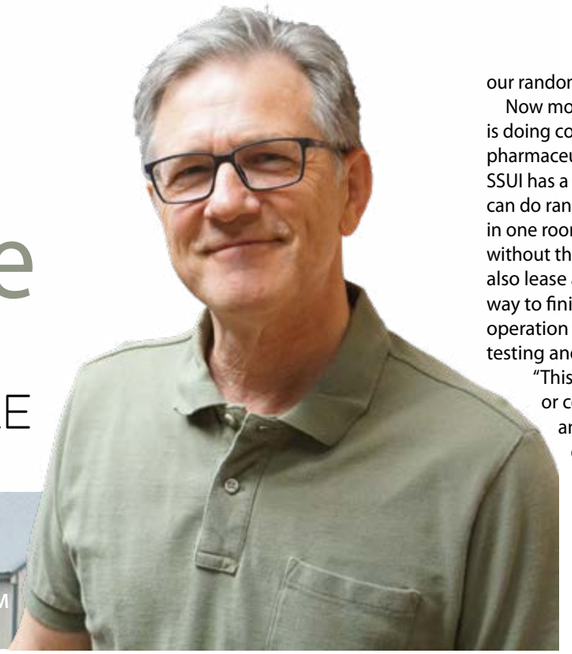
"We have a great profession in equine veterinary medicine," Dr. Macpherson continues. "It is incumbent upon all of us, both seasoned practitioners and new grads, to be creative in managing work weeks, family-friendly environments and fiscal stability so that all members of the practice thrive.

"To that end, the AAEP has just formed a Young Professionals Taskforce and we as an organization are working on these issues via mentoring, open conversations and patience. As long as both sides of this equation can openly discuss it and produce firm action plans, we will all win," Dr. Macpherson concludes.

VETERAN SWINE PRACTITIONER SAYS ...

Find Your Niche

TO MAKE PRACTICE SPECIALTY WORTHWHILE



Dr. Nate Winkelman, DVM
AASV President-Elect

Nathan "Nate" Winkelman, DVM (MN, '84), was likely the first veterinary student to go into a "swine exclusive practice" right out of veterinary school, working for renown swine practitioners Dr. Rod Johnson and Dr. Tony Scheiber.

"There were very few swine-only practices and the swine industry as we know it today was in its infancy," notes Dr. Winkelman.

Even today, the American Association of Swine Veterinarians (AASV) members consist of 47% practitioners, and only 26% are exclusively swine veterinarians.

"The complexion of being a swine-focused veterinarian has changed a lot since I first came out of veterinary school in 1984. It's fewer farm kids and more female veterinarians," says Dr. Winkelman. "However, we face the same challenge as other veterinary specialties – how can we pay them enough commensurate with their education and their student debt?

"Student debt is a huge problem for the veterinary profession," outlines the AASV's President-Elect. "We need to make sure students are paid well enough to choose this profession. A recent swine veterinary survey shows that swine veterinarians on average are making $135,000/year vs. other veterinarians paid nearly $85,000/year.

"On average," he states, "our industry is doing an excellent job of paying new swine veterinarians. And in my opinion, there is a larger need for swine veterinarians because of vertical integration."

Dr. Winkelman adds, "There is no limit to what you can make. While I wanted to be a practice owner since I came out of veterinary school, fewer younger veterinarians now want that responsibility. However, to make the most amount of money and invest in your future growth, you need to have practice ownership and find your niche."

And finding "his niche" is exactly what Dr. Winkelman has been doing since starting in swine practice some 34 years ago.

"Our business focus (and first love) is consulting with loyal, progressive pork-producer clients, some of whom we've seen each month since the beginning," stresses Dr. Winkelman.

However, along with practice partner Adam Mueller, DVM (ISU, 2012), they have developed one of the most sought-after swine contract research facilities in the country at Swine Services Unlimited, Inc. (SSUI) in Rice, MN.

Dr. Winkelman admits he fell into developing a research facility in the early 1990s while trying to figure out *Lawsonia intracellularis* or ileitis – the most common cause of grow/finish pig diarrhea in North America.

"We didn't know that much about it, so I started working with Dr. Connie Gebhardt at the University of Minnesota and developed a research disease challenge model that produced both the disease and consistent mortality and clinical signs. At that time no one was doing any commercial trials and there was a growing need for answers. Then the FDA recognized our research model as pivotal for antibiotic approvals. That allowed us to do a lot more ileitis research because we didn't have to wait for natural outbreaks of ileitis to do the studies. Instead, we could bring in the pigs, challenge them with the *Lawsonia* bacteria and do our randomized controlled research trials."

Now more than half the practice's time is doing contract research for biological, pharmaceutical and nutritional companies. SSUI has a virus-filtered facility where they can do randomized control trials with viruses in one room and control groups in another without the fear of cross contamination. They also lease a finishing facility to do trials all the way to finishing and another farrow-to-finish operation where they can do all manner of testing and comparisons.

"This research has allowed me to author or co-author many scientific papers and open doors for international consulting opportunities to gain a global industry perspective," Dr. Winkelman states.

A recent example of where the swine research facility paid dividends was where they conducted a swine influenza challenge study comparing sodium salicylate to controls. The study proved that sodium salicylate was much more effective in reducing body temperatures after a challenge of influenza virus.

They also conducted a dosing trial with Aurora's **Oral-Pro Vitamin D3 + E500** product.

"Our main objective was to determine the best dosing protocol via the water medicator," Dr. Winkelman outlines. "Up until that point, the recommendations were all over the place for these types of water- medicated products. Aurora quickly altered their label to reflect these proven rates."

AASV Challenges

Dr. Winkelman admits one of the most rewarding tasks he has ever taken on has been serving as an AASV officer. "Being asked to serve as an AASV officer is an honor and presents an opportunity for me to give back to the organization that has given so much to me," Dr. Winkelman notes.

"I'm proud to say that I have been to every AASV-AASP meeting since I was a veterinary student in 1982. Obviously, the knowledge gained, contacts made and the camaraderie with colleagues is very important to me."

In conclusion Dr. Winkelman adds, "I'm having a lot of fun giving back to the industry I love. It's time for me to do more volunteer work and try to give back what I've been given," he adds.

"Working in Washington with various senators and congressmen involved with the Farm Bill has been eye-opening," Dr. Winkelman smiles. "We're trying to secure appropriate funds, so we have a stockpile of Foot and Mouth Disease (FMD) vaccine in case we have a Foreign Animal Disease (FAD) outbreak. We're also especially concerned about African Swine Fever spreading across Eastern Europe, Russia and China.

"If we do have a FAD introduction, we want to be ready for it. In 2017, the US exported 26% of our pork. We have the safest and most consistent supply of pork in the world. If we break with a foreign animal disease, that would instantly be cut off. It's all part of the behind-the-scenes preparation that keeps swine veterinarians and producers vigilant and ready."

Swine Services Unlimited, Inc. headquarters in Rice, MN

TENNESSEE EQUINE PRACTITIONER HAS A 'TAKE NO PRISONERS' ATTITUDE

WHEN DEALING WITH LAMENESS AND INFECTION

Practicing equine medicine in Shelbyville, TN, the Tennessee Walking Horse capital of the world, provides equine veterinarian John Bennett, DVM (Auburn '80) a unique look at a wide variety of lameness issues ranging from arthritis to soft tissue injuries.

"While the Tennessee Walker is still king in these parts," Dr. Bennett notes, "we see a heavy load of Western performance horses and other gaited horses that are taking over the former Tennessee Walking Horse barns around Shelbyville," says Dr. Bennett, owner of Equine Services LLC, a four-doctor veterinary practice that focuses on lameness and equine reproductive cases.

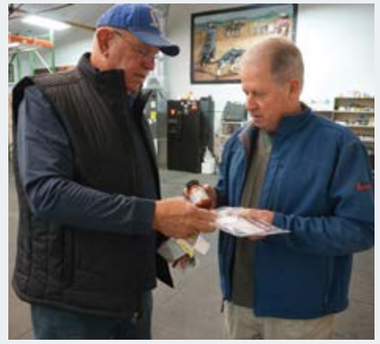
"Tarsitis (hock inflammation) is a common problem for Western performance horses, since they use their hind ends heavily during events such as reining, cutting and barrel racing," Dr. Bennett states. He believes a large percentage of high-performance Western horses have this problem and says it is hard to keep these horses in training events since they are worked so hard and there seems to be a show every weekend.

"We try and educate our horse owners that lameness results from pain coming from any part of a horse's anatomy," he explains. "This can include pain from skin wounds, connective tissue bruising, muscle pain, arthritis (joint inflammation), tendon sheath and bursal inflammation, tendon and ligament injury, and bone injury can all result in lameness that cannot be differentiated by observing the horse's gait or the way a horse moves."

Dr. Bennett notes, "Forelimb lameness is easier for most people to recognize than hindlimb lameness. The mechanics of the forelimb cause lameness to be more consistent in appearance and obvious to the untrained eye. Hindlimb lameness is generally much more difficult to visualize and diagnose. This is especially true of subtle upper hindlimb conditions. The massive musculature of the upper hindlimb makes it much harder – even for an experienced examiner – to see and feel deeper structures, and more difficult to image these structures using radiographs and ultrasound."

Dr. Bennett notes these multiple lameness issues continue to be the reason why his practice offers a wide variety of diagnostic modalities to better diagnose and treat equine lameness. These include thermography, digital radiography, digital ultrasound, acupuncture, chiropractic work as well as a lameness locator. They also offer treatments including a rehab facility, stem cell therapy, IRAP, PRP and Pro-Stride.

"We are always offering new regenerative medicine therapies, with our newest being advanced Lipogem therapy," he adds.



Aurora Equine Sales Rep Mike Duvall (L) details Dr. John Bennett on the new Altren 150 mL product.

But lameness is only part of the practice's expertise. Dealing with reproductive issues is quickly becoming a major part of the business, Dr. Bennett outlines.

"We are heavily focused on mare care, proper breeding and foal care. We have 24 stalls dedicated to breeding and mare care. A lot of customers drop off their mares here and we take care of the mare until pregnancy is confirmed. Consequently, we perform a lot of ET work, however, we do not have a recipient herd.

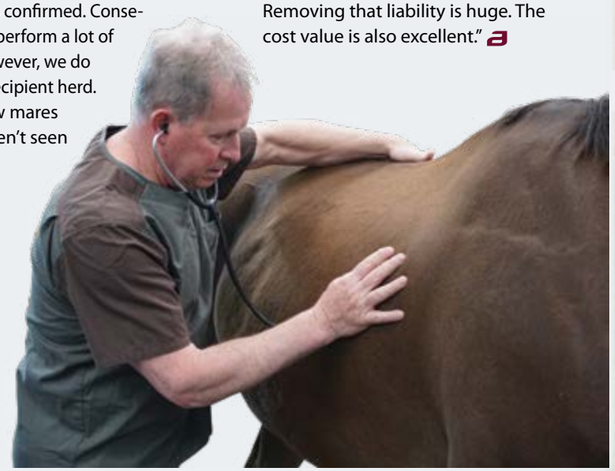
"With new mares that we haven't seen before," Dr. Bennett notes, "we highly recommend a breeding soundness examination. In most cases, procedures will include the standard rectal palpation and speculum vaginal examination, an endometrial culture and cytology exam, an endometrial biopsy, transrectal ultrasound and endocrine assays. We want to eliminate (or treat for) anything that can get in the way of a good pregnancy."

Dr. Bennett and his staff also see a lot of young horses with fever and general infections. "We don't wait around for diagnostic work to be completed when we see fever or infections," states Dr. Bennett. "We immediately put them on **Equisul-SDT®** (sulfadiazine/trimethoprim) until we run cultures and definitively identify the causative agent.

"Horses tolerate the antibiotic extremely well and the efficacy has been outstanding," he adds. "I like that we finally have an FDA-approved product to use and dispense. Now we don't have to crush sulfa pills and guess at strength and treatment time."

Dr. Bennett believes he is seeing some resistance issues building up where they are using human sulfa products. "As veterinarians we have to recognize that fact. Clients get tired of crushing pills and forcing the bitter tasting products down the horse's throat. It's not a pleasant experience for anyone, including the horse," he notes.

In conclusion Dr. Bennett stresses, "With the compounded products, the vet is responsible. If we choose to use a product off-label, we're liable. It's finally nice to have a company (and extensive FDA testing) backing up our decision. Removing that liability is huge. The cost value is also excellent."



Aurora Manufacturing Expertise

Second to None

And Proving It Daily

When the Aurora Pharmaceutical management team decided to build a dedicated manufacturing facility to start producing their line of innovative products, they knew they wanted Kevin Bell to oversee the production in Northfield, MN.

"I proudly tell people I'm employee #5," says Bell, who holds an Industrial Technology/ Manufacturing Engineering degree from the University of Wisconsin-Stout and has more than 30 years of operations and production experience – 20 of those years were with cGMP pharmaceutical and medical device manufacturers.

Since joining Aurora, Bell has one simple mantra that dictates his day – ***Safety First***, and the ***Line Always Runs***. "Everything else is secondary," says the Aurora Production Manager. "Our commitment to our customers is to provide the best product possible when they need it most. Every process we develop or refine is focused on improving line performance. We must keep the production lines running at all costs."

Aurora's first batch of product came off the line in December 2010 and it has been running ever since. "The facility is a unique design and incorporates a Quality Control laboratory that confirms Certificate of Analysis (COA) and purity of raw ingredients with high-pressure liquid chromatography (HPLC) technology," Bell outlines. "We manufacture under current FDA cGMP guidelines which include the validation of product stability of all finished products. We utilize state-of-the-art liquid fill and labeling capabilities – many of which were designed by our team – and are set up to process final liquid packaging from 50 mL bottles up to 1-gallon jugs."

Bell admits that Aurora's current core competency is water/oil/alcohol based liquid products and suspensions with a high level of competencies in powdered products as well. "That's where our veterinary founders realized the most urgent need in the animal health space. I sincerely feel that our systems, ingredients and manufacturing SOPs allow us to do this better than anyone on the market," he explains.

"We are currently looking at an additional 20+ liquid products that we still feel are necessary to fill voids in the animal health marketplace, and we are working on bringing them to market quickly."

Bell says Aurora is oftentimes referred to as a boutique manufacturer. "We can react quickly to changing industry needs and have a 'never say no' policy on products our customers are requesting or new ingredients our vendors are presenting. It keeps us cutting edge and ahead of our competitors," Bell states.

One of the new production opportunities Bell and his team are most excited about is their new injectables line. They see the need for this type of product offering and have already started on the design of the manufacturing processes, ordered and have installed key equipment and components and expect to be offering a line of injectable products soon.

Aurora Pharmaceutical headquarters in Northfield, MN

> *"You're going to get a consistently high-quality product you can rely on dose after dose"*
>
> **Kevin Bell, Aurora Production Manager**

Customer-Focused Production

Bell says Aurora is extremely fortunate that their founders are veterinarians and have been manufacturing customer-specific products for more than 20 years. "Add to that the experience of our Sales and Marketing Director, Bob Rehurek, who has been working with veterinary distributors and producers for more than 30 years, and you have a unique pulse on customers and the marketplace few companies have," Bell states.

"I firmly believe manufacturing excellence requires that manufacturers instill, and constantly reinforce within the organization, the principle that the system and everyone in it must know their customers and must seek to satisfy the needs and wants of customers and other stakeholders.

"This means that the entire organization is optimized around meeting the customers' needs, using the skills of each discipline, focusing on the real task and ultimately solving the real problems."

As Production Manager, Bell is in charge of materials, manpower and machines. While he spends a lot of time on the materials side of the business – going all over the world making sure Aurora has the best ingredients at the best cost – his overall responsibility is to tie together HR, QA/QC, materials acquisition, safety and engineering, assuring all work together.

"Our management team has done an amazing job of establishing a clear vision for the enterprise," Bell states. "When people understand this vision and have the appropriate frame of reference, information, resources, clear understanding of the task and its scope, and responsibility for accomplishing the task, they buy into the success and want to be part of that culture."

In conclusion Bell notes, "The core characteristics of manufacturing proficiency in an increasingly competitive marketplace include:

- **Superb product development skills**
- **Operations efficiency**
- **Quality conscious customer satisfaction**
- **Innovative adoption of product & process technology**

Our team of production, regulatory, quality control and product marketing experts are focused on these areas and work diligently daily to refine and adopt new technologies that bring better products to the market. "We owe that to our customers every day."

Superior People Skills and Work Ethic Keeps Henry Schein Equine Territory Manager's Life in Focus

When Donna DuRant, Equine Territory Manager for Henry Schein, started selling products in the late '90s, she worked for a manufacturer and would take her order pad from clinic to clinic, take orders for vaccines and pharma products, and then drive to the local phone booth to call in her order.

We fast forward to her current role as a distributor which has evolved from a transactional role to a more consultative one. "Oftentimes clinic staffs call on me for things that have nothing to do with our products, but may need my help setting up wet labs for continuing education, new employee training, OSHA presentations, etc. By design, my role has evolved into more of a practice management/customer service/technician/event management/product or equipment detailing/technical services role," says DuRant.

While Henry Schein has several hundred vendor partners and thousands of products, DuRant has always held to the truth that people want to work with people they trust.

"Anyone can go online and order products," DuRant states. "What I offer my clients is more of a partnership backed by Henry Schein's multiple products and services offerings. I offer them direct access to everything essential in their practice including diagnostic and imaging equipment, ultrasound equipment and training, equipment financing, pharmaceuticals, vaccines, inventory management, OSHA training, etc. But most importantly, I offer them my integrity and honesty. That's something that must be earned every day."

Horse crazy all her life, DuRant owned, trained and showed horses most of her adult life. Once she started in the animal health industry, they sold their farm and moved to town, as managing the travel for a large territory was easier to handle without all the work keeping up with livestock.

She says working in the equine industry was never in doubt. Today DuRant is widely viewed as one of the best distributor reps in the country working in the animal health industry.

Donna DuRant
Equine Territory Manager
Henry Schein

HENRY SCHEIN®
ANIMAL HEALTH

But what has always separated DuRant from many sales reps is her strong, intelligent and undeniable flair for style. Always appointed in her polished boots, starched jeans and signature smile, DuRant epitomizes the term 'have fun working.'

"I have always enjoyed working in the animal health industry," she smiles. "I'm a social butterfly. If I were on a deserted island, I would be in a lot of trouble."

Prior to joining Henry Schein, DuRant worked with the equine divisions of both Fort Dodge and Boehringer-Ingelheim. In late 2002 the West Nile Virus outbreak hit Florida. She worked closely with her clients making sure everyone had the new vaccine, as West Nile Virus was a new disease and truly an epidemic back then. It was a good time for her to really prove herself.

Five years ago, she was given the opportunity to trade in a large sales area as a manufacturer's rep and focus as a distributor rep, DuRant did what she always does — she consulted with her husband of 45 years, Jay, and her mentor at BI (and now with Aurora), Mike Duvall and colleagues who were customers of Henry Schein. The decision, according to DuRant, was not easy, but it was one she's never regretted.

"Looking back, I always enjoyed working with my distributor reps," recalls DuRant. "They always came in with new information, new products to detail and were always highly regarded by the clinics. I found out very quickly how hard they worked to stay up to date on their inventory of products, services, equipment, etc. I had no idea how hard they worked until I took on the distributor reps' role. I knew if I wanted to be respected as a Schein rep in this industry, I had to put in the time to come up to speed quickly. I read everything I could get my hands on, signed up for any service-oriented training offered, called on a lot of veterinarians (that I still rely on today) and leaned heavily on the manufacturers' reps to get up to date on their products and services."

DuRant says a good example is Aurora Pharmaceutical. "Aurora's one-price-for-all is a huge benefit to me," DuRant notes. "I know when I'm detailing Equisul-SDT® to a client, I can discuss the features and benefits of the product while not having to defend the price because there is not a discounted price online.

"Aurora reminds me of the animal health industry when I first started in it, before the companies got so big and insulated. If I need something from Aurora, I just call them and get an immediate answer. Everyone is in a hurry these days, and can't wait too long for an answer."

The ultimate success story of DuRant rests on her people skills and unflagging work ethic to make sure the Henry Schein work ethos of "making sure each customer has the best customer experience each and every day. Sometimes I ask my veterinary clients, ***What keeps you up at night?*** My job is to find something in my Henry Schein toolbox or past experience to help them stay focused on their practice.

"I enjoy the challenges presented to me every day. I love that every day is different - it revolves around horses and my clients are like family. This has never been a job for me, but rather a lifestyle. Jay and I are truly blessed, and we try to never take that for granted."

AURORA LAUNCHES COST-EFFECTIVE COCCIAID™ COCCIDIOSIS MANAGEMENT TOOL

(AMPROLIUM)

Coccidiosis is the most prevalent disease affecting the US broiler industry. An estimated $90 million is spent in the US, and over $3 billion spent worldwide, for coccidiosis prevention annually. The global impact of coccidiosis due to decreased performance, morbidity and mortality is an estimated $600 million US dollars.

Coccidia infect every poultry house worldwide. Eradication of coccidia has proven impossible, and the transmission stage of the parasite – known as oocysts – can be found in the litter of most commercial broiler houses.

Astute poultry growers will recognize coccidiosis when the birds appear depressed, have ruffled feathers and stop eating and drinking. In some cases, and depending on the *Eimeria* species involved, mortality may be significantly elevated.

Coccidia have also proven to be supremely adaptable. When the same in-feed anticoccidial drug is continuously used, the result has been the development of *Eimeria* strains that are no longer responsive to the medication (Chapman, HD 1997).

Fortunately, good control of coccidiosis is possible thanks to the availability of many effective drugs and the introduction of coccidiosis vaccines. In addition, innovative programs have been introduced that can overcome the problem of reduced *Eimeria* sensitivity to in-feed anticoccidials.

Consequently, it is beneficial to understand the disease, recognize its impact on bird health and performance and have an effective anticoccidial program implemented when outbreaks occur.

TRANSMISSION

Oocysts are passed in the feces, and infective oocysts gradually build up in the environment. Young chicks become infected from contaminated litter, housing, equipment, etc. These may have been contaminated previously by other young infected birds, or by adult birds that recovered from the condition. Areas around waterers are a prime source of infection. Oocysts remain viable in litter for many months, thereby contaminating a farm from year to year. Oocysts are only killed by freezing, extreme dryness and high temperatures.

TREATMENT

The poultry industry is facing new regulatory requirements and consumer preferences to navigate in – an addition to their normal responsibility of raising birds in a cost-efficient and wholesome manner. New challenges include changes to antibiotic use, increased food safety regulations and more concern over how birds are raised. The most significant change may be the voluntary or regulatory withdrawal of the use of antibiotics in poultry production.

In North America, this withdrawal of antibiotic use includes removal of in-ovo antibiotics, performance-improving antibiotics or antibiotic growth promotors (AGP) and the polyether ionophore antibiotics (ionophore anticoccidials).

"In general, ionophores (lasalocid, monensin, narasin and salinomycin) have a similar mechanism of action against the parasite, whereas chemicals (amprolium, decoquinate, nicarbazin) have different modes of action," states coccidiosis expert H. David Chapman, Ph.D., Professor, Department of Poultry Science, University of Arkansas. "Because of that, a strain that develops resistance to an ionophore may be controlled by a chemical, and vice versa. The poultry industry has taken advantage of this with the introduction of shuttle and rotation programs that have helped slow the development of resistance.

"The underlying assumption behind these programs," Dr. Chapman adds, "is that if the parasites develop resistance to one component, they will be eliminated by the other. The majority of poultry producers today use one or both types of programs, and this has helped achieve sustainable control of coccidiosis."

"We really are having issues with coccidiosis because we're going to more antibiotic-free programs," says Greg Mathis, Ph.D., of Southern Poultry Research, Athens, GA.

"Coccidiosis is still the poultry industry's No. 1 problem, followed closely by necrotic enteritis. We still have a very limited number of products to use. More important, we need to understand how to use the ones we have, because if not used correctly and in strict rotational programs, resistance will develop to any anticoccidial drug," he says.

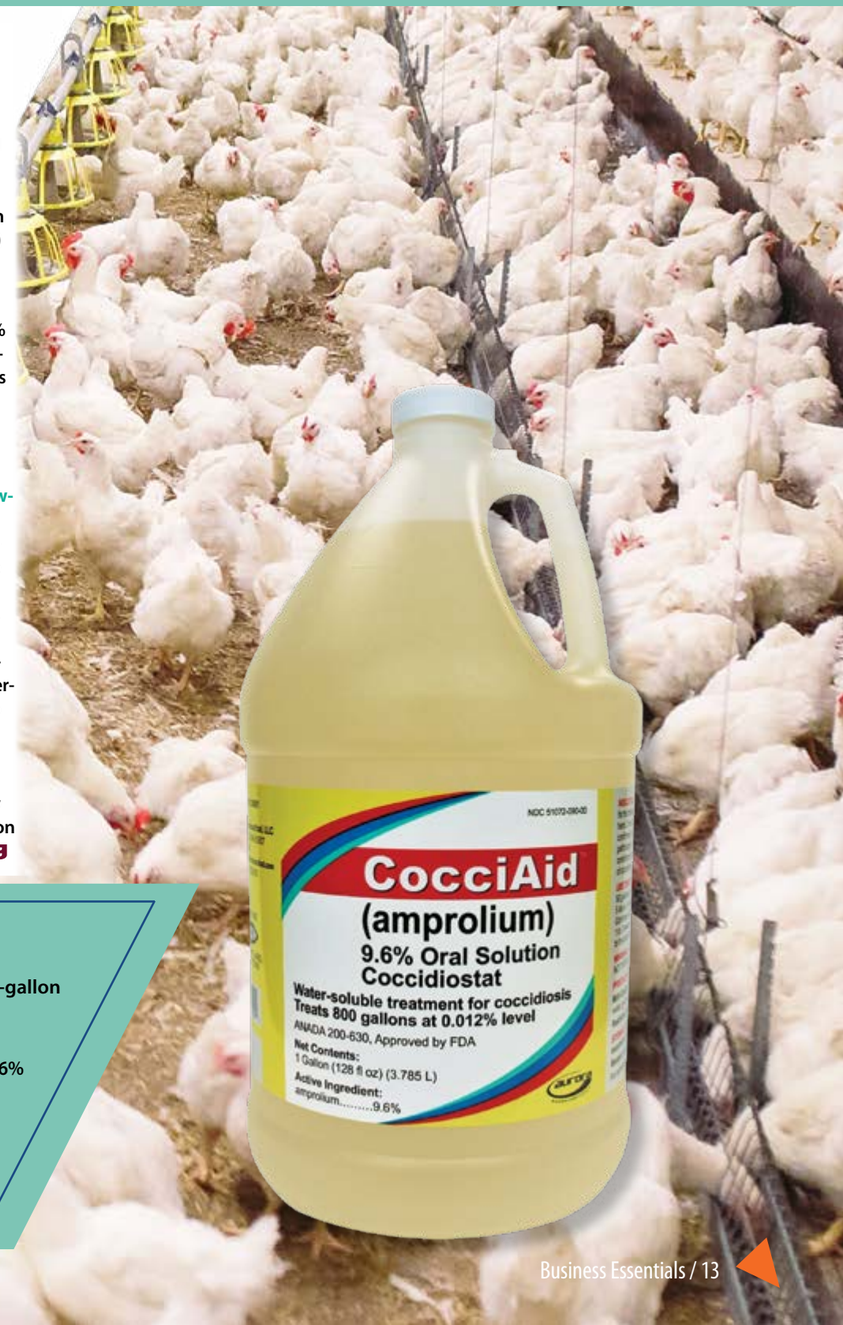
Veterinarians agree, if coccidiosis does break out, start treatment immediately. One of the most effective and proven ways to treat coccidiosis in chickens is with the proven active ingredient amprolium. Amprolium is a non-antibiotic, anticoccidial drug and has also been used for many years and needs no withdrawal time to guard against residue in the meat. It is given in the drinking water and effectively interferes with metabolism of the vitamin thiamine (vitamin B1) in coccidia.

NEW CocciAid™

Aurora's proprietary CocciAid™ (amprolium) 9.6% Oral Solution Coccidiostat is now available in a convenient 1-gallon jug for the treatment of coccidiosis in growing chickens,
turkeys and laying hens. CocciAid (amprolium) is a 9.6% oral solution coccidiostat that can be safely administered in the medicated drinking water of growing poultry and **requires no product withdrawal period for meat**.

New CocciAid can also be administered via automatic water proportioners that meter 1 fluid ounce of stock solution per gallon of drinking water.

"CocciAid 9.6% Oral Solution is not an antibiotic, but rather the newest in a series of products produced by Aurora Pharmaceutical to help veterinarians and poultry producers with a cost-effective alternative to amprolium-based coccidiostats," says Bob Rehurek, Sales and Marketing Director at Aurora. "We have used Aurora's unique solutions development technology to produce a highly-viable coccidiostat that supports a healthy water delivery system and fits beautifully in a coccidiosis rotation program where amprolium is recommended."



COCCIDIA SPECIES IN U.S. BROILERS

A 2011 sampling from US commercial broiler farms indicated 80% of field isolates had two or more species of coccidia present (Mathis, G, 2012).

The following species infect broilers:

Eimeria acervulina

- Infects upper 1/3 of small intestine
- Identified by white/gray striations on intestinal lining
- Negatively impacts feed conversion
- Weight loss in bird

Eimeria maxima

- Infects middle 1/3 of small intestine
- Causes inflammation of intestinal tract
- Weight loss in bird
- Typically leads to secondary bacterial infections: Necrotic Enteritis and Clostridium

Eimeria tenella

- Infects ceca (two blind pouches where small & large intestines join)
- Oocysts found in fecal droppings
- Causes bloody droppings
- May cause morbidity and mortality

USE DIRECTIONS

Give amprolium at the 0.012% level (8 fl. oz. CocciAid™ per 50 gallons) as soon as coccidiosis is diagnosed and continue for 3-5 days. (In severe outbreaks, give amprolium at the 0.024% level.)

Continue with 0.006% amprolium medicated water for an additional 1-2 weeks.

No other source of drinking water should be available to the birds during this time.

Use CocciAid as the sole source of amprolium.

CocciAid is available in highly cost-effective 1-gallon plastic jugs for easy handling, measuring and no-product-loss pouring.

For more information on CocciAid (amprolium) 9.6% Oral Solution Coccidiostat, contact your animal health products provider.

PRECAUTIONS: FOR ORAL USE IN ANIMALS ONLY. MAY CAUSE EYE IRRITATION. For irritation, flush with plenty of water, get medical attention.

Oral Sulfas and the 21st Century

By: Matt Klotz, DVM, Aurora Equine Technical Services Veterinarian

The advent of antibiotics started a craze that led to hundreds of compounds being developed and released in pre-WWII times. Many of these early drugs had limited efficacy at best and in some cases, profound toxicity which caused the passage of the Federal Food, Drug and Cosmetic Act in 1938.

Sulfonamides are a group of sulfa-based products that have been refined to three primary compounds used by veterinarians today: sulfamethoxazole, sulfadiazine and sulfadimethoxine. In veterinary use, these drugs are usually administered in their potentiated form where they are often combined with trimethoprim for more effective treatment.

Sulfonamides are bacteriostatic when used alone, but when combined with trimethoprim they become bacteriocidal through a synergistic interruption in folic acid synthesis. Bacterial cells must synthesize their folate versus mammalian cells which utilize folic acid from their environment (diet)[1]. This difference in cellular physiology is why these compounds will kill the infective organism without poisoning the host mammal.

Potentiated sulfonamides have been routinely used in equine practice as the primary oral antibiotic, and to a lesser extent, as an injectable that is no longer available. They have a broad spectrum of both gram negative and positive efficacy. They are widely distributed into many tissue compartments including cerebrospinal fluid, placenta, synovial fluid, subcutaneous tissue and peritoneal fluid. They are concentrated in the liver, kidney and lung[1].

Early on, certain forms were believed to be efficacious when used in a concentration dependent, single daily dose protocol. However, modern research and clinical use has established that all forms of these drugs used in horses should be administered in a time-dependent fashion of twice daily dosing to maintain constant blood and tissue concentrations above the MIC 90 for susceptible pathogens[2,3].

Adverse events with sulfonamides in horses have occurred in the form of antibiotic-induced colitis, but less commonly can induce a thrombocytopenia and anemia. Colitis is induced through disruption of the natural flora of the colon by antibiotic passthrough. This issue is hard to predict due to highly variable absorption rate of these antibiotics between individuals[1,4] and is very difficult to treat, often resulting in high mortality rates. Blood dyscrasias occur in both horses and humans and believed to be due to an immune mediated mechanism and/or bone marrow suppression and is easily reversible by discontinuing treatment[1].

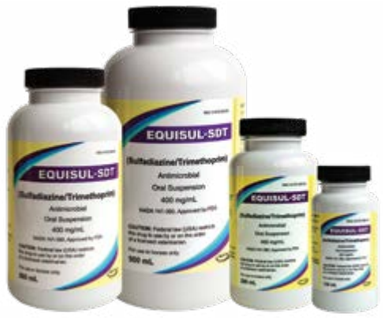
For many years, equine practitioners have relied on two primary sulfa choices in horses – the human approved sulfamethoxazole-trimethoprim (SMZ-TMP) tablets (which have only had a single pharmacokinetic trial that included only six horses)[4] and a once-a-day equine approved oral powder form of sulfadiazine-trimethoprim (Tucoprim/Uniprim)[5]. Both have proven problems with absorption, side effects and efficacy.

The human SMZ-TMP tablets are an extra label use that puts added liability on the prescriber and are thought to have wide-spread resistance in equine pathogens. Administration of the human product has to be crushed and suspended to administer and commonly cause diarrhea in certain regions. The oral powders are often administered in conjunction with food and are poorly absorbed and are limited in efficacy by the once-a-day dosing labeled recommendations[1,2,3].

In 2013, Aurora Pharmaceutical, LLC, introduced **Equisul-SDT®** (sulfadiazine/trimethoprim) – an established drug with new technology that solves many of the problems that the other sulfonamide products have for horses[6].

For example:

The micronized suspension of Equisul-SDT has none of the absorption problems seen in other sulfa drugs and has been demonstrated in a pharmacokinetic crossover study on both fed and fasted horses. This allows Equisul-SDT to maintain circulating concentrations in excess of the MIC 90 for the most common equine respiratory pathogen *Streptococcus equi* subsp. *zooepidemicus*.



Safety was demonstrated in a trial where 1X, 3X and 5X the label dosage was administered for 30 days with no statistical difference between treatment groups and placebo for adverse events.

FDA approved for twice-a-day dosing, as labeled in the horse, alleviates liability on the practitioner.

Unlike other antibiotics used in equine practice, Equisul-SDT has proven efficacy from a blinded trial treating lower respiratory infections caused by *Streptococcus equi* subsp. *zooepidemicus*.

Aurora continues with post-licensure studies and research on Equisul-SDT. In 2018, Dr. Gabriel Davolli (LSU) demonstrated that oral dosing of Equisul-SDT attains effective concentrations in the endometrium[7]. Additionally, a study at UC-Davis demonstrated that concentrations achieved by Equisul-SDT against four of the most common equine pathogens in a sensitivity analysis, demonstrated susceptibility in comparison with other sulfonamides[8]. This study is being followed by a pharmacokinetics study in foals conducted in conjunction with researchers at Colorado State University.

Aurora has taken an established antibiotic combination and reformulated it with modern technology and production methods that solves the most common safety and efficacy problems that has plagued this class of antibiotics in equine practice for decades. While development of new classes of antibiotics is slow in developing, Equisul-SDT is a forward thinking, innovative approach to a longstanding issue.

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FINAL THOUGHTS

By: Mike Strobel, DVM, MS,
President/CEO
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The Compounding Conundrum

In veterinary practice, there is an increasing use of pharmacy compounded drugs. Although primarily limited to companion animal practice and horses, there is no current legal allowance for the practice in animals from bulk drug substances.

Compounding can be legally done only from FDA approved finished dosage form of human or animal products in both large and companion animals, but a sizable percentage is done illegally from Active Pharmaceutical Ingredients (APIs) bulk drugs.

The companion animal and pharmacy industry has largely ignored the law and is steadily increasing the number of products available to practitioners. This includes copies of many FDA-approved products which are being compounded illegally under the guise that the approved products are inferior. We run into to this daily with all of our FDA-approved products.

Nothing could be further from the truth. In fact, by their very nature, drugs compounded from APIs and bulk excipients are not subjected to the same level of rigorous testing to insure they meet specifications as all FDA-approved products are required to meet. They are also not subject to the same cGMP standards all FDA products are subject to. In addition, often the bulk ingredients which are only used in animals are brought into the US under false pretenses or illegally.

The USP (United States Pharmacopeia) is the regulatory agency which governs both pharmacy compounding and FDA-approved pharmaceutical testing and manufacturing standards. The pharmacy regulations in USP are primarily focused on the human use individualized medication market because it is legal to compound from APIs in humans. They apply to all compounding activities undertaken by the practitioner or pharmacist. The veterinary market is not the same as the human market. Although there are instances where compounding is necessary and allowed as an exception under AMDUCA, there appear to be more cases where it is used as a tool to circumvent the FDA regulatory process and can increase the risk to veterinary patients.

Compounding was never intended to be a way to manufacture and sell drugs without a license. There are clear pathways for approval of new and generic drugs in the US. Our regulatory system is designed to assure both safety and efficacy of regulated products which is accomplished by rigorous testing and GLP studies to prove efficacy and safety. When pharmacists and veterinarians illegally circumvent this well-developed system, we will continue to have periodic failures, both reported and unreported, and the regulated industry will have little incentive or desire to develop both new and generic products just to be faced with low-cost and low-quality illegal competition.

The solution ultimately starts with the prescriber. Many veterinarians may not understand that this is an illegal activity that ultimately puts the patient and themselves at risk. Rather than relying on the FDA to enforce the law, practitioners can make the decision not to use these illegal drugs. Price alone is a poor reason to potentially compromise patient health and incur the liability of selling illegal drugs to your clients. Insurers are also taking note of this activity and are using it as a reason to deny claims.

It is time to put a stop to dangerous and illegal compounding of drugs for animals. Our industry should be encouraging the development of new products, not discouraging it by using illegally compounded products.

Maintenance of pregnancy in mares without a source of endogenous progesterone using Altren®

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Progestogens are needed to support equine pregnancy. Normally, the ovaries of the pregnant mare supply progesterone to maintain pregnancy for the first 3 to 3.5 months of gestation until the fetoplacental unit takes over. Occasionally, whether due to prostaglandin release from an inflammatory condition or for some other unknown reason, the *corpora lutea* do not produce sufficient progesterone to maintain pregnancy. In these situations, an exogenous source of progestogen is needed. Altrenogest, a synthetic progestogen, has been shown to be able to support pregnancy in the absence of endogenous progestogens. This study was performed to investigate the ability of Altren® (altrenogest) to maintain pregnancy in mares without endogenous progesterone support.

Briefly, ponies (n=4) and light horse mares (n=5) that were cycling normally, were examined by palpation and ultrasound. A culture swab/cytology brush and low-volume lavage of the uterus were performed and found to be free of any indication of endometritis. When in estrus with a follicle $\geq$ 35 mm, mares were bred by artificial insemination using a minimum of 1 X 10^9 motile sperm. Ovulation was induced using hCG (2,000 IU, IV).

Mares were monitored for ovulation and any evidence of delayed uterine clearance. Mares were examined for pregnancy at 14 days, and if pregnant, PGF was given to lyse the *corpus luteum* and treatment with Altren (1 mL/50 kg BW, p.o., q 24 h) was begun. Ultrasound exams per rectum were performed regularly to monitor pregnancy, and blood was drawn and assayed for progesterone. If progesterone was > 2 ng/mL, a luteolytic dose of PGF was administered to lyse any *corpora lutea* and keep endogenous progesterone below the threshold. Monitoring of plasma progesterone was continued to confirm concentrations remained <2 ng/mL.

Mares were maintained on oral Altren until 70 to 78 days of gestation at which time Altren administration was discontinued. Mares were monitored for pregnancy loss after Altren administration ceased. The conceptus was absent within 2 days and no fluid remained in the uterus by day 3. Seven of 9 mares maintained pregnancies with endogenous progesterone <2 ng/mL. One mare (203) lost her pregnancy at approx. 22 days, and a second mare (928) lost her pregnancy at approx. 36 days.

The following year, the 2 mares that failed to maintain pregnancy (203 and 928) were rebred in the same manner, following culture and cytology to verify the absence of endometritis. The mares again received Altren and PGF at the time of initial pregnancy confirmation at 14 day post-ovulation. Neither mare was able to maintain pregnancy. Mare 203 lost her pregnancy again at approx. 22 days and mare 928 lost her pregnancy at approx. 42 days. That these mares lost their pregnancies in 2 consecutive years at the same stage of gestation each year points to a more fundamental intrinsic reason for pregnancy loss other than simple progesterone deficiency.

“Altren can successfully maintain pregnancy in the absence of adequate levels of endogenous progesterone during the first trimester of pregnancy in the mare.”

Based on our results, Altren can successfully maintain pregnancy in the absence of adequate levels of endogenous progesterone during the first trimester of pregnancy in the mare.

We would like to acknowledge the following persons that assisted with this project: C Pinto, T Mavromatis, C Leisinger, M Markle, J Cruz, V Medina, B Heil.