

Message from the President



I love talking with veterinarians! Throughout my almost 50-year career, veterinarians have been central to my day-to-day work. In fact, a previous company I founded had 100 veterinarians as its founding shareholders.

The life of a veterinarian has changed dramatically over the past half-century, like most professions. These days, they work in a higher pressure environment than ever before. New and evolving diseases, new technologies, staffing challenges, and operational costs contribute to unprecedented levels of stress.

I enjoy having a conversation with these professionals about our technology platform, especially since it takes them back to their training when we discuss the principles of immunology and immune system function. It's kind of like a pop quiz to see what they can recall from their university days.

As much as it can be a refresher course for the veterinarian, I usually come away learning something new from him or her: The latest techniques for treating certain conditions; new diseases they're battling; or experimental uses and regimens for our products.

Veterinarians are a highly educated and highly regarded group of professionals. I am honoured to work with them and, I hope, to make their lives easier with the products we offer for their canine, equine and bovine patients.

U.S. bovine antibiotic regulations changing in June

The US Food & Drug Administration (FDA) has been implementing, over the past several years, a plan for supporting stewardship of medically important antimicrobials (including antibiotics) in cattle. Full implementation of the current FDA plan is expected to be completed in mid-June of this year. At that time, all remaining over-the-counter (OTC) antibiotics will be switched to prescription-only status.

The medically important antibiotics (used by humans and animals) becoming prescription-only include injectable tylosin, injectable and intramammary penicillin, injectable and oral tetracycline, sulfadimethoxine and sulfamethazine, and cephalosporins and cephalosporin benzathine intramammary tubes. In addition, lincomycin and gentamicin swine antibiotics' OTC status is switching to prescription only.

The FDA evaluates the safety of drugs used in food-producing animals, the impact drug residues have on human intestinal microflora, and the development of human antimicrobial resistance. Drug residues in

meat, milk, eggs, and honey from treated animals expose bacteria to trace amounts that don't kill them, but rather allow for the development of antibiotic resistance. Veterinarians are tasked to slow the rate of bacterial resistance by using antibiotics only when necessary to treat, control, or prevent disease. Doing so preserves antibiotic efficacy for humans and animals.

NovaVive offers an antibiotic alternative for cattle—Amplimune® - that is regulator-approved and available in the USA, Canada, New Zealand and UAE.

Amplimune is an emulsion of mycobacterium cell wall fraction (MCWF) for reducing the clinical signs and mortality associated with *E. coli* K99 diarrhea in neonatal calves. When injected into the animal, Amplimune enhances both innate and adaptive immune responses to fight bacterial infections, without the use of antibiotics.

Amplimune is OMRI listed in the USA and Canada for use in organic production.

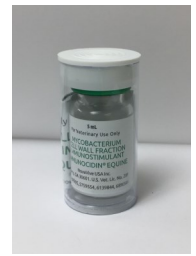
Research with Amplimune has been shown to:

- Reduce the risk of pneumonia in shipped calves
- Improve average daily gain in hutch-reared calves
- Reduce mortality and drug use in veal calves
- Improve pregnancy in embryo transfer recipient heifers
- reduce disease/improve fertility of dairy cows
- reduce morbidity and mortality in highly stressed feedlot calves

Under the new FDA rule, producers with current veterinary client-patient relationships (VCPR) may purchase antibiotics directly from their veterinarian or from a distributor with the vet's prescription.

Amplimune does not require a veterinarian prescription.

FAQs About Immunocidin® Equine



Immunocidin® Equine is our immunotherapy for the treatment of equine sarcoïd tumors. It is regulator-approved in the USA and Canada and is sold to veterinary clinics. Here are a few of the typical questions we receive from veterinarians about this product:

Q: How do I determine the amount of product required to treat a tumor?

A: The amount of product needed is based on the volume of a tumor, with an absolute minimum dose being 1ml. Most sarcoïds need to be infused with approximately 0.25 to 0.5 ml of product per cubic centimeter of tumor mass.

Q: How many treatments should be given?

A: Most tumors require three to six (generally four) treatments. Tumors that fail to respond after four treatments should be considered refractory, and therapy discontinued.

Q: Are there any special administration instructions?

A: Ensure you infiltrate as much of the actual tumor as possible. Use the smallest diameter needle available to you (a 23G or 25G needle is ideal if the tumor is not too dense, but do not use larger than 20G needle or you will have product backflow).

Try to infuse as much of the mass as possible and inject a small amount of product at the base of the tumor to contact afferent blood vessels.

Re-inject the tumor at seven- to 21-day intervals (14-day intervals are ideal) for up to four injections.

If there is no observable tumor regression after four injections, the tumor is probably refractory to immunotherapy (this occurs in less than 10% of tumors).

Q: What can I expect in terms of side effects?

A: The tumor mass will look worse

before it looks better. As the tumor cells necrose, they must either be resorbed by the body or drained to the exterior. Drainage is better.

The patient might run a mild temperature for up to 36 hours and may be somewhat lethargic and/or off-feed. This is due to IL-1 production in response to the immunotherapy.

If temperature or pain control are necessary; oral or injectable NSAIDs can be used without diminishing the immunotherapeutic/anti-cancer response.

Q: Should I expect pain at the site of injection?

A: The injection may produce pain in some animals; sedation or analgesics may be required

Q: Are there any contraindications?

A: The only contraindications to immunotherapy are corticosteroids or adrenocorticotropic hormone (ACTH).

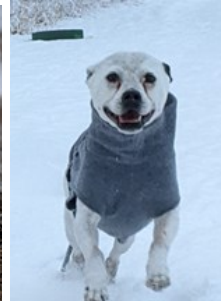
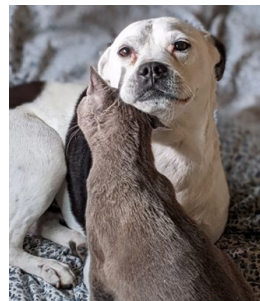
Max's Story

Max is a 12-year-old American Pitbull terrier living in Golden, CO, USA. He has Transitional Cell Carcinoma (TCC) in the bladder, and has been receiving Immunocidin immunotherapy for over 120 weeks. Here's what his guardian told us:



"I still remember getting the call from our vet that Max's Cadet BRAF test had come back positive for bladder cancer. I sank to the floor. Max had a stubborn urinary tract infection that was not responding to antibiotics.

Thirteen years earlier, our first beloved dog had died of bladder and prostate cancer. We had put him through so much trying to save his life, and I knew I couldn't do the same to Max, even though the thought of losing him was unbearable. With bladder cancer survival rates at 6-12 months, even with treatment, I was



sure we would lose our sweet boy within the year. Knowing that I would not let him suffer, but also that I was not ready to give up, I began looking into Immunocidin. The more I looked into it, the more hopeful I became. When I found a small study detailing its use in bladder cancer for dogs, and when our veterinary oncologist agreed that bathing the bladder in treatment sounded promising, I reached out to NovaVive. They worked directly with my vet, who administered the bladder infusions. I was easily able to administer oral Immunocidin at home. We had caught the cancer early - the Cadet BRAF test can detect the cancer up to four months before it becomes visible on ultrasound, and this was the case with Max. Except that his cancer did not

advance. Instead, Max's next Cadet BRAF test, and the one after that, and the one after that all came back negative. Max was diagnosed in October of 2020 and started his Immunocidin protocol in the following month. Today, more than two years later, he shows no signs of bladder cancer.

Although he completed the protocol, he continues to receive monthly bladder infusions at my request. He does have to be catheterized for his treatments, but does not require anesthesia. The vet tech gives him a pillow to rest his head on during the procedure and feeds him lots of treats afterwards. He is always excited to see her.

He has never had any negative side effects from the treatments at all. Because of Max's promising results, a TCC clinical trial may be starting soon. I hope this study shows that Immunocidin can give people more time with their beloved dogs, the way it has given us more time with our sweet boy.

We are forever grateful to NovaVive for not only saving our Max, but for doing so without him suffering."

