

Message from the President



NovaVive concludes its 2018 fiscal year on December 31st. We have been making good strides to increase awareness about our products and company this year, but we've been challenged by the slump in the U.S. dairy industry—the primary market for our top-selling product, Amplimune®. U.S. milk prices have fallen below the cost of production,

causing many dairy farmers to get out of the business.

On the positive side, we've been pleased with the inroads being made by Mark Hill and AABEX Animal Health, our marketing partners in the USA. Mark and his team are making solid connections for us and are introducing new clients to our product line.

We are optimistic that we will see continuing healthy growth in all market segments in the coming year.

As you read this issue of our newsletter, you will note the changing environment with regard to antibiotic use in livestock, including reduced direct access for producers and more stringent oversight

by veterinarians. There can be no denying the link between overuse of antibiotics in livestock and the increasing level of resistant organisms infecting humans and animals. NovaVive remains committed to offering antibiotic alternatives for animals to help reduce the reliance on traditional antibiotic drugs.

As 2018 draws to a close, I extend warmest wishes to our employees, shareholders, customers, partners and friends for a magical holiday season and a healthy, happy new year.



New Rules for Antibiotic Use in Livestock

As of December 1st, Canadian cattle producers are no longer able to buy antibiotic drugs over the counter at their local farm supply store.

About 300 products — including tetracyclines, penicillins and other drugs used to treat common animal ailments like foot rot, pink-eye, and respiratory infections — are affected by the new rules. These medically important antimicrobials for veterinary use will be sold by prescription only as a means to help preserve the effectiveness of these drugs and minimize the development and spread of antimicrobial resistance.

Now, more than ever, cattle producers need effective antibiotic alternatives to treat disease in their animals. One such alternative, Amplimune®, is fully approved in both Canada and the USA as well as Organic Materials Review Institute (OMRI) listed (for use in organ-

ic production). It is available for purchase from bovine veterinarians throughout North America.

Amplimune is an immunomodulator that enhances the natural immune function of the animal. Amplimune is made from Mycobacterium Cell Wall Fraction (MCWF) and can stimulate both innate and adaptive immunity. MCWF has been shown to interact with common signaling pathways used by different cell types of the immune system, effectively overcoming cortisol to allow the calf's immune system to naturally fight infection.

The product is approved for the treatment of bacterial scours in neonatal calves.

NovaVive has conducted research into other bovine diseases where MCWF may prove effective as an alternative to antibiotics. Data from several studies has been published/presented:

1. *Mycobacterium Cell Wall Fraction as an Aid in Reduction of Antibiotic Use in Young Calves*
2. *Efficacy of Mycobacterium Cell Wall Fraction in the treatment of clinical and subclinical endometritis in dairy cows*
3. *Efficacy of Mycobacterium Cell Wall Fraction on intrauterine influx of polymorphonuclear cells in dairy cows*
4. *Immunomodulator, Mycobacterium Cell Wall Fraction (Amplimune®), an Aid in Control of Persistent Mycoplasma bovis Infection in Dairy Cow*
5. *Effect of a Non-Specific Immune Stimulant (Amplimune®) on the Health and Production of Light Feedlot Calves*



Visit the Research section of our website (www.NovaVive.ca) for detailed data summaries. Also see page 2 for more information about Amplimune.

Immunomodulators as an Alternative to Antibiotics for Cattle

Farm animals are being repeatedly exposed to infectious microorganisms (pathogens) that are capable of causing disease; with a healthy immune system, animals are often able to overcome these pathogens.

An animal's skin provides a physical barrier to keep infection out and its bodily functions (sneezing, coughing, vomiting or diarrhea) provide "self-cleaning" processes to eliminate infectious agents that have entered the body. When there is damage to the body or the bodily functions are overwhelmed, however, pathogens can penetrate tissues and cause infection. That's when the immune system kicks in.

The immune system has both innate (non-specific) and adaptive (specific) immune responses to invading pathogens.

Adaptive immunity needs time to trigger the mechanisms required to react to an invading pathogen, whereas innate immunity involves an immediate reaction. Additionally, the adaptive immune system only protects against pathogens

the animal has already being exposed to, either by contact with a disease or by vaccination.

Vaccination works by stimulating the immune system to produce antibodies to specific pathogens that an animal may be exposed to, but vaccine efficacy can vary.

When an animal becomes infected due to exposure to bacterial or viral pathogens, a common treatment choice is antibiotics. Antibiotics can be effective if used properly, however, they have no



activity against viruses, and antibiotic resistance is an increasing concern in both humans and animals. There is mounting pressure for fewer antibiotics to be used in livestock which leads to a need for effective alternatives. Products that activate the body's natural immune system to fight infection and disease (immunomodulators) are a viable option.

Non-specific immunomodulators can be used to help the animal's immune system overcome the immunosuppressive effects of stress or exposure to infectious agents. In the calf, weaning, shipping and commingling are stressful events that create vulnerability to infection.

Immunomodulators can also enhance immune responses prior to, or at the time of, vaccination in order to help increase measurable antibody production.

Amplimune[®] is a non-specific immunomodulator that is regulator-approved in the USA and Canada for the treatment of bacterial diarrhea in newborn calves. It is OMRI listed for use in organic animals.

Antimicrobial Resistance is a Global Concern



World Health Organization

The World Health Organization (WHO) is determined to increase global awareness of antimicrobial (antibiotic) resistance (AMR). The WHO designated November 12 – 18, 2018 as World Antibiotic Awareness Week to encourage best practices among the general public, health workers and policy makers to avoid the further emergence and spread of antibiotic resistance.

"Since their discovery, antibiotics have served as the cornerstone of modern medicine. However, the persistent overuse and misuse of antibiotics in human and animal health have encouraged the emergence and spread of AMR, which occurs when microbes, such as bacteria, become resistant to the drugs used to treat them." (WHO website)

At the G20 Leaders' Summit in Argentina this month, the leaders signed a

declaration that included this statement: "We commend the progress made by the international community in developing and implementing National and Regional Action Plans on Anti-Microbial Resistance (AMR) based on One-Health approach. We recognize the need for further multi-sectoral action to reduce the spread of AMR, as it is increasingly becoming a global responsibility."

NovaVive's Mycobacterium Cell Wall Fraction (MCWF) immunotherapy technology has been proven to have antibacterial properties. To date, two products have been developed and regulator-approved (one for cattle and one for horses) that can be used as alternatives to antibiotics to treat bacterial infection.

Amplimune[®] is approved by regulators in the USA and Canada as a treatment for bacterial diarrhea in neonatal calves. Antibiotics are often used by veterinarians and

livestock producers to treat this condition, but Amplimune has been proven to be an effective treatment, often with a single dose.

Settle[®] is approved by regulators in the USA, Australia and New Zealand for the treatment of endometritis in horses. Again, this is a disease which is commonly treated with antibiotics, but a single dose of Settle, administered by I.V. injection or intrauterine flush, can help resolve a broodmare's uterine infection and the damaging inflammation it causes, often resulting in a successful pregnancy.



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