Garasol and Naxcel: Rethinking Shuttle Programs to Control Bacterial Infection at the Hatchery

Many companies use injectable antibiotics in day-old broiler chicks to reduce mortality and chronic low-grade infection due to *E. coli*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*. Garasol (gentamicin sulfate) has successfully controlled these infections for many years, with limited development of resistance. The failure of bacteria to develop widespread or rapid resistance to this product reflects a chemical structure which is difficult for the bacteria to circumvent.

In 1992, Naxcel (ceftiofur sodium) was approved for day-of-age injection in chickens. This product is being positioned as an alternative antibiotic to Garasol Injection where resistance is indicated by increased chick mortality despite antibiotic injection. Some companies, however, have experienced problems with high mortality due to bacterial infection (especially pseudomonas) after relatively short-term use of Naxcel. This can be avoided if the antibiotic program is built with an understanding of the resistance mechanisms of hatchery bacteria.

Most companies are already familiar with the resistance patterns of the coccidiostats. Some products are known for their long field life, while others are used as short-term substitutes to break resistance patterns. The short-term products may only be used for one or two cycles before performance is lost, but they effectively break the resistance. The longer-lived products can then be used for another year or longer before they show decreased performance. The same idea can be applied to hatchery antibiotics.

Naxcel has a basic ring structure common to all cephalosporin-type antibiotics. It is called a beta-lactam ring. This antibiotic is effective against many species of bacteria. Unfortunately, three common species of hatchery bacteria, *E. coli*, *Staphylococcus aureus* and *pseudomonas* have the ability to produce a cephalosporin-inactivating enzyme (beta-lactamase). This enzyme is capable of breaking the beta-lactam ring structure, making the antibiotic ineffective. The interaction between Naxcel and a typical population of hatchery bacteria is pictured on the next page.
The small number of bacteria which can produce the enzyme escape destruction by Naxcel. The enzyme breaks the ring structure and destroys the antibiotic. Initially, the bacterial population will be dramatically reduced, with only a few resistant individuals surviving. Within a few short generations, however, the majority of the population will consist of the offspring of these resistant bacteria.
Naxcel is effective against most gram-negative bacteria which are not capable of manufacturing the beta-lactamase enzyme. This leaves predominantly the bacteria which can produce this enzyme. An increase in the pseudomonas population is often associated with this resistance.

Garasol Injection does not possess this ring structure. There is no simple method for hatchery bacteria to become resistant, so development of resistance develops very slowly through many, many generations of bacteria.

Garasol Injection does not possess the beta-lactam ring structure. Bacteria which produce the beta-lactamase enzyme will not be resistant to Garasol Injection. Garasol Injection will be effective against this population. Resistance to Garasol Injection will develop slowly.

Naxcel can be used as a short-term shuttle to break resistance cycles and maintain good response to Garasol Injection. Be aware that frequent or long-term use of the product may result in sudden high mortality due to chick infection with resistant bacterial strains. Avoid this problem by limiting use to hatcheries where Garasol performance has decreased as measured by 7-day mortality.

For more information, contact Schering-Plough Animal Health Technical Services at (800) 219-9286.