INTRODUCTION

In recent years, antimicrobial resistance has become a significant public health threat. Indeed, the Centers for Disease Control (CDC) estimates that approximately 2 million people are infected with antimicrobial resistant bacteria every year and, of those infected, at least 23,000 die. In addition to death, antibiotic resistant infections add considerable costs to the healthcare system. In fact, it has been estimated that these infections add in excess of $20 billion in direct costs and $35 billion in indirect costs to the healthcare industry. The primary driving force for the increase in antimicrobial resistance is the use (or overuse) of antimicrobials in both people and animals. Antimicrobials are the most commonly prescribed drugs in human medicine and it is believed that up to 50% of all antimicrobial prescriptions may be unnecessary. In food animals (cattle, swine, chickens turkeys, etc), antimicrobials are used for promotion of growth and the prevention, treatment, and control of various diseases. While it is difficult to compare the amount of antimicrobials used in food animals to the amount used in people, it has been estimated that food animals are responsible for 80% of all reported antibiotic sales.

Concern about the development of antimicrobial resistance in bacteria responsible for outbreaks of foodborne illness in people has recently arisen. For example, *Campylobacter* is spread from animals (primarily poultry) to people through contaminated food products (raw or undercooked chicken and unpasteurized milk). *Campylobacter* is a bacterium that causes diarrhea, fever, and abdominal cramps and is responsible for 1.3 million infections and 120
deaths every year. A recent report from the CDC found that approximately 25% of all Campylobacter isolates tested in 2011 were resistant to antimicrobials commonly used for treatment compared to only 13% in 1997. In addition to Campylobacter, the prevalence of drug resistant Salmonella is seemingly on the rise. Current statistics show that drug resistant Salmonella causes 1.2 million infections and 450 deaths each year. In addition, it is estimated that these infections cost the healthcare industry $365 million a year due to increase severity of infections. Like Campylobacter, Salmonella is spread to people through the consumption of contaminated and undercooked or unpasteurized food products.

It is believed by many that the use of antimicrobials for the promotion of growth and feed efficiency (also known as subtherapeutic use) in food animals is a driving force behind the increase in antimicrobial resistance in bacterial pathogens like Campylobacter and Salmonella. It is also believed that if the use of antimicrobials for promotion of growth and feed efficiency continues, many of these infections will become untreatable. While there is evidence both for and against this theory, animal agriculture is coming under intense scrutiny from both governmental regulators and private organizations. As a result, the United States Food and Drug Administration (FDA) recently published two documents (FDA Guidances for Industry 209 and 213) that detail their views on the judicious use of antimicrobials in food animals and restrict the use of medically-important antimicrobials in feed for the purposes of promoting growth and feed efficiency. The purpose of this document is to summarize these guidances and detail the impact that they will have on the use of antimicrobials in beef cattle in the state of Georgia.

FDA GUIDANCE FOR INDUSTRY 209

Published by the FDA in April 2012, Guidance for Industry 209 represents the FDA’s current thinking on the topic of judicious antimicrobial use in food animals. In this document,
the FDA proposed measures to promote more judicious use of antimicrobials in food animals in two ways:

1) Limiting the use of medically important antimicrobials to uses that are considered necessary for assuring animal health and

2) Limiting the use of antimicrobials to uses that require veterinary oversight or consultation.

In other words, the FDA considers the use of antimicrobials for promotion of weight gain and feed efficiency unnecessary and a potential contributor to the increase in the prevalence of antimicrobial resistant bacteria. However, the use of antimicrobials to prevent, treat, or control specific diseases is considered reasonable and necessary for assuring the health of food animals. For example, if it is believed that a group of cattle are at risk of developing respiratory disease because of their history or specific production practices used by a producer, treating this group of cattle with an antimicrobial approved for prevention of respiratory disease would be reasonable. However, administration of a drug to overtly healthy animals in the absence of specific information suggesting increased risk of disease is not judicious use. Furthermore, the FDA believes that all antimicrobial use, whether the drug is given by injection or administered in the feed or water, should involve the oversight or consultation of a veterinarian. Currently, many of the antimicrobial drugs approved for use in-feed are available over-the-counter. With Guidance for Industry 209, the FDA has suggested that the ability to purchase antimicrobials over-the-counter be phased out and moved to a prescription only process. As a result, the FDA has recommended that veterinarians be involved with all decisions regarding antimicrobial use, whether it be treating individual animals or periodic consulting to establish management protocols, to further combat and slow the development of antimicrobial resistant bacteria.
FDA GUIDANCE FOR INDUSTRY 213

Guidance for Industry 213 was published by the FDA in December 2013 and this document established recommendations for pharmaceutical companies to gradually and voluntarily phase out the use of in-feed antimicrobials for the promotion of weight gain and feed efficiency. In addition, Guidance for Industry 213 recommended that all antimicrobial use involve the input of a licensed veterinarian. In more basic terms, Guidance for Industry 213 was the implementation of the recommendations contained in Guidance for Industry 209. From the date of passage, the FDA gave the pharmaceutical industry 3 years to adopt these changes and, should compliance be low, further action potentially taken. While this document only provided recommendations and all changes to drug labels were voluntary, all major pharmaceutical companies quickly made changes to their labels to meet the new FDA guidelines.

IMPLICATIONS OF GUIDANCES 209 AND 213 FOR THE GEORGIA BEEF INDUSTRY

Guidances for Industry 209 and 213 clearly laid out the FDA’s position on the in-feed use of antimicrobials in food animals for promotion of growth and feed efficiency. As a result of these documents, in-feed antimicrobials can no longer be used to promote growth or feed efficiency, regardless of the existence of a valid prescription. As a result, the use of in-feed antimicrobials for this purpose would be considered illegal. In addition, any antimicrobial use, particularly in-feed use, requires a prescription from a veterinarian. Moreover, the veterinarian writing the prescription must have an established veterinary-client-patient relationship before a prescription can be written. In other words, the veterinarian writing the prescription must have sufficient knowledge of the operation in question, have examined the animals or group of animals, and must have assumed responsibility for treating the animals on that operation. In
addition, the veterinarian needs to periodically visit the operation and review protocols regularly to maintain this relationship.

CONCLUSIONS

While cumbersome and difficult to understand, these guidelines are designed to promote better antimicrobial use in food animals and reduce the selection pressure for antimicrobial resistant bacteria. While antimicrobial use in food animals is only a small part of the antimicrobial resistance puzzle, animal agriculture is under intense scrutiny from both governmental agencies and public advocacy groups. The long-term effects of these changes are yet to be seen, however, the events of the next 5-10 years will be telling. Regardless of our views on the topic, our patterns of antimicrobial use must change or more restrictive rules may be put in place.