

PORK SAFETY

Title: Effects of Subtherapeutic Antibiotics on Antibiotic Resistance and Virulence Gene Transfer in Swine Intestinal Bacteria – **NPB #08-002**

Investigator: Steve Carlson DVM, PhD

Institution: Iowa State University

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Scientific Abstract:

Subtherapeutic antibiotics have been used for decades as growth promotants and prophylactic agents. The following antibiotics are approved for use as feed additives in swine: tetracyclines, roxarsone, hygromycin, tylosin, oleandomycin, penicillin G, sulfathiazole, carbadox, sulfamethazine, erythromycin, flavomycin, bacitracin, virginiamycin, lincomycin, apramycin, tiamulin, efthromycin, neomycin, tilmicosin, and florfenicol.

A recent study indicates that subtherapeutic chlortetracycline can be associated with an increase in multiresistance for swine intestinal microbes. Other studies also suggest that subtherapeutic antibiotics can lead to the propagation of an antibiotic resistant “superbug” (*Enterococcus*) in swine (Poole, *et al.*, 2001). On the other hand, some subtherapeutic antibiotics have not yet been associated with this problem (Donabedian, *et al.*, 2003). These three studies do not, however, address gene transfer events that precipitate resistance and virulence. That is, little is known about the effects of these antibiotics on gene transfer events in enteric bacteria.

The overall objective was to determine which subtherapeutic antibiotics contribute to the transfer of antibiotic resistance and virulence genes while also identifying the subtherapeutic antibiotics that do not contribute to this problem in swine. Three main objectives involved assessing various transfer events mediated by subtherapeutic antibiotics *in vitro* and in swine. These three transfer events involved determining the relative rates of transfer of plasmids, integrons and the *Salmonella* pathogenicity island. Transfer was measured from commensal *E. coli* to six different pathogenic bacteria- *Salmonella*, *Yersinia*, *Pseudomonas*, *Shigella*, ETEC, and *Proteus*.

Results from these studies revealed that certain antibiotics were more likely to mediate gene transfer events. Animal studies revealed numerous subtherapeutic antibiotic-mediated transfer events. The worst offending antibiotics were, in order of rank, lincomycin > apramycin = neomycin = sulfamethazine > tylosin = florfenicol. Sulfamethazine mediated an increase in transfer of both a plasmid and an integron. Lincomycin, apramycin, and neomycin caused an increase in the transfer of two different plasmids whereas sulfamethazine mediated an increase in transfer of just one plasmid type. Lincomycin mediated the highest increase in plasmid transfer.

The results indicate that certain subtherapeutic antibiotics have a higher risk for mediating unwanted gene transfer into pathogenic bacteria. These six antibiotics include sulfamethazine, lincomycin, apramycin, neomycin, tylosin, and florfenicol. Other subtherapeutic antibiotics appear to have a less significant risk.

These research results were submitted in fulfillment of checkoff-funded research projects. This report is published directly as submitted by the project's principal investigator. This report has not been peer-reviewed.

For more information contact:

National Pork Board • PO Box 9114 • Des Moines, IA 50306 USA • 800-456-7675 • Fax: 515-223-2646 • pork.org
