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SHEA

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Department of Health and Human Services
Food and Drug Administration
Docket No. 98D-0969

Comment from the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) on:

Risk Assessment of the Public Health Impact of Streptogramin Resistance in *Enterococcus faecium* Attributable to the Use of Streptogramins in Animals; Request for Comments and for Scientific Data and Information.

IDSA and SHEA are highly supportive of the FDA Center for Veterinary Medicine plan to develop a risk assessment (RA) model to account for the potential transfer of resistance determinants from bacteria in food-producing animals to bacteria in humans. These data are essential to establishing the risk of transfer of streptogramin resistance from farm animals to humans as a result of the use of virginiamycin in food animal production. The streptogramin combination, quinupristin/dalfopristin (Q/D), is one of only two FDA-approved human antimicrobials that are effective for the treatment of vancomycin-resistant *Enterococcus faecium* (VREF) infections in humans. We would like to make the following specific comments:

III. Risk Assessment Plan

For the on-farm component, it will be critically important to establish rates of *E. faecium* streptogramin resistance in herds and flocks that are untreated as well as treated with virginiamycin in order to establish a relationship between use of the drug and any increased incidence of resistance in *E. faecium*. Molecular typing of the resistant isolates will also be critically important to establishing a credible link between on-farm isolates and isolates found post-slaughter on carcasses, in meats for human consumption, and in humans who may enter the hospital already colonized with Q/D-resistant *E. faecium*. For testing humans for colonization with Q/D-resistant *E. faecium*, the sensitivity of the culture procedure will be critically important as demonstrated by the previous studies in Belgium that detected VREF in the stools of healthy subjects only when a vancomycin-containing selective media was used. (Ref: Van der Auwera et al. J Infect Dis 1996; 73:1129-36) of equal importance will be the determination of the mechanism and genetics of Q/D resistance, particularly the presence of plasmids or transposable elements that may carry the resistance genes. This will be critical to tracing the genetic transfer of resistance genes among different strains of *E. faecium*, or other species of enterococci.

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IV. Data and Information Requested

Under item 7, the prevalence of Q/D-resistant/vancomycin-resistant *E. faecium* was documented to be 1.4% (4/291) in patients at baseline prior to treatment with Q/D (Ref: Moellering et al J Antimicrob Chemother 1999; 44:251-261). These patients were studied in the United States and worldwide.

Under item 9, the enterococcal disease infection rate among humans harboring (colonized with) vancomycin-resistant *E. faecium* has been reported in a number of publications with the following rates:

<u>Reference</u>	<u>Infection</u>	<u>Disease Rate</u>
Roghamann et al Clin Infect Dis 1997; 25:1056-9	Bacteremia	10/56 (18 %)
Montecalvo et al Infect Cont Hosp Epid 1995; 16:680-5	Not Stated	1.57/16.6 (9.4%)

The study by Montecalvo lists the rate of colonization as 16.6 patients per 1,000 patient hospital days, a rate that is 10.6 times greater than the VREF infection rate which translates into a disease rate of 9.4% if all disease occurs in previously colonized patients. Disease rates in colonized patients are likely to vary with the degree of illness of the patients. The above rates are for hospitalized patients with leukemia or on oncology units. Patients with less severe underlying illness are not expected to have as high a rate of clinical VRE infection.

Conclusion

IDSAs and SHEAs enthusiastically support the undertaking of this RA by the FDA Center for Veterinary Medicine. We also request that FDA survey the extent of virginiamycin usage in food animal production, and determine the available evidence to support its use as a growth promoter in each class of animals in which it is currently in use. The members of IDSAs and SHEAs play an active role in the diagnosis, prevention, and treatment of VREF infections in hospitalized patients. We are very concerned about the possible development of resistance to Q/D in VREF and will be actively monitoring the resistance rates to Q/D in patients infected or colonized with VREF.

Sincerely,



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