STOCHASTIC MODELING OF PHARMACOKINETICS TO MEASURE RISK AND EFFICACY OF ANTIMICROBIC USE IN DAIRY CATTLE

BARRETT D. SLENNING, MS, DVM, MPVM
College of Veterinary Medicine, North Carolina State University
4700 Hillsborough Street, Raleigh, North Carolina, 27606, U.S.A.

Recently, the veterinary profession, industry, regulators, and consumers have become increasingly aware of antimicrobic residue problems in meat and milk. Regulations regarding approved use of antimicrobics are becoming more strict and limiting, while simultaneously practitioners are faced with new, likely effective, yet unapproved formulations, along with research on new, unapproved applications for existing formulations. This places the practitioner in a dilemma: Optimal therapy may indicate extra-label use, meaning no official rules exist for recommending withdrawal periods. Hence, clinicians have no defense against liability for therapeutic failures or residue violations.

The purpose of this work is to develop a microcomputer-based analytical tool that uses available literature on food animal pharmacokinetics in assessing varying therapeutic regimens with regards to efficacy and safety for the animal, quality of the food chain, and liability for the producer and practitioner. Meta-analytic techniques are used on a pharmacokinetic database to make across study estimates of means and variations for distribution of regimen-specific indices such as serum, tissue, and mammary absorptions and half-lives for a variety of antimicrobics. With information on sensitivities, the model can also estimate variations in test-specific detection levels and pathogen-specific inhibitory concentrations. A spreadsheet-based stochastic model develops a probabalistic, distribution-sensitive simulation of variation in antimicrobic pharmacokinetics. Application of economic decision analysis, hazard assessment, and optimization procedures to the model's output allow for in-depth quantitative appraisals of the complex effects of physiology, pharmacokinetics, and bacterial susceptibilities on drug distribution and response to therapy. The output from this process establishes a practical and defensible foundation for risk and benefit determinations and residue avoidance in therapeutic decision-making.

Proceedings of the 6th International Symposium on Veterinary Epidemiology and Economics, 1991
Available at www.sciquest.org.nz