SUMMARY MINUTES
FOOD AND DRUG ADMINISTRATION
VETERINARY MEDICINE ADVISORY COMMITTEE

MEETING
JANUARY25-26, 1999
HELD AT
HOLIDAY INN GAITHERSBURG
2 MONTGOMERY VILLAGE AVENUE
GAITHERSBURG, MD 20879

These summary minutes for the January 25-26, 1999, meeting of the Veterinary Medicine Advisory Committee, were approved on April 16, 1999. "I certify that I attended the January 25-26, 1999, meeting of the Veterinary Medicine Advisory Committee and that these minutes accurately reflect what transpired."

Keith E Sterner DVM

Keith Sterner, D.V.M.
Chairperson, Veterinary
Medicine Advisory Committee

Richard E. Geyer
Executive Secretary
Veterinary Medicine Advisory
Committee

MEETING OF THE VETERINARY MEDICINE ADVISORY COMMITEE

January 25-26, 1999
Holiday Inn
Gaithersburg, Maryland

Veterinary Medicine Advisory Committee members present: Frederick Angulo, D.V.M., Ph.D.; Steven Barker, Ph.D.; Oscar Fletcher, D.V.M., Ph.D.; Wanda Haschek-Hock, B.V.Sc., Ph.D.; Robert Holland, D.V.M.; Vernon Langston, D.V.M., Ph.D.; Keith Sterner, D.V.M. (chair); Richard Wood

Consultants present: George Cooper, Ph.D. (January 26); Peter Galbraith, D.M.D., M.P.H.; Diane Gerken, D.V.M., Ph.D.; Carl Norden, M.D. (member, Division of Anti-Infective Drugs Advisory Committee); Thomas O'Brien, M.D.; Donald Lein, D.V.M., Ph.D.

Department of Health and Human Services Speaker: Nicole Lurie, M.D., M.S.P.H.

Food and Drug Administration and USDA: Michael Friedman, M.D.; Stephen F. Sundlof, D.V.M., Ph.D.; Mark Goldberger, M.D., M.P.H.; Margaret A. Miller, Ph.D.; Linda Tollefson, D.V.M., M.P.H.; Albert Sheldon, Ph.D.; Eric Flamm, Ph.D.; Kaye Wachsmuth, Ph.D.; Jesse Goodman, M.D., M.P.H.; and Joy Whetstone Dawson, Esq.

Guest Speakers: David Bell, M.D., Centers for Disease Control and Prevention; Scott McEwen, D.V.M., D.V.Sc., University of Guelph; Patricia Liebemman, Ph.D., Center for Science in the Public Interest; Lyle Vogel, D.V.M., M.P.H., American Veterinary Medical Association; J.M. Rutter, D.V.M., Veterinary Medicines Directorate, UK; Abigail Salyers, University of Illinois, Ph.D.; Sherwood Gorbach, M.D, Tufts University

Animal Health Institute Speakers: Dr. Brendan Fox; Dr. Richard Carnevale; Mr. Alex Mathews

Public speakers: Margaret Mellon, Union of Concemed Scientists; Dr. Rebecca Goldberg, Environmental Defense Fund; Dr. Tom Burkgren, American Association of Swine Practitioners; Dr. Diane Fagerberg, Colorao Animal Research Enterprises; Thomas Shryock, Ph.D., National Committee for Clinical Laboratory Standards and Elanco Animal Health; Barb Determan, National Pork Producers Council; Dr. Lester Crawford, Georgetown University; Joel Brandenberger, Coalition for Animal Health; Dr. Clyde Thornsberry, MRL Pharmaceutical Services; Dr. Harless A. McDaniel, AVID; Dr. Dennis Wages, American Association of Avian Pathologists; Dr. Mike Apley, Academy of Veterinary Consultants; Dr. Robert Walker, Michigan State University; Dr. Larry Glickman, Purdue University; Dr. James S. Cullor, University of California (Davis); Dr. Barbara Glenn, Federation of Animal Science Societies; Dr. Jim Jarrett, American Association of Bovine Practioners; Dr. Ran P. Smith, National Cattleman's Beef Association.

SUMMARY MINUTES

The January 25-26, 1999 meeting was held to assess the proposed CVM Framework Document as it would impact human health through the veterinary drug approval process. The following summarizes the committee responses to questions posed by the FDA.

Question 1 Framework Concept

Question

FDA's goal is to protect the public health by ensuring that the efficacy of human antimicrobial therapies is not compromised due to use of antimicrobials in food animals while providing for the safe use of antimicrobials in food animals. Do the concepts laid out in the document entitled "A Proposed Framework for Evaluating and Assuring the Human Safety of Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals" provide a sound scientific basis for achieving this goal if implemented?

Committee Recommendations

The committee understands that the framework document is to help FDA respond, in its regulatory role, to a legal dilemma in the approval of drugs for the animal drug industry. The committee also understands that the agency proposes the framework for consistency in the drug approval process.

The committee concludes that the proposed framework to protect public health by ensuring that the efficacy of human antimicrobial therapies is not compromised due to the use of antimicrobials in food animals, while providing for the safe use of antimicrobials in food animals, provides a basis for achieving this goal. A sound scientific basis for the framework must be put together, utilizing a diverse group of experts working in microbiology from government, industry and academia. This should be done quickly.

The committee recommends that CVM state publicly how it will handle current and future applications until this process is completed.

Question2 Categorization of Antimicrobial Drugs Based on Their Importance to Human Medicine

Question

The agency is proposing that the categorization of antimicrobial drugs for human medicine take into account the usefulness of drugs in both foodborne disease and non-foodborne infectious diseases, when evidence exists that the use of the drug may result in the induction of resistant pathogens or the transfer of resistant elements to human pathogens.

This approach recognizes not only the well known risk of resistance transfer through classical foodborne pathogens but also the threat of transfer of resistant bacteria or resistance genes from other intestinal bacteria of food producing animals resulting in resistant infections of humans with other types of pathogens (e.g., resistant E. coli or Enterococcus). Does the committee agree with this approach?

Committee Recommendations

The committee concludes that categorization of antimicrobial drugs for food animals considering the importance of antimicrobial drugs for human medicine is a workable concept. Antimicrobial resistant microbes and the ability of transfer of resistance genes from other bacteria of food animals must be considered. The committee heard several comments from many members requesting that CVM attempt to simplify the categorization. The committee also voted to have they agency consider adding a fourth category.

The committee recommends that the following sentence from the third paragraph, page 14 of the Framework Document be deleted: "Given our current understanding of the mechanisms of resistance, FDA believes that, generally, it would not appear biologically plausible for resistance to be transferred from animal enteric pathogens to the human respiratory pathogen."

Question 3 Monitoring Threshold Levels

Question

A) Should multiple monitoring threshold levels be established and should they be based on animal data, human data or both? Should the levels be tied to specific actions -- e.g., need for further investigation, need for mitigation strategies, need for withdrawal of product from the market?

B) What organism(s) should be the basis for the monitoring thresholds? In the interest of cost containment, would sentinel organism(s) be designated or should a foodborne pathogen(s) be used?

Committee recommendations

A) Monitoring threshold levels of antimicrobial resistance is the important tool for the proposed framework, and assures the human safety of the microbial effects of new animal drugs. We encourage the use of human, food-producing and pet animal, and other environmental data such as slaughterhouse samples, for making these decisions. The levels should be tied to specific actions.

B) Some members felt that a broad range of gram negative and gram positive organisms

should be used for monitoring antimicrobial resistance and others felt that we do not have enough data to make statements about what organisms should be the basis for monitoring thresholds. The committee agreed that the sole use of sentinel organisms would be inappropriate.

Antimicrobial resistance data should be monitored through the National Antimicrobial Resistance Monitoring Survey (NARMS), animal health diagnostic laboratory data, FSIS HACCP program within plants, the quality assurance programs that various associations are implementing, and an independent central laboratory for on-farm data using sentinel farms. These activities should be supported by government and industry.

Question 4 Resistance Threshold Levels

Question

The agency has proposed the creation of different levels of resistance transfer to humans that would be acceptable based on the importance of the drug or drug class in human medicine. Category I antimicrobial drugs would require that the use in food producing animals results in little or no resistance transfer to humans. Category II antimicrobial drugs would require that a predefined level of maximum resistance transfer be established prior to approval that would depend on several factors, such as the existence of alternatives to the drug, the human pathogens of concern, etc. The level of resistance transfer must be low enough that there is a reasonable certainty of no harm to humans associated with the use of the product in food animals. What criteria should the agency use to safely define the acceptable level of resistance transfer, if any, for antimicrobial drugs that fall into categories I and II?

Committee recommendations

The committee agrees that resistance levels for Category I antimicrobial drugs would require that use in food animals result in little or no resistance transfer to pathogens of human importance. If resistance transfer is detected, FDA and an expert group would review the data and discuss mitigation for the future use of the drug in food animals.

Question 5 On-Farm Post Approval Monitoring Programs

Question

On-farm post-approval monitoring programs will be necessary for certain antimicrobials (Category I, Category II High, and some Category II Medium products). Should on-farm monitoring be instituted immediately post-approval, or triggered by a change in the data generated from other sources such as NARMS?

Committee Recommendations

Slaughterhouse antimicrobial resistance data is of paramount importance to the framework document for making post-approval monitoring decisions. On-farm antimicrobial resistance monitoring utilizing on-farm health quality assurance programs is encouraged by the committee for post-approval antimicrobial resistance levels of high category antibiotics. Diagnostic laboratory data and an accredited central laboratory should be developed utilizing government and industry money.