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Dr. Lester Crawford, Acting Director
Food and Drug Administration
5600 Fishers Lane, Rm 1471
Mail Stop HF-1
Rockville, Maryland 20857

Dear Dr. Crawford:

We, the Board of the American College of Poultry Veterinarians, on behalf of our membership, are writing this letter to express our concern regarding the decision by Administrative Law Judge Davidson to withdraw the approval for the use of Baytril in poultry.

The American College of Poultry Veterinarians (ACPV) is a veterinary specialty organization (RVSO) of the AVMA. Our veterinary specialists have made poultry the focus of their professional expertise. Our group includes pathologists, researchers, educators, and practicing veterinarians, all of whom are board-certified experts in the field of poultry medicine. Many of our members have advanced degrees in their areas of specialization.

We are very aware of the current climate of public concern regarding the safety of our environment and our food supply as it relates to the practices of corporate poultry farming. We understand the political pressure that this concern generates, and many of us are actively involved in developing economically acceptable alternative practices to address some of the key concerns. Nevertheless, we are trained scientists. We resist the pressure to make changes that could harm the welfare of our flocks and ultimately food safety without solid scientific evidence that such a change is also protecting human health.

Baytril is a unique antibiotic. It is expensive and therefore reserved for use only in seriously ill flocks. These flocks are at high risk of excessive mortality and morbidity with serious economic loss. Baytril is never used as a preventative medication or a growth promotant in healthy flocks. Because it is used very judiciously, Baytril is the *only* antibiotic that has remained highly effective for the treatment of serious bacterial diseases in chickens and turkeys.

Poultry veterinary medicine is highly focused on disease prevention; *not* therapeutic treatment of sick animals. Our strategies have been highly successful as the

incidence of disease in poultry has declined steadily for the past 50 years. Disease outbreaks still do occur, however, in spite of our best on-going efforts. When flocks succumb to bacterial diseases, such as *E. coli* airsacculitis, it is imperative that we have a highly effective tool to stop the outbreak before it spreads beyond the limits of the immediately affected flock. Baytril is that tool.

Industry estimates by NCC (National Chicken Council) and NTF (National Turkey Federation) have placed Baytril use at no more than about 1–2% of the annual U.S. broiler chicken flock and about 4% of the annual U.S. turkey flock annually. Current usage in broilers is likely in the 0.2% range. Although it is used infrequently, it is vital in the face of disease outbreaks.

The scientific evidence does not support withdrawal of approval of Baytril for poultry:

- **Scientific evidence suggests that judicious use of antibiotics actually improves the wholesomeness and safety of the poultry meat supply.** Untreated ill individuals within a flock are often anorexic. The intestines of an anorexic bird are more fragile and are easily broken by the eviscerating equipment. The result is a higher level of fecal contamination from ill flocks that can cross-contaminate healthy birds. Fecal contaminants include *Campylobacter spp., Salmonella spp. and E. coli.* Dr. Scott Russell, Ph.D., University of Georgia presented scientific studies demonstrating this very real consequence of automated processing of untreated flocks. This testimony is included in your materials for the review of this case.

- **Statistics from the CDC FoodNet and the Tollefson cross-examination do not support a correlation between the incidence of fluoroquinolone-resistant *Campylobacter* infections and the introduction of Baytril for use in poultry.** Baytril was introduced to U.S. poultry in 1996. From 1997 to 2001, the incidence of fluoroquinolone-resistant *Campylobacter* infections has <u>decreased</u> from 3.28 to 2.62 cases per 100,000 population. In fact, the overall incidence of campylobacteriosis in persons decreased from 2.4 million to 1.4 million from 1996-1997 to 1999. During that same time, chicken consumption was on a sustained increase. <u>This is exactly opposite of what CVM contends</u> yet may correlate well with Dr. Russell's hypothesis that resolving airsacculitis cases allows the veterinarian to relieve pain and suffering while improving the overall food safety profile.

- **HACCP implementation by poultry processors has resulted in continually decreasing pathogen counts on poultry carcasses since Baytril's approval.** Both FSIS studies and independent research shows that CFU's and carcass prevalence of Campylobacter are decreasing in broilers. Comparison of the 1995 and 2000 FSIS broiler baseline studies shows a small drop in prevalence coupled with a large drop in CFU/carcass during the HACCP era. A recent study by Stern and Robach (J. Food Protection; 66, 1557-63, 2003) support the

FSIS data. This report shows a 90% drop in Campylobacter CFU over the same approximate time period. These data in conjunction with the poultry use data, make chicken an unlikely and decreasing source for human fluoroquinolone-resistant Campylobacteriosis.

- **Microbiologic data are also suggestive that chicken is not a significant source of *Campylobacter* for humans nor is it a source for cross-contamination of kitchens or other foods.**
  Live *Campylobacter* cells cannot be directly cultured from processed chicken. It is generally known among poultry microbiologists that *Campylobacter* can only be recovered when a pre-enrichment step is used to bring back to life cells that are injured during the sequential heating, cooling and chlorine treatments that accompany poultry processing. Unlike *Salmonella* and *E. coli, Campylobacter* is a fastidious organism that only multiplies in the confines of a host G.I. tract. It is simply not logical then, that even raw chicken has a high enough infectious organism load to cause or spread human disease in a significant way.

- **Fluoroquinolone-resistant Campylobacters, regardless of source, do not exhibit higher virulence than susceptible ones.**
  It is well defined in the scientific literature that a single mutation in the DNA gyrase gene is able to confer fluoroquinolone resistance. This mutation has never been shown in any published science to affect *Campylobacter*'s pathogenicity or virulence.

- **An assessment of CVM's position by the European Agency for the Evaluation of Medicinal Products (the European equivalent to the FDA) supports the position that the use of Baytril in poultry poses no public health threat.**

The ACPV membership directly involved in turkey health and production are most disturbed by the attack on Baytril approval for use in turkeys using CVM data generated only in chickens. We believe that the CVM data is flawed as it applies to chickens, and most certainly that CVM is unjustified in applying chicken data to turkeys.

- **There are *no* compelling studies linking turkeys to fluoroquinolone-resistant Campylobacteriosis in humans.** To our knowledge, the only study associating turkeys with fluoroquinolone-resistant Campylobacter comes from a report in the hearing evidence in which independent chicken and turkey variables were not significant in a univariate ANOVA model. These independent variables were combined to produce a new significant "poultry" variable. Two insignificant, unrelated variables cannot be combined to create one "significant" variable.

- **Approval of any vaccine or drug for use in turkeys requires extensive testing in a turkey model.** Turkeys are different animals than chickens, and they are managed differently on the farm. Very few diseases are common to both species of poultry.

  Turkeys are brooded in one facility for the first 6 to 8 weeks, and then transferred to a different facility to reach market age. Baytril is used almost exclusively in the brooding facility. Turkey brooding facilities are cleaned out after each brood which makes development of resident resistant bacteria less likely. The fact that Baytril is still a highly effective treatment for turkeys after 8 years of field use demonstrates the impact of routine facility cleanout on the sensitivity of the bacterial population.

  At processing, turkeys undergo manual evisceration instead of the automated evisceration typically used in broilers. As a result, they have far less opportunity for fecal carcass contamination at processing. Neither turkey field management nor the processing methodology logically supports a causal relationship with human fluoroquinolone-resistant campylobacteriosis.

  The loss of Baytril for the treatment of young turkeys based on CVM chicken models is not scientifically valid. Baytril is a valuable tool used to protect the welfare of our turkey flocks and the safety of our food supply. The product is used judiciously, responsibly and safely. It should not be withdrawn for use in turkeys.

We, the board-certified poultry medicine specialists of the AVMA ask you to carefully consider the scientific evidence supporting the continued use of Baytril in chickens and turkeys. The ALJ ruling largely ignored important facts from highly credible poultry veterinarians. We encourage you to include individuals who are experienced in the areas of poultry production and the practice of poultry veterinary medicine on the review committee. Please give the scientific evidence in support of Baytril its' due weight. We strongly urge you to overturn Judge Davidson's ruling.

Very sincerely,

Board of Governors of the American College of Poultry Veterinarians

cc: Dockets Management Branch, ref #00N-1571

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

October 29, 2004

American College of Poultry Veterinarians
382 West Street Road
Kennett Square, Pennsylvania 19348

Dear Board of Governors:

Thank you for your letter addressed to Dr. Crawford regarding the proposed withdrawal of the approval of enrofloxacin use in poultry. As described below, this matter is now pending before Dr. Crawford.

Under longstanding federal regulations governing the withdrawal of approval of a new animal drug, communications about this proposed withdrawal are not allowed between the Commissioner, officials advising the Office of the Commissioner, and persons outside the Food and Drug Administration (FDA). See Title 21 Code of Federal Regulations, Section 10.55(d)(1) (21 CFR 10.55 (d)(1)). Therefore, Dr. Crawford is unable to respond to the specific issues regarding enrofloxacin that you raise in your letter. For your information, under these regulations, a copy of your correspondence and this response must be placed in the FDA docket and served on the participants. See 21 CFR 10.55(d)(3).

However, I am able to provide the following information on the regulatory process for FDA's formal evidentiary hearings and a brief outline of selected milestones in the case of enrofloxacin. The FDA's formal hearings are conducted by an administrative law judge under regulations found at 21 CFR part 12. These regulations set out the procedures that FDA must follow when conducting formal hearings.

The Center for Veterinary Medicine (CVM) proposed to withdraw approval of the New Animal Drug Application (NADA) 140-828, pursuant to Section 512(c)(1)(B) of the Federal Food, Drug, and Cosmetic Act. That section requires that a new animal drug must be shown to be safe and effective for its intended uses. On October 31, 2000, CVM published a notice of opportunity for hearing (NOOH) in the *Federal Register*. On November 29, 2000, Bayer filed a request for a hearing. The FDA Commissioner agreed and published a Notice of Hearing on February 20, 2002, in the *Federal Register*.

After submission of documentary evidence, written direct testimony, and joint stipulations by CVM, Bayer Corporation, the sponsor of the animal drug, and non-party participant Animal Health Institute (AHI), an oral hearing for cross-examination of witnesses was held between April 28 and May 7, 2003, with Administrative Law Judge Daniel J. Davidson presiding. The parties and AHI filed post-hearing briefs and replies in the summer of 2003 and the administrative law judge issued an initial decision on March 16, 2004. The parties have filed exceptions to the initial decision.

A public docket was established at the time the NOOH was published in October 2000. The record of the hearing, which includes the NOOH, referenced scientific studies, briefs, hearing transcripts, the initial decision of the administrative law judge, and subsequent filings by CVM, Bayer, and AHI, can be found in this public docket (Docket No. 2000N-1571).

I hope this information is helpful. Thank you for your interest in this issue.

Sincerely,

LaJuana D. Caldwell
Director
Office of Executive Secretariat

cc: Dockets Management Branch (HFA-305)