

fieldale farms corporation

July 28, 2004

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

Dear Dr. Crawford:

I am writing to urge FDA to continue the approval of NADA 140-828 for the use of enrofloxacin (Baytril® 3.23% solution, Bayer) in poultry and to urge you to select truly independent scientific and legal experts for the final review.

I submitted written testimony in support of Bayer's position for the hearing before the administrative law judge. I am a practicing poultry veterinarian, working for a large integrated broiler producer in Georgia since 1991. I received the DVM degree in 1975, an MS in Medical Microbiology in 1983, and the Master of Avian Medicine in 1991, all from the University of Georgia. I am certified by the American College of Veterinary Internal Medicine (Large Animal) and the American College of Poultry Veterinarians. Among other industry activities, I am currently chair of the Committee on Transmissible Diseases of Poultry and Other Avian Species of the United States Animal Health Association.

Judge Davidson ignored or struck important testimony from qualified experts. His conduct of the hearing and his initial decision were, in my opinion, clearly and unjustifiably biased in favor of the position held by the Center for Veterinary Medicine. There are risks and benefits inherent to the use of virtually any xenobiotic, particularly in food-producing animals. The balance of those risks and benefits to all involved parties—the animals, farmers, consumers, and public health—must be considered in the approval and use of any food animal drug. Without doubt, public health must carry the most weight by far. However, in this hearing, the purported (and again in my opinion, highly debatable) risks to public health received almost exclusive attention, and any consideration of the clearly demonstrated benefits of continued use of this drug in poultry to the birds, farmers, producers, consumers, and even to public health was virtually excluded. Compelling evidence was presented (and ignored) that withdrawal of this drug from use in poultry could very conceivably have adverse impacts on human health due to increased fecal and pathogen contamination resulting from the processing of untreated or unsuccessfully treated flocks of sick birds. FDA should carefully consider the possibility that the withdrawal of this NADA could actually result in a net increase in the incidence

and severity of food-borne illness. The risk of such an outcome likely outweighs the highly debatable risk of continued use. Bear in mind that during the roughly 8 years that Baytril has been used in poultry in the US, both the incidence of human campylobacteriosis and the proportion of fluoroquinolone-resistant cases has decreased, while the consumption of poultry has increased. The authorities in Europe have so far concluded that this drug is safe for use in poultry.

As a practicing poultry veterinarian working for a producer, I am most qualified to re-emphasize the benefits to the birds, farmers, and producers, and to highlight the potentially devastating effects of withdrawal of this approval. Enrofloxacin is clearly and without doubt the *only* effective drug available to poultry veterinarians for treating *Escherichia coli* infections in broiler and breeder chickens. While it is almost exclusively a secondary infection, *E. coli* infection is by far the most common and important disease condition in broiler production. Our goal as poultry veterinarians is to prevent this disease (mainly by preventing the primary inciting viral diseases), and we are generally quite successful. However, there are times when our efforts temporarily fail, and effective antibiotic treatment becomes critical. Contrary to the claims of CVM, the other available drugs, which are few, are poor substitutes at best. The most commonly used alternative drug, tetracycline (including oxytetracycline and chlortetracycline), is almost totally ineffective in most operations. It is often little more than a placebo. The next line of defense, Rofenaid (ormetoprim and sulfadimethoxine) is only slightly more effective than the tetracyclines and has several major drawbacks. Rofenaid is available for use only in the feed, which is much less flexible and greatly complicates administration. It has a five-day withdrawal period. Being a sulfonamide, it represents a much greater residue hazard than the other alternatives. Finally, Rofenaid is not approved for use in breeder hens. Sensitivity to enrofloxacin continues at almost 100% of isolates tested. Due to its expense and our sensitivity to drug resistance issues, this drug is used sparingly and typically as a last resort in cases with severe disease. Consequently, the loss of enrofloxacin would represent a major blow to our ability to deal with *E. coli* infections, and could have serious and wide-ranging adverse effects. Those companies that have foresworn the use of Baytril have done so at the behest of their marketing departments, under activist pressure, and not with the willing acquiescence of their veterinarians. Here are a few of the likely effects of withdrawal of this NADA.

1. Animal welfare will decrease, and animal suffering will increase. We grow these birds for the sole purpose of eating them. They depend on us for all of their needs. It is a moral imperative that we treat them humanely. Leaving our poultry veterinarians with no effective drugs to treat the most common bacterial disease in these birds is morally indefensible.
2. The inevitable disease outbreaks that do occur will have more severe consequences. Morbidity, mortality, dead-on-arrivals at the processing plant, and condemnations will all increase. Flock uniformity and gut integrity will suffer. This in turn affects automated processing equipment, leading to higher rates of contamination, reduced microbial quality, shorter shelf life, more spoilage, and an increased risk of food-borne illness. It is unlikely that sicker, less healthy chickens will result in safer, more wholesome chicken meat.

3. Individual private family farmers may be severely impacted when untreatable infections occur in their flocks.
4. Prophylactic use of older, less effective drugs will probably increase if enrofloxacin is removed. Without the security of an effective backup, managers will be more prone to strike preemptively at the first hint of a disease problem in one house, and treat all houses on the farm prophylactically with over-the-counter drugs such as tetracyclines. Medicated pre-starter programs may increase. Doses and duration of treatment with older, less effective drugs will likely increase, possibly to extra-label levels, in an effort to get these older drugs to work. Extra-label drug combinations (some of which may not be rational) may become more common. All of these practices may actually increase total drug use, while having questionable benefits. Such practices may also increase the possibilities of drug toxicities and adverse interactions in the birds, and tissue residues in the meat.
5. The disposal of increased numbers of dead chickens will tax the disposal methods, and may have adverse environmental impacts, whether the carcasses are composted, buried, incinerated, or rendered.

In summary, it is far from clear that the removal of enrofloxacin from poultry production will have any impact on the incidence of antibiotic treatment failures in humans. I believe that Bayer has demonstrated that the risk assessments and epidemiological associations that have been used to infer such cause-and-effect relationships are seriously flawed and not supported by scientific facts. Conversely, there is ample direct evidence that removal of enrofloxacin will seriously and adversely impact the practice of poultry medicine, the health and welfare of poultry, and the economics of poultry production. The loss of this drug may well adversely impact the quality and safety of poultry products and the incidence of food-borne illness in humans. The concrete reasons to continue the NADA for enrofloxacin in poultry far outweigh the questionable benefits of possible harm. The NADA for enrofloxacin in poultry should remain in place. I urge you to appoint dispassionate, objective, knowledgeable experts to assist you in your final review of this critical issue.

Sincerely,



John A. Smith DVM, MS, MAM

Cc: Docket OON-1571



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

September 29, 2004

John A. Smith, D.V.M., M.S., M.A.M.
Fieldale Farms Corporation
P.O. Box 558
Baldwin, Georgia 300511

Dear Dr. Smith:

Thank you for your letter of July 28 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

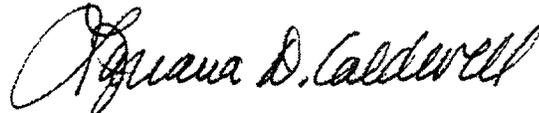
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administrative law judge issued an initial decision on March 16, 2004. The parties have filed exceptions to the initial decision.

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,

A handwritten signature in cursive script that reads "LaJuana D. Caldwell".

LaJuana D. Caldwell
Director
Office of Executive Secretariat

cc: Dockets Management Branch (HFA-305)