

**JUL 17 2003**

The Honorable Jeff Sessions
United States Senate
Washington, D.C. 20510

Dear Senator Sessions:

This letter is in response to your request for the Food and Drug Administration's (FDA) comments on statements made in a letter received by your office from various groups concerning the Minor Use Minor Species (MUMS) Animal Health Act of 2003 (S. 741). Specifically, your staff provided FDA a copy of a letter addressed to "Dear Senator," dated April 4, 2003, (hereafter referred to as "interest group letter"), and asked us to provide the Agency's comments on the letter based on our understanding of S. 741.

As you know, Public Law 104-250, the Animal Drug Availability Act (10-09-96), directed the Secretary of Health and Human Services to develop proposals for ways to achieve the goal of increasing the availability of safe and effective drugs to alleviate animal suffering and improve animal care for minor species and minor uses, while ensuring appropriate safeguards for animal and human health.

FDA believes that the MUMS legislation is important because it will promote and protect public health and animal health by having healthier animals and safer food. In addition, it will provide additional mechanisms by which the Agency can scrutinize new animal drugs. Similar to the plight of human orphan drugs, the markets are small for treatments for minor species, yet the need is crucial. Veterinarians, animal owners and livestock producers have limited legal options for treating these sick animals. This bill may be viewed as the orphan drug program for rare, exotic, and other minor species and for minor (or orphan) uses. The bill includes a provision to provide incentives for sponsors to seek approval of these new animal drugs that parallel those offered by the very successful Orphan Drug Program for human drugs.

Inadequate treatment of diseased animals because of a shortage of FDA approved drugs may pose a public health hazard. For example, the transmission of parasites or pathogens from animals to humans, or the shedding of disease producing organisms by untreated animals into the environment may increase health risks to humans as well as other animals. In many cases the choices are to leave a sick animal untreated or treat the animal with unapproved drugs that may lead to adverse effects, including death, in the treated animal and may pose a drug residue or microbial risk to humans consuming food derived from treated animals. In addition, a paucity of approved antimicrobial drugs leads to overuse of the few approved

drugs, which actually increases the selective pressure that can lead to the development of antimicrobial resistance and ultimately further diminishes veterinary care options. For example, there is only one antibiotic approved for the treatment of American Foulbrood in honeybees. After over 30 years of use, resistance has developed in several areas of the country. New treatments are needed to protect the bees that pollinate important agricultural crops as well as produce honey.

While infection prevention is an important benefit of the bill, the bill will address many other needs. There is a need for anesthetics and analgesics (dosage information, precautions, etc.) for most of the zoo and wildlife species. Exotic pets are on the rise, and we lack drugs for treatment of many of the ailments they may develop. There is a very critical need for tranquilizers and restraint agents for use in capturing wildlife for examination, tagging purposes, or treatment procedures. Any of the organ systems can develop problems that will often respond to therapeutic intervention, provided accurate information is available regarding species, indication, dosage, contraindications, etc. Consider glaucoma in a rabbit, arthritis in a zebra, chronic congestive heart failure in a monkey, urinary calculi (stones) in a goat, mange mite in a parakeet, gout in an iguana, or tumors that would respond to therapeutic agents.

**This Legislation Maintains FDA's Rigorous Drug Safety Requirements --
Including Safeguards to Prevent Antibiotic Resistance**

An Efficient Process for the Approval of Antibiotics for Use in Food-Producing Animals is Not Inappropriate.

The interest group letter asks Senators to ensure that "legislation to streamline approvals of certain drugs for use in animals does not apply inappropriately to antibiotics in food-producing animals." Minor species animals, including food-producing animals, should not be subjected to unnecessary suffering and even death due to lack of approved safe and effective antimicrobial therapy. Bacterial infections can occur in any animal, and, just like with people, there can be adverse reactions to certain antibiotics based on species and to incorrectly used antibiotics. Data to demonstrate that these products are safe must conform to the same standard as that for major species. The goal of MUMS must be to protect, not endanger, both human and animal health through proper regulation of safe and effective drugs.

The MUMS Animal Health Act of 2003 establishes two new ways to lawfully market new animal drugs while maintaining the rigorous public safety requirements of FDA. Under section 571 - Conditional Approval, and section 572 - Index, new animal drugs, including antimicrobial new animal drugs, are subject to the same food safety standard that would be applied to such drugs under section 512 of the Federal Food, Drug, and Cosmetic (FD&C) Act.

Conditional approval is a way for small companies appealing to niche markets to regain some capital investment by marketing the new animal drug for a short period (a maximum of five years, renewed annually) after meeting the full safety standard but prior to meeting the full effectiveness standard currently required for a new animal drug application (NADA).

Conditional approval can only be obtained from FDA once all of the rigorous safety components are completed including target animal safety and human food safety in accordance with current standards of the FD&C. FDA does a complete review of toxicity, residue, and antimicrobial resistance data (as needed) as part of the food safety review. The only difference between this type of approval and a regular NADA is the delay in submission and review of full effectiveness data. Moreover, a conditionally-approved antimicrobial can be quickly removed from the market after refusal by FDA to renew the conditional approval followed by an informal hearing after the conditional approval is withdrawn.

This bill does provide for drug indexing which can accelerate legal marketing of new animal drugs, but it is important to understand that the drug index is intended for non-food minor animal species only, such as zoo, laboratory, and exotic animals and early life stage food-producing minor animal species. FDA will authorize index drugs only for those minor species for which there is reasonable certainty that humans or other animals will not consume edible products from the animal or for early life stage minor species where human food safety can be demonstrated by the same standard applied under the current statute to ensure that there are no human health consequences. An NADA level Food Safety Review must be done before the product is even eligible to be sent to an expert panel to assess the target animal safety and effectiveness of the product. Labeling of a new animal drug that is the subject of an index shall prominently and conspicuously state that extra-label use is prohibited. Additionally, to ensure adherence to specified conditions of use and to provide for expeditious consideration of new information, the legislation provides the Secretary explicit authority to remove or suspend a new animal drug from the index.

Criteria for Listing Drugs on the Index is Not Limited to Drug Residue Information.

The interest group letter claims: "Although drug-residue issues are to be evaluated, the criteria for listing drugs on the index do not allow for consideration of any other issue related to antibiotic resistance." This statement is incorrect. To have a product considered for indexing, an individual must first submit a request to the Secretary for a determination whether the product would be eligible for indexing. If the product is for the early life stage of a food-producing animal, a full human food safety review will be done at that time, including assessment of the risk of antimicrobial resistance. That request must include an environmental assessment or information to support a categorical exclusion from the requirement to prepare an environmental assessment. In addition, FDA has the authority to request "any other information as the Secretary may deem necessary to make the eligibility determination" regarding whether a new animal drug may be included in the index. Furthermore, the legislation states that the Secretary will make a determination of eligibility for a product to be indexed only if the proposed use does not raise concerns related to safety. For a product for which the Secretary makes a determination of eligibility for indexing, the sponsor must request that the product be indexed, and the sponsor must provide information on any additional requirements that the Secretary may prescribe. Clearly, FDA can address any aspect of human safety deemed necessary when determining whether or not a drug can be indexed.

The Appropriate Use of Antibiotics for Minor Use/Minor Species Will Not Endanger Public Health

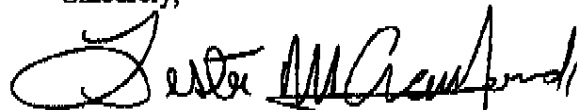
The concern that antimicrobial drugs will not be reviewed sufficiently with respect to antimicrobial resistance to ensure public safety is unfounded. While the Agency recognizes and shares the concern regarding a potential increase in antimicrobial resistance associated with the use of antimicrobials in animals, the Agency believes its approval standards will minimize this potential risk. Furthermore, with regard to the MUMS legislation, this bill does not diminish the food safety, including microbial safety, or environmental safety requirements for a new animal drug from the current standard for any new animal drug approved by FDA. Increasing the availability of legally marketed drugs for minor species or minor uses, while maintaining the current high standards for human and environmental safety, has been the primary goal of the legislation from its inception. Contrary to the contention in the letter, FDA does not believe that the bill creates “short cuts” or “loopholes” with respect to the required demonstration of food safety and environmental safety.

MUMS Will Provide FDA Mechanisms to Provide Greater Scrutiny to the Uses of Antibiotics in Agriculture and Aquaculture

The interest group letter states: “Congress should be telling FDA to apply more, not less, scrutiny to uses of antibiotics in agriculture and aquaculture.” It is in the best interest of all parties that drugs are manufactured and labeled in accordance with FDA standards, including dosage and withdrawal period information based on evidence that the products are safe and effective, rather than the current state of affairs where unapproved products are used because of a lack of alternatives and FDA does not have the resources for effective enforcement. The MUMS bill will encourage development of new products and approved uses with properly manufactured and labeled products. This will favor animal health through the availability of safe and effective products. It will favor human health through decreased exposure to diseased animals and through accurate dosing and observation of approved withdrawal periods.

We thank you for the opportunity to provide these Agency comments regarding the MUMS legislation. If we can be of further assistance, please let us know.

Sincerely,



Lester M. Crawford, D.V.M., Ph.D.
Deputy Commissioner