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Division of Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2011-D-0889; Draft Guidance for Industry on New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions With GFI #209; Availability

The Animal Health Institute (AHI) submits these comments to Docket No. FDA-2011-D-0889, "Draft Guidance for Industry on New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions With GFI #209; Availability." AHI is the national trade association representing manufacturers of animal health products -- the pharmaceuticals, biological products and feed additives used in modern food production, and the medicines that keep livestock and pets healthy.

The industry appreciates the release of this guidance which provides a pathway for antibiotic sponsors to work voluntarily with the agency to implement the principles contained in final Guidance for Industry #209. The guidance proposes to revise labeling of certain medically important antibiotics used in animal feeds by altering current approved indications for improving growth and or feed efficiency and changing the legal availability of these products from over the counter to veterinary feed directive only.

AHI understands that FDA is concerned that current production claims may not represent judicious antibiotic use for an antibiotic classified by the agency as medically important. However, food animal producers have relied on the benefits of these products for many years to keep animals healthy, reduce the environmental impact on land and resources, and provide healthful and affordable meat and poultry to consumers. Therefore, any changes to indications and availability of these products must be undertaken carefully to reduce unnecessary negative impacts to animals, producers, and veterinarians. In this regard we have the following comments and questions relative to the guidance:

IV. Voluntary Adoption of Judicious Use Principles

B. Need for Veterinary Oversight of Medically Important Antimicrobial Drugs used in the feed or water of Food-Producing Animals

- It's not clear why the agency is specifically singling out water soluble antibiotic products for conversion to prescription status at this time. These products, with some rare exceptions, have never had production indications. The products are virtually all labeled for treatment of active infections at therapeutic levels for limited durations.
- Is CVM considering certification programs to allow for trained professionals (veterinarians, nutritionists, feed mills, etc.) to carry out the function of the VFD in the remote local areas? Are there opportunities for an education campaign or web-based training tools?

V. Timeline for Voluntarily Implementing Changes

- To what extent is the proposal binding on a sponsor to notify the Agency 3 months after publication of final GFI #213 of its intentions to engage in the voluntary process to modify their product labeling?

VI. Supplemental New Animal Drug Applications

c. Human Food Safety

Microbial Food Safety

- The guidance states an intention by the agency to limit any new therapeutic indications to an "*explicitly defined duration of dosing*". Since these products will be used only by or on the order of a licensed veterinarian how will this requirement be balanced against a veterinarians' medical judgment as to the extent of medication needed depending on the particular disease conditions in a herd or flock?
- The agency should clarify how the information to assess microbial food safety discussed under (1) differs from a complete qualitative microbial food safety risk assessment described in GFI #152.
- Under (3), information is requested of the sponsor to include how a loss of susceptibility of organisms of concern to human health could impact human clinical medicine. AHI believes this is not an appropriate requirement for animal drug sponsors, and, moreover is unnecessary. Not only are there numerous variables with respect to clinical outcomes of individual patients making it difficult to assess the impact of changes *in vitro* susceptibilities, but DA has already determined that certain antibiotics are important to human health which is the agency's stated basis for regulating them differently from other antibiotics.

- Item (4) requests information on how FDA's general elements of judicious use have been addressed. "*Specifically, all approved indications should be for therapeutic/preventive use, require veterinary oversight, and restrict use to an explicitly defined duration of dosing.*" Does this imply that the agency intends to require changes to currently approved therapeutic/preventive labeling indications?

e. Evidence of Effectiveness

- The guidance states that in supporting a new therapeutic claim "*...at least some data should come from studies conducted in vivo in the target species and production class.*" Should this not be left to how well the sponsor can document a new claim utilizing in vitro data or other information available on the product rather than pre-judging what is necessary? In 21 CFR "substantial evidence" means evidence consisting of one or more adequate and well controlled investigations, such as—
(E) an in vitro study; by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.
Is the *in vivo* requirement beyond the scope of the substantial evidence regulation if this standard can be met?

VII. Generic Drugs and Combinations

- What assurance will sponsors have if a product in a class of antibiotics is changed to VFD, that FDA will require timely VFD changes across all similar products, specifically:
 - If the approved conditions of use for a new animal drug application for a medically important antimicrobial new animal drug are revised under draft guidance #213 by voluntarily withdrawing a production use, must the approved labeling for any currently approved generic application(s) that references the original new animal drug application generally be revised in a similar fashion? What assurance is there that FDA will be able to force generics to comply with pioneer label changes?
 - If the pioneer sponsor spends additional resources (expertise, study costs & time) to expand or add additional claims via GFI #213, will generic sponsors be required to conduct their own studies to modify existing product labels? Will the sponsor receive any data exclusivity for new indications?
 - How will FDA force compliance by non-generic companies that do not voluntarily engage the agency to affect labeling changes?

B. Combination New Animal Drugs

- How will the CVM handle non-VFD drugs as part of a combination that includes a VFD product?

As a final comment, AHI requests FDA comment as to what metrics the agency will utilize to measure progress in implementing the principles in GFI #209 and #213.

In conclusion, AHI and its member companies support the process FDA is proposing in order to preserve the availability of medically important antibiotics to prevent, control, and treat animal disease while extending additional controls over their use. AHI is committed to working cooperatively with the agency to effect these changes in an orderly manner so as to minimize disruption to animal production and minimize adverse impacts to animal health and food safety.

Thank you in advance for your consideration of these comments. Should you have any questions, please do not hesitate to contact AHI at (202) 637-2440.

Sincerely,



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