March 5, 2012

Kevin J. Greenlees, Ph.D, DABT
U.S. Delegate, CCRVDF, Senior Advisor for Science & Policy
Office of New Animal Drug Evaluation, HFV-100
USFDA Center for Veterinary Medicine
7520 Standish Place
Rockville, MD 20855

RE: Clarification of CSPI’s Comments during the CCRVDF U.S. Delegation Meeting on March 2, 2012

Dear U.S. Delegate Greenlees:

The Center for Science in the Public Interest (CSPI)\(^1\) appreciates the opportunity to participate in the delegation meetings and provide the U.S. Delegates with comments to aid in the development of their positions for the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) 20\(^{th}\) Session. CSPI represents over 850,000 consumers and urges the U.S. Delegation to consider the following issues when preparing to make interventions.

- **Agenda Item 6(b) “Proposed Draft Maximum Residue Limits for Veterinary Drugs”**
  - CSPI requests that the U.S. Delegation state, for each of the veterinary drugs reviewed, whether the drug is classified by the World Health Organization (WHO) or by the U.S. Food and Drug Administration as a critically important or a highly important antimicrobial for human medicine.
  - As an example, the WHO classifies amoxicillin as a critically important drug to human medicine. This prioritization means that amoxicillin requires the most urgent development of risk management strategies in order to preserve its effectiveness in human medicine.\(^2\)
  - Antibiotic resistance (ABR) due to the overuse, misuse, and/or inappropriate use of veterinary drugs is a significant cross-cutting issue for the CCRVDF committee to consider and it is well within the expertise of the committee members. When making decisions on the use and allowable levels of veterinary drug residues in food products, issues surrounding the potential to promote the spread and development of ABR pathogens should be noted.

- **Agenda Item 7(b) “Proposed Revisions of the Risk Analysis Principles Applied by the CCRVDF and the Risk Assessment Policy for the Setting of Maximum Limits for Residues of Veterinary Drugs in Foods”**
  - CSPI asks that the U.S. Delegation not oppose line (e) in Annex 1: *to consider other matters in relation to the safety of food containing residues of veterinary drugs and make relevant recommendations.* Removal of this sentence would weaken the CCRVDF

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\(^1\) The Center for Science in the Public Interest is a nonprofit health advocacy and education organization focused on food safety, nutrition, and alcohol issues. CSPI is supported principally by subscribers to its *Nutrition Action HealthLetter* and by foundation grants. It does not accept government or industry funding.

\(^2\) Critically Important Antimicrobials for Human Medicine:
and limit its ability to take into consideration other matters connected to veterinary drug use.

- For the new form, “Form for Expressing Concerns with Advancement of an MRL or Request for Clarification of Concerns,” CSPI recommends that the U.S. Delegation request that additional information be provided when filling out the form related to the drug’s producers. For example, after “Veterinary drugs concerned,” there should be a section to provide the “Names and locations of the drug’s producers.” Asking for this information will provide background on which companies and countries are most invested in this drug’s trade and revenue. Transparency related to production and trade interests should be part of the form.

- Agenda Item 10 “Risk Management Recommendations for the Veterinary Drugs for which no ADI or MRL has been Recommended by JECFA due to Specific Human Health Concerns”
  
  - As a general comment, CSPI is concerned that the U.S. Delegation is not being consistent with the FDA’s position on at least four of the drugs reviewed in this section. Malachite green, nitrofurans, carbadox, and chloramphenicol have all appeared in FDA’s Import Alerts due to specific human health risks. Below are two examples of Import Alerts.
    
    - **Import Alert # 16-131: Detention Without Physical Examination of Aquacultured Catfish, Basa, Shrimp, Dace, and Eel from China - Presence of New Animal Drugs and/or Unsafe Food Additives.**
      
      Please note that this alert states, “The use of unapproved antibiotics or chemicals in aquaculture raises significant public health concerns. There is clear scientific evidence that the use of antibiotics or chemicals, such as malachite green, nitrofurans, fluoroquinolones, and gentian violet during the various stages of aquaculture can result in the presence of residues of the parent compound or its metabolites in the edible portion of the aquacultured seafood. The presence of antibiotic residues may contribute to an increase of antimicrobial resistance in human pathogens. Moreover, prolonged exposure to nitrofurans, malachite green, and gentian violet has been shown to have a carcinogenic effect.”

    - **Import Alert # 16-129: Detention Without Physical Examination of Seafood Products Due to Nitrofurans.**
      
      Please note that this alert states, “Studies have shown that residues of nitrofurans ingested by consumption of contaminated product are bioavailable. When consumed, nitrofuran residues are absorbed by the consumer’s body and again form tissue-bound residues. Since the compound is considered to be carcinogenic and genotoxic, consumption over time of product contaminated with nitrofurans may present a human health risk. In 1991, FDA withdrew several approved food animal nitrofuran products because of our concerns regarding their carcinogenicity. Nitrofurazone, one of the nitrofurans, has been shown to produce mammary tumors in rats and ovarian tumors in mice. Additionally, some people may be hypersensitive to this product. Nitrofurazone containing products are required to have a warning statement to alert hypersensitive individuals. Nitrofurans are on the list of drugs prohibited from extra-label use in food animals. See http://www.fda.gov/cvm/index/uploads/amducaup.html.”

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3 [http://www.accessdata.fda.gov/cms_ia/importalert_33.html](http://www.accessdata.fda.gov/cms_ia/importalert_33.html)

4 [http://www.accessdata.fda.gov/cms_ia/importalert_31.html](http://www.accessdata.fda.gov/cms_ia/importalert_31.html)
o CSPI strongly supports Option A, as the most protective management measure to public health, for each of the drugs under review (with the exception of nitroimidazoles due to the deficiencies in the databases available to JECFA).

o In reference to Option B, CSPI requests that the U.S. Delegation propose to have the 3rd and 4th bullet points deleted.
  - 3rd bullet: Basing the risk management conclusion on approaches to determine an acceptable level of risk and residue concentrations that result in consumers not exceeding the level of risk (such as an acceptable margin of exposure or extrapolation of the dose response curve to the specified risk level)
  - 4th bullet: Basing the risk management conclusion on development of scientific data to address the concerns identified in the JECFA risk assessment

o The term “approaches” used in the 3rd bullet has no context or clear guidance. Additionally, the term “development of scientific data” in the 4th bullet is vague and does not require that the data be at a scientifically comparable level as JECFA. These segments of Option B should be removed because consumer protection requires clear and understandable tools to be used by nations, and these bullets do not provide guidance on identifying those tools.

o Furthermore, with regard to the 3rd bullet, allowing governments/competent authorities to use undefined “approaches to determine an acceptable level of risk” runs counter to treaty obligations that require use of a science-based risk assessment that applies techniques developed by relevant international organizations.

o Regarding the 4th bullet, risk management decisions that lower health protections based on unqualified scientific data should not be allowed to challenge as being trade restrictive to those protections based on well-founded risk assessments. Again, the 3rd and 4th bullet points should be removed as inconsistent with international treaty obligations.

Sincerely,

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