ANIMAL HEALTH INSTITUTE
Representing manufacturers of animal health products

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

Re: Docket No. FDA-2001-N-0075 (formerly Docket No. 2001-N–0284) and RIN 0910-AF78; Import Tolerances for Residues of Unapproved New Animal Drugs in Food; Proposed Rule

The ANIMAL HEALTH INSTITUTE ("AHI") submits these comments to Docket No. FDA-2001-N-0075; Import Tolerances for Residues of Unapproved New Animal Drugs in Food; Proposed Rule**.** 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. AHI member companies represent the majority of animal pharmaceuticals and animal insecticides, as well as serving a significant segment of the world market.

AHI supports the proposal to create a categorical exclusion from the requirement to submit environmental assessments for import tolerance requests. The proposed rule states that, if appropriate information is available, FDA will consult the Council on Environmental Quality regarding establishment of categorical exclusions for import tolerance requests.

Page 3655 of the Federal Register notice I. Background, Issue 4: Import Tolerances Effect on the Environment indicates:

> *FDA is considering amending the regulations at 21 CFR 25.33 to allow a categorical exclusion for import tolerances under the National Environmental Policy Act, if there is information that shows that establishing import tolerances does not have a significant effect on the environment. The Agency is seeking information on whether import tolerances will have a significant effect on the environment.*
>
> *The consensus of VMAC was that they could not think of any instance relative to residues within animal derived food products that would have a significant environmental impact.*
>
> *Other public comments on this issue included that categorical exclusion from the requirement to submit an environmental assessment would be appropriate for import tolerances on a case-by-case basis, if no extraordinary circumstances exist.*

In addition, Page 3657 of the Federal Register notice, II. Summary of the Proposed Rule, C. Requests To Establish or Amend an Import Tolerance (Proposed § 510.205), 2. Content and Administration of a Request (Proposed § 510.205(b)) indicates:

> *Under this proposed rule, if finalized, a requester would be required to submit an environmental assessment, as described in 21 CFR 25.40, to facilitate the Agency's assessment of potential environmental impacts under the National Environmental Policy Act; Executive Order 12114, ''Environmental Effects Abroad of Major Federal Actions,'' of January 4, 1979 (44 FR 1957, January 9, 1979); and 21 CFR 25.60. As previously discussed in this document, the Agency solicited comments on the issue of whether import tolerances will have a significant effect on the environment in the August 2001 ANPRM and January 2002 VMAC. Although categorical exclusions are not addressed in this proposed rule, the Agency is still considering the comments received in response to the August 2001 ANPRM and January 2002 VMAC. If, in the future, the Agency determines it to be appropriate, FDA will consult with the Council on Environmental Quality (CEQ) regarding the establishment of categorical exclusions for certain import tolerance requests. FDA reiterates its previous requests for comments and supporting information relevant to the issue of whether import tolerances will have a significant effect on the environment in the United States or abroad.*

AHI believes the action of approving an import tolerance for residues of an unapproved new animal drug in food presents no appreciable risk to the environment. A categorical exclusion from the requirement for environmental assessments for this action would be consistent with criteria that already exist. A categorical exclusion is already in place for total residues of pharmaceuticals discharged from sewage treatment facilities at concentrations less than 1 mcg/L (21 CFR 25.31 (b)) because that concentration normally presents no significant risk to the environment. Aquaculture products introduced into the aquatic environment at concentrations of total residues less than 1 mcg/L and veterinary products introduced into the terrestrial environment at total residue concentrations less than 100 mcg/kg soil are not considered a significant risk and do not require an environmental assessment (US FDA/CVM Guidance for Industry #89[1]). Only the calculations which demonstrate the potential occurrence of these low concentrations are needed to demonstrate minimal risk. Also, veterinary products that are extensively metabolized in treated animals, such that the metabolites are not structurally similar to the animal drugs, do not require environmental assessments. In all of these cases, minimal risk to the environment is expected and a detailed environmental assessment is not required. These existing criteria could be used to demonstrate that a categorical exclusion for import tolerance requests would not be expected to appreciably affect the environment.

The only routine point of entry of residues into the domestic environment after consumption of food by humans would be in the discharge from sewage treatment facilities. Active ingredients in pharmaceuticals and aquaculture products are normally considered to present no significant environmental risk at concentrations less than 1 mcg/L. The FDA guidance for calculating concentrations of pharmaceuticals discharged from sewage treatment facilities provides a daily volume of effluent from all US facilities equal to 1.214×10^{11} liters (FDA, 1998[2]). The US EPA provides guidance for the average amount of food consumed per capita each day by the population of the United States (US EPA, 2011[3]). From this information, the residue level in imported meat can be calculated that would have to be eaten daily by every person in the United States in order to reach the concentration of 1 mcg/L in effluent of a sewage treatment facility:

[1] http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052424.pdf
[2] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070561.pdf
[3] http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf

Daily amount of residue needed to reach 1 mcg/L in effluent from sewage treatment facilities:
1 mcg/L x 1.214 X 10^{11} L/day = 1.214 X 10^{11} mcg/day x 0.001 mg/mcg = 1.214 X10^{8} mg/day

Concentrations of residues in tissues needed to reach 1 mcg/L in effluent:
Beef (70 kg person x average of 0.77 g consumed per capita/kg /day = 54 g/person/day)
(1.214X10^{8} mg residue/day)/(0.054 kg consumed/person/day)(300,000,000 people) = 7.5 ppm

Pork (70 kg person x average of 0.39 g consumed per capita/kg/day = 27 g/person/day)
(1.214X10^{8} mg residue/day)/(0.027 kg consumed/person/day)(300,000,000 people) = 15 ppm

Poultry (70 kg person x average of 0.77 g consumed per capita/kg/day = 54 g/person/day)
(1.214X10^{8} mg residue/day)/(0.054 kg consumed/person/day)(300,000,000 people) = 7.5 ppm

Finfish (70 kg person x average of 0.16 g consumed per capita/kg/day = 11.2 g/person/day)
(1.214X10^{8} mg residue/day)/(0.0112 kg consumed/person/day)(300,000,000 people) = 36 ppm

Tolerance limits for residues of animal drugs in edible tissues are normally far below these calculated values. Therefore, discharge of residue from human consumption through sewage treatment facilities will be at concentrations below 1 mcg/L and should not be considered to present any appreciable risk to the environment.

The only other domestic point of entry for residues of unapproved new animal drugs might be from shipments of meat seized and disposed of in domestic municipal solid waste landfills. Risk from this disposal practice in an environmental assessment would be difficult to quantify since information about the amount of meat seized and the concentration of residue in the meat would not be available. However, the risk to the environment from meat disposed of in landfills should not be significant. Municipal landfills in the United States operate under strict rules from the US EPA (40 CFR 258, Subtitle D of Resource Conservation and Recovery Act[4]). Landfills are lined and have leachate recycling or capture and treatment systems. Materials placed in landfills are mixed, compacted and covered with soil from the landfill. Concentrations of any residue of new animal drug in seized meat would be diluted by soil and other material in the landfill. An extraordinary amount of meat would have to be disposed of for the overall concentration of residue in the entire landfill to be 100 mcg/kg or higher. Concentrations lower than 100 mcg/kg have already been identified as presenting little chance of resulting in appreciable environmental risk from veterinary products. Disposal of seized meat in municipal solid waste landfills is highly unlikely to result in appreciable environmental risk.

Current extraordinary circumstances identified in 21 CFR 25.21 and other FDA guidance could be evaluated to determine if particular examples are relevant to the action associated with a request for a tolerance limit for an unapproved new animal drug.

Approval of an import tolerance request should also have no appreciable effect on environments outside the United States associated with Executive Order 12114 and with 21 CFR 25.60. The use of a new animal drug in animals that enter the human food supply requires approval and registration in the country where the product is approved for use. Along with this approval comes an evaluation

[4] http://www.epa.gov/osw/nonhaz/municipal/landfill.htm

of the potential for the product to affect the environment. If the product is not expected to present an appreciable risk to the environment in the country where it is registered for use, it is hard to imagine a situation where movement of residues to another country or into the global commons, such as the open ocean, would present a significant environmental risk. Dispersion and degradation of residues would only serve to reduce their concentrations presenting fewer risks. Movement of residues, even those of marine-based aquaculture products from net pens, should result in diluted concentrations well below 1 mcg/L before the residues reached the open ocean or the coastal environment of a neighboring country. Importation of foods with residues of new animal drugs, appropriately registered in the country where they are used, are not likely to result in an environmental impact on neighboring countries or in the global commons, such as the oceans.

The Animal Health Institute would support a proposal from the FDA for a categorical exclusion from the need for an environmental assessment for an Import Tolerance Request. We would appreciate consideration of our support for a categorical exclusion as part of your final evaluation and implementation of the proposed rule for import tolerances for residues of unapproved new animal drugs in food.

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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