

### Comment Form

				Date June 30, 2003	Document GFI #144 Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food-Producing Animals with Respect to Antimicrobial Resistance VICH GL27
Commenter	Section	Paragraph Figure/ Table Line No.	Proposed Change	Comment/ Rationale	
AHI Comment 1	Cover Page	Para 1	Additional sentence at end of paragraph "This information should help to characterize the potential for the use of the product to select for antimicrobial-resistant bacteria of human health concern.	Provides additional clarification of the purpose of the document by incorporating the language from the Introduction section of the document	

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AHI Comment 2	Introduction	Para 1	<p>New first paragraph and additional language to what would now become paragraph two.</p> <p>“The use of antimicrobial agents is likely to lead to selection of resistance whether administered to humans, animals or plants. Zoonotic organisms such as non-typhoid Salmonellae, Campylobacter spp. and enterohaemorrhagic E. coli (e.g. O157) can, by definition, be transferred to humans from animals. Therefore, it stands to reason that resistant zoonotic organisms can also be transferred to humans. It is recognized that antimicrobial resistance in some of these pathogens can arise during therapy of infected people as well. The transfer of antimicrobial-resistant commensal bacteria or their genetic material from animals to humans via the food chain is also possible, but the data are conflicting. Data demonstrating the magnitude and importance of such transfer, or whether transfer occurs via consumption of contaminated meat or via contamination of water or vegetables by animal excreta are limited.<sup>1,2,3</sup></p> <p>It is clear that food-producing animals represent a potential reservoir of antimicrobial-resistant microorganisms for humans. It is also recognized that humans are a potential reservoir of resistant microorganisms for animals.<sup>4,5</sup> Therefore, prudent use of antimicrobial agents is needed in veterinary as well as in human medicine. The extent to which animals are a source of human exposure to antimicrobial-resistant microorganisms remains to be quantified. In addition, methods for assessing the magnitude of the animal source of exposure have not been totally defined. However, when evaluating the safety. .”</p>	<p>This is the original agreed upon language from VICH GL27. Inclusion of this language was discussed at length within the Expert Working Group and agreed upon by all parties. This language and the five references provide a balanced discussion of the issue for the reader and should be included in the document.</p>
AHI comment 3	Introduction	Para 1, first sentence	<p>Rewrite end of sentence: “...antimicrobial agents to select for <u>antibiotic</u> resistant bacteria <u>of human health concern</u>.”</p>	Clarification

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AHI comment 4	Introduction	Para 1, second sentence	Substitute the word <b>provided</b> for "reported."	Clarification
AHI comment 5	Introduction	Para 1, last sentence	Replace the phrase "to contribute to" with <b>as part of</b> .	Clarification
AHI comment 6	Objectives	Para 1, first sentence	Replace sentence with "The objective of this document is to provide harmonized technical guidance in the EU, Japan and the US for registration of thereapeutic antimicrobial veterinary medicinal products intended for use in food-producing animals with regard to characterization of the potential for a given antimicrobial agent to select for resistant bacteria of human health concern.	Clarification
AHI comment 7	Objectives	Para 3, first sentence	Replace "for" with <b>of</b> .	Clarification
AHI comment 8	Objectives	Para 3, second sentence	Replace "principle" with <b>fundamental</b> .	Clarification
AHI comment 9	Data recommend	Para 2, first sentence	Editorial recommendation to latter half of the sentence to now read...sponsors may choose to also include some of all of those data.	Clarification
AHI comment 10	1.4	First and second sentences	Combine into a single sentence with additional clarifying phrases to now read: "...to the antimicrobial drug substance contained in the product should be provided and may come from literature..."	Clarification
AHI comment 11	1.4	Third sentence	Add a clarifying phrase in the middle of the sentence so that it will now read: "Information from related analogs within the same drug class should be provided..."	Clarification

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AHI comment 12	1.5	Second sentence	Combine with the first sentence by the elimination of the phrase "This information may come"	Clarification
AHI comment 13	1.6	Second sentence	Combine with the first sentence by the elimination of the phrase "This information" and insertion of the word <b>and</b> .	Clarification
AHI comment 14	New Section		<p>Inclusion of five references noted in AHI comment 2:</p> <p><b>References</b></p> <p>1. Ministry of Agriculture Fisheries and Food. A Review of Antimicrobial resistance in the Food Chain: A Technical Report for MAFF. July 1998 <a href="http://www.foodstandards.gov.uk/maff/pdf/resist.pdf">http://www.foodstandards.gov.uk/maff/pdf/resist.pdf</a>.</p> <p>2. European Commission. Opinion of the Scientific Steering Committee on Antimicrobial Resistance. May 1999. <a href="http://europa.eu.int/comm/food/fs/sc/ssc/out50_en.pdf">http://europa.eu.int/comm/food/fs/sc/ssc/out50_en.pdf</a>.</p> <p>3. Commonwealth Department of Health and Aged Care and the Commonwealth Department of Agriculture, Fisheries and Forestry-Australia. The use of antibiotics in food-producing animals: antibiotic-resistant bacteria in animals and humans. Report of the Joint Expert Advisory Committee on Antibiotic Resistance (JETACAR). September 1999. <a href="http://www.health.gov.au/pubs/jetacar.pdf">http://www.health.gov.au/pubs/jetacar.pdf</a>.</p> <p>4. H. Kinde, et.al. Sewage Effluent: Likely Source of Salmonella enteritidis, Phage Type 4 Infection in a Commercial Chicken Layer Flock in Southern California. Avian Diseases 40:672-679, 1996.</p> <p>5. H. Kinde, et.al. Prevalence of Salmonella in Municipal Sewage Treatment Plant Effluents in Southern California. Avian Diseases 41:392-398, 1997.</p>	See AHI comment 2.