



1931 N. Meacham Rd.
Suite 100
Schaumburg, IL
60173-4360
phone 847.925.8070
800.248.2862
fax 847.925.1329
www.avma.org

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Dr. Michael David, Director
National Center for Import and Export
International Animal Health Standards Team
USDA, APHIS, Veterinary Services
4700 River Road, Unit 33
Riverdale, MD 20737
E-mail: michael.j.david@aphis.usda.gov; debra.beasley@aphis.usda.gov

VIA E-MAIL ONLY

Dear Dr. David,

The AVMA appreciates the opportunity to provide comments on the following revised document (Chapter 6.9.; Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine) extracted from the report of the September 2011 meeting of the OIE Terrestrial Animal Health Standards Commission (TAHSC). As requested, when we have comments on revised text, our responses are formulated for this Chapter as follows:

- a. identification of the text, as written in the TASHC report, on which we are commenting;
- b. description of the changes we believe should be made to the text, assuming approval of changes proposed by the TASHC, to include suggested language, if any, to implement the changes we believe should be made; and
- c. scientific justification or rationale for such changes; or comments if no specific changes are suggested.

When language revisions are suggested under “b.,” our recommended deletions are ~~struck through~~ and additions are underlined.

CHAPTER 6.9.—RESPONSIBLE AND PRUDENT USE OF ANTIMICROBIAL AGENTS IN VETERINARY MEDICINE

1. Article 6.9.1.—Purpose, second sentence

- a. TEXT: “It defines the respective responsibilities of the...”
- b. CHANGES & REVISIONS SUGGESTED: “It defines the respective ~~responsibilities~~ responsibilities of the...”
- c. RATIONALE: “Responsibilities” was spelled incorrectly.

2. Article 6.9.2.—Objectives of responsible and prudent use, new paragraph 4

- a. TEXT: “...contribute to maintaining the efficacy and usefulness of *antimicrobial agents* used ...”
- b. CHANGES & REVISIONS SUGGESTED: Delete the phrase “and usefulness” as follows: “...contribute to maintaining the efficacy ~~and usefulness~~ of *antimicrobial agents* used ...”
- c. RATIONALE: In this context, “usefulness” would mean the same as “efficacy,” which has previously been stated. Hence, it is redundant and should be deleted.

3. **Article 6.9.3.—Responsibilities of the regulatory authorities; Section 2 (*Submission of data for the granting of marketing authorisation*), new sentence 3**
 - a. TEXT: “...each individual antimicrobial ~~agents product~~ and the...”
 - b. CHANGES & REVISIONS SUGGESTED: “...each individual antimicrobial ~~agents~~ agent and the...”
 - c. RATIONALE: Grammatical error; “agent” should be singular, not plural.

4. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 3 (*Market approval*), line 1**
 - a. TEXT: “...that the market approval process of a ~~new~~ VMPs containing antimicrobial...”
 - b. CHANGES & REVISIONS SUGGESTED: “...that the market approval process of ~~a~~ VMPs containing antimicrobial...”
 - c. RATIONALE: Grammatical error; “VMPs” is plural, so does not require the article “a.”

5. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 4 (*Registration procedures*), line 2**
 - a. TEXT: “...the quality, safety and efficacy of the VMPs containing antimicrobial...”
 - b. CHANGES & REVISIONS SUGGESTED: “...the quality, safety and efficacy of ~~the~~ VMPs containing antimicrobial...”
 - c. RATIONALE: Grammatical error; “VMPs” is plural, so does not require the article “the.”

6. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 4 (*Registration procedures*), final sentence**
 - a. TEXT: All Member eCountries should make every effort to actively combat the manufacture, advertisement, trade, distribution and use of unlicensed and counterfeit ~~bulk active pharmaceutical ingredients and products~~ including bulk active ingredients.
 - b. CHANGES & REVISIONS SUGGESTED: All Member Countries should make every effort to actively combat the manufacture, advertisement, trade, distribution and use of unlicensed and counterfeit bulk active ingredients and other products ~~including bulk active ingredients~~.
 - c. RATIONALE: The changes proposed by the TAHSC made it somewhat unclear as to whether the recommendation referred to all bulk active ingredients. Thus, we have suggested language in an attempt to clarify this statement. AVMA policy on *Compounding from Unapproved (Bulk) Substances* (www.avma.org/issues/policy/compounding_bulk.asp) indicates that such compounding may be medically necessary in non-food producing animals and as such, offers guidance on best practices. The FDA offers guidance also (see: www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074656.htm).

7. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 6 (*Assessment of therapeutic efficacy*), subsection “b” (*Clinical trials*), point ii)**
 - a. TEXT: “...such as Veterinary International Cooperation of Harmonisation (VICH) guidelines...”
 - b. CHANGES & REVISIONS SUGGESTED: No specific changes; please refer to COMMENTS.
 - c. COMMENTS: Although the TAHSC did not propose changes to this text, the AVMA noted that in Article 6.9.3., Section 4, second paragraph, the full name of the VICH is already written, albeit differently than in Section 6. Because the full name is written correctly in Section 4, we suggest either correcting the full name in Section 6 or, alternatively, deleting the full name and replacing it with the acronym “VICH.”

8. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 7 (*Assessment of the potential of antimicrobial agents to select for resistance*), paragraph “c”**
 - a. TEXT: “...the degree of cross-resistance within and between antimicrobial classes;
 - b. CHANGES & REVISIONS SUGGESTED: “...the degree of cross-resistance ~~within and between~~ antimicrobial classes;
 - c. RATIONALE: It is well understood that cross-resistance can occur both within and between classes of antimicrobials. Thus, the above suggested edit is offered for clarity.

9. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 10 (*Establishment of a summary of product characteristics for each veterinary medicinal products containing antimicrobial agent(s)*), title**
 - a. TEXT: “...of product characteristics for each veterinary medicinal products containing...”
 - b. CHANGES & REVISIONS SUGGESTED: “...of ~~product~~ characteristics for each veterinary medicinal ~~products~~ product containing...”
 - c. RATIONALE: The use of “product” multiple times in the title is redundant. The first use is not needed and should be deleted. In addition, since reference is made to “each” VMP, “product” should be singular and not plural.

10. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 10 (*Establishment of a summary of product characteristics for each veterinary medicinal products containing antimicrobial agent(s)*), paragraph “d”**
 - a. TEXT: “target animal species and as appropriate age or production category”
 - b. CHANGES & REVISIONS SUGGESTED: “target animal species and, as appropriate, age or production category”
 - c. RATIONALE: Adding commas to set-off the phrase “as appropriate” clarifies the sentence.

11. **Article 6.9.3.—Responsibilities of the regulatory authorities, Section 14 (*Training of antimicrobial users*), paragraph “a”**
 - a. TEXT: “information on *disease* prevention, ~~and~~ management and mitigation strategies;”
 - b. CHANGES & REVISIONS SUGGESTED: None
 - c. COMMENTS: Just to clarify, this sentence is meant to mean that training should include information on disease prevention, disease management, and disease mitigation strategies, correct?

12. **Article 6.9.6.—Responsibilities of veterinarians, Section 1 (*Use of antimicrobial agents*), paragraph “b”**
 - a. TEXT: “make an appropriate choice of ~~the~~ antimicrobial agent based on treatment experience and diagnostic laboratory information (pathogen isolation, identification and antibiogram) where possible.”
 - b. CHANGES & REVISIONS SUGGESTED: “make an appropriate choice of antimicrobial agent based on ~~treatment~~ clinical experience and diagnostic laboratory information (pathogen isolation, identification and antibiogram) where possible.”
 - c. RATIONALE: We believe that “treatment experience” as used by the TAHSC in his paragraph refers to treatment in a clinical, rather than an experimental, setting, and so suggest changing “treatment” to “clinical” for added clarity.

- 13. Article 6.9.6.—Responsibilities of veterinarians, Section 2 (*Choosing an antimicrobial agent*), second-to-last paragraph, final sentence**
- TEXT: “In the absence of such results, an appropriate antimicrobial agent belonging to a different class should be used.”
 - CHANGES & REVISIONS SUGGESTED: “In the absence of such results, an appropriate antimicrobial agent belonging to a different class should be considered ~~used~~.”
 - RATIONALE: The specifics of antimicrobial selection should be left to the individual veterinarian, who might have good reason to select an antimicrobial from the same class of the first-line drug in the case of disease recurrence or treatment failure.
- 14. Article 6.9.6.—Responsibilities of veterinarians, Section 6 (*Training/continued professional development*), final sentence**
- TEXT: “...American Veterinary Medical Associations).”
 - CHANGES & REVISIONS SUGGESTED: Change to “American Veterinary Medical Association Associations”
 - RATIONALE: Grammatical error. “Association” should be singular, not plural.
- 15. Article 6.9.7.— Responsibilities of food-animal producers, Section 2, paragraph “c”**
- TEXT: “...including maintenance of the storage conditions as appropriate,...”
 - CHANGES & REVISIONS SUGGESTED: “...including ~~maintenance of the storage of the~~ product conditions as appropriate,...”
 - RATIONALE: The change in verbiage proposed by the TAHSC appears to indicate that each food-animal producer might need to maintain a storage facility specifically for VMPs with antimicrobial agents. The AVMA suggests the revisions above to add clarity to this statement.
- 16. Article 6.9.7.—Responsibilities of food-animal producers, Section 2, new paragraph “i,” point (vii)**
- TEXT: “...(including date of the end of the withdrawal periods);”
 - CHANGES & REVISIONS SUGGESTED: “...(~~including date of the end~~ date of the withdrawal periods);”
 - RATIONALE: The suggested revision streamlines verbiage and adds clarity.

As always, we appreciate the opportunity to provide input. Should you have questions or require additional information about our comments, please do not hesitate to contact Dr. Beth Sabin, International Coordinator and Assistant Director in our Education and Research Division (esabin@avma.org; 800-248-2862, ext 6675).

Sincerely,



W. Ron DeHaven, DVM, MBA
Executive Vice President and CEO