DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-D-0165]

# International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products; Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Validation of Analytical Methods Used in Residue Depletion Studies; Revised Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised guidance for industry (GFI #208) entitled "Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Validation of Analytical Methods Used in Residue Depletion Studies" (VICH GL49(R)). This revised guidance, which provides minor updates to a final guidance on the same topic for which a notice of availability was published in the Federal Register of September 15, 2011, has been developed for veterinary use by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). This revised VICH guidance document is intended to provide a general description of the criteria that have been found by the European Union, Japan, United States, Australia, New Zealand, and Canada to be suitable for the validation of analytical methods used in veterinary drug residue depletion studies.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of the guidance to the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your request. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the revised guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Julia Oriani, Center for Veterinary Medicine (HFV-151), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240-402-0788, julia.oriani@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

## I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote the international harmonization of regulatory requirements. FDA has participated in efforts to enhance harmonization and has expressed its commitment to seek scientifically based harmonized technical procedures for the development of pharmaceutical products. One of the goals of harmonization is to identify, and then reduce, differences in technical requirements for drug development among regulatory agencies in different countries.

FDA has actively participated in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use for several years to develop harmonized technical requirements for the approval of human pharmaceutical and

biological products among the European Union, Japan, and the United States. The VICH is a parallel initiative for veterinary medicinal products. The VICH is concerned with developing harmonized technical requirements for the approval of veterinary medicinal products in the European Union, Japan, and the United States, and includes input from both regulatory and industry representatives.

The VICH Steering Committee is composed of member representatives from the European Commission, European Medicines Evaluation Agency, European Federation of Animal Health, Committee on Veterinary Medicinal Products, FDA, U.S. Department of Agriculture, the Animal Health Institute, Japanese Veterinary Pharmaceutical Association, Japanese Association of Veterinary Biologics, and Japanese Ministry of Agriculture, Forestry, and Fisheries.

Six observers are eligible to participate in the VICH Steering Committee: One representative from the government of Australia/New Zealand, one representative from the industry in Australia/New Zealand, one representative from the government of Canada, one representative from the industry of Canada, one representative from the government of South Africa, and one representative from the industry of South Africa. The VICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation for Animal Health (IFAH). An IFAH representative also participates in the VICH Steering Committee meetings.

## II. Revised Guidance on Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Validation of Analytical Methods Used in Residue Depletion Studies

In June 2014, the VICH Steering Committee agreed that a revised guidance document entitled "Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Validation of Analytical Methods Used in Residue Depletion Studies" (VICH GL49(R)) should be made available to the public. This revised guidance is a revision of a final guidance on the same topic for which a notice of availability was published in the Federal Register of September 15, 2011 (76 FR 57056). The revised guidance makes minor changes such as correcting a typographical error in table 2 (Annex 3). Also, the explanatory text for table 2 (Annex 3) was revised to correct a description of the statistical model and to provide an explanation of the procedure used to generate the data in the table. This revised guidance is a product of the Metabolism and Residue Kinetics Expert Working Group of the VICH.

During the veterinary drug development process, residue depletion studies are conducted to determine the concentration of the residue or residues present in the edible products (tissues, milk, eggs, or honey) of animals treated with veterinary drugs. This information is used in regulatory submissions around the world. Submission of regulatory methods (i.e., postapproval control methods) and the validation requirements of the regulatory methods are usually well defined by various regulatory agencies worldwide and might even be defined by national or regional law. However, the residue depletion studies are generally conducted before the regulatory methods have been completed. Oftentimes the in-house validated residue methods provide the framework for the methods submitted for regulatory monitoring. Harmonization of the validation requirements for methodology used during residue depletion studies and submitted to the regulatory agencies in support of the maximum residue limits and withdrawal periods should be achievable. It is the intent of this document to describe a validation procedure that is acceptable to the regulatory bodies of the VICH regions for use in the residue depletion studies.

This validated method could continue on to become the "regulatory method" but that phase of the process will not be addressed in any detail in this guidance. For purposes of this guidance, the term "acceptable" refers to the scientific evaluation of the analytical method in terms of the described validation criteria, not to acceptance of the analytical method as satisfying the applicable national/regional laws and regulations of any of the relevant regulatory bodies.

## III. Significance of Guidance

As a result of Level 2 revisions, this VICH revised guidance is being issued in final, consistent with FDA's good guidance practice (GGP) regulations at 21 CFR 10.115(g)(4). This guidance, developed under the VICH process, has been revised to conform to FDA's GGP regulation (21 CFR 10.115). For example, the document has been designated "guidance" rather than "guideline." In addition, guidance documents must not include mandatory language such as "shall," "must," "require," or "requirement," unless FDA is using these words to describe a statutory or regulatory requirement.

This VICH guidance represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of applicable statutes and regulations.

## IV. Paperwork Reduction Act of 1995

This revised guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 514 have been approved under OMB control number 0910-0032.

## V. Comments

Interested persons may submit either electronic comments regarding this document to www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

## VI. Electronic Access

Persons with access to the Internet may obtain the guidance at either http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm or http://www.regulations.gov.

Dated: March 3, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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