and review staff entitled ''Recommended Approaches to Integration of Genetic Toxicology Study Results.'' This guidance is intended to inform industry and the review staff in the Center for Drug Evaluation and Research (CDER) on how CDER views positive findings in genetic toxicology assays during drug development. The guidance provides recommendations on how to proceed with clinical studies while ensuring the safety of study participants when results in genotoxicity studies suggest a potential cancer or genetic hazard.

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

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: David Jacobson-Kram, Center for Drug Evaluation and Research (6411), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6488, Silver Spring, MD 20993, 301–796–0175.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry and review staff entitled ''Recommended Approaches to Integration of Genetic Toxicology Study Results.'' Pharmaceuticals administered through oral, intravenous, topical, and other routes, as appropriate, are subject to this guidance.

In the **Federal Register** of December 2, 2004 (69 FR 70153), FDA announced the availability of a draft version of the guidance entitled ''Recommended Approaches to Integration of Genetic Toxicology Study Results.'' When the draft guidance was published, FDA requested comments on the document. Some changes were made to the draft document based on comments submitted to the docket including the following changes: (1) The guidance now suggests that for a compound giving positive results in a genetic toxicology assay, an alternative to demonstrating ''mechanism of action'' would be ruling out mechanisms involving direct interaction with dexoyribonucleic acid (DNA) and (2) alkaline elution is included as an example of an assay for measuring DNA damage. Other editorial changes were also made.

A number of comments to the docket suggested that the fourth test in the International Conference on Harmonisation (ICH) battery should be an option for compounds giving a positive response in one of the initial assays. This change was not included. Positive responses are primarily seen in the in vitro chromosomal aberration assay and/or the mouse lymphoma assay. Because these two tests measure common genetic lesions and have similar drug exposure protocols, the data from the two assays can be used to corroborate results.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking on recommended approaches to integration of genetic toxicology study results. 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 the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the guidance at any time. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: December 21, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E5–8224 Filed 1–3–06; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 1999D–2215] (formerly 99D–2215)

International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products; Draft Revised Guidance for Industry on Impurities in New Veterinary Drug Substances (Revision); Request for Comments; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability for comments of a draft revised guidance for industry (#92) entitled ''Impurities in New Veterinary Drug Substances (Revision)'' VICH GL10(R). This draft revised guidance, which updates a final guidance on the same topic for which a Notice of Availability was published in the **Federal Register** of July 7, 2000 (the 2000 guidance), has been developed for veterinary use by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). The draft revised document is intended to provide guidance for registration applicants on the content and qualification of impurities in new veterinary drug substances produced by chemical syntheses and not previously registered in a country, region, or member state.

DATES: Submit written or electronic comments by February 3, 2006 to ensure their adequate consideration in preparation of the final guidance document. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Communications Staff (HFV–12), Center for Veterinary Medicine (CVM), 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 draft revised guidance document.

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

Comments should be identified with the full title of the draft revised guidance and the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Dennis Bensley, Center for Veterinary Medicine (HFV–143), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–6956, e-mail: *dbensley@cvm.fda.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 Harmonization of Technical Requirements for Approval 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. VICH is a parallel initiative for veterinary medicinal products. 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; the U.S. Department of Agriculture; the Animal Health Institute; the Japanese Veterinary Pharmaceutical Association; the Japanese Association of Veterinary Biologics; and the Japanese Ministry of Agriculture, Forestry, and Fisheries.

Four 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, and one representative from the industry of Canada. 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. Draft Revised Guidance on Impurities in New Veterinary Drug Substances

In May 2005, the VICH steering committee agreed that a draft revised guidance entitled ''Impurities in New Veterinary Drug Substances (Revision)'' VICH GL10(R) should be made available for public comment. The draft 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 July 7, 2000 (65 FR 42020). The draft revised guidance clarifies the 2000 guidance, adds information, and provides consistency with more recently published VICH guidances. The draft revised guidance is the product of the Quality Expert Working Group of VICH. Comments about this draft will be considered by FDA and the Quality Expert Working Group.

This draft revised document is intended to provide guidance for registration applications on the content and qualification of impurities in new veterinary drug substances intended to be used for new veterinary medicinal products, produced by chemical syntheses and not previously registered in a country, region, or member state.

The draft revised guidance includes revised text on recommended threshold limits and revised text on recommended specification limits for impurities. Additions to the glossary include definitions for the terms ''identification threshold'' and ''qualification threshold.'' References to validated limits of quantitation were removed. In addition, minor editorial changes were made to improve the clarity and consistency of the document.

III. Paperwork Reduction Act of 1995

This draft revised guidance contains information collection provisions that 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 this draft revised guidance have been approved under OMB control number 0910–0032.

IV. Significance of Guidance

This draft revised document, developed under the VICH process, has been revised to conform to FDA's good guidance practices 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,'' ''required,'' or ''requirement,'' unless FDA is using these words to describe a statutory or regulatory requirement.

The draft revised VICH guidance represents the agency's current thinking on impurities in new veterinary drug substances. This draft revised guidance does not create or confer any rights for or on any person and will not operate to bind FDA or the public. An alternative method may be used as long as it satisfies the requirements of applicable statutes and regulations.

V. Comments

This draft revised guidance document is being distributed for comment purposes only and is not intended for implementation at this time. Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this draft revised guidance document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. A copy of the draft revised guidance and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VI. Electronic Access

Electronic comments may also be submitted on the Internet at *http://www.fda.gov/dockets/ecomments*. Once on this Internet site, select Docket No. 1999D–2215, entitled ''Draft Revised Guidance for Industry on Impurities in New Veterinary Drug Substances (Revision)'' VICH GL10(R), and follow the directions.

Copies of the draft guidance document entitled ''Draft Revised Guidance for Industry on Impurities in New Veterinary Drug Substances (Revision)'' VICH GL10(R), may be obtained on the Internet from the CVM home page at *http://www.fda.gov/cvm*.

Dated: December 21, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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