In the **Federal Register** of December 24, 1997 (62 FR 67377), FDA published the ICH draft guidance for industry entitled ''Q3C Impurities: Residual Solvents.'' The draft guidance makes recommendations as to what amounts of residual solvents are considered safe in pharmaceuticals. The draft guidance recommends use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents. Upon issuance in 1997, the text and appendix 1 of the draft guidance contained several tables and a list of solvents categorizing residual solvents by toxicity, classes 1 through 3, with class 1 being the most toxic. The ICH Quality Expert Working Group (EWG) agreed that the PDE could be modified if reliable and more relevant toxicity data were brought to the attention of the group and the modified PDE could result in a revision of the tables and list.

In 1999, ICH instituted a Q3C maintenance agreement and formed a maintenance EWG (Q3C EWG). The agreement provided for the reconsideration of solvent PDEs and allowed for minor changes to the tables and list that include the existing PDEs. The agreement also provided that new solvents and PDEs could be added to the tables and list based on adequate toxicity data. In the **Federal Register** of February 12, 2002 (67 FR 6542), FDA briefly described the process for proposing future revisions to the PDEs. In the same notice, the agency announced its decision to delink the tables and list from the Q3C guidance and create a stand alone document entitled ''Q3C: Tables and List'' to facilitate making changes recommended by ICH.

In the **Federal Register** of February 12, 2002 (67 FR 6542), FDA also announced the availability of draft recommendations for the revision of the PDE for NMP and THF according to the Q3C maintenance procedures. The notice gave interested persons an opportunity to submit comments by March 14, 2002.

II. Revised PDEs for NMP and THF

After consideration of the comments received, the EWG's recommendations to revise the PDEs for NMP and THF were submitted to the ICH Steering Committee and agreement was reached by the three participating regulatory agencies in September 2002.

A. N-Methylpyrrolidone (NMP)

The Q3C EWG received new toxicity data for the solvent NMP in late 1999. In February 2002, FDA made available for comment the EWG's draft recommendation for the revision of the PDE for NMP (67 FR 6542 at 6543). At the September 2002 ICH meeting, the Steering Committee agreed to the EWG's recommendation to keep NMP in Class 2. A PDE of 5.3 milligrams per day (mg/day) and a concentration limit of 530 parts per million (ppm) are being declared for this solvent.

B. Tetrahydrofuran (THF)

The Q3C EWG reviewed new toxicity data for the solvent THF. In February 2002, FDA made available for comment the EWG's draft recommendation for the revision of the PDE for THF (67 FR 6542 at 6543). At the September 2002 ICH meeting, the Steering Committee agreed to the EWG's recommendation to move THF from class 3 to class 2. A PDE of 7.2 mg/day and a concentration limit of 720 ppm are being declared for this solvent.

The analyses and recommendations for NMP and THF are available for review at *http://www.fda.gov/cder/audiences/iact/iachome.htm*. They are also available from the Division of Drug Information (HFD–240) (see **ADDRESSES**). The agency will revise the tables and list in the guidance ''Q3C: Tables and List'' to reflect the ICH final recommendations for NMP and THF.

The revised PDEs for the two solvents contained in the revised guidance ''Q3C: Tables and List'' represent the agency's current thinking on this topic. They do not create or confer any rights for or on any person and do 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.

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

III. Internet Access to Documents and the Maintenance Procedures

Persons with access to the Internet may obtain the Q3C documents at *http://www.fda.gov/cder/guidance/index.htm*, or *http://www.fda.gov/cber/guidelines.htm*. Information on the Q3C maintenance process, and proposals, recommendations, and agreements for revisions to the tables and list are made available at *http://www.fda.gov/cder/audiences/iact/iachome.htm*. The electronic address for the Division of Dockets Management is *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: November 4, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 03–28372 Filed 11–12–03; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2002D–0368]

International Cooperation on Harmonisation of Technical Requirements for Approval of Veterinary Medicinal Products; Guidance for Industry on ''Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Repeat-Dose (90-Day) Toxicity Testing'' (VICH GL31); Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry (#147) entitled ''Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Repeat-Dose (90-Day) Toxicity Testing'' (VICH GL31). This guidance has been developed by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). The objective of this guidance is to establish recommendations for an internationally harmonized 90-day repeat-dose testing.

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

ADDRESSES: Submit written requests for single copies of this 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 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*. Comments are to be identified with the

docket number found in brackets in the heading of this document. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Louis T. Mulligan, Center for Veterinary Medicine (HFV–153), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–6984, e-mail: *lmulliga@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. 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; the U.S. 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. Guidance on Toxicity Testing

In the **Federal Register** of September 4, 2002 (67 FR 56569), FDA published the notice of availability of the VICH draft guidance, giving interested persons until October 4, 2002 to submit comments. After consideration of comments received, the draft guidance was changed in response to the comments and submitted to the VICH Steering Committee. At a meeting held from October 10 to 11, 2002, the VICH Steering Committee endorsed the guidance for industry, VICH GL31.

A variety of toxicological evaluations are performed to establish the safety of veterinary drug residues in human food. The objective of this guidance is to establish recommendations for an internationally harmonized 90-day repeat-dose testing.

III. Significance of Guidance

This 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.'' Because guidance documents are not binding unless specifically supported by statute or regulation, mandatory words such as ''must,'' ''shall,'' and ''will'' in the original VICH documents have been substituted with ''should'' or ''it is recommended.''

This guidance document represents the agency's current thinking on establishing the safety of veterinary drug residues in human food. This 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.

IV. Comments

As with all of FDA's guidances, the public is encouraged to submit written or electronic comments pertinent to this guidance. FDA will periodically review the comments in the docket and where appropriate, will amend the guidance. The agency will notify the public of any such amendments through a notice in the **Federal Register**.

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this 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 should be identified with the docket number found in brackets in the heading of this document. A copy of the guidance document and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

V. Electronic Access

Persons with Internet access may obtain copies of the guidance document entitled ''Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Repeat-Dose (90-Day) Toxicity Testing'' (VICH GL31), from the CVM home page at *http://www.fda.gov/cvm*.

Dated: October 31, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2003D–0474]

International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products; Draft Guidance for Industry on ''Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Establish a Microbiological Acceptable Daily Intake;'' Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability for comments of a draft guidance document for industry (#159) entitled ''Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Establish a Microbiological ADI'' (VICH GL–36). This draft guidance has been developed for veterinary use by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH).