

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**[Docket No. 2004D-0377]**

**International Conference on Harmonisation; Draft Guidance on E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs; Availability**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled “E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guidance provides recommendations to sponsors concerning clinical studies to assess the potential of a new drug to cause cardiac arrhythmias, focusing on the assessment of changes in the QT/QTc interval on the electrocardiogram as a predictor of risk. The draft guidance is intended to encourage the assessment of drug effects on the QT/QTc interval as a standard part of drug development and to encourage the early discussion of this assessment with FDA.

**DATES:** Submit written or electronic comments on the draft guidance by December 13, 2004.

**ADDRESSES:** Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.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>. Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. The guidance may also be obtained by mail by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800. Send two self-addressed adhesive labels to assist the office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:**

*Regarding the guidance:* Douglas C. Throckmorton, Center for Drug Evaluation and Research (HFD-1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

*Regarding the ICH:* Michelle Limoli, Office of International Programs (HFG-1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4480.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health, Labour, and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada, and the European Free Trade Area.

In June 2004, the ICH Steering Committee agreed that a draft guidance entitled “E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs” should be made available for public comment. The draft guidance is the product of the Efficacy Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the Efficacy Expert Working Group.

The draft guidance provides guidance on the design, conduct, analysis and interpretation of clinical studies to assess the potential of a new drug to cause cardiac arrhythmias, focusing on the assessment of changes in the QT/QTc interval on the electrocardiogram as a predictor of risk. The draft guidance is intended to encourage the assessment of drug effects on the QT/QTc interval, along with the collection of adverse cardiac events related to arrhythmias, as a standard part of drug development, and to encourage the early discussion of this assessment with the FDA. The goal of such discussions is to reach a common understanding of the effects as early in development as practical, with the goal of enhancing the efficiency of data collection later in drug development.

This draft guidance, when finalized, will represent 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 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 draft guidance. 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 draft 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  
<http://www.fda.gov/ohrms/dockets/default.htm>,  
<http://www.fda.gov/cder/guidance/index.htm>, or  
<http://www.fda.gov/cber/publications.htm>.

Dated: September 3, 2004.

**William K. Hubbard,**  
*Associate Commissioner for Policy and Planning.*