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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

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Certifier A. Corbin

[Docket No. FDA-2008-D-0449]

**Draft Guidance for Industry on Integrated Summary of Effectiveness;  
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**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Integrated Summary of Effectiveness.” This draft guidance describes how an integrated summary of effectiveness (ISE) should be prepared by industry for new drug applications (NDAs) and biologics license applications (BLAs). This guidance, when final, will supersede section G, Integrated Summary of Effectiveness Data, of the 1988 guidance on “Format and Content of the Clinical and Statistical Sections of an Application” (Clin-Stat guidance). This guidance also incorporates the conceptual framework of section 2.7.3, Summary of Clinical Efficacy, from the International Conference on Harmonisation (ICH) guidance for industry “M4E The CTD —Efficacy.” This guidance is intended to improve the quality of product applications by describing what efficacy information should be submitted so that FDA can make a regulatory decision on an application.

**DATES:** Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit

written or electronic comments on the draft guidance by [*insert date 60 days after date of publication in the Federal Register*].

**ADDRESSES:** Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002; or the Office of Communication, Training, and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research, 1401 Rockville Pike, Rockville, MD 20852-1448. The guidance may also be obtained from the Center for Biologics Evaluation and Research by mail by calling 1-800-835-4709 or 301-827-1800. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document. Send one self-addressed adhesive label to assist that office in processing your requests.

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.regulations.gov*.

**FOR FURTHER INFORMATION CONTACT:**

Howard Chazin, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6470, Silver Spring, MD 20993-0002, 301-796-0700; or

Leonard Wilson, Center for Biologics Evaluation and Research (HFM-25), Food and Drug Administration, 1401 Rockville Pike, suite 576N, Rockville, MD 20852, 301-827-1053.

**SUPPLEMENTARY INFORMATION:**

## I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Integrated Summary of Effectiveness.” This draft guidance describes how an ISE should be prepared by industry for NDAs and BLAs. The ISE has been required as part of an NDA submission (21 CFR 314.50(d)(5)(v)) since 1985, but the regulation does not describe the specific components of the ISE. The Clin-Stat guidance provides a description of what FDA recommends be included in an ISE. However, since the Clin-Stat guidance was published, several International Conference on Harmonisation guidances, including the ICH guidances for industry “E3 Structure and Content of Clinical Study Reports,” “E10 Choice of Control Group and Related Issues in Clinical Trials,” and “M4E The CTD—Efficacy,” have provided further recommendations for describing individual trials and providing results of efficacy analyses. This guidance, when final, will supersede section G of the Clin-Stat guidance to reflect FDA’s current thinking regarding the format and content of the ISE to provide a truly integrated analysis, rather than a summary of efficacy results from individual clinical trials, and to satisfy FDA regulatory requirements. Although there are no corresponding regulations requiring an ISE for BLA submissions, applicants are encouraged to provide these analyses.

Regarding the common technical document, the ISE is often confused with the document included in Module 2, section 2.7.3, Summary of Clinical Efficacy. Although one of the goals of the ISE is to summarize the available effectiveness data, the ISE primarily is intended to be an integrated analysis of these data, going beyond a simple summary. The focus of the ISE is not on the detailed results of the individual studies, which are described in individual study reports, but a comprehensive, detailed, in-depth analysis that

goes beyond individual study results to examine the basis for the entire approach taken.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on the content and format of the ISE. 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. The Paperwork Reduction Act of 1995**

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR part 314 have been approved under 0910–0001. The collections of information for submission of data in a BLA under 21 CFR 601.2 have been approved under 0910–0338.

## **III. Comments**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this 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. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system.

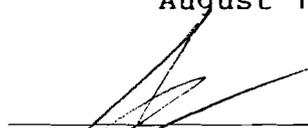
Electronic comments or submissions will be accepted by FDA only through FDMS at <http://www.regulations.gov>.

#### **IV. Electronic Access**

Persons with access to the Internet may obtain the document at <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/cber/guidelines.htm> or <http://www.regulations.gov>.

Dated: 8/19/08

August 19, 2008.



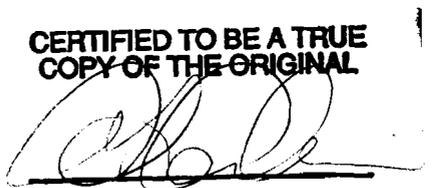
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Jeffrey Shuren,  
Associate Commissioner for Policy and Planning.

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