

[www.fda.gov/dockets/ecomments](http://www.fda.gov/dockets/ecomments). See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:**

Margaret Kober, Center for Drug Evaluation and Research (HFD-580), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4243.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In March 1995, the agency issued a guidance entitled "Guidance for Clinical Evaluation of Combination Estrogen/Progestin-Containing Drug Products Used for Hormone Replacement Therapy of Postmenopausal Women". The agency was revising the 1995 guidance when the results of a substudy of the National Institutes of Health (NIH) Women's Health Initiative (WHI) trial were made available to the public.<sup>1</sup> In light of the interim results of the WHI substudy, on September 10, 2002 (67 FR 57432), the agency withdrew the 1995 guidance. Once finalized, this guidance will replace the 1995 guidance.

In the WHI substudy, postmenopausal women who took conjugated estrogen 0.625 milligram (mg) combined with medroxyprogesterone acetate 2.5 mg had higher risks of several serious adverse events relative to those women who took placebo. Conjugated estrogens alone also increased the rates of cardiovascular disease compared to placebo. Other doses of conjugated estrogens and medroxyprogesterone acetate and other combinations of estrogens and progestins were not studied in the WHI. However, in the absence of comparable data, the risks of serious adverse events should be assumed to be similar because other studies show that estrogens and progestins are associated with these types of events.

This draft guidance revises the 1995 guidance in several ways. For example, the draft guidance no longer uses the phrase "hormone replacement" because neither estrogen alone nor estrogen/progestin treatments for symptoms of menopause should be considered replacement hormones. The guidance only addresses two indications (moderate to severe vasomotor symptoms and moderate to severe vulvar and vaginal atrophy symptoms) and explains under what conditions both indications can be studied concurrently in a single trial. For other indications, such as the prevention of

osteoporosis, sponsors are asked to direct inquiries to the appropriate review division in the Center for Drug Evaluation and Research. A section entitled Primary Endpoints has been added for each indication, and the Study Analysis section has been modified to clarify analyses of the primary endpoints. The Monitoring section for drug products containing estrogen plus progestin has been expanded. The additions to this section were made to address diagnostic ambiguities in the efficacy evaluation for protection of the endometrium.

This level 1 draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance represents the agency's current thinking on recommendations for clinical evaluation of estrogen and estrogen/progestin drug products to treat vasomotor symptoms and vulvar and vaginal atrophy symptoms. 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 Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding the draft guidance. Submit a single copy of electronic comments to <http://www.fda.gov/dockets/ecomments> or two hard copies of any written comments, except that individuals may submit one hard 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 Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

**III. Electronic Access**

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

Dated: January 23, 2003.

**Margaret M. Dotzel,**

*Assistant Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. 01D-0488]

**Guidance for Industry on Food-Effect Bioavailability and Fed Bioequivalence Studies; 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 entitled "Food-Effect Bioavailability and Fed Bioequivalence Studies." This guidance provides recommendations to sponsors and/or applicants planning to conduct food-effect bioavailability (BA) and fed bioequivalence (BE) studies for orally administered drug products as part of investigational new drug applications (INDs), new drug applications (NDAs) and abbreviated new drug applications (ANDAs), and supplemental applications.

**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 Dockets Management Branch (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:**

Ameeta Parekh, Center for Drug Evaluation and Research (HFD-870), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-5919.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a guidance for industry entitled "Food-Effect Bioavailability and Fed Bioequivalence Studies." This guidance document is intended to provide information to sponsors and/or applicants planning to include food-effect BA and fed BE studies for orally

<sup>1</sup> The results of the NIH Women's Health Initiative trial were reported in the *Journal of the American Medical Association*, 288: 321-333, 2002.

administered drug products in INDs, NDAs, ANDAs, and supplemental applications. This guidance provides recommendations for when studies are appropriate, as well as recommendations on study design, data analysis, and product labeling.

In the **Federal Register** of November 28, 2001 (66 FR 59433), FDA published a draft guidance entitled "Food-Effect Bioavailability and Fed Bioequivalence Studies: Study Design, Data Analysis, and Labeling." Based on comments received on the draft guidance and the refinement of agency thinking on the conduct of such studies, FDA has revised the guidance.

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 submitting food-effect BA and fed BE information as part of INDs, NDAs, and ANDAs. 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 statute and regulations.

## II. Comments

Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments on the guidance at any time. Two copies of mailed 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 guidance and received comments are available for public examination in the Dockets Management Branch 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: January 21, 2003.

**Margaret M. Dotzel,**

*Assistant Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Health Resources and Services Administration

#### Agency Information Collection Activities: Proposed Collection; Comment Request

In compliance with the requirement for the opportunity for public comment on proposed data collection projects (section 3506(c)(2)(A) of Title 44, United States Code, as amended by the Paperwork Reduction Act of 1995, Public Law 104-13), the Health Resources and Services Administration (HRSA) publishes periodic summaries of proposed projects being developed for submission to Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995. To request more information on the proposed project or to obtain a copy of the data collection plans and draft instruments, call the HRSA Reports Clearance Officer at (301) 443-1129.

Comments are invited on: (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) ways to enhance the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology.

#### Proposed Project: Ryan White CARE Act: Title III Client-level Demonstration Project (CDP)—New

The CDP was originally established in 1994 to collect information from grantees and their subcontracted service providers funded under Titles I and II of the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act of 1990, as amended by the Ryan White CARE Act Amendments of 1996 (codified under Title XXVI of the Public Health Service (PHS) Act). This new effort will collect client level data from

a sample of Ryan White CARE Act Title III Grantees. The HRSA's HIV/AIDS Bureau administers funds for all titles of the CARE Act. The Title III program is authorized by Section 2651 of the PHS Act.

The PHS Act specifies that HRSA is responsible for the administration of grant funds, the allocation of funds, the evaluation of programs for the population served, and the improvement of the quantity and quality of care. Accurate records on the grantees receiving CARE Act funding, the services provided, and the clients served are critical to the implementation of the legislation and thus are necessary for HRSA to fulfill its responsibilities.

Client level information will be collected from a sample of Title III CARE Act funded grantees regarding the number of clients served, services provided, demographic information about clients served, and health status of clients served. In addition, client level information will be collected that measures mortality status and additional indicators of health status and whether standards of care are being followed by providers.

The primary purposes of the CDP are to examine client level demographic and service data on HIV/AIDS infected/affected clients being served by the Ryan White CARE Act and demonstrate the usefulness of these data for planning and evaluation purposes at both the local and national levels. Through this system, HRSA seeks to supplement the information collected in the CARE Act Data Report (CADR). Because there is no nationwide acceptance of client level reporting for HIV/AIDS services, the CADR collects data aggregated at the grantee level and contains duplicated counts of clients who have received services from more than one provider during a given reporting period.

Based on data from eligible grantees, the number of clients that a grantee serves ranges from 125 to 2748, with 422 being the median number of clients. About 30 minutes is required to respond to these questions and the data are collected 4 times a year.

The burden estimate for this project is as follows:

Grantee	Number of respondents	Responses per respondent	Total responses	Burden hour per respondent	Total burden hours
<500 Clients .....	15	250	3,750	2	7,500
500+ Clients .....	10	1,232	12,320	2	24,640
Total .....	25	.....	16,070	.....	32,140