

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N-0064]

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Certifier L. CLAWSON  
DDM

**Electronic Case Report Form Submission; Notice of Pilot Project**

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

**ACTION:** Notice.

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**SUMMARY:** The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration (FDA) are seeking sponsors interested in participating in a pilot project to test the submission of case report form (CRF) data provided electronically in extensible markup language (XML) based on the Operational Data Model (ODM) developed by the Clinical Data Interchange Standards Consortium (CDISC). This pilot will test the ability of a new data format to support all review activity, which our current submission format is incapable of doing. Data supplied in ODM format by sponsors during the pilot project will not replace any regulatory requirements for submitting CRFs. We anticipate that a successful pilot will allow CDER and CBER to routinely accept CRFs from studies employing electronic data capture (EDC) in ODM format in marketing applications provided in electronic format.

**DATES:** Submit written or electronic requests to participate in the pilot project by *[insert date 180 days after date of publication in the Federal Register]*.

General comments on the pilot project are welcome at any time.

**ADDRESSES:** Submit written requests to participate and comments regarding this pilot project 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>.

**FOR FURTHER INFORMATION CONTACT:** Armando Oliva, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6310, Silver Spring, MD 20993-0002, 301-796-0514.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the opportunity to participate in a pilot project being conducted by CDER and CBER involving the testing of the ODM standard developed by the CDISC, with the goal of replacing the existing portable document format (PDF)-based CRFs derived from clinical trials that use EDC and, therefore, lack paper CRFs. CDISC is an open, multidisciplinary, nonprofit organization that has established worldwide industry standards to support the electronic acquisition, exchange, submission, and archiving of clinical trial data and metadata for medical and biopharmaceutical product development (<http://www.cdisc.org>).

Under existing Federal regulations (21 CFR 314.50), applicants must provide CRFs with a marketing application. Since November 1997, under 21 CFR part 11, we have accepted CRFs in electronic format instead of paper. FDA has issued several guidances that provide recommendations concerning electronic submissions. In the **Federal Register** of October 19, 2005 (70 FR 60842), FDA announced the availability of a guidance entitled "Providing Regulatory Submissions in Electronic Format—Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications" (<http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/cber/gdlns/esubapp.htm>). In section III.E.3. of that guidance, FDA recommends that

applicants submit an individual subject's complete CRF as a single, PDF file. The guidance recommends that if a paper CRF was used in the clinical trial, the submitted CRF should be a scanned image of the paper CRF, including all original entries with modifications, addenda, corrections, comments, annotations, and any extemporaneous additions (i.e., audit trail). The guidance further recommends that if EDC was used in the clinical trial, the applicant should submit a PDF-generated form or other PDF representation of the information (e.g., subject profile).

Based on our experience, PDF-based CRFs from clinical trials that employ EDC are not ideal to support all review activity. Although the PDF-based CRFs for trials that use EDC can provide a record of the observations collected during the trial (i.e., the data) and additional information about what was collected (metadata), they typically do not provide an audit trail. CDER and CBER are interested in adopting a new, standard format that can replace the PDF-based CRF and that can reliably provide all three components of the CRF in an electronic format: Data, metadata, and audit trail.

The ODM is an XML-based standard that facilitates the electronic exchange of clinical trial data, metadata, and audit trail. We are working with CDISC to develop the capabilities within CDER and CBER to review CRFs using ODM. CDISC employed the current production version (Version 1.2) of the ODM on the CDISC Web site, and we performed some initial testing of limited CRF data in ODM. To help in this development, we are launching this pilot project and seeking sponsors willing to provide CRFs in ODM format to test our capabilities to review these files. However, data supplied during the pilot project will not replace any regulatory requirements for submitting CRFs.

The purpose of this pilot project is to obtain additional experience with ODM-based CRFs. We anticipate that a successful pilot will allow CDER and CBER to routinely accept CRFs from studies that employ EDC in ODM format in marketing applications submitted in electronic format.

## **II. Pilot Project Description**

This pilot project is part of an effort to improve the quality of CRFs provided to CDER and CBER in electronic format and to improve the centers' capability to review these files. Eventually, CDER and CBER expect to recommend new technical specifications for the submission of CRFs that are derived from clinical trials that employ EDC and, therefore, lack paper CRFs.

### *A. Initial Approach*

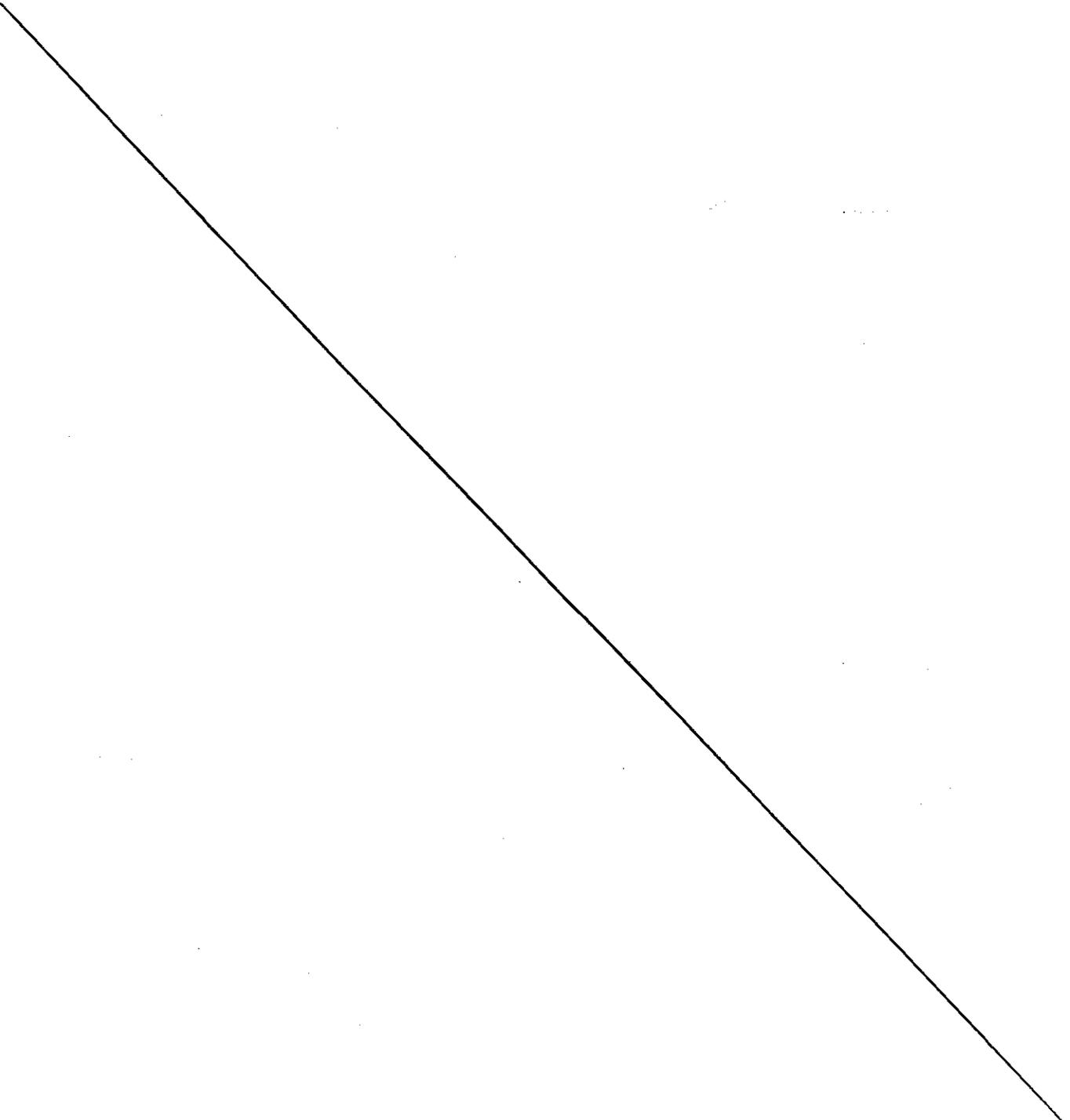
Because only a limited number of sponsors are needed (i.e., approximately five), CDER and CBER will use their discretion in choosing participants, based on participants' previous experience submitting CRFs in accordance with existing guidance. Participants should be willing to provide the same CRFs in two formats: PDF, in accordance with existing guidance, and ODM. If PDF-based CRFs have already been submitted as part of an existing new drug application or biologics license application on file with the agency, then participants need only provide the ODM-based CRFs with the same information. Having the same information available in both PDF and ODM provides the best opportunity to compare the two formats.

### *B. How to Participate*

Written requests to participate in the pilot project should be submitted to the Division of Dockets Management (see **ADDRESSES**). Requests are to be identified with the docket number found in brackets in the heading of this document.

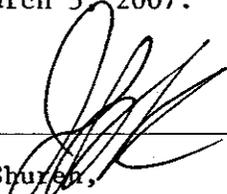
### III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this pilot project. 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.

Dated: 3/5/07  
March 5, 2007.

  
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Jeffrey Shuren,  
Assistant Commissioner for Policy.

[FR Doc. 07-????? Filed ??-??-07; 8:45 am]

**BILLING CODE 4160-01-S**

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