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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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Certifier D. Hawkins

[Docket No. 2007N-0343]

Electronic Nonclinical Study Data Submission; Notice of Pilot Project

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Center for Drug Evaluation and Research (CDER) is seeking sponsors interested in participating in a pilot project to test, in a regulatory setting, the electronic submission of nonclinical study data using the Standard for Exchange of Nonclinical Data (SEND). The purpose of this pilot is to test the ability of a new electronic data format to support nonclinical review activity. The pilot also will involve a collaboration of FDA, available pilot participants, and the SEND Consortium to update and create a new draft SEND implementation guide. FDA anticipates that a successful pilot will enable CDER to routinely accept nonclinical study data electronically in SEND format, instead of paper or portable document format (PDF), in investigational new drug applications (INDs), new drug applications (NDAs), and biologics licensing applications (BLAs).

DATES: Submit written or electronic requests to participate in the pilot project by *[insert date 90 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

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Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Bobbie Witczak, Food and Drug Administration, 5600 Fishers Lane HFD-070, Rockville, MD 20857, 301-827-3938.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing an opportunity to participate in a 3-year pilot project in a regulatory setting being conducted by CDER involving the ongoing testing of SEND, a nonclinical data model developed by the Clinical Data Interchange Standards Consortium (CDISC). The ultimate goal of the pilot is to replace the existing paper/PDF-based listings of nonclinical study data.

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>). CDISC is currently facilitating the extension of the same standard for nonclinical data, termed SEND, through the efforts of the SEND Consortium. Where possible, the standards developed for clinical datasets and metadata, as described in the overall Study Data Tabulation Model (SDTM), are being used to develop a standardized dataset format for nonclinical studies.

Under current regulations, applicants must provide tabulated nonclinical data from animal toxicity studies as part of NDA (21 CFR 314.50) and IND (21 CFR 312.23) applications. In a guidance for industry titled "Providing Regulatory Submissions in Electronic Format—Human Pharmaceutical Product Application and Related Submissions Using the eCTD Specifications," FDA

makes recommendations about how to submit documents in electronic format to INDs, BLAs, and NDAs using the electronic common technical document (eCTD) specifications. CDER currently receives nonclinical study data either on paper or as electronic PDF files. These formats do not support the agency's ability to easily receive, validate, display, or evaluate the data using modern, computer-based review and analysis tools. As part of FDA's effort to modernize its information technology systems and improve efficiency, the agency is planning to transition from the traditional paper/PDF formats to a true electronic data format for submission of nonclinical data for regulatory review.

Recently, CDER has adopted a standard for clinical study data based on the CDISC SDTM standard. In addition, CDER entered into a CRADA (cooperative research and development agreement) with PharmQuest Corporation, Inc., for the development of data validation, viewing, and analysis tools to evaluate standardized nonclinical datasets based on SEND. The FDA believes the use of standardized SEND datasets, together with new and better analysis tools, will increase the efficiency of agency review and evaluation of nonclinical data.

CDER recently completed a related pilot project (phase 1) that asked for volunteers from industry to submit sample nonclinical datasets in the SEND format outside of a regulatory setting (68 FR 3885; January 27, 2003). The phase 1 pilot also evaluated data validation and analysis tools specifically designed to validate datasets according to the current SEND standard and to enable a reviewer to efficiently display and evaluate data from animal toxicity studies submitted in the SEND format. The phase 1 pilot resulted in development of a SEND Implementation Guide (Version 2.3; November 2005), which is available on the CDISC Web site (<http://www.cdisc.org/models/send/v2.3/>)

SENDV2.3ImplementationGuide.pdf). The SEND Implementation Guide describes the process for formatting nonclinical data from single- and repeat-dose animal toxicity and carcinogenicity studies for submission purposes. The pilot also resulted in the development of specialized software tools for validating, displaying, and analyzing SEND-formatted nonclinical data.

As a continuation of this testing process, this new pilot (phase 2) will enable FDA to evaluate animal toxicity data submitted in SEND format in a regulatory setting by comparing SEND-formatted data provided electronically as SAS transport file (XPT version 5) datasets with data provided in PDF.

In addition, in the intervening time period between the publication of the SEND implementation guide version 2.3 (November 2005) and now, some changes have been made to the SDTM for clinical data, making it desirable to update the SEND implementation guide to ensure harmonized implementation of the CDISC study data standard across both clinical and nonclinical data. There is also a plan to expand the SEND implementation guide to include a pharmacokinetics domain, more detailed implementation examples, and, eventually, other nonclinical study types. As a result, FDA will not conduct the pilot using the existing SEND implementation guide version 2.3. Instead, phase 2 will include an initial collaboration among FDA, available pilot participants, and the SEND Consortium to update and create a new draft SEND implementation guide before FDA receives any datasets for regulatory review. The current status of both the pilot project and the draft SEND implementation guide can be found on the FDA SEND Web page at <http://www.fda.gov/oc/datacouncil/send.html>. Before creating and submitting nonclinical datasets, pilot participants should ensure that they use the most recent draft version of the SEND implementation guide.

II. Pilot Project Description

This pilot project is part of an ongoing effort to improve the efficiency of the review of nonclinical data within CDER. Eventually, as experience from the ongoing pilot is gained with various types of nonclinical studies, CDER expects to recommend new technical specifications as part of a continuing process for the submission of nonclinical study data provided electronically and eliminate the need to provide paper/PDF-based data listing.

A. Approach

CDER is seeking a limited number of sponsors (i.e., approximately five to eight) to participate in the phase 2 pilot. The duration of the pilot is expected to be approximately 3 years, but it may be extended as needed. Participants should be familiar with SEND (e.g., from involvement in the phase 1 pilot) and be willing to provide the same nonclinical study data in both PDF and SEND formats to an existing IND. The PDF must comply with all applicable regulations, including those in part 11 (21 CFR part 11)¹. To achieve the goals of the pilot, FDA intends to exercise additional enforcement discretion with regard to part 11 requirements as applied to data submitted in SEND format under this pilot. That is, we do not intend to take enforcement action against data submitted in SEND format, under this pilot, to enforce compliance with those portions of part 11 that remain in effect. The SAS transport files (version 5) should be based on the SEND format. Having the same data available in both PDF and SEND formats provides the best opportunity to compare the two and evaluate the accuracy and reliability of the SEND format. Although the PDF version will continue to be the version used for archival purposes during the pilot, both data formats (i.e., PDF and

¹ See, "Guidance for Industry; Part 11, Electronic Records; Electronic Signatures—Scope and Application," August, 2003; <http://www.fda.gov/Cder/guidance/5667fnl.htm>

SEND) will be used by FDA for regulatory review purposes. Before receiving any SEND data, FDA and pilot participants will work with the SEND Consortium to update the SEND implementation guide, which will then be used during the pilot.

For the purposes of this phase 2 pilot, full study reports of the following types of animal toxicity studies will be requested for submission to an existing IND in the appropriate CDER review division: (1) Repeat-dose toxicity studies of 14 days duration to 12 months duration in any species, (2) life-time carcinogenicity studies in rats or mice, or (3) 6-month carcinogenicity studies in transgenic mice. Studies should include toxicokinetic data, if available. For submission of carcinogenicity studies, the appropriate CDER and International Conference on Harmonization (ICH) guidances should be consulted. The submission should contain both the “Tumor Dataset for Statistical Analysis” (i.e., tumor.xpt, as described in Appendix 1 of the Study Data Specifications document; version 1.3; dated 2006–11–27) as well as the SEND-formatted datasets for the entire study. Depending on the ongoing efforts of the SEND Consortium to expand the SEND implementation guide, additional nonclinical study types may be piloted in the future. If so, FDA will post on the FDA SEND Web page an updated list of study types the agency will accept in this and any future pilots. We anticipate that a successful phase 2 pilot, which includes implementation of any needed changes to the SEND implementation guide and/or the data validation, viewing, and analysis tools, will allow CDER to routinely accept specific types of nonclinical study data provided electronically as SAS transport file (XPT version 5) datasets based on the SEND format. In the case of carcinogenicity studies, a successful phase 2 pilot will enable submission of the entire carcinogenicity study data in the electronic

SEND format, thus eliminating the need for a separate submission of the electronic tumor dataset (i.e., tumor.xpt).

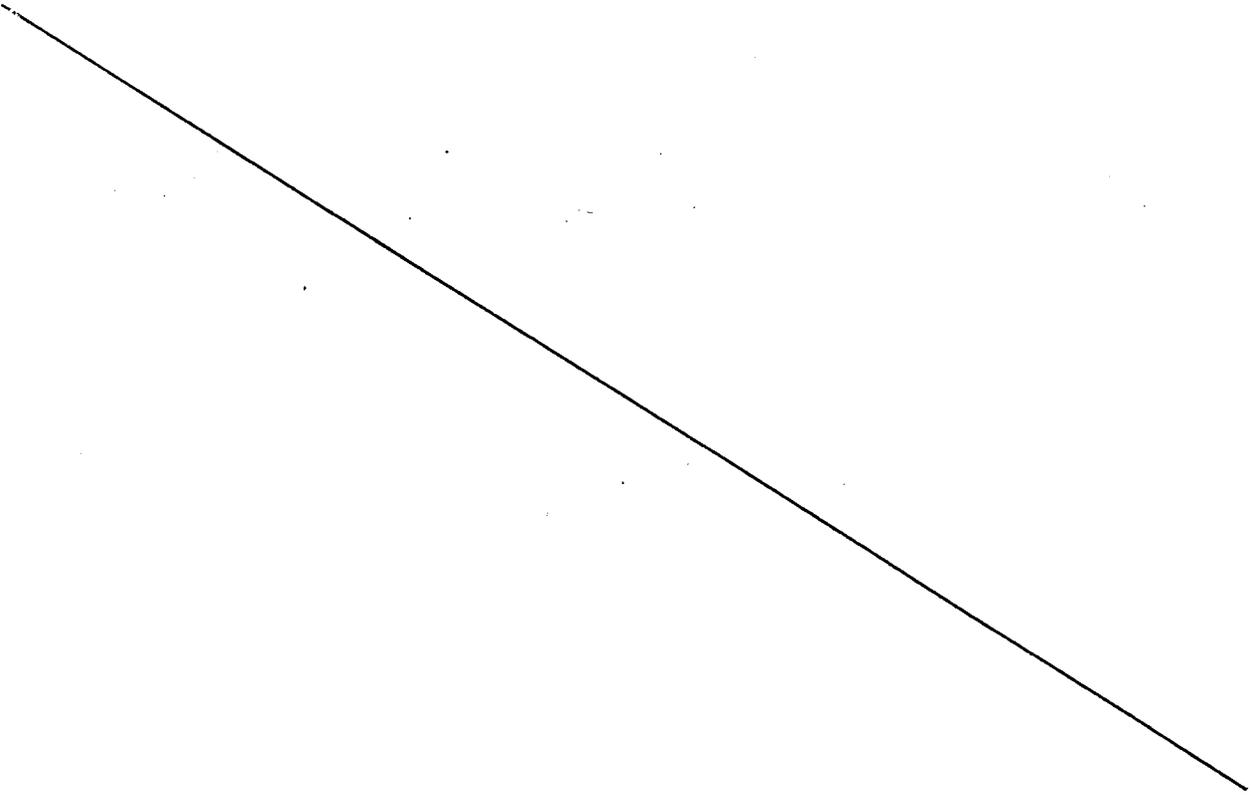
B. How to Participate

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.

As mentioned above, it is recommended that interested participants be familiar with SEND and/or have been involved in the previous phase 1 pilot.

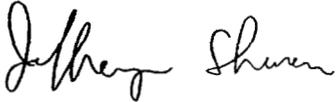
III. Comments

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: SEP 26 2007
September 26, 2007.



Jeffrey Shuren,
Assistant Commissioner for Policy.

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