

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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9-28-06  
9-29-06  
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[Docket Nos. 1999D-0054, 2001D-0475, and 2003D-0364] (formerly Docket Nos. 99D-0054, 01D-0475, and 03D-0364, respectively)

**Guidances on Providing Regulatory Submissions in Electronic Format;  
Withdrawal of Guidances**

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

**ACTION:** Notice; withdrawal.

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**SUMMARY:** The Food and Drug Administration's (FDA) Center for Drug Evaluation and Research is announcing the withdrawal of three guidances for industry: "Providing Submissions in Electronic Format—NDAs," "Providing Regulatory Submissions in Electronic Format—ANDAs," and "Providing Regulatory Submissions in Electronic Format: Annual Reports for NDAs and ANDAs." These guidances are being withdrawn because they are no longer consistent with more recent guidance and no longer reflect the agency's preferred format for receiving electronic submissions.

**DATES:** [*Insert date of publication in the Federal Register*].

**FOR FURTHER INFORMATION CONTACT:** Armando Oliva, Center for Drug Evaluation and Research (HF-18), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1512, e-mail: *armando.oliva@fda.hhs.gov*, or

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**SUPPLEMENTARY INFORMATION:**

## I. Background

During the past decade, FDA has been working to expand its ability to receive and review marketing applications electronically. In addition, the agency has been working through the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) to harmonize the formats being used for marketing applications.

Beginning in 1999, FDA issued two guidances and one draft guidance for industry that made recommendations to applicants wishing to submit applications to FDA in electronic format: (1) "Providing Regulatory Submissions in Electronic Format—NDAs" (e-NDA guidance) (64 FR 4432, January 28, 1999), (2) "Providing Regulatory Submissions in Electronic Format—ANDAs" (e-ANDA guidance) (67 FR 43331, June 27, 2002), and (3) "Providing Regulatory Submissions in Electronic Format—Annual Reports for New Drug Applications and Abbreviated New Drug Applications" (draft) (68 FR 51788, August 28, 2003). In general, these guidances recommended submitting documents as portable document files (PDF), electronic data/case report tabulations as SAS transport files, and the NDA table of contents in PDF format. In the meantime, however, the FDA adopted the ICH Common Technical Document (CTD) headings and subheadings for marketing applications. ICH then issued specifications for the electronic version of the CTD (e-CTD).

In October 2005, FDA issued the guidance "Providing Regulatory Submissions in Electronic Format—Human Pharmaceutical Product Applications and Related Submissions Using the e-CTD Specifications" (the e-CTD guidance) (70 FR 60842; October 19, 2005). This guidance differs from

the e-NDA and e-ANDA guidances in one significant aspect: The application table of contents is no longer submitted as a PDF file, but is submitted as an XML (extensible markup language) file. This XML file has numerous advantages over the older PDF format, most significant of which is the ability to update the application table of contents automatically as new amendments are received. With the e-CTD format, sponsors and reviewers now have access to a real-time, up-to-date, cumulative table of contents that provides easy and immediate access to all files included in an application, regardless of when they were included, or in what submission they are located. This has never previously been possible. Another advantage is that the table of contents can be displayed in various ways, allowing discipline-specific views of an application, further promoting review efficiency. This is especially important for agency review staff. For example, although all portions of an application are always available to all reviewers, a chemist would be interested in different portions of the application than a clinical reviewer. The XML table of contents permits reviewers to view the application in a manner that makes the most sense to support their particular review activity.

Despite the release of the e-CTD guidance describing the use of the XML format, FDA has continued to make all three guidances available with their differing recommendations. As a result, applicants have had three choices when submitting a marketing application electronically: (1) Use the e-NDA/e-ANDA format, (2) use the e-CTD format, or (3) use what we call a "hybrid" submission (the older e-NDA format with the table of contents organized using the newer CTD headings). In addition, FDA still receives submissions that are a combination of paper and electronic formats. Of course, this would not be appropriate for sponsors who are using the e-CTD format, as doing this would

negate the intent of having all portions of the application readily available for review via the XML table of contents. A result of having this variety of choices is confusion and frustration for industry, who are not receiving consistent recommendations about how to submit marketing applications. It is also confusing and frustrating for our review staff. In addition, our willingness to receive applications in a variety of different forms has forced the agency to maintain expensive and duplicative processes and systems for receiving and archiving these various application types.

## **II. Withdrawal of Guidances**

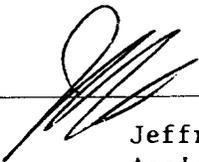
The e-CTD format is preferred by FDA because it is more efficient than the other choices and consistent with FDA's technical capabilities. The e-CTD format is also the preferred ICH format. As a result, the agency is withdrawing the earlier guidances. In addition, we will remove references to these guidances from the electronic submissions docket on December 31, 2007. Further information on providing regulatory submissions in electronic format can be found on Docket No. 1992S-0251 (formerly Docket No. 92S-0251) (<http://www.fda.gov/ohrms/dockets/dockets/92s0251/92s0251.htm>). We are recommending that sponsors wishing to submit applications electronically use the most efficient and internationally agreed to formats recommended in our most recent guidance.

Although the Center for Biologics Evaluation and Research (CBER) supports the use of the e-CTD format and encourages its sponsors to use this format when creating its submissions, CBER also recognizes that in certain situations a sponsor may not be capable of providing submissions in that format at this time. Therefore, CBER recommends that sponsors who cannot use the e-CTD format consult guidance for industry "Providing Regulatory

Submissions to the Center for Biologics Evaluation and Research (CBER) in  
Electronic Format—Biologics Marketing Applications [Biologics License  
Application (BLA), Product License Application (PLA) / Establishment License

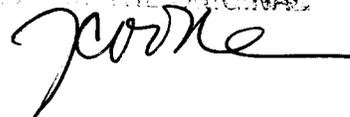
Application (ELA) and New Drug Application (NDA)] (11/12/1999) (available online at <http://www.fda.gov/cber/esub/esubguid.htm>).

Dated: 9/22/06  
September 22, 2006.



Jeffrey Shuren,  
Assistant Commissioner for Policy.

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[FR Doc. 06-????? Filed ??-??-06; 8:45 am]

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