Instructions for Submitting Protocols Intended for Electronic Submissions

In order to begin submitting documents electronically to the FDA, CTEP/PIO is providing instructions to you, the protocol authors, on the formatting of protocol documents. CTEP/PIO encourages the use of the formatted Protocol Template and the submission of protocols as MS Word documents rather than files already converted to Portable Document Format (PDF). A 2007 MS Word version of the Protocol Template (and its instructions for use) is available on the CTEP website; following this template will ensure that the formatting requirements are met.

FDA requires that the Protocol Document and Informed Consent Document (ICD) are submitted as two separate electronic files. Additionally for amendments, the accompanying change memo must be the first page of the Protocol or IC Document. The change memo must have hyperlinks to the affected section of the Protocol or ICD.

If you will be using your own MS Word protocol template, please note that the final MS Word document when converted to PDF should be compliant with PDF file requirements specified in FDA guidelines summarized below. MS Word offers a variety of formatting options and methods; please refer to the user manual for version-specific instructions.

CTEP cannot accept MS Word files that:

- are read-only
- are password protected
- contain macros
- are saved with a file extension other than .doc or .docx

If you will be submitting your protocols in PDF format, you are required to follow the instructions below.

CTEP cannot accept Portable Document Format files that are:

- password protected
- saved as portfolios
- saved in a subset format (PDF/A, PDF/X, FDF, etc.)
- saved with attachments

1. PDF Format Specifications

- Use PDF versions 1.4 through 1.7, which are for use with Adobe Acrobat 5.0 or higher.
- Create PDF files from source documents using the “Optimize the PDF for fast web view” option to reduce file sizes and opening times.
- All PDF files should be text-based (created directly from an electronic source such as a word processing file) rather than image-based (scanned paper source document). Image-based documents are more difficult to read and cannot be electronically searched.

- If necessary, scan paper source documents at resolution that will ensure the pages are legible both on the screen and when printed. To balance legibility and file size, the recommended resolution for black ink is 300 dpi; b/w photographs – 600 dpi (8 bit gray scale); and color photographs – 600 dpi (24 bit RGB). After scanning, avoid re-sampling to a lower resolution.
- Embed all fonts used in the PDF file to ensure that they are available to the reviewer. Since font embedding does not always solve the problems that occur when a reviewer tries to paste text from a PDF document into another software format, limit fonts to those listed below:

Font Type	**Font Name**
Sans Serif	Arial
	Arial Italic
	Arial Bold
	Arial Bold Italic
Non proportional	Courier New
	Courier New Italic
	Courier New Bold
	Courier New Bold Italic
Serif	Times New Roman
	Times New Roman Italic
	Times New Roman Bold
	Times New Roman Bold Italic
Other	Symbol
	Zapf Dingbats

- Use font sizes between 9 and 12 points. Times New Roman, 12-point font is recommended for narrative text; point sizes 9-10 are recommended for tables; 10-point fonts are recommended for footnotes. Smaller point sizes should be avoided.
- Black is the recommended font color except that blue can be used for hypertext links. Avoid light colors since they do not print well on grayscale printers.

2. Page Layout

- Pages should be properly oriented. For example, you should set the page orientation of landscape pages to landscape prior to saving the PDF document in final form to ensure correct page presentation.
- The print area for pages should fit on a sheet of paper that is 8.5” by 11”. Allow a margin of 1” on all sides. Header and footer information should not appear within 3/8” of the edge of the page.
- Number the initial page of the document as page one (1) so the page numbers for the document and the PDF file are the same.

3. PDF Bookmarks, Hypertext Links, and Thumbnails

- Use hypertext links throughout the body of the document to link to related sections, references, appendices, tables, or figures that are not located on the same page as the narrative text. Hypertext links can be designated by blue text. Using relative paths when creating hypertext links minimizes the loss of hyperlink functionality when the document is moved to a different location.
- For documents with a table of contents (TOC), provide bookmarks and hypertext links for each item listed in the table of contents. Make the bookmark hierarchy identical to the TOC. CTEP expects the bookmarks at least at the second level headers (i.e., 1.1).
- PDF documents do not need embedded thumbnails.
- Set the Navigation Tab to open to "Bookmarks Panel and Page" as initial document view option.

4. PDF File Submission

- In order to reduce file size, use the following lossless file compression methods: Zip/Flate or CCITT Group 4.
- Use lower case characters and avoid using special characters, except hyphens and underscores, in file names. Special characters to avoid include punctuation, spaces, or other non-alphanumeric symbols (e.g., \ / : * ? < > | " % # +).
- Submit each document (e.g., protocol, informed consent form) as a separate PDF file. For revisions and amendments, the change memo must be the first page of each document, with hyperlinks to the corresponding change in the document.

References:

1. FDA PDF Specification: Portable Document Format Specifications, Version 3.1 http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163565.pdf

2. Final Guidance for Industry: Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions Using the eCTD Specifications , June 2008 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072349.pdf