Preparing Protocol Documents for eCTD Submissions to the FDA

In order to submit documents electronically to CBER and CDER, FDA, CTEP/PIO is providing instructions to you, the protocol authors, on the formatting of protocol documents. CTEP/PIO encourages the use of the Protocol and Informed Consent templates available on the CTEP website (http://ctep.cancer.gov/protocolDevelopment/templates_applications.htm) and the submission of protocol documents in MS Word format rather than in Portable Document Format (PDF).

FDA requires that the Protocol and Informed Consent documents are submitted as two separate electronic files. If you will be using your own MS Word protocol/informed consent templates, please note that the final MS Word documents when converted to PDF format 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 documents that are:

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

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

CTEP cannot accept PDF documents that are:

- password protected or have any security settings
- saved as portfolios
- saved with attachments, annotations, JavaScript, or dynamic content

1. **PDF Format Specifications**

- Use PDF versions 1.4 through 1.7.
- 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 documents should be text-based (created directly from an electronic source such as MS Word) 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.

NCI CTEP Protocol and Information Office
November 2015

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- Fully 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 document format, limit fonts to those listed below:

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

- Use font sizes ranging from 9 to 12 points. Times New Roman, 12-point font is recommended for narrative text; point sizes 9-10 are recommended for tables and 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.
- Avoid using image-based graphics as they will not be searchable when converted to PDF. If images are used, they should be high resolution.

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"x11" (landscape: 11"x8.5"). Allow a margin of at least 3/4" (preferably 1") on all sides. Header and footer information should not appear within 3/8" from the edge.
- Set tables to a maximum width of 6.5" (landscape: 9").

- Use *Insert Page Number* function to add consecutive page numbers to each document, including appendices. Use Roman numerals (I, II, III, IV, etc) for the Change Memo/Summary of Changes and Arabic numerals (1, 2, 3, 4) for the document's main content.

3. PDF Bookmarks, Hypertext Links, and Thumbnails

- PDF documents do not need embedded 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. Use *Insert Hyperlink/Link to Place in This Document* to ensure that links have relative paths. Hypertext links can be designated by blue or blue-underlined text. A consistent method of designating links in a document avoids confusion.
- Include a hypertext linked Table of Contents (TOC) and bookmarks in documents 5 pages or longer. Provide bookmarks for each item listed in the TOC. Make the bookmark hierarchy identical to the TOC. CTEP expects the bookmarks at least at the second level headers (i.e., 1.1). Include a Bookmark for the Title Page, Table of Contents, and Schema.
- Set the Navigation Tab to open to *Bookmarks Panel and Page* as initial document view option, and the Page Layout and Magnification to *Default*.
- Set the magnification of bookmarks to *Inherit Zoom*.

4. PDF File Submission

- Submit each document (e.g., protocol, informed consent) as a separate PDF file. For revisions and amendments, the Change Memo/Summary of Changes must be included at the beginning of the document and have hypertext links to the corresponding affected document Sections.

References:

1. FDA PDF Specification: Portable Document Format Specifications, Version 4.0
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

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