

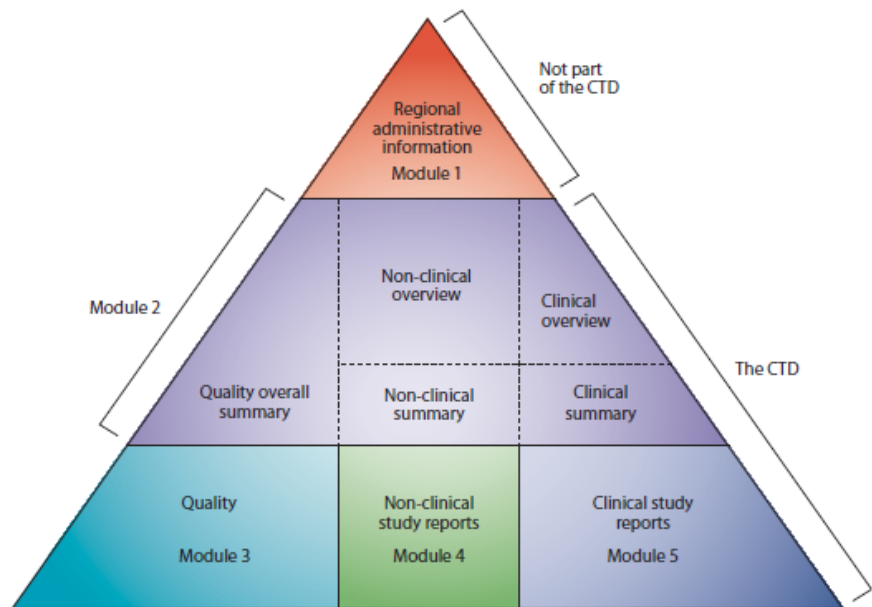
# Preparing Protocol Documents for eCTD Submissions to the FDA

November 2015



# What is eCTD?

- Electronic transfer of information to the FDA based on Common Technical Document (CTD) format.
- eCTD is the only acceptable format for electronic submissions to CDER and CBER.
- Set of PDF documents linked via XML backbone.
- Relies on formatted files, hyperlinks and bookmarks for ease of navigation.



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

# eCTD Style Guide

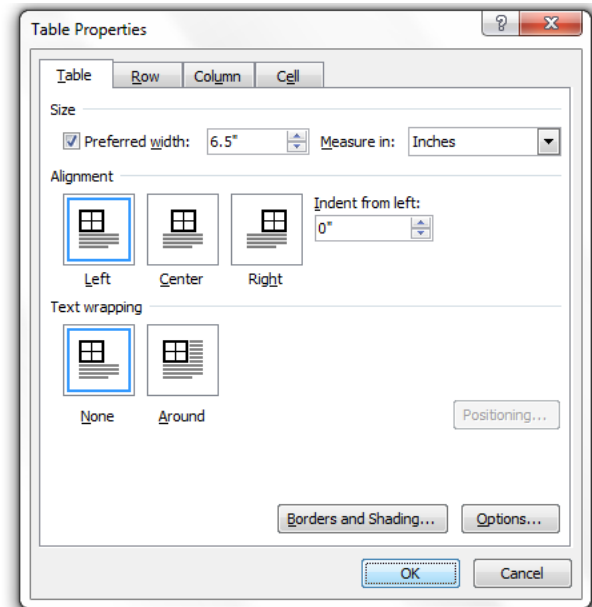
- FDA has specific requirements for the formatting of eCTD documents, including content appearance as well as electronic navigation (PDF Bookmarks and hypertext links).
- FDA requires that the Protocol and Informed Consent documents are submitted as two separate electronic files.
- CTEP would like to encourage the use of the formatted Protocol and Informed Consent templates available at [http://ctep.cancer.gov/protocolDevelopment/templates\\_applications.htm](http://ctep.cancer.gov/protocolDevelopment/templates_applications.htm) and the submission of protocol documents in MS Word format rather than PDF.
- CTEP templates ensure fonts, margins, page orientation, header and footer information, and heading styles are correct and suitable for eCTD submission.

# eCTD – MS Word Format Specifications (1)

- 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 and summarized on the following slides.
- CTEP cannot accept MS Word files that are:
  - ✓ read-only
  - ✓ password-protected
  - ✓ contain macros
  - ✓ saved with a file extension other than .doc or .docx
- 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.

# eCTD – MS Word Format Specifications (2)

- The print area for pages should fit on a sheet of paper that is 8.5” x 11” (landscape: 11” x 8.5”). 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** to add consecutive page numbers to each document, including appendices.
- Use Roman numerals (I, II, III or I, ii, iii, etc.) for the Change Memo/Summary of Changes and Arabic numerals (1, 2, 3, 4) for the document’s main content.

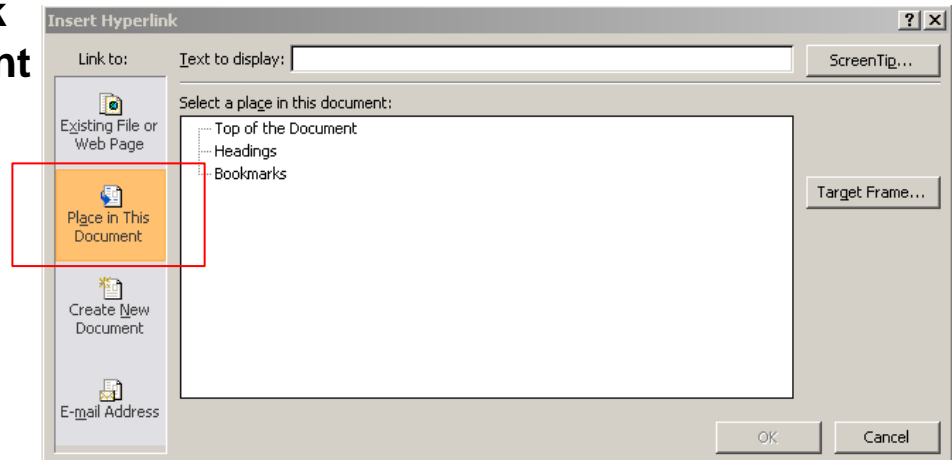


# eCTD – MS Word Format Specifications (3)

- 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](#) or [blue underlined](#) text. A consistent method of designating links avoids confusion.

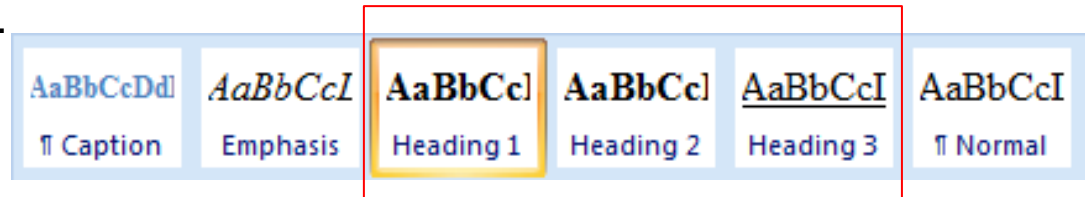
The patient will be requested to maintain a medication diary (see [Appendix F](#)) of each dose of medication. The medication diary will be returned to clinic staff at the end of each course. Patients will be instructed to record doses as they take them (and not to batch entries at a later time) and how to correct errors if they occur.

- Use **Insert Hyperlink/Link to Place in This Document** to ensure that links have relative paths.



# eCTD – MS Word Format Specifications (4)

- Use Word **default Heading Styles** for your document's headings, i.e., Heading 1, Heading 2, etc. Always start with Heading 1 as the top level heading. Include at least two and up to three levels of headings in the protocol document.



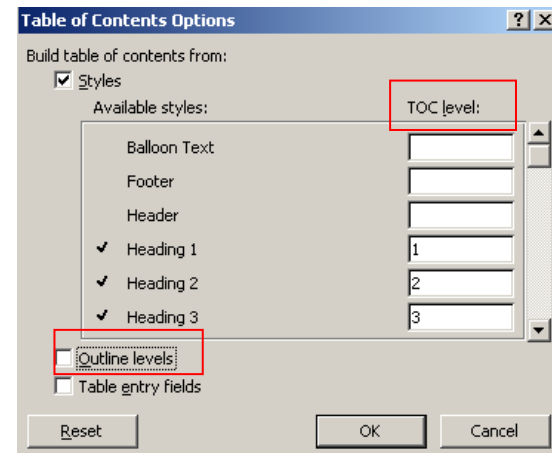
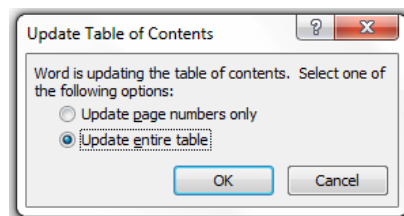
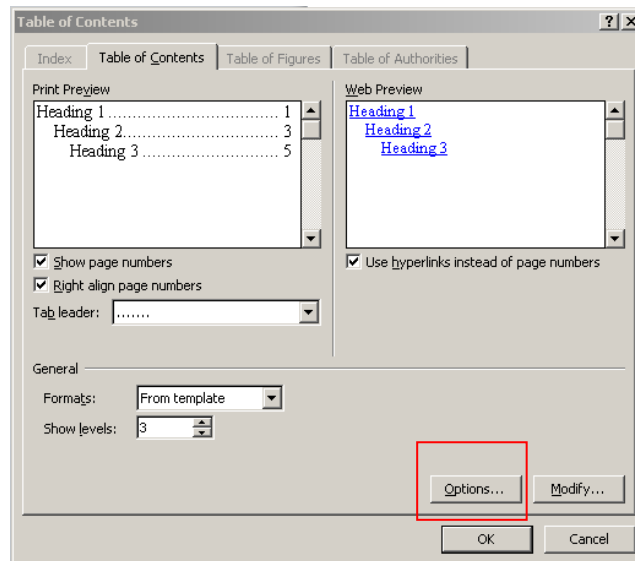
<b>BACKGROUND</b>	→	<b>Heading 1</b>
<b>Introduction/Rationale for Development</b>	→	<b>Heading 2</b>
<i>Antitumor Activity</i>	→	<b>Heading 3</b>

To modify the default font formatting (font type/size/color, etc.), so that it matches your document's formatting:

1. Highlight the paragraph where you want to apply the Heading Style.
2. Right-click the appropriate Heading (e.g., Heading 1) in the *Quick Style Gallery*. Note: If it is not displayed, find it in *Styles* (Alt+Ctrl+Shift+S).
3. Click on *Update Heading 1 to Match Selection*.

# eCTD – MS Word Format Specifications (5)

- Include a Table of Contents in every document that is 5 or more pages long. Use **Insert Table of Contents** to create the TOC. Update the TOC after you make content changes.



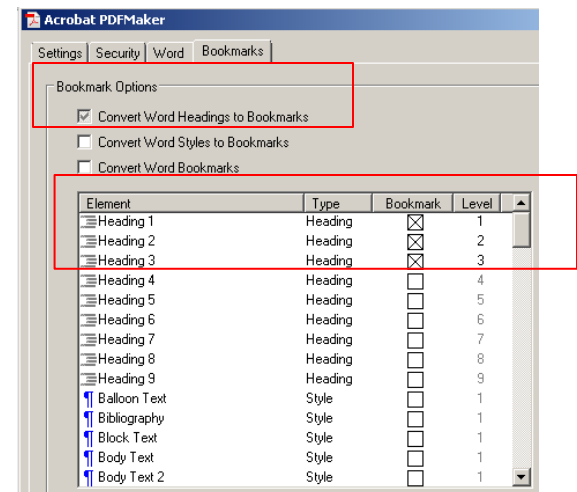
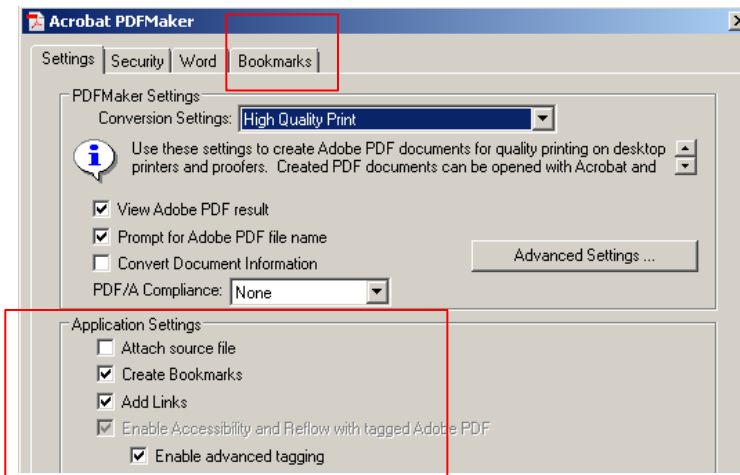
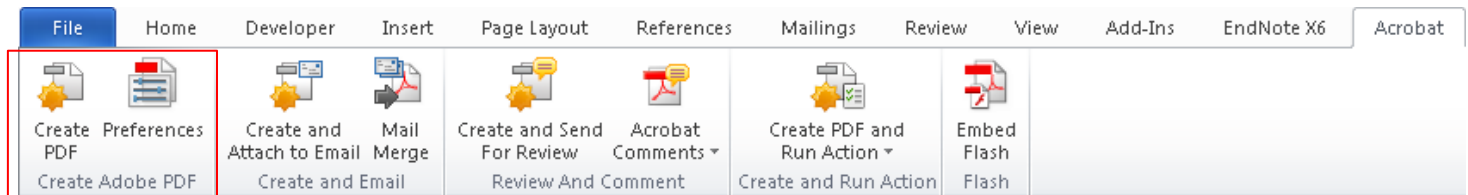
To designate Headings for inclusion in the TOC:

1. Click on *Options*.
2. Uncheck *Outline levels*.
3. Choose the appropriate Headings and assign *TOC level*.



# eCTD – MS Word Format Specifications (6)

- Use Adobe **Acrobat PDFMaker** (an add-in application to MS Word) to create the PDF files. First, click on *Preferences/Bookmarks/Convert Word Headings to Bookmarks* to designate the appropriate Headings for conversion. Then, click on *Create PDF*.

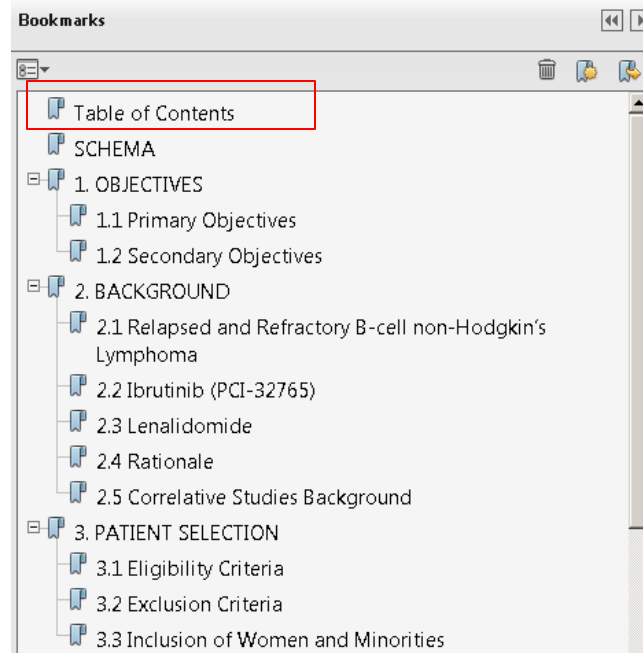


# eCTD – MS Word Format Specifications (7)

- The designated headings will convert to PDF Bookmarks. Provide PDF Bookmarks for all items listed in the TOC and preserve the hierarchy (sequence and nesting of headings).

Include a Bookmark for the Title Page, Table of Contents, and Schema.

- Please note that PDF Bookmarks are required.



## TABLE OF CONTENTS

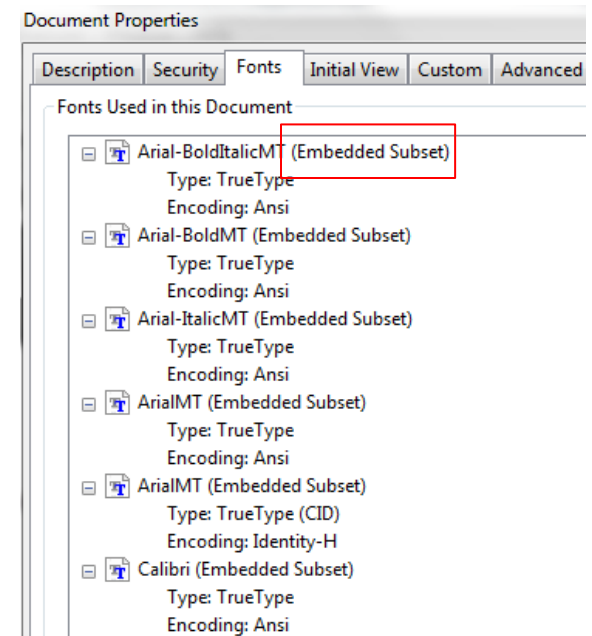
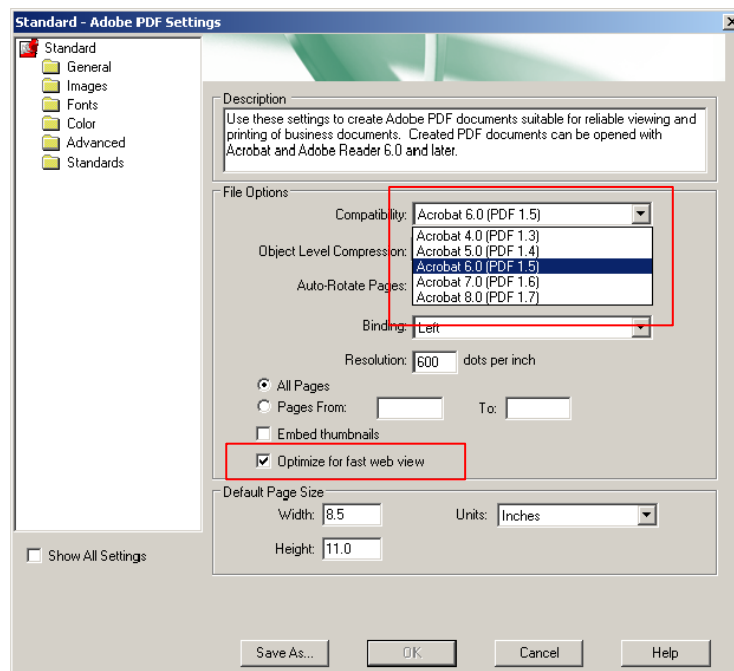
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# eCTD – PDF Format Specifications (1)

- If you will be submitting your protocols/informed consents in PDF format, you are required to also 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
- All PDF documents should be text-based (created directly from an electronic source such as a Word document) rather than image-based (scanned paper). 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. 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.

# eCTD – PDF Format Specifications (2)

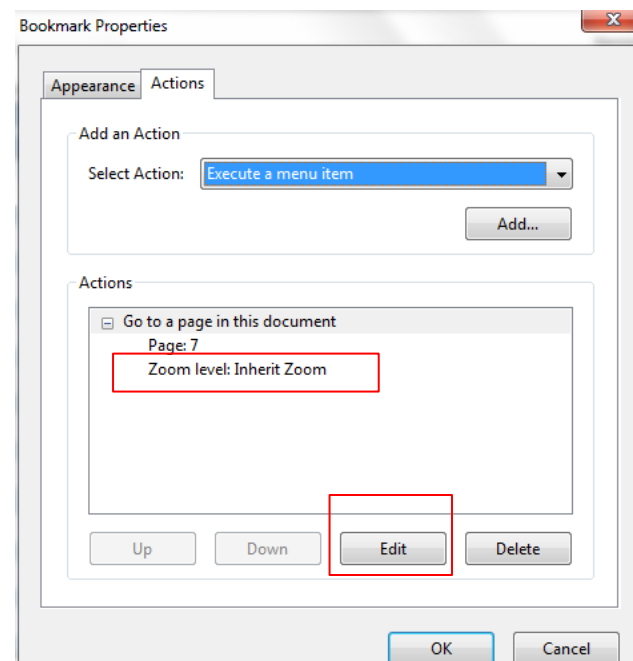
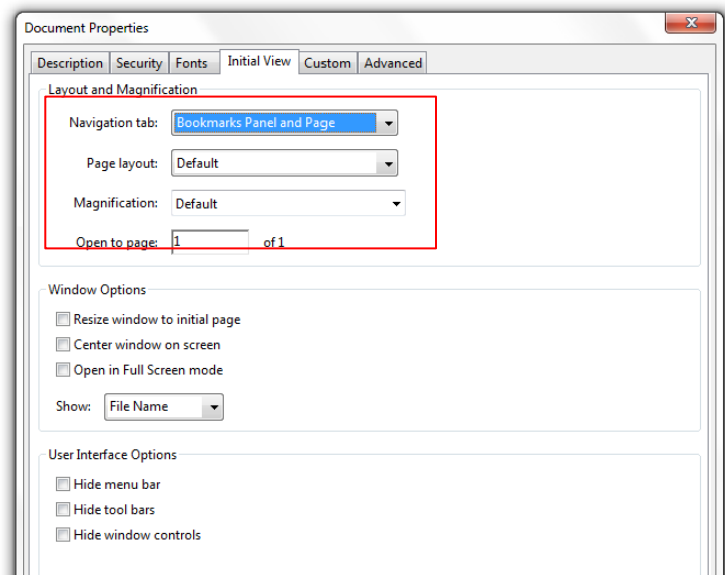
- Use PDF versions 1.4 through 1.7.
- In *Adobe PDF Settings*, check off *Optimize for fast web view* to reduce file sizes and opening times.



- Embed all fonts (including subsets) to ensure that they are available to the reviewer.

# eCTD – PDF Format Specifications (3)

- In the **Initial View** tab, set the *Navigation tab* to open to **Bookmarks Panel and Page**, *Page layout* and *Magnification* to **Default**, and *Open to page* to the first page of the document.
- Set the magnification of PDF Bookmarks to *Inherit Zoom*.



# eCTD – CTEP Requirements

- Following FDA's requirements, CTEP PIO is asking sites to submit the protocol and informed consent documents as two separate electronic files.
- Include the NCI Protocol # and Version Date in all protocol and informed consent document headers.  
*NCI Protocol #: 9426*  
*Version Date: 10/01/2012*
- For protocol and informed consent amendments, include the Change Memo/Summary of Changes at the beginning of the document and hyperlink to the corresponding document Sections.

#	Section	Page(s)	Change
1.	<a href="#">3.1.2.2</a>	35	Eligibility Criteria: History of congenital long QT syndrome has been added as a third bullet.
2.			
3.			
4.			
5.			

- The Protocol Submission Worksheet is available at <http://ctep.cancer.gov/protocolDevelopment/default.htm>. This document contains prompts for required administrative information.

# References and Contact Information

- This presentation is based on the following FDA documents:
  1. FDA PDF Specification: Portable Document Format Specifications, Version 4.0  
<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormSubmissionRequirements/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>
- For problems or questions, please contact the CTEP Protocol and Information Office (PIO) by telephone (240-276-6535), or e-mail at [pio@ctep.nci.nih.gov](mailto:pio@ctep.nci.nih.gov)

Thank you