

Electronic ANDA Top 10

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Agenda

- **Reviewer's Standpoint**
- **eCTD Myths**
- **Top Ten Issues for Success**
- **The "DO" List**
- **The Do Not Do List**
- **References**



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Reviewer's Standpoint

Consider application from reviewer's standpoint

- **Navigation via bookmarks and links**
- **Legible/Viewable documents**
- **Ability to copy and paste text, tables and figures from documents**



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eCTD Myths

Myth #1

“Now that we have the XML backbone, we don’t need to put a TOC in our documents”

Truth: Imagine your document were paper. If you need a TOC to navigate it, include it for each electronic file that needs it.



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eCTD Myths

Myth #2

“The leaf title should include the eCTD numbering so the reviewers will know what they’re looking at”

Truth: the reviewer is usually just looking for the succinct title of a study, and additional numbering is redundant and confusing



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eCTD Myths

Myth #3

“Scanned images, text, tables and figures are just as useful as the electronically converted versions”

Truth: Scanned images, text, tables and figures are very difficult, aggravate reviewers and can impede a review. Source documents converted to pdf or OCR'd pdfs are much more user-friendly from a reviewer's perspective.



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Top 10 Issues for Success



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10. Be Sure to Reference All Files in the XML Backbone(s)

- Unreferenced Files Result from
 - Missing/Mislocated Directory references in `xlink:href`
 - “Extra” files
 - Failing to Repeat Complete Directory Structure on each media component in a set
- Unreferenced Files cannot be located by reviewers



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9. Include Module 1 in All eCTD Submissions

- Every eCTD Submission Requires Module 1**
- Module 1 Identifies important information**
 - Company Name**
 - Drug Name**
 - Submission Type**
 - Submission Date**
 - Application Number**
 - Sequence Number**



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8. Make Sure All Application Numbers are 6 Digits

- Application-number values must be 6 digits -**
 - No Alpha Characters**
 - No “-” “,” or other punctuation**
 - No spaces**
 - Six Numbers – pad left “0” if 5 digits are given**
- Application number is key - ties all submissions together as an application**



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7. Make Sure All Sequence Numbers are 4 Digits

- Sequence-number values must be a unique number and it must be 4 digits**
 - No Alpha Characters**
 - No “-” “,” or other punctuation**
 - No spaces**
- Sequence number is key and relates all submission components together**
- Sequence numbers need not be received/submitted in “sequence”**



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6. Ensure we receive what you intended

- Ensure what we receive is what you wanted to send**
 - No blank electronic media**
 - No empty folder**
 - No unloadable media**



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5. Documents Conform to eCTD Granularity

- **Avoid “combining” documents at higher parent leaf level (allowed by Module 3)**
 - **Tempting - small initial savings in combining**
 - **Large cost in life cycle complexity**
 - **“Legacy” Study Reports make for life cycle issues down the road**
- **eCTD Leaf titles - Short, meaningful & indicative of the contents - Use clear, concise, leaf titles**



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4. All XML must use Standard Components

UTIL Folder

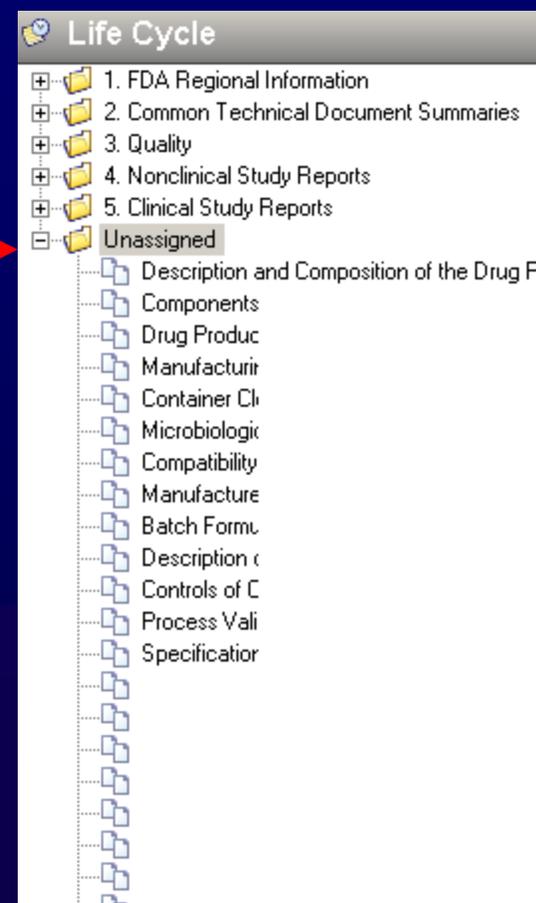
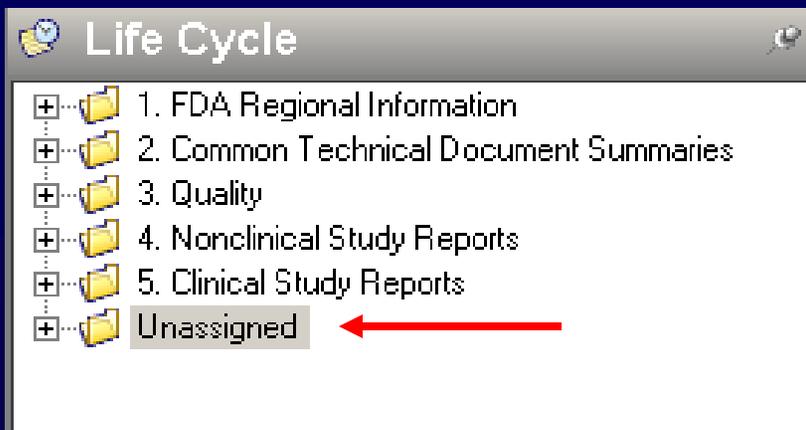
- 3 Standard DTDs**
 - 3 Standard Styles Sheets in UTIL folder**
 - Custom components create issues in FDA Processes – Defeat standards efforts**
- Avoid GIFs, custom CSS, custom DTDs, custom elements with standard DTDs**



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4. All XML must use Standard Components

This is one of the results when standards are not followed



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3. PDF contains Recognizable Text

- **Scanned images, text, tables and figures**
 - **Are not very useful**
 - **Irritate reviewers**
 - **More cumbersome to work with**
 - **Are larger in size compared to electronic files converted to pdf**
 - **Can impede the review**
- **Whenever possible source documents should be converted to pdf or provided as OCR'd pdfs**
 - **Are much more user-friendly from a reviewer's perspective**



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2. PDF Hyperlinks/Bookmarks are Valid and Correct

- Validate all Hyperlinks and Bookmarks – Correct location**
- Broken hyperlinks and bookmarks diminish reviewer confidence in the submission**
- Test before you submit**
- Blue text should be reserved for links**



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2. PDF Hyperlinks/Bookmarks continued

- **Reviewability and Navigation is very important!**
- **Bookmarks and Links enhance navigation & can improve reviewability**
 - **When to provide them? Anytime the text refers to a reference (table, figure, section, etc.) that is not on the same page**
- **Create document level Tables of Content with appropriate bookmarks and links**

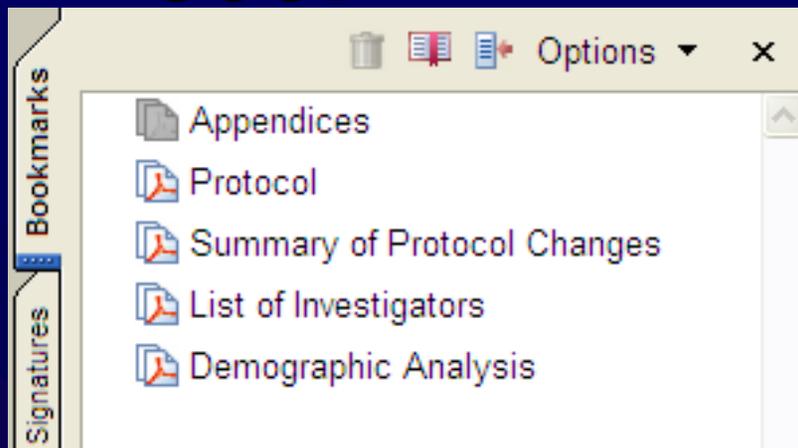


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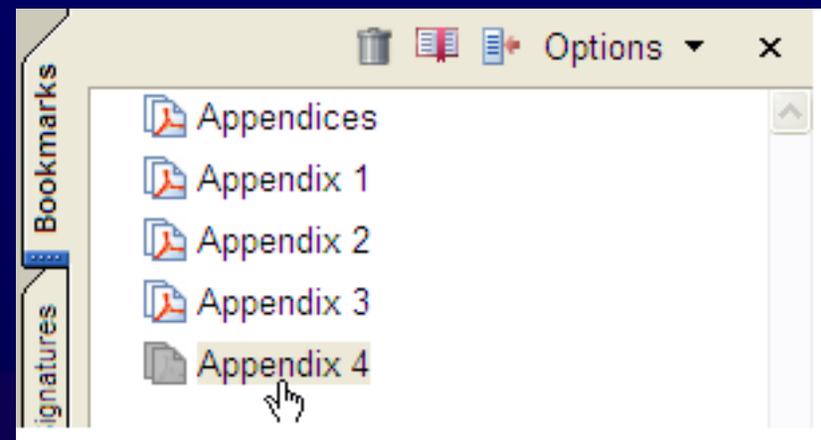
Example of Bookmark Issue #2

Provide Bookmarks With Intuitive Names

GOOD

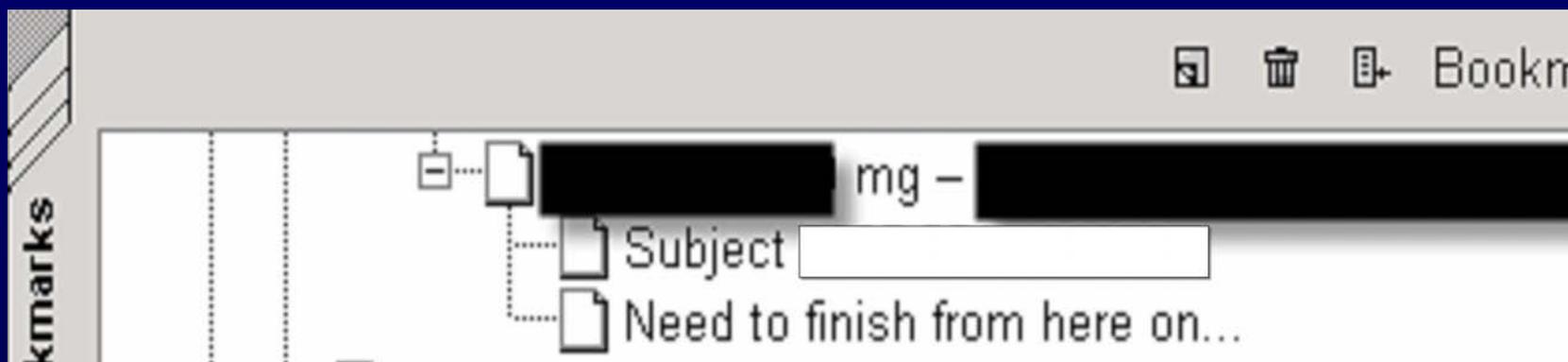


BAD



Example of Bookmark Issue #2

Bookmark Issue Example



Having No Bookmarks is a serious issue!



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1. PDF Documents include TOCs

For each Document -

- If a paper document needs a TOC, a PDF document needs a hyperlinked TOC**
- No change from eANDA – TOC should include bookmarks and hyperlinks**
- Cross Document Links still work in an eCTD**
- TOCs should begin a PDF document if possible**



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Top 10 Issues for Success

10. Files Referenced in the XML Backbone(s)
9. eCTD Submissions Include Module 1
8. Application Numbers are 6 Digits
7. Sequence Numbers are 4 Digits
6. Ensure we receive what you intended
5. Documents Conform to eCTD Granularity
4. XML must be Standard Components
3. PDF contains Recognizable Text
2. PDF Hyperlinks/Bookmarks are Correct
1. PDF Documents include TOCs



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Ensuring Success

Submitting Electronic Submissions

- Send physical media to the OGD document room or electronically via the Gateway (ESG)
- Use the correct electronic media and choose type appropriate to size of submission
- Send only ONE copy of the electronic submission
- If Part 11 compliant electronic signatures are available otherwise only documents requiring original signatures



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eCTD: To Do List

- **Do Submit eCTD**
- **Follow Regulations, Guidance & Specifications**
- **6-digit application # and 4 digit sequence #**
- **Take advantage of granularity**
- **Send submissions to the OGD Document Room**
- **Include all required eCTD files**
- **ALL files submitted are referenced in XML backbone**
- **Only send 1 copy of the electronic submission**
- **Same application # is in the us-regional.xml, FDA form and cover letter**



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The eCTD Do Not Do List:

- X Don't submit a duplicate sequence**
- X Don't send one submission for multiple applications**
- X Don't use node extensions in preparing eCTD**
- X Don't send customized style sheets**
- X Don't send electronic desk copies**
- X Don't send Word files or file formats not requested or specified in the guidance**



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The eCTD Do Not Do List:

X Don't use "356-form" as the file name for more than one file in a submission

X Don't use spaces and non-allowable characters in file and folder names



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References

Requesting an Electronic Common Technical Document (eCTD) Application Number

<http://www.fda.gov/cder/ogd/#enumber>

**Common Technical Document (CTD)
Modules/Sections Corresponding to Summary
Data Tables in Bioequivalence Submissions to
ANDAs**

http://www.fda.gov/cder/ogd/Summary_BioTables_CTD.htm

CDER Office of Generic Drug website

<http://www.fda.gov/cder/ogd/>



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References

FDA eCTD website: <http://www.fda.gov/cder/Regulatory/ersr/ectd.htm>

FDA presentations are available at
<http://www.fda.gov/cder/Regulatory/ersr/default.htm#Presentations>

ICH M2 EWG eCTD Specification:
http://estri.ich.org/eCTD/eCTD_Specification_v3_2.pdf

Comprehensive Table of Contents Headings and Hierarchy:
<http://www.fda.gov/cder/Regulatory/ersr/5640CTOC-v1.2.pdf>
Review the mapping sections (IND, NDA, ANDA) on page 12

eCTD validation, visit
http://www.fda.gov/cder/Regulatory/ersr/validation_specs.htm

CDER Contact for information on eCTD and CTD submissions
eSub@cder.fda.gov



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