HOW TO GET READY FOR eCTD SUBMISSION?

With China aiming to vigorously encourage its innovative drug development, an overhaul of regulatory practices for the life science industry is underway to facilitate and accelerate the process. In recent years, China joined the ICH to add more laws and regulations to support the world's drug developers. There were many attempts to implement eCTD in an effortless manner, but there are still a few challenges that authorities are facing.

WHAT IS eCTD?

eCTD, which stands for Electronic Common Technical Document, is the electronic version of common technical document (CTD). The new submission format would be equipped with XML backbone.

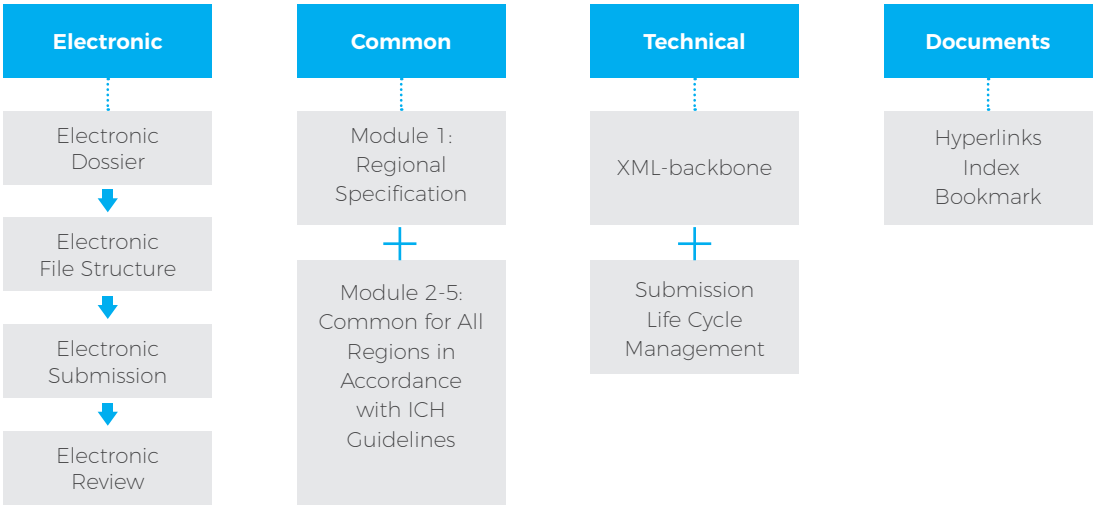

Figure 1: eCTD Module

WHY eCTD?

Looking at the global landscape, EU mandated eCTD for Centralized Procedures in 2010 and the U.S mandated eCTD for all submissions since 2018 (Yang, 2019). With the Chinese pharma industry looking to align itself with global industry standards, adopting the eCTD would be an inevitable move towards international harmonization for China.

SUBMISSION OF ELECTRONIC FORMAT OF CHINESE eCTD FILES

eSubmission Advantages

· Transparency
· Efficiency
· Cost-effectiveness

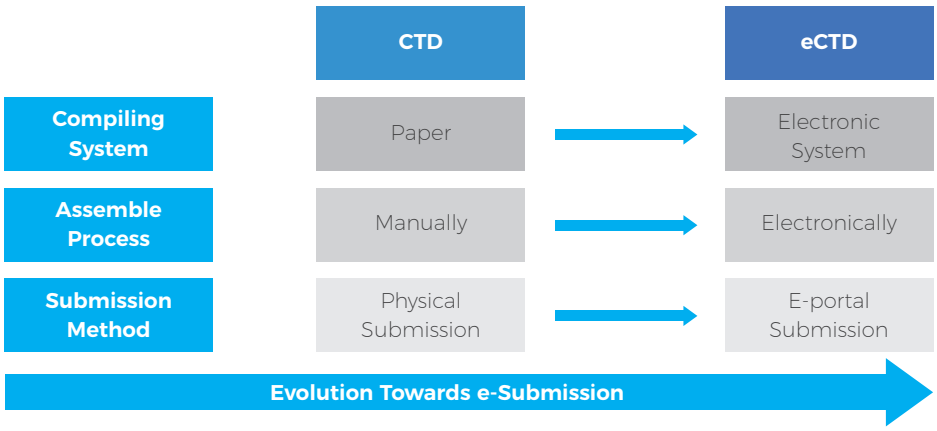

Figure 2: CTD vs eCTD

MAIN CHALLENGE

To implement eCTD smoothly, the pharmaceutical industry and drug regulatory authorities are facing a few challenges. The main challenge is not having enough professionals conforming to eCTD format requirements as well as having the ability to translate it. Therefore, eCTD translation requires extra effort from the medical translator to produce exceptional quality work.

SPECIAL FORMAT REQUIREMENTS OUTLINE

· Bookmarking
· Internal Hyperlinking – Sections, Tables, Figures, References, and Appendices
· Table of Contents – Overall, Tables, Figures, and Appendices
· Embeded Fonts
· Consistent Headers/Footers and Page Orientation
· Converting PDF documents into MS Word file through OCR (Optical Character Recognition)

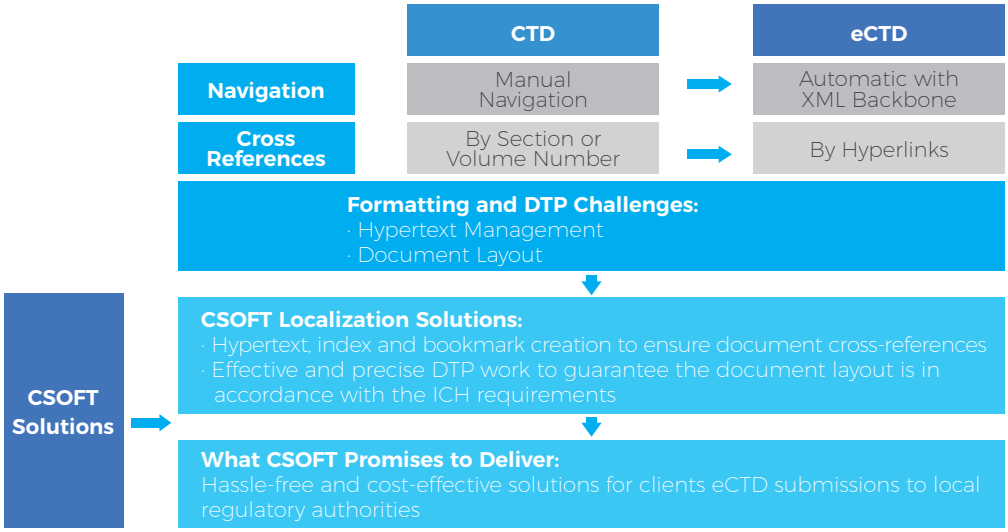

Figure 3: CSOFT solutions

CSOFT SOLUTIONS CASE SHARE

eCTD submission requires intensive effort and time to learn the new regulatory requirements and develop an efficient strategy. In 2018, ICH published the "Specifications for Submission Formats" for eCTD that described the way files structured for inclusion in the eCTD (illustrated in Figure 2.1).

CSOFT offer solutions to help pharmaceutical companies to easily create files that strictly comply with the latest regulatory rules. Here are some examples that show how CSOFT managed to deliver the right type of files:

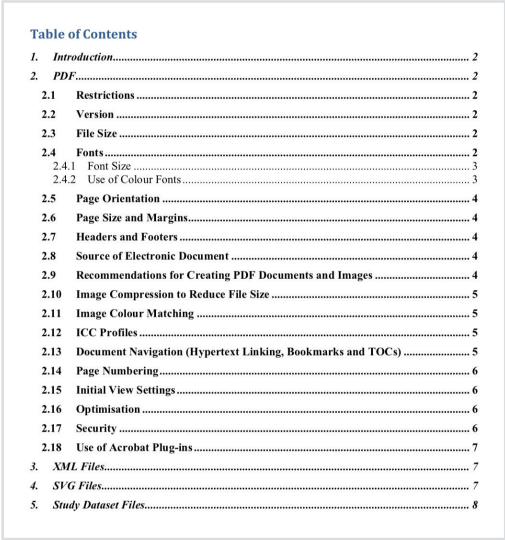
Table of Contents

Figure 4: Specification for Submission Formats for eCTD c1.2

CASE ONE: HYPERLINKED – TABLE OF CONTENTS

Here is an example of a toxicology written summary that required a hyperlinked "Table of Contents." After translating the files, CSOFT DTP team will hyperlink different sections and test them to ensure functionality.

2.6.4 药代动力学-书面-总结 第 1 页

目录

页码

2.6.4 pharmkin-written-summary Page 1

Table of Contents

Page

Figure 5: Table of Contents (TOC) example of before and after translated

CASE TWO: CREATING A MASTER FILE

In this index, one of the top pharmaceutical companies needed CSOFT not only localize their content, but also allocate the content from the scattered files into one piece and ensure all cross-references functioned flawlessly. The engineering team delivered the file as shown below:

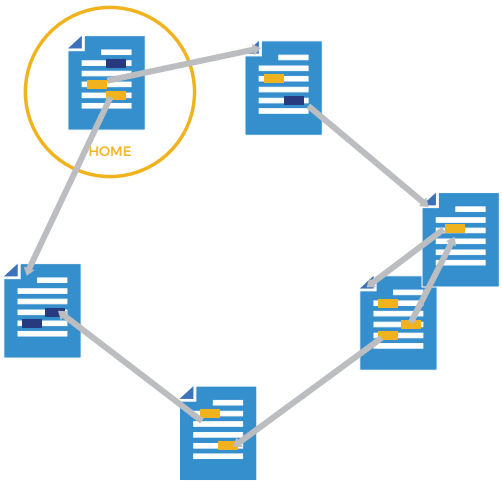

Figure 6: Explanation of Hypertext

模块 3 药学部分资料目录

文件编号（原液部分）	申报文件	文件编号（制剂部分）	申报文件
3.2.S.1.基本信息	3.2.S.1.基本信息.docx	3.2.P.1.制剂描述和组成	3.2.P.1.制剂描述和组成.docx
3.2.S.2.生产	3.2.S.2.生产.docx	3.2.P.2.药物开发	3.2.P.2.药物开发.docx
	3.2.S.2.生产附图.docx		3.2.P.2.药物开发附图.docx
3.2.S.3.特性鉴定	3.2.S.3.特性鉴定.docx	3.2.P.3.生产	3.2.P.3.生产.docx
3.2.S.4.质量控制	3.2.S.4.质量控制.docx	3.2.P.4.辅料控制	3.2.P.4.辅料控制.docx
3.2.S.5.对照品	3.2.S.5.对照品.docx	3.2.P.5.质量控制	3.2.P.5.质量控制.docx
3.2.S.6.容器密封系统	3.2.S.6.容器密封系统.docx	3.2.P.6.对照品	3.2.P.6.对照品.docx
3.2.S.7.稳定性	3.2.S.7.稳定性.doc	3.2.P.7.容器密封性	3.2.P.7.容器密封性.docx
	3.2.S.7.稳定性附图.docx	3.2.P.8.稳定性	3.2.P.8.稳定性.docx

Figure 7: Screenshot of Master File

CSOFT'S eCTD WORKFLOW

To make sure the format of the eCTD document delivered to the clients is 100% flawless, CSOFT has developed a sophisticated workflow from years of experience.

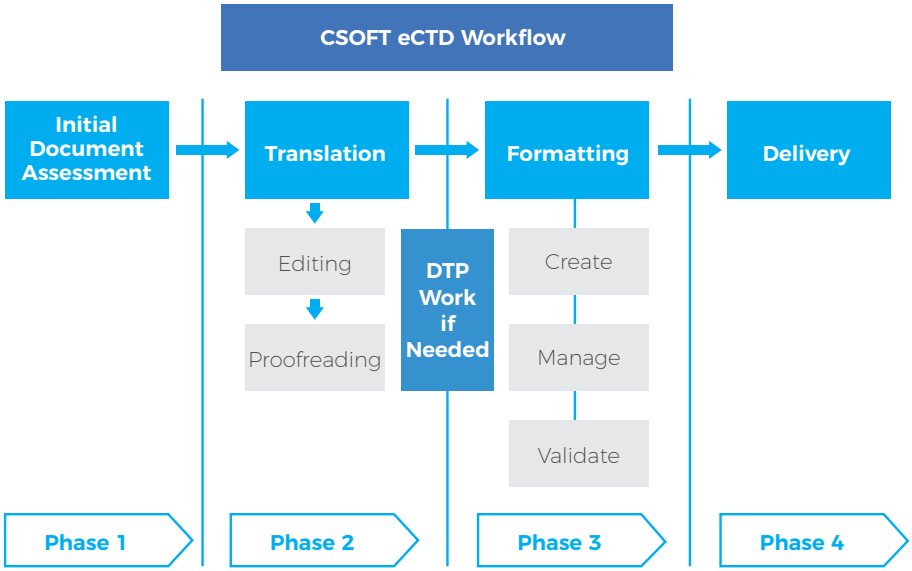

Figure 8: CSOFT eCTD workflow

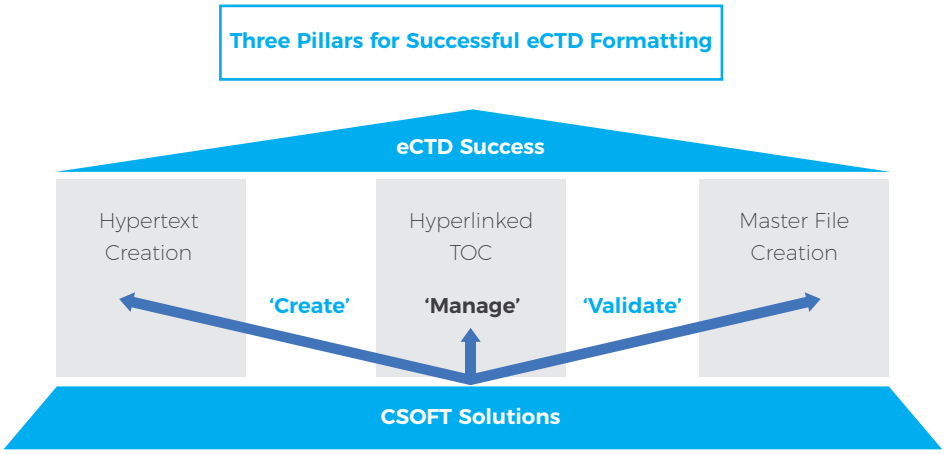

Figure 9: Three Pillars for Successful eCTD Formatting

EXTRA TIPS

Ginny Ventura, a Regulatory Information Specialist in the Center for Drug Evaluation and Research, suggested in a recent Drug Information Association (DIA) conference some tips for eCTD success:

1. Include Table of Contents (TOC) in all PDF documents. For each document

a) If a paper document needs a TOC, a PDF documents needs a hyperlinked TOC.

b) No change from eNDA – both must have bookmarks and hyperlinks.

c) Ensure that cross-document links still work in an eCTD.

2. Be sure all PDF hyperlinks and bookmarks are correct

a) Validate all hyperlinks and bookmarks.

b) Provide bookmarks with intuitive names.

c) It's useful to have a bookmark link back to higher levels of the submission.

d) Broken hyperlinks and bookmarks diminish reviewer confidence in the submission.

e) Test before submitting.

3. All XML documents must use standard components

a) UTIL Folder.

b) Three standard DTDs.

c) There are three standard style sheets in the UTIL folder.

d) Custom components create issues in FDA processes and defeat standards efforts.

e) Avoid GIFs, custom CSS, custom DTDs, and custom elements with standard DTDs.

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