

## 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.

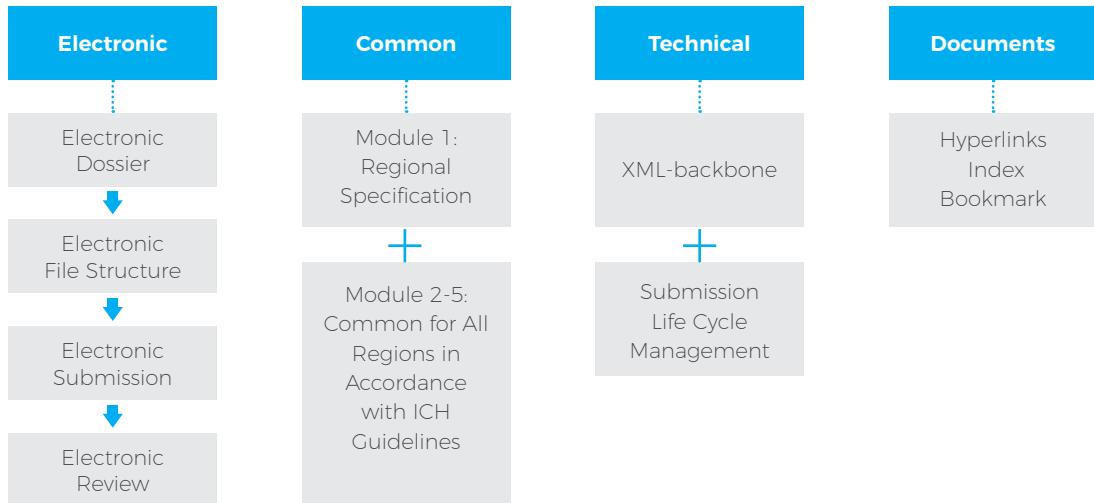


Figure 1: eCTD Module

## 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

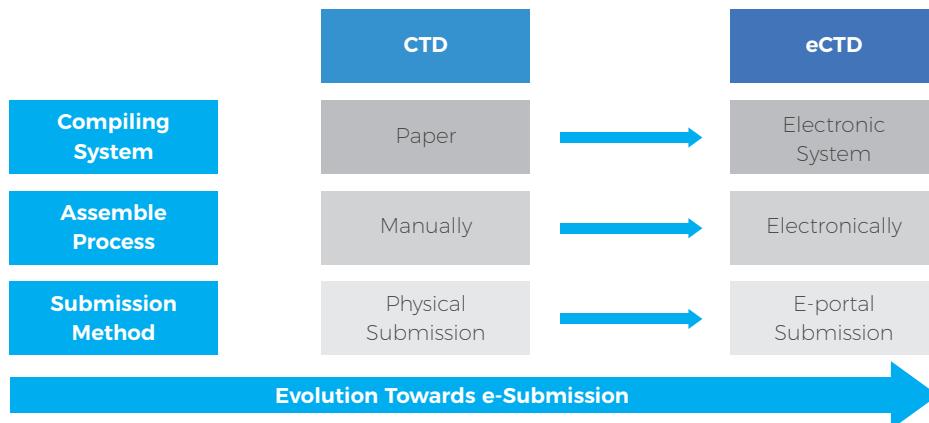


Figure 2: CTD vs eCTD

## 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
- Embedded Fonts
- Consistent Headers/Footers and Page Orientation
- Converting PDF documents into MS Word file through OCR (Optical Character Recognition)

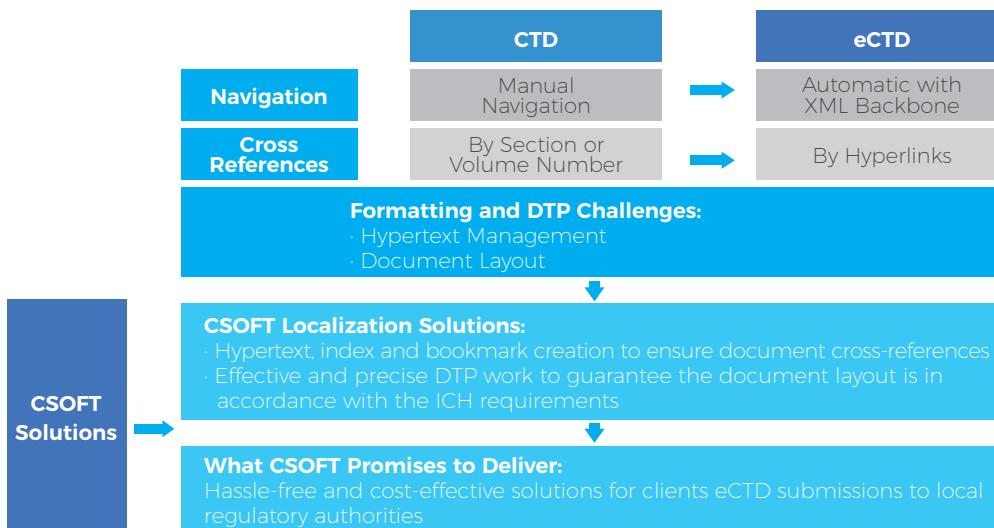


Figure 3: CSOFT solutions

## 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	
1. Introduction.....	2
2. PDF.....	2
2.1 Restrictions .....	2
2.2 Version .....	2
2.3 File Size .....	2
2.4 Fonts.....	2
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2.4.2 Use of Colour Fonts .....	3
2.5 Page Orientation .....	4
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2.8 Source of Electronic Document .....	4
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2.10 Image Compression to Reduce File Size .....	5
2.11 Image Colour Matching .....	5
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2.13 Document Navigation (Hypertext Linking, Bookmarks and TOCs) .....	5
2.14 Page Numbering .....	6
2.15 Initial View Settings.....	6
2.16 Optimisation .....	6
2.17 Security .....	6
2.18 Use of Acrobat Plug-ins .....	7
3. XML Files.....	7
4. SVG Files.....	7
5. Study Dataset Files.....	8

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.

<p><b>2.6.4 药代动力学-书面-总结</b></p> <p style="text-align: right;">第 1 页</p> <p><b>目录</b></p> <p style="text-align: right;"><b>页码</b></p> <tbody> <tr> <td>2.6.4 药代动力学书面总结目录.....</td> <td>1<sup>vi</sup></td> </tr> <tr> <td>2.6.4.1 简要总结.....</td> <td>4<sup>vi</sup></td> </tr> <tr> <td>2.6.4.2 分析方法.....</td> <td>5<sup>vi</sup></td> </tr> <tr> <td>2.6.4.3 吸收.....</td> <td>5<sup>vi</sup></td> </tr> <tr> <td>    2.6.4.3.1 单次给药药代动力学.....</td> <td>5<sup>vi</sup></td> </tr> <tr> <td>    2.6.4.3.2 多次给药毒代动力学.....</td> <td>7<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.3.2.1 大鼠.....</td> <td>7<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.3.2.2 前导性妊娠大鼠.....</td> <td>8<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.3.2.3 前导性妊娠兔.....</td> <td>9<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.3.2.4 犬.....</td> <td>10<sup>vi</sup></td> </tr> <tr> <td>    2.6.4.3.4 分布.....</td> <td>11<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.4.1 组织分布.....</td> <td>11<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.4.2 蛋白结合率.....</td> <td>11<sup>vi</sup></td> </tr> <tr> <td>        2.6.4.4.3 血细胞分布.....</td> <td>12<sup>vi</sup></td> </tr> <tr> <td>    2.6.4.4 代谢.....</td> <td>12<sup>vi</sup></td> </tr> <tr> <td>    2.6.4.6 排泄.....</td> <td>13<sup>vi</sup></td> </tr> <tr> <td>2.6.4.7 药代动力学药物相互作用.....</td> <td>14<sup>vi</sup></td> </tr> <tr> <td>2.6.4.8 其他药代动力学研究.....</td> <td>14<sup>vi</sup></td> </tr> <tr> <td>2.6.4.9 讨论和结论.....</td> <td>14<sup>vi</sup></td> </tr> <tr> <td>2.6.4.10 表和图.....</td> <td>15<sup>vi</sup></td> </tr> <tr> <td>2.6.4.11 参考文献.....</td> <td>15<sup>vi</sup></td> </tr> </tbody>	2.6.4 药代动力学书面总结目录.....	1 <sup>vi</sup>	2.6.4.1 简要总结.....	4 <sup>vi</sup>	2.6.4.2 分析方法.....	5 <sup>vi</sup>	2.6.4.3 吸收.....	5 <sup>vi</sup>	2.6.4.3.1 单次给药药代动力学.....	5 <sup>vi</sup>	2.6.4.3.2 多次给药毒代动力学.....	7 <sup>vi</sup>	2.6.4.3.2.1 大鼠.....	7 <sup>vi</sup>	2.6.4.3.2.2 前导性妊娠大鼠.....	8 <sup>vi</sup>	2.6.4.3.2.3 前导性妊娠兔.....	9 <sup>vi</sup>	2.6.4.3.2.4 犬.....	10 <sup>vi</sup>	2.6.4.3.4 分布.....	11 <sup>vi</sup>	2.6.4.4.1 组织分布.....	11 <sup>vi</sup>	2.6.4.4.2 蛋白结合率.....	11 <sup>vi</sup>	2.6.4.4.3 血细胞分布.....	12 <sup>vi</sup>	2.6.4.4 代谢.....	12 <sup>vi</sup>	2.6.4.6 排泄.....	13 <sup>vi</sup>	2.6.4.7 药代动力学药物相互作用.....	14 <sup>vi</sup>	2.6.4.8 其他药代动力学研究.....	14 <sup>vi</sup>	2.6.4.9 讨论和结论.....	14 <sup>vi</sup>	2.6.4.10 表和图.....	15 <sup>vi</sup>	2.6.4.11 参考文献.....	15 <sup>vi</sup>
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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:

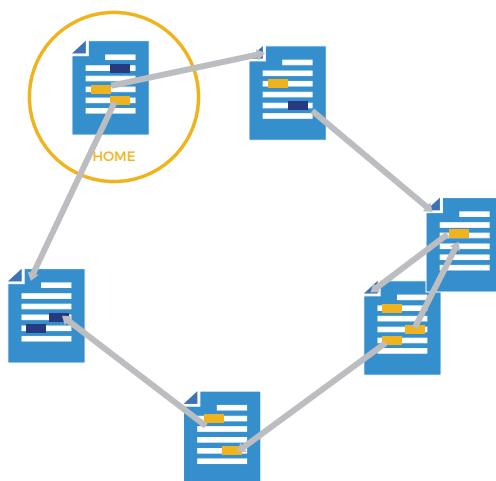


Figure 6: Explanation of Hypertext

模块 3 药学部分资料目录			
文件编号# (原被部分)	申报文件#	文件编号# (制剂部分)	申报文件#
3.2.5.1.基本信息-	3.2.S.1.基本信息.d ocx	3.2.P.1.制剂描述和组成-	3.2.P.1.制剂描述和组成.docx
3.2.5.2.生产-	3.2.S.2.生产附图.d ocx	3.2.P.2.药物开发-	3.2.P.2.药物开发附图.docx
3.2.5.3.特性鉴定-	3.2.S.3.特性鉴定.d ocx	3.2.P.3.生...	3.2.P.3.生...docx
3.2.5.4.质量控制-	3.2.S.4.质量控制.d ocx	3.2.P.4.辅料控制-	3.2.P.4.辅料控制.d ocx
3.2.5.5.对照品-	3.2.S.5.对照品.d ocx	3.2.P.5.质量控制-	3.2.P.5.质量控制.d ocx
3.2.5.6.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.d ocx
3.2.5.7.稳定性-	3.2.S.7.稳定性.d ocx	3.2.P.7.容器密封性-	3.2.P.7.容器密封性.d ocx
		3.2.P.8.稳定性-	3.2.P.8.稳定性.d ocx

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.

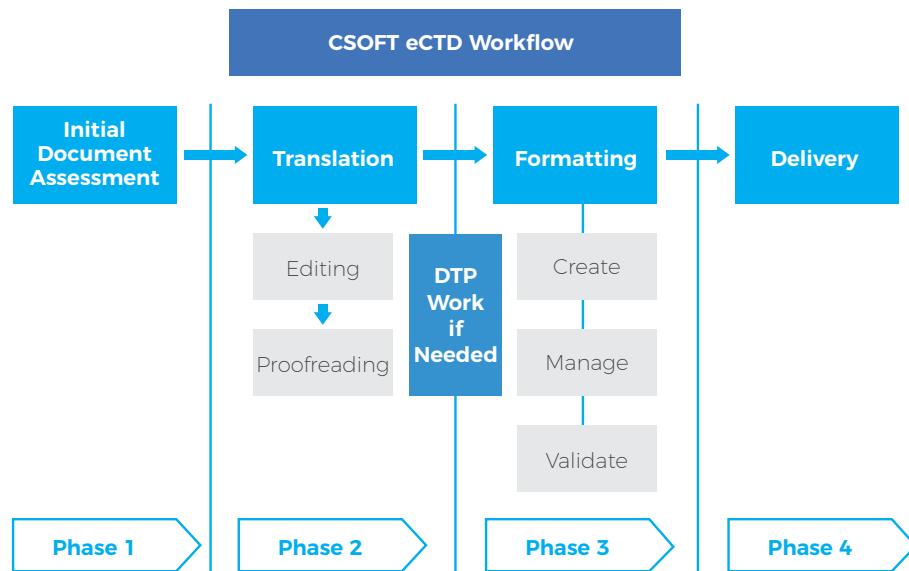


Figure 8: CSOFT eCTD workflow

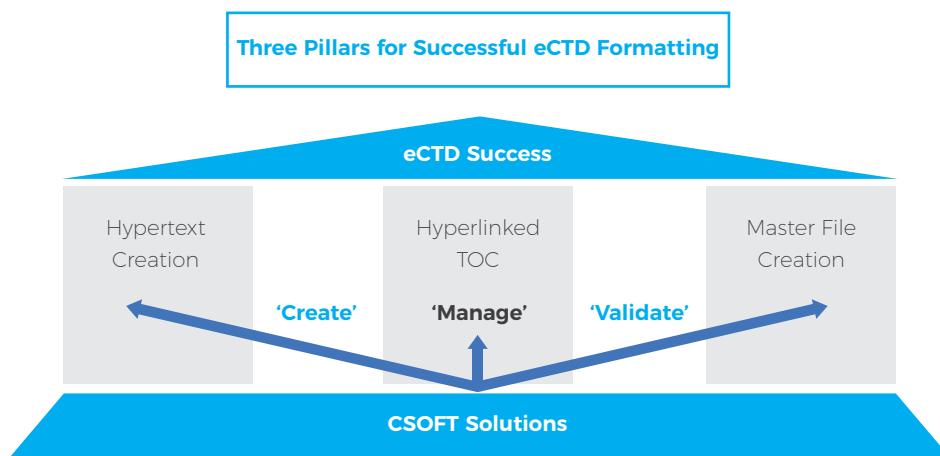


Figure 9: Three Pillars for Successful eCTD Formatting

## 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.

## REFERENCES

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## ABOUT CSOFT LIFE SCIENCES

CSOFT Life Sciences has over 15 years of experience providing end to end medical translations for all stages of the product life cycle, from pre-clinical to post-launch. We also specialize in China market access consulting and CTD/eCTD submission with EMA and NMPA. The operation is compliant with ISO 17100 and certified in ISO 9001:2015 and ISO 13485:2016, providing customized solutions to meet the rigorous regulatory requirements in global submission.