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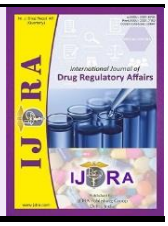

**Review Article**

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# The Status of the Electronic Common Technical Documents Implementation in China: A Comparative Study Based on the USA and EU

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## Abstract

Objective

This paper aims to analyze the problems that China may face in the eCTD implementation process and provide corresponding solutions so as to promote the stable and high-speed development of China's eCTD construction.

Method

This study mainly uses literature research method and comparative analysis method. By searching and analyzing relevant literatures, laws and regulations at home and abroad, this study chooses the USA, the EU and China as objects and makes comparative analysis from three aspects of policy tools, regulatory guidelines and implementation situation among three regions.

Results

As for policy tools, the USA and EU rely on environmental tools, while provide less support for supply-oriented and demand-oriented tools. As for regulatory guidelines, the guidelines of the USA are more comprehensive and detailed; while the guidelines of the EU are looser and focus on practice, but both maintain a high updating frequency. As for implementation situation, from recommendation to compulsory implementation, the USA and EU both give up the one-step approach, and the situation is generally good.

Conclusion

The obstacles to the promotion of eCTD in China mainly focus on the implementation status of CTD, the perfection degree of policy system, the level of software construction and the status of professional personnel training. Therefore, government should set up reasonable transition mode, improve the policy system and infrastructure construction, and cultivate professional talents. Enterprises should take an active part in the implementation of eCTD, choose the appropriate way of cooperation with software suppliers, and build internal professional registration teams.

**Keywords:** Drug registration, eCTD, USA, EU, China

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## 1. Introduction

With the rapid development of pharmaceutical industry and the significant improvement of the level of research and development of pharmaceutical enterprises, the number of drug registration applications around the world has shown a blowout growth. The preparation, submission and review of drug registration documents are the key links before marketing. In addition, paper documents occupy a lot of space and resources. For drug reviewers, how to receive, review, comment and save the mountain of paper application files has also become a major problem at present.

To solve these problems, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) proposed the solution of Electronic Common Technical Document (eCTD), and issued the first edition of guideline in 2003, which promotes application materials to be declared and

reviewed in this format. The current version - v3.2.2 and v4.0 are widely used in the world. As a modern information-based form of drug registration, eCTD can make the preparation, declaration, acceptance, review and storage of application materials more convenient, safe and effective, and also improve the review efficiency of regulatory authorities and shorten the time to market. It caters to the common needs of drug administrations and enterprises of all countries, the goal of international coordination and unification, and the needs of development of the times. It has gradually become an important trend of global drug registration and application, and has been widely used and highly recognized by the international medicine community. At present, it has been carried out or enforced by more than 40 countries and regions in the world. (1)

*China's 2019 Annual Drug Evaluation Report* shows that in 2019, the Center for Drug Evaluation(CDE) accepted 8,082 new registration applications (including 5 device combination products), among which, the number of applications requiring technical evaluation continued to increase in recent years, to 6,199 in 2019, an increase of 11.21% compared with 2018. (2) At present, CDE still has a large workload and review pressure, and has a strong demand for efficient technical review work and rigorous registration and application management. With the release of *the Opinions on the Reform of the Drug and Medical Device Evaluation and Approval System* [(2015)No. 44] on August 18, 2015 , the drug evaluation and approval system reform implement fully, China has also begun to carry out the construction of eCTD and actively promote the integration of drug registration technical standards with international standards. (3) On June 19, 2017, the National Medical Products Administration (NMPA) announced formally that it became a member of ICH, which means that China will participate in drawing up international drug registration standards for human use, also means that China must gradually transform and implement more than 70 technical guidelines released by ICH in the past more than 20 years. Therefore, it is imperative to incorporate eCTD into China's drug registration system gradually. This paper makes a comparative analysis of eCTD policy system, regulatory guidelines and implementation status among the USA, the EU and China, and then finds out problems and put forward corresponding strategies to promote the real implementation of eCTD in China, so as to facilitate the rapid listing of drugs in China and abroad, and truly realize the international integration.

## 2. Analysis of Policy Tools

Policy tools are the general term of all kinds of governance means used by the government to achieve policy goals. Rothwell and Zegveld proposed three types of tools: supply-oriented, environmental and demand-oriented tools. (4) Supply-oriented tools mean that the government provides support for eCTD system and software suppliers through infrastructure construction, public service, talents and information and so on. Environmental tools mainly refer to improving the level of eCTD and creating a favorable policy environment for it by means of target planning and regulatory control. To stimulate the demand of pharmaceutical enterprises for eCTD application, demand-oriented tools can be applied, such as reducing fees, providing convenience, etc.

Relevant policies on eCTD issued by European, American and Chinese drug regulatory departments are listed in table 1. The policy collection time is up to March 10th, 2021, and policies included in the analysis are classified and summarized in three tool dimensions.

**Table 1.** eCTD policy system of the USA, EU and China

| Policy tool | Subdivided Type | Specific Meaning | USA | EU | China |
|---|---|---|---|---|---|
| **supply-oriented** | information support | build technology infrastructure such as information network, eCTD electronic management system and electronic submission channel | √ | √ | - |
| | capital investment | provide financial support for eCTD software and platform construction, such as providing research and development funds and setting up special funds | × | × | × |
| | educational training | according to the application requirements of eCTD, set up a professional team, and carry out training and technical guidance | √ | √ | √ |
| **environmental** | goal planning | make an overall plan for the future development of the eCTD implementation | √ | √ | × |
| | regulation control | set departmental rules，working system and other mandatory measures to strengthen the implementation and supervision of eCTD | √ | √ | × |
| | policy guidelines | formulate eCTD standards and guidelines | √ | √ | - |
| **demand-oriented** | policy preference | formulate policies such as encouraging innovation, encouraging the introduction of technology, giving fast-track access, or reducing registration fees | × | × | × |
| | service outsourcing | outsource the required government services to enterprises, or purchase software and provide it for applicants for free | √ | √ | √ |

| | | | | | |
|---|---|---|---|---|---|
| | trade security | provide protection for eCTD service and trade | × | × | × |
| | enterprise communication | conduct eCTD academic exchanges and cooperate with domestic enterprises or regulatory authorities of other countries | √ | √ | √ |

**Note: "-" indicates that it is under construction.**

As is shown in the Table 1, the supply-oriented policies mainly provide eCTD electronic management platform and electronic submission gateway platform. The USA has reached a long-term cooperation with GlobalSubmit since 2005, using its REVIEW and VALIDATE platforms as the sole official review and validation software. Most EU member states use eCTDmanager and EURSvalidator supplied by EXITDO to examine and validate eCTD format. (5) In 2018, CDE in China selected Shanghai Baoxin Software Co., Ltd. to build the eCTD data management system.

In the EU and the USA, except for personnel training, the demand-oriented policies focus on the communication with domestic enterprises and regulatory authorities of other countries. According to the information published on the official website of the USA, FDA has organized nearly 30 training sessions and seminars related to eCTD since 2003, while China is far from it. During the implementation of the eCTD, the EU, the USA and China have not given special preferential policies or trade security to the enterprises. But the EU provides the free verification software for enterprises, in order to reduce the cost of implementing the eCTD.

In the EU and the USA, environmental policies make up the majority, including the goal planning, regulation control and policy guidelines. Both the EU and USA give up the one-step approach and adopt a transitional period to gradually expand the type, and set up an implementation schedule at the initial stage to give all kinds of enterprises time, capital and manpower to adapt to the reform. It has been nearly 15 years since the implementation of eCTD in the USA and nearly 10 years in the EU. It can be seen that the transition from CTD to eCTD cannot be accomplished overnight.

According to different political environment and enterprise conditions, the eCTD implementation details differ between the USA and the EU. For the USA, it required NDA, BLA and ANDA to apply the eCTD at first, while commercial IND and DMF were latter. Then, it extended the eCTD format to medical devices, periodic safety update reports, promotional materials and labels, drug risk assessment and mitigation strategies. For the EU, all applications under the centralized review procedure are required to apply the eCTD firstly. Later, the EU expanded eCTD format application to non-centralized review procedure and mutual recognition application procedure. At present, the eCTD format submissions include periodic safety update reports (PSURs), active substance master files (ASMFs), plasma master files (PMFs), etc.

### 3. Analysis of regulatory guidelines

There are 15 eCTD relevant laws and regulations in the USA, and FDA provided a list for enterprises to search and read. The programmatic document is *Providing Regulatory Submissions in Electronic Format-Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*, it specifies the execution schedule and submission details, while *eCTD Technical Conformance Guide* is its supplementary document, providing the submit methods and FDA's technical recommendations. Related to the module 1 of ICH M4, FDA issued 3 guidelines: *The eCTD Backbone Files Specification for Module 1*, *eCTD Table of Contents Headings and Hierarchy v1.3 and v2.3*, *Example Submissions using the eCTD Backbone Files Specification for Module 1 Version 1.4*. For others, *Specifications for eCTD Validation Criteria* provides validation criteria for eCTD. The above documents are the basic documents for the preparation and the introduction of procedures of eCTD application, which are the leading documents for FDA to apply for the eCTD. And *Electronic Submissions Gateway，Getting Started: Creating an ESG Account* is the relevant guidance for electronic submission.

The eCTD regulations of the EU are relatively simple, a total of seven except for Q&A. The master guidelines are: *The EU Harmonised technical eCTD guidance*, *Best Practice Guide on the use of eCTD in the MRP/DCP*. The former pays attention to the specification of regulations, the latter focuses on practice guidance. The professional guidelines include eCTD number and format, electronic submission, verification standard, module 1 specification and eCTDv4.0 implementation draft. And *EU Module 1 eCTD Specification* and *eCTD validation criteria* are the two most important guidelines for compiling eCTD documents. The Q&A involves the explanation of compulsory program execution，UUID usage，life cycle management and eCTD format.

From the setting of regulations, the USA and the EU have developed their own eCTD technical guidelines, verification standards, module 1 specifications, format specifications and submission guidelines. The USA pays more attention to the policy improvement, proposing electronic submission of promotional materials and labels, and standards for non-clinical data exchange. While the EU focuses more on the practical issues of eCTD specifically publishing Q&A on UUID and life cycle etc. In general, the FDA regulations are more complete and provide more detailed information to facilitate self-inspection; and the EU regulations are more flexible for enterprises. In addition, the EU and the USA have a high frequency of updating their guidelines and specifications for eCTD. At present, the FDA module 1 eCTD version is v1.3 and v2.4, the DTD version is v2.01 and v3.3, and the verification standard is v3.9. The versions for the EU are v3.0.3, v3.0.1 and v7.1 respectively. And FDA will make the use of Module 1v2.4 and DTDv3.3 mandatory from March1st 2022.

Enterprises need to pay attention to this problem when preparing the application materials of eCTD.

According to the guidelines issued by China so far, China's eCTD will be based on the content of ICH eCTD v3.2.2 version, and drawing on the rules of STF in the USA, relevant regulations of non-English documents and the use of controlled vocabulary of eCTD v4.0 in Japan.

It is clear that China plans to directly transit from paper submission to the eCTD v3.2.2, and gradually introduces the rules of eCTD 4.0. Compared with the EU and the USA, the construction of China's guidelines is still in the initial stage. Except for basic guidelines, there are no practical guidelines such as submission method, Q&A, format specification, etc. The eCTD regulations of the EU, the USA and China are listed in Table 2.

**Table 2.** eCTD regulations of the EU, the USA and China

| Country | Type | Guideline name | Note |
|---|---|---|---|
| **US** | master guidelines | *Providing Regulatory Submissions in Electronic Format-Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications Guidance for Industry（R7）* | platform guideline |
| | | *eCTD Technical Conformance Guide v1.5* | technical guideline |
| | professional guidelines | *Specifications for Files Format Types Using eCTD Specifications v5.0* | file format type |
| | | *Specifications for eCTD Validation Criteria v3.9* | validation criteria |
| | | *Electronic Common Technical Document (eCTD) v4.0 Technical Conformance Guide and Implementation Package* | eCTD v4.0 implementation package |
| | | *The eCTD Backbone Files Specification for Module 1 v1.3 and v2.5* | module 1 specification |
| | | *eCTD Table of Contents Headings and Hierarchy v1.3 and v2.3* | modules 1-5 structure |
| | | *Example Submissions using the eCTD Backbone Files Specification for Module 1 Version 1.4* | module 1 zone XML file |
| | | *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs* | advertising labels and promotional materials |
| | | *Transmission Specifications v1.8* | transmission mode |
| | | *New Requirements for Electronic Submissions of DMFs* | DMF electronic submission |
| | | *FDA Electronic Submissions Gateway：Getting Started: Creating an ESG Account* | electronic gateway platform |
| | | *eCTD Submission Types and Sub-Types* | type description |
| | | *Portable Document Format (PDF) specifications v4.1* | PDF format specification |
| | | *Providing Regulatory Submissions in Electronic Format-Standardized Study Data* | SEND |
| **EU** | master guidelines | *Best Practice Guide on the use of eCTD in the MRP/DCP* | practice guideline |
| | | *The EU Harmonised technical eCTD guidance v4.0* | technical guideline |
| | professional guidelines | *Requirements on submissions（number and format）for New MA Applications within MRP, DCP or National procedures* | numbering and format |
| | | *Final HMA eSubmission Roadmap* | electronic submission roadmap |
| | | *eCTD validation criteria v7.1* | validation criteria |
| | | *EU module 1 Specification v3.0.3* | module 1 specification |
| | | *eCTD v4.0 Implementation package* | eCTD v4.0 implementation package |
| | Q&A | *Q&A on how to handle ongoing procedures in relation to mandatory eCTD format* | eCTD mandatory program |
| | | *Q&A on mandatory eCTD in National Procedures (NP)* | NP mandatory program |

| | | | |
|---|---|---|---|
| | | *Q&A on merging or splitting eCTD lifecycles for different strengths and/or forms of medicinal products* | lifecycle management |
| | | *Q&A on the use of UUID in eCTD* | UUID usage |
| | | *Variations in eCTD format Q&A document* | eCTD format |
| **China** | master guidelines | *eCTD technical specification (draft for comments) and annex* | technical specification |
| | | *Guidelines for eCTD declaration (draft for comments)* | application guideline |
| | professional guidelines | *eCTD Verification Criteria (draft for comments)* | validation criteria |
| | | *M4 module 1 administrative documents and drug information* | module 1 specification |

## 4. Analysis of difference of eCTD implementation

Both the EU and the USA give enterprises enough experience accumulation and buffer period when making the execution plan of eCTD. The compulsory implementation of eCTD is based on a full understanding of eCTD of enterprises.

### *4.1 The implementation of eCTD in the USA*

The USA recommended the use of eCTD in 2003, and enforced it in 2017. By this time, pharmaceutical enterprises in the USA have already had a relatively good foundation for eCTD, specific data can be seen in Figure 1. (6) As of 2016, nearly 90% of NDA, BLA and ANDA applications were in the form of eCTD, according to data released by the official YouTube account of FDA. Therefore, the eCTD compulsion of these application types was successfully completed in 2017. However, compared with other applications, it is more difficult to apply for the eCTD of raw materials, auxiliary materials and packaging materials. At the end of 2014, FDA statistics show that just over 50% of the files in the DMF's quotable list exist in the form of eCTD. (7) Therefore, the USA issued notices to extend the submission of DMF in the eCTD format in April 2017, and further extended the submission of DMF Type III in the eCTD format in April 2018 and January 2019, with the final date set at May 2020. It can be seen that the adaptability of different application types to eCTD is different.

In addition, the USA has adopted a "forward, not backward" approach to the update of the version since 2015. (8) It began to implement M1 v2.4 and DTD v3.3, and the previous M1 v1.3 and DTD 2.01 were also accepted by the FDA for some time. Enterprises can use DTD v3.3 when they submit eCTD files, and enterprises that already use DTD 2.01 can also convert to DTD v3.3 actively, but once convert to DTD v3.3, they cannot revert back to DTD 2.01 and paper submission.

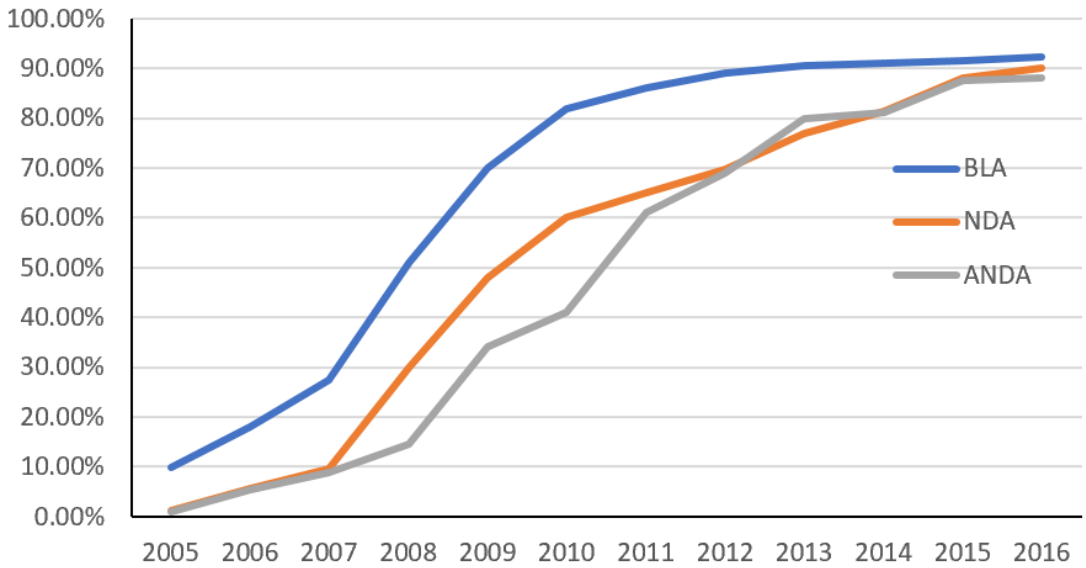


**Figure 1.** eCTD submission rates of different application types from 2005 to 2016 in FDA

### *4.2 The implementation of eCTD in the EU*

The EU's unified drug regulation is carried out by a group composed of at least 30 national or regional drug regulatory authorities plus the EMA , so it is complex and difficult to introduce new systems and processes. The EU did not go well in early stages of the process. As can be seen in Figure 2, in the second quarter of 2010, just nearly 15% of all application files in Europe were submitted in the eCTD format. (6) There is a big gap from the roughly 60 percent of eCTD application rate for NDA in the US in 2010.

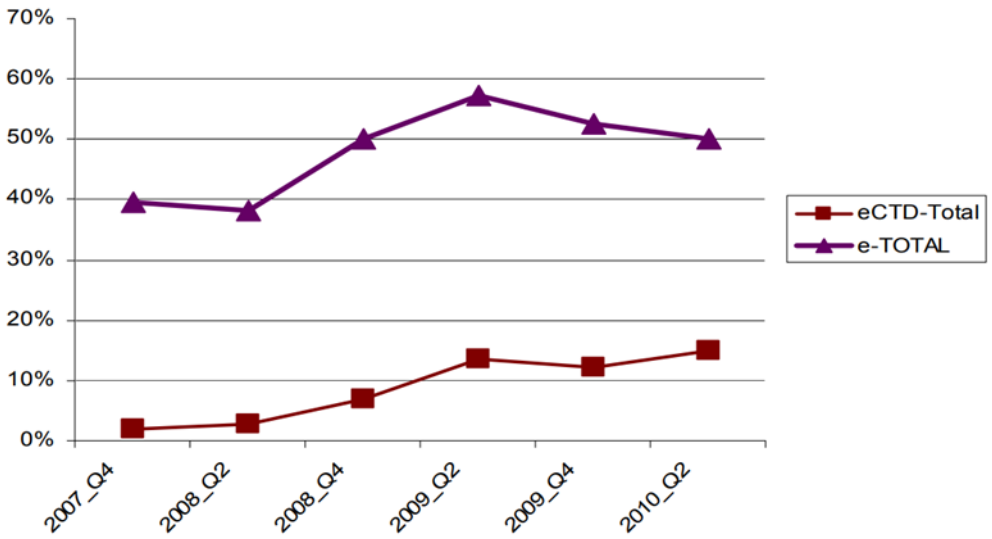


**Figure 2.** The proportion of eCTD application from 2007 to 2010 in EMA

Due to the low adoption level of eCTD in the pharmaceutical industry of other countries and regions (importing countries or regions of EU drugs), the EU introduced NeeS in 2007 as a transitional way to implement eCTD, and promulgated guidelines , such as module 1 and verification standards of NeeS. Until 2017, the NeeS form was gradually phased out. (9) The format and organization of NeeS are consistent with that of eCTD. They both split into various sub-files according to the hierarchy, and then make these subfiles into file packages in a PDF or Word format. (10) Unlike eCTD, however, it does not contain XML files or util folders, and relies on electronic directories, bookmarks, and hyperlinks to navigate and replace files. (11) The EU seized the opportunity to force the implementation of eCTD as pharmaceutical companies have gained greater understanding of the electronic application of CTD through NeeS. An international survey supported by the EMA showed that three quarters of those with experience with eCTD thought that the benefits of eCTD outweighed the disadvantages and it is worth promoting. (12) This transition mode was based on the imperfection of information technology at that time and the complex national geographical environment in Europe, and subsequent countries such as Canada did not adopt the transition mode from NeeS to eCTD. (13,14)

### *4.3 The implementation of eCTD in China*

China's work on eCTD has just begun, with only draft technical guidelines and other guidelines being issued for consultation. The first edition of CTD guidelines was published by the ICH expert working group on M4 in July 2000, which has had a history of more than ten years. For China, the construction of CTD regulatory system was completed in 2020, with the release of M4 module 1 administrative documents and drug information. In addition, the promotion of CTD format in China is faced with many problems, and the transition from CTD to eCTD is lack of enough time accumulation.

Compared with developed countries, relevant regulations and guidelines on eCTD in China are quite backward. FDA has issued nearly 20 guidelines on eCTD, while there are currently 3 relevant guidelines in China, all of which are still in the stage of soliciting opinions. eCTD is closely related to computer technology, and drug regulatory authorities need to support relevant software to manage the life cycle of eCTD application materials, such as supplements, changes, and annual reports ; to verify the integrity of eCTD files. In 2018, China already has suppliers of eCTD data management systems, including verification subsystems, review subsystems and document management subsystems, but the progress of the platform's construction has not yet been announced, and the stability, security, storage of systems and other problems are not known. Furthermore, the ideal way to submit eCTD files is by electronic gateway. Both FDA and EMA take CD and U disk as the secondary solution, but there is no electronic gateway platform in China. At last, the lack of professionals on eCTD also seriously affects the use and promotion of eCTD.

## 5. eCTD implementation problems in China

### *5.1 Limitations on the CTD implementation*

The CTD implementation time in China is short, with little advancement. Since September 2010, China has implemented eCTD. A decade later, China has issued the M4 module 1, drug information and other guiding principles, but enterprises and review staff need more time to adapt to a more standardized CTD format. China is a big market of generic drugs and APIs, with a large number of small-scale pharmaceutical companies and unsound R&D systems. It has been difficult to implement CTD format, so the transition from CTD to eCTD need a long-time accumulation.

### *5.2 Backwardness of the policy system*

China's relevant regulations and guidelines lag behind the USA and the EU in terms of quantity, comprehensiveness and operability. Firstly, the USA has issued 15 guidelines on eCTD, while China's current key guidelines are at the stage of soliciting opinions, lacking target planning documents, and the transition time and

mode are unclear. Secondly, China has not provided enterprises with proper guidelines for production declaration, Q&A, format specifications, content templates, practice guidelines and other practical guidelines. Thirdly, China's support for the supply and demand is relatively weak, such as the lack of professionals training and technical guidelines for enterprises; and China has not yet used economic means or preferential policies to reduce the burden on enterprises to implement eCTD.

### *5.3 Deficiency of the software facilities construction*

The drug administration departments need relevant software platforms to support document verification, data review, annotation, storage and life cycle management. The construction of eCTD data management system in China is at the initial stage. In 2018, Shanghai Baoxin Software Co., Ltd. became the supplier of China's eCTD data management system, building verification subsystem, review subsystem and document management subsystem for China, but the construction of the platform has not yet been announced.

In addition to the drug administration departments, enterprises also need a series of professional softwares to make and generate eCTD documents. At present, pharmaceutical enterprises in the EU and the USA usually cooperate with external software suppliers. The mainstream software suppliers in the market mainly include foreign enterprises such as CSC, EXITDO, GlobalSubmit, Lorenz, Doublebridge and Liquent. The external software suppliers cooperated by Chinese pharmaceutical enterprises include Suzhou Creet, Yiruisi and Haijinge, which provide services such as document editing, format conversion, production and verification. However, there are problems that enterprises do not trust software outsourcing services and the cost of software construction is high. (15)

### *5.4 Lack of the professionals*

eCTD is the integration of multiple disciplines and specialties, and it is so complex that once it fails, it will cause losses that enterprises cannot estimate and make up for. So configuring the professionals and organizing professional registration teams have become an important factor and the primary problem faced by pharmaceutical enterprise when preparing eCTD applications. In China, most of the current drug registration practitioners lack relevant experience and detailed understanding of regulations and guiding principles, and cannot efficiently complete editing and generating eCTD data and electronic application projects. Moreover, drug registration projects have joint effects on many departments and personnel of enterprises. For example, the marketing department needs to plan the layout strategy according to the registration schedule. Therefore, the change of application form drives the uncertainty of process design, application duration and success rate of registered projects, which will increase the decision-making pressure, the risk of enterprise management and other department personnel, thus reducing the support of enterprises for eCTD implementation.

## 6. eCTD implementation strategies in China

### *6.1 Set up transition mode*

The implementation of eCTD in the USA has gone through a process from recommendation to mandatory, and the mandatory time varies for different types of applications. The EU uses NeeS to let enterprises get familiar with the structure of eCTD, and then considers the compilation of XML trunk files, so as to gradually transition to eCTD. In addition, both the EU and the USA set up buffer periods and issue time schedules to give enterprises enough time and experience to cope with the mandatory implementation of eCTD. Therefore, China must give full consideration to its national conditions and the specific situation of enterprises, set a reasonable and clear buffer period by conducting research on enterprises and give respective considerations to different types of applications. Furthermore, eCTD v4.0 will also be formally implemented in the EU, the USA and other places. At the early stage of the eCTD implementation, China must consider how to upgrade the latest version smoothly, and how to be geared to the most advanced international drug evaluation system, in order to reduce the human and material resources required for version conversion.

### *6.2 Improve the policy system and infrastructure construction*

To truly implement the eCTD, Chinese government first need to improve the policy system covering CTD and eCTD including supply-oriented, environmental and demand-oriented policy tools. Publish more regulatory guidelines, such as CTD and eCTD templates, eCTD practice Q&A, STF guidance files, and so on. On this basis, the government can establish the eCTD project pilot, collect feedback information and suggestions, and provide preferential policies, such as shorten the approval time limit, give fast track, reduce fees and so on, to encourage enterprises to apply for drug registration in the eCTD format.

Pharmaceutical enterprises have high requirement on the confidentiality, integrity and security of electronic application of eCTD. Therefore, in the construction of eCTD information system, enterprises must support the construction of security management system, storage management system, electronic transmission platform, to enhance the network anti-attack ability and ensure that the electronic data will not be modified and stolen by others. Domestic enterprises are more inclined to buy cheap and high-quality domestic software, while foreign enterprises prefer service outsourcing. However, in the China's eCTD popularization process, the key factor to be considered is how to help eCTD software enterprises develop compliant, reliable and affordable software and service suitable for Chinese market.

### *6.3 Improve and diversify the cooperation with software suppliers*

Pharmaceutical companies can promote the diversification of cooperation with software suppliers, such as renting or purchasing software, outsourcing to software suppliers, developing software independently

or cooperatively and other ways to conduct eCTD application. According to the survey, most American enterprises choose to edit CTD documents by outsourcing to software suppliers. Because of the differences in national eCTD systems within the EU, enterprises find that most foreign programs can be localized and compliant with domestic regulatory requirements only after major modifications. As a result, many active multinational companies choose to cooperate or develop software independently and applicate independently. Based on this, Chinese enterprises should consider a series of professional factors, such as the location of the company, the number of projects, the number of employees, the corporate culture and the willingness of capital investment, when choosing the way to cooperate with software suppliers.

### *6.4 Train the professionals*

China officially joined ICH in 2017, and China's pharmaceutical enterprises and center for drug evaluation are not familiar with the basic knowledge, technical specifications and verification standards of eCTD. From the perspective of the government, firstly, the government needs to participate in more international experience exchange meetings, organize domestic relevant technical specification training meetings, seminars, and enterprise communication meetings, to help domestic enterprises and personnel to break operational barriers, learn mature experience, master the legal scale, understand the international industry dynamics, and truly understand the application of eCTD. Secondly, the center for drug evaluation should establish and build a large-scale talent team including computer professionals and compound professionals to deal with various problems that may arise in the future. At the same time, it is suggested that the center for drug evaluation open the trial submission channel, so as to accumulate operational experience for reviewers and enterprises to master the new review method and the electronic submission of eCTD application. Besides, training courses on eCTD data management system operation and eCTD technical specifications should be carried out for the internal accepting personnel, reviewers and system management personnel of the drug control center, so as to ensure the smooth implementation and transition of eCTD electronic application. Finally, we should not neglect the publicity and training of the enterprise's senior management personnel, and enhance the recognition of the enterprise as a whole.

From the perspective of the enterprises, whether enterprises outsource or buy software by themselves, an electronic application project generally involves three basic roles: (1) document writers, who are responsible for compiling data, charts and other data collected by all parties into professional reports and application materials, and need to be familiar with the classification of granularity and the basic format specification of eCTD, so as to save more time for document segmentation and format adjustment in subsequent links; (2) document editors, who can skillfully apply various kinds of software to edit the format of documents, complete the work from Word form to PDF form to eCTD structured documents, and be responsible for communication and cooperation with software companies; (3) project managers, who should control the declaration process and quality, be responsible for formulating the declaration plan and controlling the declaration progress, manage the electronic declaration documents, and coordinate all departments to work together efficiently. These three roles are indispensable and meet the basic requirements of eCTD application. Therefore, enterprises need to train and set up registered project teams with these three roles, so as to enhance the professionalization of staff.

## 7. Conclusion

China officially joined ICH in 2017, and most pharmaceutical enterprises are not familiar with the basic knowledge, technical specifications, verification standards and other aspects of eCTD. Therefore, the guidance of the drug regulatory authorities is very necessary. Drug administration and other departments need to organize more relevant training meetings, seminars, and enterprise communication meetings to help domestic enterprises and professionals to break operational barriers, learn mature experience, master laws and regulations, understand the international industry dynamics, and truly adapt to the application of eCTD. At the same time, it is suggested that CDE open the trial submission channel to help enterprises fully understand eCTD and find and solve problems as soon as possible. In addition, training on the operation of eCTD data management system and eCTD technical specifications should be carried out for CDE internal acceptors, reviewers and system administrators to ensure the smooth implementation and transition of eCTD electronic application.

Although eCTD is still a long way from being mandatory in China, the authorities have issued several drafts on eCTD for consultation. Chinese enterprises need to act as soon as possible and actively express their opinions, and provide convenience for the review agencies and enterprises themselves in the process of making rules, so that the policies formulated will be more in line with the actual situation of Chinese enterprises. In addition, enterprises should change their concept, actively participate in the eCTD training meetings and seminars organized by all parties, cultivate professional talents, and realize the strategic preparation and risk control of eCTD application.

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**Conflict of Interest**

The authors declare that there is no conflict of interest regarding the publication of this article.

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