European Economic Letters
ISSN 2323-5233
Vol 9, Issue 1 (2019)
http://eelet.org.uk

Streamlining eCTD Submissions for Biotech and Pharmaceutical Products: Best Practices

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Abstract:
The eCTD is a means of improving compliance, efficiency, and timeline for authoring and regulatory submissions of common application documents for the pharmaceutical and biotechnology industries. In this paper, discussed the challenges and practices of the automation, accuracy of the document, and functional team collaboration in eCTD submissions. Based on Merck KGaA, Shenzhen Hepalink Pharmaceutical and Fresenius Kabi case studies, The integration and compliance strategies benefit based on these cases. Using automation, structured workflows and parallel to international rules of enforcement increases accuracy whilst reducing delay in submissions. However, this will be integrated with AI, security risk, and comparative analysis of regulatory agency to optimise the eCTD submission process even more.

Keywords: eCTD, Regulatory Submissions, NDA, IND, Pharmaceutical

I. INTRODUCTION

A. Background to the Study

The "electronic Common Technical Document (eCTD)" is generally a submission and standard format of applications, reports, and amendments, and supplements to FDA's "Centre for Drug Evaluation and Research (CDER)" and "Centre for Biologics Evaluation and Research (CBER)". There are some different submission types for eCTD, which helps in submission for biological products, as therapeutic proteins and vaccines are "New Drug Application (NDA)" and "Biologics Lisence Application (BLA)" [1]. Submission for conducting clinical trials of a new drug, "Investigational New Drug Application (IND)", are also used as a common type of submission format for eCTD.

B. Overview

The biotech and pharmaceutical industry standard for regulatory submissions is the "electronic Common Technical Document (eCTD)". This does not require streamlining of eCTD submissions, compliance, optimisation, and without delay of approvals. Such as early planning, using the eCTD compliant software, document quality, and adhering to the regulations. Additionally, it also continues to enhance the lifecycle management process, collaboration and process automation [2]. The teams can accept what is new in the regulations and thereby train to get better. These strategies, submission accuracy, time to approval and time to market of new pharmaceutical and biotech products have become faster.

C. Problem Statement

Reviewing and validation, along with maintaining the consistency for submitting eCTD submissions of biotech and pharmaceutical companies, brings in challenges with handling sophisticated regulatory standards, new guidelines and strict documentation specifications. Some of them are formatting inconsistent documents, no version control, lack of a good following between teams and a failing technical validation [3]. In addition, the agency's regulatory standards of submission have changed over time. Otherwise, all firms run the risk of rejected applications, longer time to market approval and missing market windows. Meanwhile, to address these challenges of producing efficient, accurate and compliant eCTD submissions, best practices and automation are needed.

D. Objectives

The aim of this study is to streamline eCTD submission for biotech and pharmaceutical products by aligning best practices which help to improve the operational efficiency, decrease delays of approval and ensure regulatory complinaces. 1. To evaluate a structure workflow process of submission, and ensure that all docs are accurate, as well as to automate the process to make certain elements more efficient. 2. To align with the eCTD global regulations, in order to improve the regulations by keeping consistency in regulation and to follow validation tools in the documentation. 3. To enable communication between the IT department, the clinical team, and the regulatory affairs which will help for better process of submission to resolve their process failures.

E. Scope and Significance

The research investigates such best practices that expedite eCTD submissions for biotech as well as pharmaceutical products, and compliance with the regulations. Automation, document management, validation tools and cross functional collaboration are optimised tools to achieve submission processes. It is important to this study because it can allow companies to short circuit delay approval, reduce compliance risks, and improve operations. The research tackles typical issues typical of the inconsistency formatting and changing regulatory requirements to offer the organisation some insights concerning the improvement in formatting submission strategy and reducing the time to market for new biotech and pharmaceutical innovations.

II. LITERATURE REVIEW

A. The eCTD's role in the pharmaceutical industry

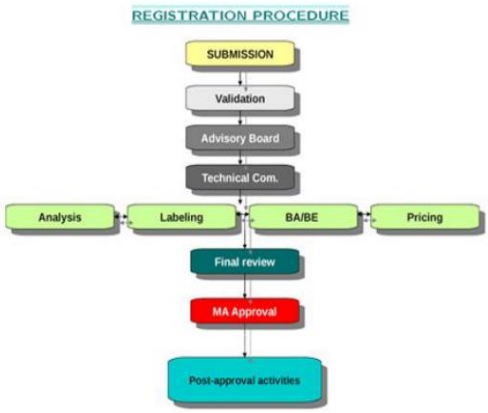

Figure 1: Registration Procedure of NDA

[5]

An NDA is a type of application that has to be filled up with FDA to approve a new medicine on the market. A sponsor then provides preclinical and clinical test data to the NDA for analysis of the drug information and manufacturing process description to receive this license. Following receipt by the agency, the NDA is subjected to a technical review and assessment. This assessment and supporting paperwork guarantee that enough information has been provided in each section to support applying for formal FDA review [5]. One essential division in the pharmaceutical industry is drug regulatory affairs. The pharmaceutical industry is expanding so quickly that regulatory affairs specialists are needed to meet the industries' present demands in the face of global competition. The vital connection between the pharmaceutical industry and international regulatory bodies is provided by drug regulatory affairs specialists. The approval process for pharmaceutical products ought to be a crucial step in guaranteeing that people have access to safe and efficient medications. In addition to facilitating the production, evaluation, life-cycle management, and archiving of the electronic submission, the eCTD will act as an interface for the transfer of regulatory information from industry to agencies.

The article describes the challenges related to eCTD and CTD filing processing for regulatory submission in the US and Canada. It also lists out the problems like technical validation error, regional submission format variation and compliance of handling evolving regulatory guidelines. The study highlights the importance of having precise structuring of documents, managing documents at their lifecycle in proper manner and executing documents in a manner that complies with agency specific requirements [6]. It also elaborates on the issues of electronic submission tools, validation checks, and automation to minimize errors and speed up eCTD submissions for regulatory approval.

B. Regulatory Frameworks and Compliance Strategies

The drug or biological information of products are pre-filled syringes information of products and also related to engineering and manufacturing information should be located in the eCTD that would provide similar information for the drug or biological product alone [7]. The study explores the regulatory documentation that refers to the structured collection of documents that are mandated by the government and industry-regulated bodies to ensure safety and compliance in the field of the pharmaceutical industry. Different regulatory agencies govern eCTD with specific requirements, such as the FDA, EMA, and PMDA.

Various features of CTD have been examined, including its multiple modules and structure. Moreover, a comparative analysis of the contents and formats of different regulatory agencies has also been presented. Every country has its own regulatory processes that can provide the format for the submission of different industries, such as the pharmaceutical industry. The

regulatory bodies are the “Food and Drug Administration (FDA)” in the US, the UK “European Medicines Agency (EMA)” in the UK, and Japan's Ministry of Health, Labour, and Welfare (MHLW)” [8]. The regulatory bodies from different countries have their own format for filing an application seeking approval for marketing a drug.

C. Collaboration in eCTD Processes

Collaboration is an important aspect of the accuracy, compliance, and efficiency of the eCTD submissions. Regulatory affairs teams can also benefit from document preparation, validation, and lifecycle management easier, both together with IT specialists, and with global teams. Early interaction can allow to deal proactively with compliance issues to reduce delays in approval. Errors can be brought down, and submissions are kept consistent by real-time collaboration through the cloud [9]. The automation and optimization of workflow also involves coordinating third-party vendors. Therefore, cross-functional collaboration that results in an increased quality of submission, reduction in time to approval and compliance with other jurisdictions’ regulations is encouraged by favorable interactions with pharmaceutical companies.

The importance of the data sharing for regulatory submission as well as the promotion of the healthcare innovation through the help of different frameworks based on the global collaboration. As eCTD is also marking the importance of a single common data exchange between various regulatory authorities and pharma companies to shorten time duration while travelling the data. The study highlighted the use of digital platforms and structured data sharing networks to speed up regulatory filing and decrease error rates in the document as well as the time to approval [10]. The approach implements learning health systems through promoting collaboration between academic institutions, regulatory agencies, and industry stakeholders for adaptation, transparency, and the capability of safely adapting continuously to compliance requirements in eCTD submissions.

III. METHODOLOGY

A. Research Design

The data collected is used by the research design framework for this study to address and decide the path of the investigation. The study used an **explanatory research approach** that is aligned with the topic of eCTD submissions for Biotech and Pharmaceutical Products. This research approach helps the study to explore the eCTD submission process, which helps to enhance the efficiency of the pharmaceutical and biotech products. This research approach also enhances the understanding of the topic with limited information available and is also useful in future occurrences.

B. Data Collection and Analysis

“Secondary qualitative and quantitative” data collecting is the method adopted for this investigation. Numerous sources, including industry reports, journals, papers, websites, and many more, are reviewed by the qualitative data technique. On the other hand, the quantitative data approach looks at a variety of graphs and charts that can be used to analyse precise data related to eCTD submission for biotech and pharmaceutical products. All information that is collected is from accurate and reliable sources, providing precise knowledge and research-related facts.

C. Case Studies/Examples

Case Study 1: Merck KGaA: Improving efficiency of submission through system integration

A leading pharmaceutical company from Germany, Merck KGaA, integrated its intelligent Content Services Platform, CARA, with a product provider, eCTD manager, to streamline its eCTD submission processes. This becomes a simple and easy way to access the document, facilitating version control and easier metadata mapping, which removes some of the manual errors and also improves efficiency. By allowing direct assess to the regulatory documents that are sorted in the Merck’s Document Management System (DMS) which help to optimise the submission workflow to streamline its global regulatory compliance [11]. The improved system made the process of preparing submittals faster, decreased the rework and improved regulatory operations as a whole.

Case Study 2: Shenzhen Hepalink Pharmaceutical: Ensuring Global Regulatory Compliance

Fulfilling the global regulatory requirements such as FDA, EMA and EDQM standards, Shenzhen Hepalink Pharmaceutical optimised its eCTD submission process. In the process of implementing EXTEDO eCTDmanager, the company realises time, accuracy, consistency and compliance reduction across multiple markets. It made it easier to organise documents, check for errors, and reduce submission errors, thus speeding up approvals. As a means of subduing regulatory complexities, Hepalink adopted strategically the international scheduling and was thus able to achieve positive international presence [11]. Thus, the digital solutions introduced by the company enabled an efficient submission process that protects the company from compliance risks and quickly reaches critical pharmaceutical products to global markets.

Case Study 3: Fresenius Kabi: Streamlining eCTD Submission Processes

Infusion therapy and clinical nutrition European leader Fresenius Kabi exploited EXTEDO's eCTD manager to improve its eCTD submission process. This implementation helped to speed up the regulatory submission publishing, made document management, version control and regulations compliant with the new evolving global regulations. Hence, it assisted in saving manual preparation and errors while submitting the files [12]. The ability to increase automation and compliance to regulatory requirements, Fresenius helped to speed up the approval timelines. They settled into the new regulatory hand at the cost of good submissions at all phases of pharmaceutical approval and with high-quality standards in global markets.

IV. RESULTS

A. Data presentation

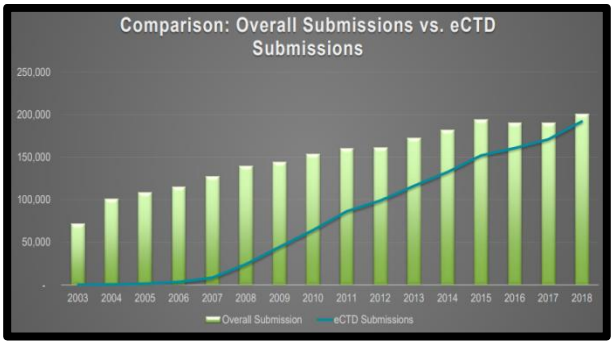

Figure 2: Overall submission Vs. eCTD Submission
[13]

This graph compares the total number of electronic submissions with eCTD submissions between 2003 and 2018. Over 90,000 eCTD submissions have been submitted in FY 2018, out of over 100,000 total, which is a strong adoption. The evidence of this growth drives the need for more streamlined, automated workflows, regulatory alignment, and interdepartmental alignment processes to reduce the e-CTD submission process for biotech and pharma products [13].

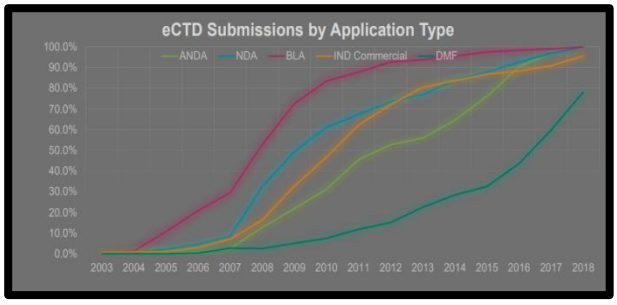

Figure 3: Application types of eCTD Submission
[13]

The above graph depicts the percentage of eCTD submissions by application type year 2003 to 2018. By FY 2018, eCTD was nearly 100% used in NDA, BLA, ANDA submissions, 96% for commercial IND, and 78% for DMF. Rapid adoption across categories shows how the industry is transitioning to standardised electronic submissions. However, more highlights because there needs to be standardisation of workflows, regulatory harmonisation, and more coordination across departments in the eCTD process for biotech and pharmaceutical companies [13].

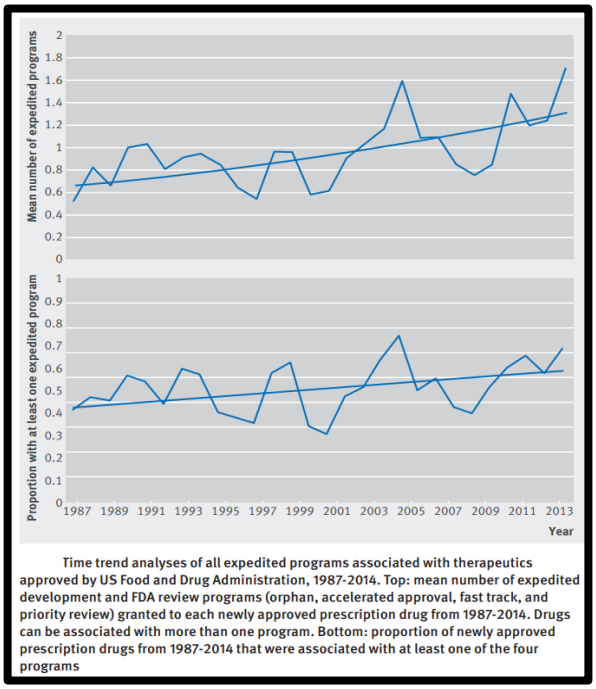

Figure 4: Trends in FDA Expedited Program Use per Approved Drug (1987–2014)
[14]

This graph is quite related to this ongoing research on streamlining of eCTD submissions. From 1987 to 2014, it demonstrates a steady increase in the use of expedited FDA programs (orphan, fast track, accelerated, priority). The first graph shows how the mean number of expedited designations per drug is increasing, and the second one shows the increasing proportion of drugs that use at least one program. This implying the necessity for faster, more effective eCTD submission.

B. Findings

This has found that the adoption of eCTD rose from less than 10% in 2003 to 96% to 100% for NDAs, BLAs and ANDAs by 2018. This paralleled a wider shift in industry towards electronic submissions [13]. At the same time, FDA expedited program designations per drug and each drug's use of at least one program increased (1987–2014), stressing the importance of timely, automated eCTD workflows, regulatory convergence, and cross-functional partnership [14].

C. Case Study Outcomes

Case Study	Key Findings	Relevance
Case Study 1: Merck KGaA: Improving efficiency of submission through system integration	● Integrated CARA with eCTDmanager. ● Improved version control and metadata mapping [11].	Enhances efficiency in regulatory submissions
Case Study 2: Shenzhen Hepalink Pharmaceutical: Ensuring	● Adopted EXTEDO eCTDmanager for streamlined compliance. ● Improved	Ensures compliance with global regulatory

Global Regulatory Compliance	accuracy, consistency, and reduced submission errors [11].	standards
Case Study 3: Fresenius Kabi: Streamlining eCTD Submission Processes	● Implemented EXTEDO's eCTDmanager. ● Improved document management ● Reduce manual errors	Enhances automation, reduces workload, and ensures high-quality global submissions [12].

Table 1: Case Study Outcomes
(Source: Self-developed)

Table 1 highlights the outcomes of the case studies where key findings and relevance are discussed. Merck KGaA implement CARA with eCTDmanager to enhance their operations. On the other hand, Shenzhen Hepalink Pharmaceuticals also ensure EXTEDO eCTDmanager to improve their compliance. Lastly, Fresenius Kabi also ensure EXTEDO eCTDmanager to decrease manual errors.

D. Comparative Analysis

Authors	Focus Area	Key Findings	Limitations
[5]	NDA Registration & eCTD Role	eCTD improves submission structure and compliance [5].	Validation errors and format differences.
[6]	Challenges in eCTD Submissions	Issues with validation, structuring, and evolving guidelines.	Needs better automation and management [6].
[7]	Regulatory Frameworks & Compliance	Different agencies have unique requirements [7].	Lack of global standardisation.
[8]	Comparative Regulatory Analysis	Approval processes vary by country [8].	Complex cross-border submissions.

[9]	Collaboration in eCTD	Cloud-based collaboration enhances efficiency [9].	Tech reliance and security risks.
[10]	Data Sharing & eCTD Optimisation	Digital platforms speed up approvals [10].	Requires strong governanc e and coordinati on.

Table 2: Comparative Analysis
(Source: Self-developed)

The features of eCTD submissions are summarized in the table, which describes improvements in compliance, collaboration and efficiency. This lists the problems such as validation errors, changing guidelines, and variations at the agencies. Although digital platforms and cloud based solutions make the submission process easier, they still face problems ranging from security risks to automation needs to global standardisation.

V. DISCUSSION

A. Interpretation of Results

eCTD is one of the most advanced and useful submission formats for different regulatory agencies such as the FDA, NDA, and many more. The shift had been processed due to the efficiency in the submission, which takes less time and increases accountability. On the other hand, eCTD enhances the structure of submission, which decreases the validation error and human error [5]. The different regulatory agencies, such as the FDA, use this technique of submission to enhance their accountability and decision-making process. eCTD is a superior technology that establishes a single application format for all applications and also avoids expensive internal processes and systems for receiving and archiving applications. Due to the introduction of eCTD, the traditional submission process is not encouraged by different countries' regulatory agencies.

Conversely, considering the additional quantitative discussion there are highlighted some different valuable insights. The data show comprehensive digital transformation in regulatory submissions. eCTD filings increased from nearly zero in 2003 to almost universal use (96–100%) by 2018 across application types [13]. Simultaneously, the increasing average and proportion of FDA expedited program designations per drug (1987–2014) indicate increasing regulatory urgency [14]. These trends highlight the need for automated, standardised eCTD workflows and validation tools, and better collaboration between IT, clinical and regulatory functions to keep pace with the increasing speed to approval.

B. Practical Implications

The eCTD must be implemented since it would thus bring the actual advantage of lessened compliance with regulatory requirements, submission accuracy and shorter regulatory approvals. These automated validation tools reduce errors in all the global regulatory agencies to reduce or eliminate errors. Furthermore, the document management can be real time accessible by the regulatory team and stakeholders via the cloud. The standardised submission format takes the number of delays in getting things approved by agencies such as the FDA and EMA. In addition to pharmaceutical approvals transparency, it also increases pharmaceutical approvals transparency and efficiency through structured data networks. Nevertheless, such companies need to ensure how to face these automation, data security risks and regulatory compliance expectations in such a way that the eCTD processes get optimised for global regulatory success.

C. Challenges and Limitations

The challenges and limitations with the secondary data collection method for the study of eCTD submission have impacted the study. The limited source of data is one of the most important challenges that this method provides. The thing with the study, which is not well explained and the data is not available on different sources, is that the information is not well explained. Additionally, the available data are not specifically applicable to the compliance strategy. Finally, this study does not specifically deal with the lack of differences between different regulatory agencies.

D. Recommendations

Finally, the study should include the difference of the regulatory agencies of different countries, and this will contribute to strengthen the study in the future. There is the need for missing AI and automation discussion that should be added to the study studying the information and data of multiple secondary sources as well as its effect on the eCTD submission format. Apart from that, the study should also examine the difficulties that occur in the advanced submission format of eCTD in terms of data security and compliance. It helps to improve the cybersecurity of the eCTD as well as digital document management.

VI. CONCLUSION AND FUTURE WORK

The eCTD which has been the one to change the game for the pharmaceutical industry in terms of format of submission, revolutionising the global standard, compliance and the efficiency. Validation error and data security are challenges that exists in eCTD that otherwise improves the pharmaceutical industry accountability and decision-making process. The topic has been illustrated in a detailed manner through the help of different case studies.

Future study will be on challenges and comparative analysis by various regulators FDA and NDA. The systematic review will be analysed for future study, which will enhance the information and data related to the eCTD submission format in pharmaceutical industry.

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