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RESEARCH ARTICLE

Prospective Study of Good Practice for Management of Comments / Deficiencies in CTD/eCTD

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ABSTRACT
eCTD or electronic common technical document is an interface designed for the pharmaceutical industry to transfer regulatory information. This module-based regulatory application format was developed by the International Conference on Harmonization (ICH M2 EWG). In 2008 the FDA (Food and Drug Administration) made eCTD format compulsory for all electronic submissions. The role of eCTD is to help pharmaceutical companies enhance the submission procedure by bridging the gap between the time and market and minimizing expenses. However, a recent analysis made by the Open Text™ Corp (a leading company in enterprise content management), it's found out that most of the pharmaceutical companies are struggling hard to meet the deadline created by FDA to comply with the standard using eCTD format.
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1. Introduction

The Common Technical Document (CTD) provides a globally harmonized format that is accepted in many regions, avoiding the need to compile different registration dossiers for different regulatory authorities. It is organized into five modules. Module 1 is region specific, while Modules 2, 3, 4, and 5 are intended to be common for all regions. A regional component is included in Module 3. The review of information provided in a well-structured regulatory activity will improve the efficiency of the screening and review of that regulatory activity. The FDA

is looking towards moving to an all-electronic submissions system for regulatory information in all of its divisions to facilitate easier reviews and information sharing. All submitted documents, such as new drug applications and marketing materials, will come in electronic common technical document (eCTD) form.

The main role of eCTD in pharmaceutical industry is regulatory submissions. And it is done by harmonizing the blueprint and module-based format of pharmaceutical submission applications. This kind of submission ensures convenient and faster filing of applications. This interface is also upgraded by the ICH at regular intervals so as to make it more user friendly.

Good Practice Management in CTD and eCTD:

This document outlines the CTD format for the submission of information in relation to drugs for human use, which is filed over the lifecycle of that product in Canada. Table 1 provides an overview of the presentation of the drug regulatory activity, out- lining the modular structure and main headings, which should be used. The CTD format also provides the structure for the eCTD format; therefore some documents are specific to the format in which a regulatory activity is submitted. For example, the Table of Contents is only required in the CTD format, where the Life Cycle Management Table is only required in the eCTD format. The first draft of the CTD Guidance (2003) was for the use of the CTD format with New Drugs Submission (NDS) regulatory activities only. With this guidance, Health Canada as moved to a more inclusive approach for the CTD format, with the inclusion of documents that may only be submitted for specific regulatory activity types or upon request; therefore many sections and subsections may not be applicable for a given regulatory activity.

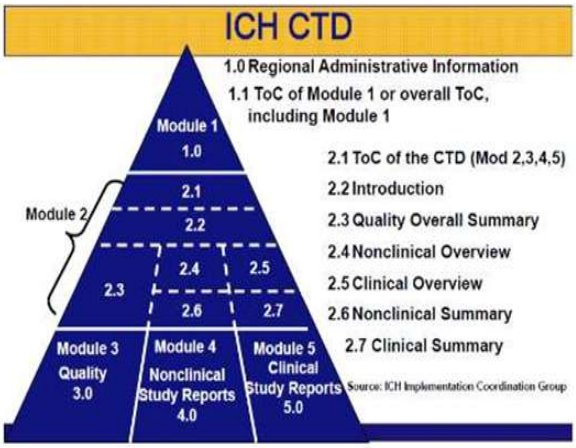

Figure 1

Module 1: Administrative and Product Information

Module 1 identifies placeholders, defined by the numerical items listed in the Module 1 Table of Contents (ToC), for all administrative and product information documentation. Sponsors should use their own discretion based on the number of documents being provided in a given folder in order to decide if those documents should be organized using subfolders.

Module 2:

Note 1: Optionality of granularity for the Quality Overall Summary is provided in order to accommodate different levels of complexity of products. The applicant can choose the level at which the QOS is managed.

Note 2: One document should be submitted for each drug substance.

Note 3: For a drug product supplied with reconstitution diluent(s), the information on the diluent(s) should be provided in a separate part "P" document.

Note 4: One document for each indication should be submitted, although closely related indications can be within a single document.

Module 3:

Note 1: In choosing the level of granularity for this Module, the applicant should consider that, when relevant information is changed at any point in the product's lifecycle, replacements of complete documents/files should be provided in the CTD and eCTD.

Note 2: For a drug product containing more than one drug substance, the information requested for part "S" should b provided in its entirety for each drug sub- stance.

Note 3: For a drug product supplied with reconstitution diluent(s), the information on the diluent(s) should be provided in a separate part "P", as appropriate.

Note 4: The lower level of headings included in CTD-Q at this point are unlikely to be individual documents or files.

Note 5: Refer to regional guidances.

Note 6: Literature References should be listed in the tables of contents

Module 4:

Note 1: Typically, a single document should be provided for each study report included in Module 4. However, where the study report is large, (e.g., a carcinogenicity study), the applicant can choose to submit the report as more than one document. In this case, the text portion of the report should be one document and the appendices can be one or more documents. In choosing the level of granularity for these reports, the applicant should consider that, when relevant information is changed at any point in the product's lifecycle, replacements of complete documents/files should be provided.

Note 2: Literature References should be listed in the tables of contents.

Module 5:

Note 1: The applicants should ordinarily provide the study reports as multiple documents (a synopsis, a main body of the study report and appropriate appendices). Appendices should be organized in accordance with the ICH E3 guideline, which de- scribes the content and format of the clinical study report. In choosing the level of granularity for reports the applicant should consider that, when relevant information is changed at any point in the product's lifecycle, replacements of complete documents/files should be provided.

Note 2: For applications in support of more than one indication, this section should be repeated for each indication.

Note 3: Literature References should be listed in the tables of content.

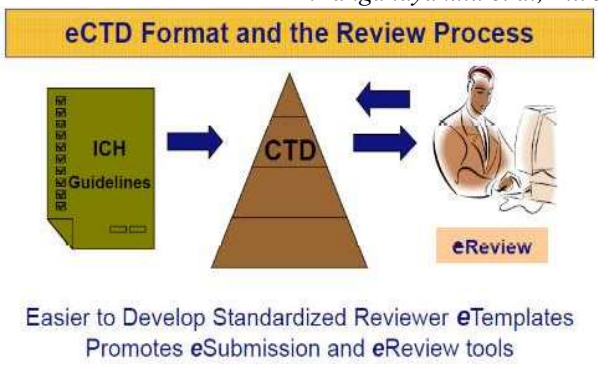

Figure 2

2. Presentation of Regulatory Activities

This section describes the physical specifications for submitting paper regulatory activity in CTD format. The paper format is to serve as the official Central Registry (legal) copy for paper-based regulatory activity. Organization and Identification of Regulatory Activity Volumes. The regulatory activity should be bound in three-ring binders.

Example of bangladesh adapting to ctd and ECTD formats: This report focuses on improvement of the regulatory capacity of the DGDA in regard to the registration process to ensure that the products manufactured or circulating in the country are of good quality and effective and safe for human use. The two main objectives aligned with regulatory system strengthening are to:

- Build the capacity of DGDA officers and major stakeholders to improve the re- view of medicines for registration, to adopt the CTD format for registration, and to move the DGDA toward practices more consistent with international standards.
- Implement an online drug registration management system (using Pharmadex) to effectively track the process of drug registration, including licensing, inspection, and overall regulatory management at DGDA.

TORs for the Taskforce Members:

Identify the structure of the review team, flow of work for medicine registration, and provide recommendations to the DGDA officers that would be designated for each category of work, e.g., the deputy directors were assigned as moderators and assistant directors as reviewers.

Provide further feedback for improvement of Pharmadex, once it has been tailored to suit the new forms and flows.

Provide inputs and feedback in the development of the Bangladesh CTD guide- lines and other documents, including SOPs, user manuals, etc.

Continue to oversee the overall adoption of CTD and implementation of Pharmadex.

Official Launch of Pharmadex and CTD Guidelines:

The registration module of the Bangladesh-specific Pharmadex has been completed and is ready to be launched in September 2016 on a pilot basis at a few selected pharmaceutical companies. To further prepare for the pilot launch, four sets of on- the-job training were also organized for DGDA officers to enable them to practice reviewing actual CTD-based dossiers that were submitted by four pharmaceutical companies, who were participating to show their support for the directorate and the new review process. The practice session was planned such that the staff performed dossier reviews based on their functional roles as outlined in the Pharmadex work- flow. Furthermore, as a part of the positioning of Pharmadex, a user/applicant request form was developed for DGDA, which has been sent to selected pharmaceutical companies to collect legacy data and information to build a Pharmadex database comprising all the necessary data required to launch the system. Once this step is completed, DGDA will send out an official letter to selected manufacturers requesting them to submit a CTD-based dossier to register a product and also to submit their application through Pharmadex.

3. Conclusion

eCTD or electronic common technical document is an interface designed for the pharmaceutical industry to transfer regulatory information. eCTD format enables pharmaceutical companies to submit applications to various regulatory authorities such as FDA without altering the data. This XML-based electronic version of the CTD is now widely used as preferred submission format for the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). eCTD format is now widely used in the United States, Japan, the European Union and Canada. As per Harv Martens, a member of the ICH M2 Expert Working Group, Electronic Common Technical Document comprises of 5 modules Administrative information and prescribing information Common technical document summaries Quality Non- clinical study reports Clinical study reports And it is further divided into 2 categories

-Regional module: 1.

Common module: 2-5. The main role of eCTD in pharmaceutical industry is regulatory submissions. And it is done by harmonizing the blueprint and module-based format of pharmaceutical submission applications. This kind of submission ensures convenient and faster filing of applications. This interface is also upgraded by the ICH at regular intervals so as to make it more user friendly. As eCTD format has become mandatory in the key markets, it has become essential for the companies to conceive a unified environment that aids the lifecycle of every kind of inherent submission. In this way, they can effortlessly manage the exhaustive system of accumulating, acclaiming, releasing and documenting new drug/medical device applications.

However, in most of the cases, companies lack such an integrated platform. Even though some pharmaceutical companies have some of the components, there are still many fields where key functionality is incorporated in silos. There are firms, who still follow the traditional paper-based methods, thus wasting both considerable amount of time and money. In order to successfully carry out the eCTD submission, pharmaceutical companies must grasp all documents, including assortments, responses to questions, modifications and restorations in a consistent electronic

format. The primary component of eCTD submission is XML "backbone" file which offers metadata about content files. It also gives lifecycle instructions for explaining the submission and each document within the submission. Life sciences companies should follow this data structure, as it greatly helps them with effective submission of their documents at faster rate. The pharmaceutical companies should use a primary software product to manage the integrated regulatory data and regulatory submissions process.

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