cunesoft
compliance delivered

A View to Tomorrow's Electronic Submission - eCTD v4.0

Benefits, challenges and transition

October 2018

Content

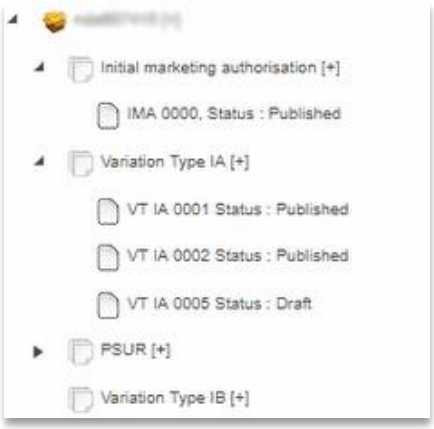
Introduction

Since the early 2000's, the electronic Common Technical Document (eCTD) has been accepted by many health authorities. Introduced as a globally harmonized means of transitioning paper submissions to electronical methods, its implementation led to the creation of eCTD submission software tools and new submission management processes. Changes to the eCTD version are not uncommon yet the transition from eCTD version 3.2.2 to eCTD version 4.0 is, in fact, quite substantial. It will ultimately deliver entirely new value and will also bring some new challenges on the way.

Understanding eCTD Changes

A key change we see with eCTD v4.0 is the organization of your dossier and submissions. While traditionally you have organized everything by sequence, eCTD v4.0 gives a more structured approach.

Figure 1. Product application tree view



In the Figure 1. you can see a tree view of a product application, and different submissions within this application. Each submission contains various *submission units* – traditionally called sequences for eCTD up to version 3 – and each *unit* will have a lifecycle stage associated with it. The structure of *submission unit* will look familiar to what you can see in eCTD v3, as the logical structure of eCTD v4.0 will not change dramatically. Creating, editing and using submission units will closely resemble today's sequence preparation process, with some altered details.

One more important change we see in moving from eCTD v3, to eCTD v4.0 is *transition mapping message*. While this message does not include any actual content, it will set the stage

for the ongoing lifecycle management of submission activity that already started but is in the process on moving from old eCTD version to eCTD v4.0

In terms of the submission assembly, the actual view of the assembly will look much the same as it does today. What will most likely be different is the fact that the output itself could, at least in theory, be delivered as a flat structure.

eCTD v4.0 Validation & Viewing

Submission validation will now occur at two levels. The first following the ICH validation rules and, if those are passed, the regional validation rules. Both ICH and regions that are accepting eCTD v4.0, have provided or will provide the specifications for validation rules so that vendors, industry and health authorities can create mechanisms for validating submissions.

Advantages of eCTD v4.0

After working closely with local health authorities in various eCTD v4.0 workshops and functional analysis days and working on preparation to eCTD v4.0 – we believe there are several distinct advantages when moving to eCTD v4.0:

- *Harmonized submissions* - All content from Module 1 through Module 5 is contained in one exchange message – i.e., 1 XML file covers both ICH and regional information.
- *Expanded Document reuse* - Once a document has been submitted, eCTD v4.0 will allow for the document to be reused by referencing its unique ID from the same or different submission unit.
- *Enhanced lifecycle via Context of Use* -The Context of Use concept allows for advanced life cycle management operations. A Context of Use may be replaced by one or more Context of Use elements and vice versa (i.e., many to one) through the context of use life cycle.
- eCTD v4.0 also introduces the ability to apply changes to keyword definition display name values (e.g., drug substance/product names, manufacturers, dosage forms, indication, excipient, group title, etc.) without resubmitting the physical files or the Contexts of Use element.
- *Built-in grouping* - The Context of Use code and Keyword code combination will function to create a group of documents in a specific context.
- One use of context groups includes the replacement for STFs in Modules 4 and 5 to organize multiple files relating to a single clinical study as noted in the eCTD specification v3.2.2.

- *Eventual support for two-way communication (regional)* - The regulatory authority can use eCTD v4.0 to send correspondence to the submitter.

Cunesoft & eCTD v4.0

Upcoming Changes and Adaptations

Cunesoft designed and built cune-eCTD and the Regulatory Operations platform with the knowledge of eCTD v4.0 coming in the next few years. As a result, we have a solution that can already adapt to new submission requirements with its schema-driven submission publishing capabilities, its adaptive submission structure templates that are built in and its ability to seamlessly utilized document metadata that is applied during publishing. Nonetheless, some of the changes will need to be adapted to our solution.

eCTD's v4.0 Construct of "Applications"

eCTD v4.0's concept of the Application and how it is used to help group submission information will be introduced to cune-eCTD. Applications effectively map to what has historically referred to as a "Dossier". Within each application there will be submissions which map to a specific 'Regulatory Activity'. Within each submission there will be 'submission units' which align with today's concept of 'sequence'.

Adapting document attributes for 'keywords'

Another change - mapping document attributes to eCTD's v4.0. keywords concepts and ultimately replacing current constructs such as the study tagging file (STF). Cunesoft's submission templates, with context of use codes, will be configured to identify which keywords are to be inherited from the document.

Flexibility with Context of Use

In eCTD v4.0, Context of Use (CoU) is similar to a leaf and indicates the type of document. The code for each Context of Use specifies where documents are to be inserted into the CTD/eCTD TOC when presenting a reviewable structure. A CoU will become where lifecycle actions occur and may contain 1 or more individual documents. This will be part of the submission templates we provide where the context of use code will be provided and both product and document attributes (i.e. substance & manufacturer) will be leveraged and utilized as keywords.

Sophisticated Lifecycle Actions

Another change will be in the handling of content lifecycle. With eCTD v4.0, the ability to have 1-to-many and many-to-1 types of lifecycle actions that will become available. For submission contents within the same context of use and keyword(s), replacing (or versioning) the documents within that CoU can occur 1-to-1, 1-to-many, many-to-1 and many-to-many.

Once replaced, prior content becomes 'obsolete' and the new content becomes 'active'.

Transition Mapping Message

The transition mapping message (TMM) will contain data elements to enable the following two objectives: a.) maintain Context of Use lifecycle in new submissions/regulatory activities; b.) enable the reuse of documents within and across applications. Cunesoft will implement the ability to create this message from the current view of historical eCTD sequences using our standard publishing request interface and adding the option for creating the transition mapping message.

Submission Assembly

Behind the scenes, our submission templates will have the additional mapping to the appropriate Context of Use codes and their related coding systems. These templates will also know which product and document attributes should be mapped as keywords for the context of use.

Validation & Viewing

As ICH and regional validation rules become finalized and available, Cunesoft will be determining its strategy for incorporating as many of these rules as possible so that they are applied and enforced as early in the submission process as possible.

Contact us for more information and Product Demo

Cunesoft offers a ready to use, pre-validated and highly secure cloud based regulatory compliance suite for Life Science companies. Contact us for a live demo.

Cunesoft GmbH
Luise-Ullrich-Strasse 20
80636 Munich
Germany
Phone: +49-(0)89-235 14741
Website: www.cunesoft.com
E-mail: info@cunesoft.com

Cunesoft Inc.
103 Carnegie Center Drive, Suite 300
Princeton, NJ 08540
USA
Website: www.cunesoft.com
E-mail: info@cunesoft.com