

Document Management for Labeling

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The management of label documents of medicinal products is complicated and time consuming with many parties involved. The right document version must be approved by the relevant stakeholders, provided to the affiliates for local implementation, submitted to the Health Authorities meeting stringent time lines, distributed to several departments, included in xEVMPD update notifications and used for the assessment of adverse events by the Pharmacovigilance department.

The labeling department must have an overview of the current label documentation, pending requested changes and the history of changes. They need to inform affiliates about revisions to core documents and need to ensure that local labels are updated in time. In addition they need to make sure that the electronic handling and storage of label documents is done in a compliant way and that unauthorized persons cannot access or change labels.

A document management system for labeling can help to meet these requirements. It should consist of the following components:

- Standard Electronic Document Management System (EDMS)
- Read-only portal
- Affiliates collaboration platform
- Tracking database
- Interface to the electronic Publishing System

Standard Electronic Document Management System (EDMS)

An EDMS for labeling does not need to be set up in a complicated manner. Only few users mainly from the Labeling and Regulatory

Affairs department and the labeling committee members need to use the system. It will not be used by affiliates and other departments. This presumes that the affiliates are responsible for the management of local labels using local systems and procedures. The central labeling department only handles the Company Core Data Sheet (CCDS), common / core labels and documents which are included in eCTD submissions.

A typical lifecycle of a CCDS consists of only few steps like draft, review and approve. Common and local labels have additional steps to capture the interaction with the Health Authority (HA). During the review and approval of the CCDS and common labels, members of the internal labeling committee are involved. Being senior management they require an easy to use and mobile way of reviewing and approving the document.

The biggest challenge for an EDMS is to manage parallel changes to the same source label. For instance a new document version for a variation is created, internally approved and submitted to the HA waiting for approval. Meanwhile another label change is required. A new version needs to be created which is not based on the variation with pending HA approval but on the previous HA approved document. This cannot be reflected by a sequential version history. One possible approach is to have version branches. Another is to create completely new documents and to set relations between the source mother and child document.

Finally an EDMS helps to meet compliance requirements. It controls the document lifecycle, meta-data and storage location, handles different versions, records an audit

trail of changes and enforces a permissions system.

Read-only Portal

Pharmacovigilance and other internal departments and affiliates need to have access to approved label documents. They need to obtain a CCDS once it is company internally approved and the national Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) once approved by the HA.

This access can be achieved by a read-only portal which is synchronized with the EDMS. The portal needs to display certain document attributes like for instance product name, active ingredient, form, strength and country. A filtering function is required so that it is easy to find the relevant documents.

External staff needs to have access to this portal as smaller countries like Malta or Cyprus are very often handled by consultants. Other areas of business are nowadays also outsourced to partner companies. This access demands a permission system so that external users can only see the product / country information relevant to them.

Affiliates collaboration platform

A collaboration platform streamlines the communication between the labeling department and the affiliates. The user fills out a business case specific data entry form and follows a lifecycle updating the form at different time points.

Two typical scenarios for such a collaboration lifecycle are:

1. The labeling department notifies concerned affiliates about a new version of a CCDS. Labeling operations provides the document and informs which text was changed, the reason for change and till when the national

labels must be adapted based on for instance the safety grading. As a next step the affiliates send a new version of the local label for inclusion in the eCTD submission. Finally they send an update when the label was submitted to and approved by the HA.

2. Affiliates need to inform the labeling department when the HA requests a change to a local label and provide additional information about it.

An integration or synchronization with the EDMS for providing the documents and uploading them would be beneficial but is difficult to implement. A labeling operations manager needs to check the received document and place it at the right location in the EDMS.

Likewise an integration of the collaboration platform with a tracking database would be beneficial as event dates like "submitted to" and "approved by the HA" must be captured. But also here the headquarter Regulatory Affairs department wants to check these dates before storing them in the tracking database.

Tracking database

Pharmaceutical legislation requires that a change of the base label has to be locally implemented after 30 or 60 days or another pre-defined period depending on for instance the safety grading. The timely implementation of label changes is checked during HA inspections. An overview of the changes, the status of the local implementation and the history must be available. In order to trigger corrective actions it is important for the labeling department to know in which countries the label submission is already delayed and where it soon will be.

The label tracking cannot be done using the document meta-data of the EDMS. The data structure is complex and the reporting requirements are high and therefore a

separate tracking database is used. Mid-sized and large biopharmaceutical companies have a Regulatory Information Management (RIM) System in use and it is advisable to extend this system to also meet the label tracking requirements. The RIM system needs to provide the relevant data and label documents for the xEVMPD submissions and therefore the link to labeling management is anyways given.

Interface to Publishing System

Label documents are included in eCTD or Nees. A publisher retrieves the document in the EDMS and associates it to the submission sequence. Typically publishing systems are set up so that it is only possible to associate internally approved documents stored in the corporate EDMS.

The EDMS and publishing system also need to be able to process XML documents. The Structured Product Label (SPL) format is based on ANSI/HL7 and mandated by the US Food and Drug Administration (FDA) for medical product labeling. For Europe a similar project called Product Information Management (PIM) was stopped by the European Medicines Agency (EMA) in March 2011.

About the Author

Sven Harmsen is an independent consultant specializing on Electronic Document Management and Regulatory Affairs IT systems. Since beginning of 2008 he has managed various global implementation projects in this area.

Prior to being self employed Sven Harmsen worked six years at Astellas Pharma and was responsible for R&D related Document Management and Regulatory IT systems.

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