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WHITE PAPER

Labeling Digitization: Manage Data, not Documents

A prescription drug product label is a compilation of information about the safe and effective use of the product prepared by the manufacturer or marketing authorizing holder (MAH) and approved by the health authorities in the respective marketed zones. Drug labeling is becoming more prominent that involves dealing with multiple functional dynamics with required specialized attention, stakeholders (supply chains), and constantly evolving regulatory environment across the globe. Marketing authorization holder is responsible to maintain the valid and updated information in their approved or marketed product labels throughout of its lifecycle globally where the products are being marketed.

Creation and maintenance of labels or label documents is a continual process to any MAH since they have to collect and implement all the necessary changes in the label documents for regulatory approvals and compliance. Health authorities also communicate to the MAHs on updating information via notifications/amendment notification letters. In this regard, MAHs are responsible to collect product specific updated information from various sources and update core label information for each product on a time basis.

Core Data Sheet (CCDS/CDS) Importance

Core information or core label data (Core Data Sheet or CDS) is an ***internal regulatory document*** which serves as the ***company's global reference document for a product***. It is used to communicate the company's position to appropriate stakeholders worldwide for the inclusion of safety and efficacy information on country-specific labels. The core safety information includes mainly therapeutic class, indications, dosage and administration, contraindications, drug interactions, pregnancy/lactation, special populations, adverse drug reactions, warnings/precautions, and over dosage.

HQ Role

Global labeling management or headquarters team is responsible to prepare and maintenance of CCDS for each marketed product of the company. Once the CCDS is prepared and approved it should be distributed to all the local country affiliates where the product is being marketed. However, CCDS maintenance is a widen challenge to the MAHs that requires timely receive, review, validate and update the information pertaining to safety & efficacy changes to the marketed products. There are several ways to obtaining safety updates such as periodic safety reports, PMS, health authority notifications, and regulatory platform information (FDA, PRAC recommendations, etc). The headquarter team is responsible to get all the above information to meet regulatory compliance in the existing documents. Once the CCDS is updated and approved the same document will be distributed to all the country affiliates to implement the necessary changes in the local labels as applicable. In case of any difference in the label content from core information to local labels, headquarter team will provide the response for each difference in local labels after evaluating and concerning the country or region-specific requirements. Thus headquarter team will provide continuous support to all the local affiliates on labeling information.

How Core Data Sheet is Different from a Label

Drug label refers to all the printed information included with prescription drugs, over-the-counter medicine, and any dietary supplements that constitute the agency-approved information on the use of the product in a specific country or region. The approved labels were prepared according to the regulatory authority's standards and templates. Drug labels include usage instructions, ingredient details, and a lot more information about the product. All the drug distributors must comply with the Health Authority standards to get approval and market their products in a specific country or region.

Health authority regulations and standards are different from one country or region to other country or region for dossier submission (label documents) for its market approval. In the Europe region, all the marketing authorization holder should submit label information as per the SmPC/SPC (Summary of Product Characteristics) format as defined by the EMA, whereas in United States region, label information should be in USPI (United States Prescribing Information) format by FDA. These two labels (SmPC and USPI) are mainly considered as regulatory labels and many other emerging countries or regions are adopting these standards and preparing their local labels by considering their local country-specific requirements.

"Regional or Local label does not fully represent the company position, therefore not the best solution as an internal regulatory tool although there might be some reasons to do so".

However, there are no fixed regulatory or standard templates available for CDS document creation. CCDS constitutes the company position based on the data developed for its marketing positions worldwide. CCDS should not be a regulatory agency position from any MAH prospective. CCDS discloses the company's view of safety profile to regulators. If regulatory authorities disagree with statements in the CCDS, the company can reconsider, disregard or adopt their position for the CCDS.CCDS format and content is an internal company decision, but can be based on a label format of SPL, USPI. But not limited, CDS document can also be prepared by using a region-neutral structure of hybridization format for its better representation of data.

Label Data Points

As per the FDA & EMA guidelines, USPI contain 17 sections and SmPC contains 10 sections in the label document. Companies that are serving globally have different labeling requirements based on the products and different requirements of each country and region. The number of sections from local labels to SPC/USPI may vary for one country to another country. But the local label information must be in line with the company core information (CDS/CSI). In addition, some countries will have additional sections which are not available in SPC/USPI and those sections may be considered as local country requirements for that particular country or region.

Example of Local Label Requirements

South Africa	Panama	Costa Rica
Scheduling status	Trademark or generic name of product	Generic name and concentration of the pharmaceutical product
Proprietary name	Name and address of manufacturer and distributor	Pharmaceutical form
Composition	Dosage form and route of administration	International Common Denomination (INN) of the active principle
Pharmacological classification	Name of the responsible pharmacist	Clinical pharmacology
Pharmacological action	Details of therapeutic class	Indications
Indications	A sample of the container	Contra-indications
Contra-indications	Complete formula of finished dosage	Precautions and warnings
Warnings and special precautions	Draft of proposed packaging copy and package insert	Interactions
Interactions	Active ingredients	Adverse effects
Pregnancy and lactation	Indications	Dosage and administration
Dosage and directions for use	Contraindications	Recommendation in case of overdosing
Side-effects and special precautions	Warnings, precautions	Abuse and addiction (when applicable)
Known symptoms of overdosage and particulars of its treatment	Recommended route of administration	Date of review of the monograph
Identification	Draft outline of proposed information to the medical profession	Complete bibliographical references
Presentation	Recommended dosage: usual dose, frequency, range	
Storage instructions	Summary of pharmacological data and data relevant to proposed use	
Registration numbers	Summary of all clinical trials	
Name and business address of the applicant	Data on adverse reactions and drug interactions	
Date of publication of this package insert		

Local label Content Management

As mentioned earlier local countries follow different label formats and capturing all the information from SPC/USPI to local label is a big challenge to any MAH. The different sections or section names in local labels are based on local requirements/regulations and data representation also may be different for some of the sections. Some of SPC/USPI sections might be called with other names and data representation also might be different in the local labels, and some of the sections' information may be split into more than one section. This is the prime criteria and must be thoroughly compiled and validated before capturing appropriate data into label documents. Generally, local labels contain limited labeling information as compared with SPC/USPI.

Local labels have different section names in their country label templates; however, those sections are very similar in the meaning with the other sections in regulatory label of SPC/USPI. For example, **South Africa** local label contains identification & presentation sections, but these sections are not available in SPC/USPI. However, the same information is available in both the SPC/USPI under the dosage form and strength, Nature and contents of container & how supplied sections. In **Panama**, local label contains section "sample of container" and this is equal to 6.5 & 16 sections in SPC & USPI, respectively. Whereas in **Costa Rica**, INN of active substance and complete bibliography sections are similar with sections 11 & 15 in USPI, and section 2 in SPC. However, SPC doesn't constitute any bibliographical related section. Below table shows some of local label sections deviating with SPC/USPI sections and meeting the same information in other sections (refer below table).

Label Digitization

Maintaining Regulatory compliance at all times coupled with stringent timelines is an ongoing obligation. Currently, this is done with a lot of manual processes that repetitive in nature and sometimes causing people burnout. Resorting to offshoring doesn't help much because of continuous oversight and attritions.

Digitization labels and utilizing technology solutions for end-to-end labeling operations using automation and some artificial intelligence (AI) will be your future. Every company needs to adapt to these and the faster companies adapt, the more they can ease the current pain. In these automation technologies, most of the labeling activities are performed using automation processes such as create, update, maintain and compare the documents for different versions and give the compliance report for each labeling activity. Technology involves business rules management to help keep some flexibility to adapt to customizations on the fly. This technology also helps in raising the alerts/notifications for regulatory changes in labeling documents and accordingly MAHs can take a proactive approach to update the data in the documents.

This also improves HQ control yet helps in reducing their burden by allowing a standardized and centralized approach with the ability to allow for localized autonomy as applicable. This allows everyone to be aligned while meeting the needs of the region where they're conducting business.

Advantages with Digitization & Automation

Over 30% time saving

Higher efficiency and productivity gains

No need of offshoring

Less or No manual QC

Meet Label Compliance goals more effectively

Less HA label findings

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