WHITEPAPER

Labeling findings from FDA and other Agencies audits summary

Regulatory environment has become increasingly complex and making drug labeling a highly regulated and closely monitored activity. As some of you are aware, Health authorities are specific to regulatory requirements for medicinal products on labeling requirements such as patient information leaflets, package inserts and prescribing information packaging and artwork.

Industry experts estimate that between 35 to 40 percent of all product recalls are attributed to packaging and labeling errors as well as omissions. In fact, a recent report by AMR Research cited from Food and Drug Administration statistics which includes 455 product recall notices, 51 percent of them are because of mislabeling, and 13 percent are because of faulty packaging. Most of the regulatory inspection findings are associated with labeling issues by Health authorities such as US FDA, EMA, Canada, and others. All of them have a basic expectation "Product labeling must be compliant with the applicable local health authorities' requirements for content, format, organization and structure. Labels should comprise of information on the safe and effective use of the drug. The label must be informative, accurate, not promotional, false or misleading. No implied claims or suggestions for use if evidence of safety or effective is lacking". Let us see why this is complex when it comes to implementing the above.

The management of both global and local labeling process is a complex process, it includes maintaining and updating the CCDS and local labels. If any label deviations or compliance issues, it would lead to regulatory actions, recalls and fines as well sometimes.

So what are the Challenges?

There are several challenges impacting product labeling process with respect to global and local regulations. Most of Labeling challenges stem from some common events like company acquisitions and mergers, multiple products approved in multiple countries, changes in the local labeling (country specific regulations). The global labeling process is very complex and there are often functional dependencies between different departments such as regulatory affairs, medical, safety, manufacturing, supply chain, marketing, packaging, and local affiliates.

At present, mergers or portfolio acquisitions are frequent among global companies. These activities combined with in-licensing of products at all stages of development and marketing, can also disrupt any compliance process as companies try to reallocate global resources and re-adjust processes for the new organizational structures or entities. Compliance gaps and risks internal to these activities may not be immediately identified when teams are restructured, resulting in unclear ownership and responsibility for a critical process. The following are extreme challenges during mergers and acquisitions which include inadequate transition process, lack of an appropriate tracking system, poor communication between head quarter labeling teams, local affiliates and regulatory teams.

Companies having several products marketed across multiple regions with country specific requirement(s) to comply with their regulations, this is complex and also increases costs exponentially. Most importantly, labeling challenges in labeling process are regulatory compliance, global process standardization, automated inspection, version control, data management, and impact of changes. Over a period, the label content in different jurisdictions continues to "drift" away from the content presented in CCDS, disintegrating the intention of a "core" as the misalignment continues to expand. This is one of the main reasons in large companies that are marketing potentially hundreds of products in multiple markets.

In addition, the frequent changes in drug labeling regulations in the emerging markets contribute to another important challenge. Local Product Label (LPD) must comply with local regulations (applicable country specific) failing to compliance with the regulations would lead to health authority actions, product recalls or withdrawal from the market. Local labeling challenges are mainly due to lack of coordination between labeling head quarters and affiliates, inconsistency with CCDS and CSI information, delays in updating the local label and implementing the new changes, content and language translations.

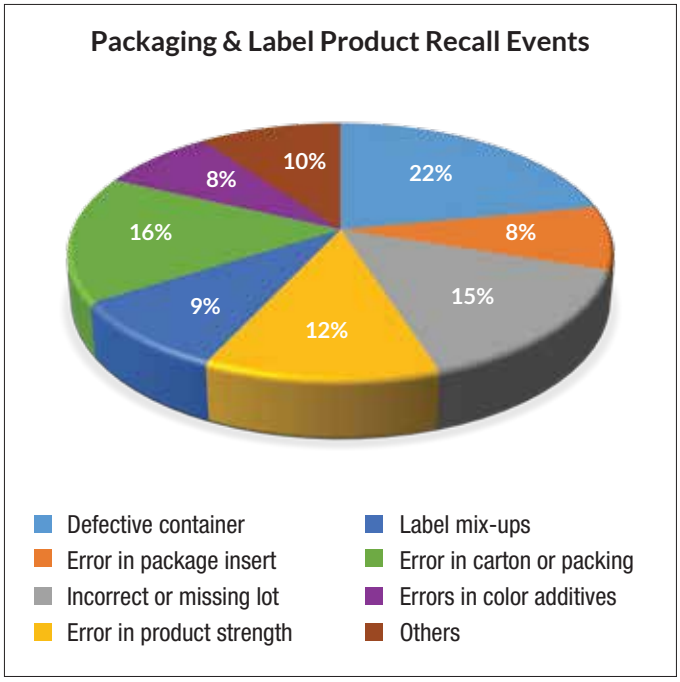
Category	Label Challenges	Percentage	Total %
Multiple products multiple countries	Frequent safety updates in CCDS for newly approved drugs	4	34
	Label content in different jurisdictions	9	
	Non-consistency in label formats and submission methods	3	
	Tight budgets and schedules	8	
	Language and content changes	5	
	Poor strategic plans	5	
Mergers & Acquisitions (M&As)	Unclear ownership	15	45
	Inadequate transition process	6	
	Lack of an appropriate tracking system	8	
	Poor communication between head quarter labeling teams	11	
	Label version history management	5	
Local regulations	Coordination between labeling head quarters and affiliates	11	23
	Delays in updating local labels and implementing new changes	2	
	Inconsistency with CCDS and CSI information	2	
	Content and language translations	3	
	Timeline management for label updation and deviations	5	

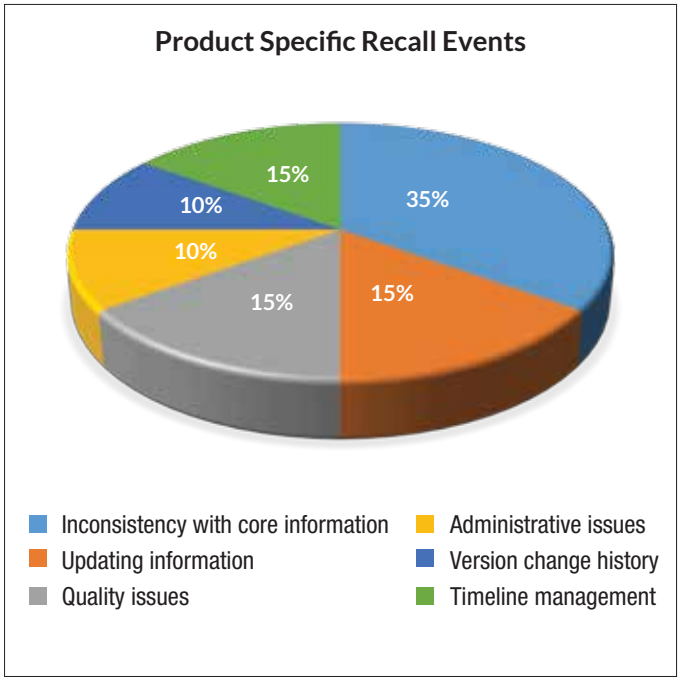
Package & Labeling Compliance

With high importance of regulatory compliance, data accuracy is one of the most important criteria in drug labeling; approximately 51% of auditing issues are related to labeling associated documents from various audits conducted by FDA and MHRA reports. Lack of effective control measures and processes to eliminate labeling errors could result in serious health hazards, regulatory actions, and a flawed reputation for a company; sometimes labeling non compliance issues may lead to product recalls, partial or complete withdrawals from the markets as well.

The label compliance issues are associated mainly with packaging related (defect container, miscarton information, label mix-ups, etc) and product related that includes dosage form, strength, warnings, contraindications, ADRs, and others.

Package & Labeling must comply with applicable regulatory requirements such as US FDA, Health Canada, and MHRA. In USA, drug product packaging and labeling should comply with US FDA 21 CFR 211 Subpart G. It includes Material examination and usage criteria, labeling issuance, Packaging and Labeling (P&L) Operations, Tamper-evident packaging, Drug Product (DP) Inspection and Expiration dating. In the same way, for emerging markets packaging and labeling must be done as per applicable country specific Health Authority regulations.





Source: Regulatory Education for Industry (REdI): Focus on CGMPs & FDA Inspections Silver Spring, MD , July 15-16, 2015