Report

Mastering the translation of clinical trial labels

Creating local language labels with consistency, accuracy and speed

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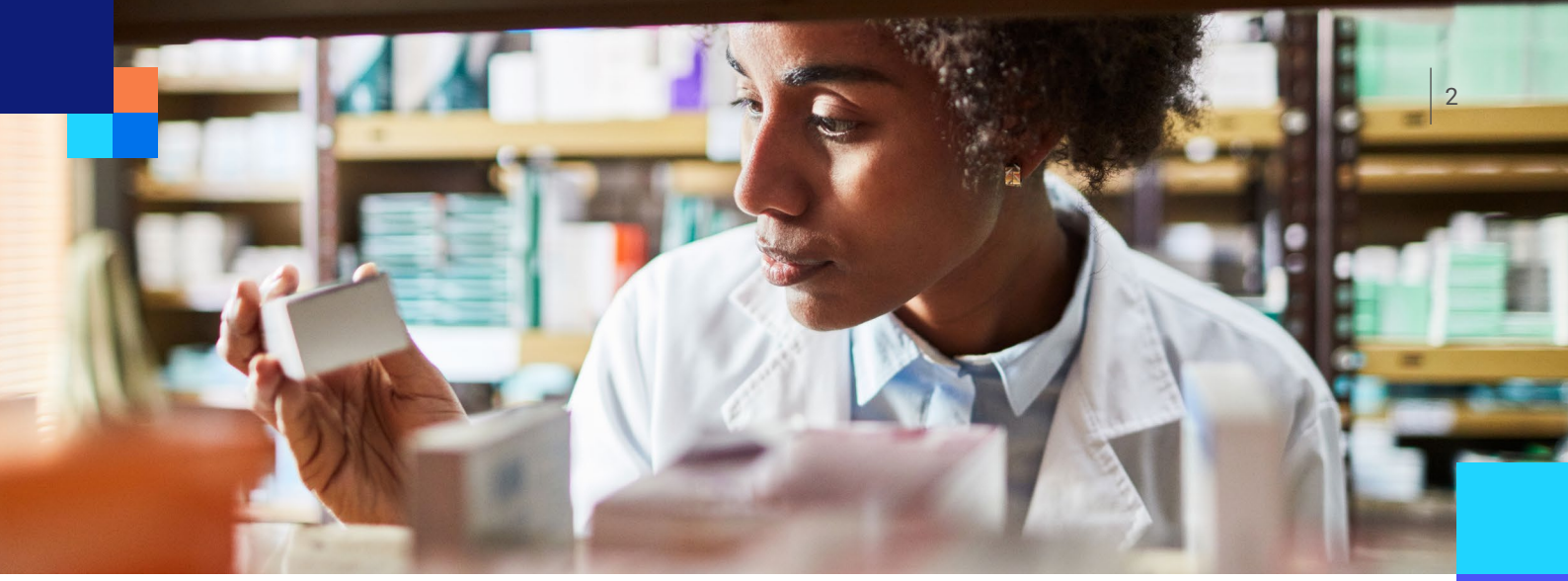

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Background

Without careful management, labeling can quickly become a significant bottleneck in the clinical trial supply chain, with any delays potentially derailing the progress of a study. One of the most complex and lengthiest aspects of clinical trial labeling is efficiently managing the wide array of country-specific labels that are required for a multi-national trial, ensuring that all the label information is correctly translated and that the design and other label elements comply with the relevant local regulations. Without the use of integrated systems, this activity is incredibly labor-intensive, and as trials get more complex and geographically diverse, it gets exponentially harder.

This challenge is compounded whenever a clinical trial opts to use multi-page booklets; a common practice when IMPs (Investigational Medicinal Products) are destined for multiple countries as a single panel label typically only has sufficient space for a couple of languages. Each booklet is effectively a collection of single-panel labels, each of which can cause delays to booklet creation while its content is being approved, if for instance, countries are added at a late stage to address issues with patient recruitment. Consequently, it is not uncommon for booklet label creation, approval, and printing to take over 16 weeks.

The shift to agile trial protocols has also complicated matters, with some materials now needing to be produced on-demand to incorporate the latest changes to patient information.

Events of the past few years have led to a reset of sponsor expectations thanks to conclusive proof that trials can be conducted at speed without excessive cost or risk to patient safety. This has resulted in demand for all therapies in development to benefit from an accelerated clinical trial process, allowing them to reach patients faster and offering an improved experience. This supports pledges to deliver more patient-centric care, while also fast-tracking the route to market and maximizing the return on investment before patent expiration.

As sponsors and their partners in the outsourcing community seek to identify how they can find efficiencies in the clinical trial process, the clinical supply chain is in the spotlight with organizations recognizing that automation and the creation of streamlined workflows can deliver results.

The translation challenge

A clinical trial label or booklet contains many different elements that need to be managed for country specific labels, with a combination of text, phrases, variables, barcodes, and graphics. All content, whether it is text or image based, must go through an approval process before it is added to a label.

Some of the regulatory requirements that need to be printed include:

- Name of the main sponsor, clinical research organization or investigator
- Name of local sponsor as well as or in replacement of main sponsor
- Trial reference code to allow identification of clinical trial
- Trial subject identification number/ treatment number
- Expiry dates (subject to revision as data becomes available about stability)
- Regulatory phrases such as “Keep out of the reach and sight of children” and “For clinical trial use only” or similar wording
- Quantity of dosage units
- Route of administration
- In case of open trials, the name/identifier and strength/potency
- Batch or code number to identify the contents and packaging operation
- Storage conditions
- Period of use to allow return of IMP after expiry

When creating labels for a clinical trial, it is normal practice to create a ‘master label’ in English from which country-specific labels are derived; translations of the master-level phrases need to be sourced before the localized labels can be created and sent for approval.

There are occasions where a booklet is likely to be required even if the trial is being conducted within a single country. For example, some countries have multiple official languages and numerous regional dialects, such as India which is playing an ever-greater role in clinical research. Each of these languages and dialects need to be accounted for in labeling to ensure patient adherence and safety throughout each study.

In addition to ensuring that label content is correctly translated, organizations need to maintain compliance with other local and regional regulations, which could dictate the use of specific fonts or symbols. Despite most national regulators opting to set regulations based on US or EU standards, there are still numerous country-specific requirements, even for EU member states; it is a challenge to ensure that label designs comply with all regulations for many different territories covered by a multi-national trial.

With a general industry emphasis on speed of delivery, there is now an increased likelihood that target countries taking part in the trial will change at short notice due to the availability of eligible subjects. Organizations need to be able to quickly source translations for label content and ensure that their label template design adheres to local regulations.

Fundamentals of a GxP-compliant phrase library

Phrase libraries allow organizations to safely recycle content, providing a repository of approved translated master-level phrases that can be used without reference to an external translation house and repeating lengthy internal approval processes every time a phrase is used. This method can effectively save time and reduce costs without having an impact on safety.

All the 'approved phrases' and 'sets of phrases' should be managed and stored independently of specific trial information and the platform should offer tools to help language experts monitor the impact of proposed and actioned changes to phrases.

The library allows for more effective standardization of phrases across different studies. Most phrases can be correctly expressed in a variety of ways and while technically correct, inconsistent phrasing is frowned upon by regulators due to the potential for patient confusion and health risk.

Phrases should be stored as Unicode with a specification for the approved font, point size, spacing, kerning etc. This ensures that phrases are used in the format that they were originally approved, ensuring legibility.

Are universal phrase packs the future?

It has been argued that the industry could compile a common phrase pack containing translations of master-level phrases common to all companies and trials e.g., "Keep out of reach of children" to provide consistency across studies (regardless of the sponsor and trial delivery partners). This pack could be used as the foundation of an organization's wider phrase library and could potentially also include images and iconography.

This would emulate practices used in other industries, for example:

- The medical device sector now has an ISO standard symbol library available which has been widely adopted.
- The Global Harmonization Standard (GHS) has been widely adopted by organizations transporting hazardous material across Europe. A standardized set of risk and safety phrases and pictograms are now used, with specialist companies maintaining commercially available phrase packs.

Translation management basics

For efficient GxP compliant translation management, any software-based system must involve:

- Robust security features including granular access permissions
- Detailed user activity logs
- Version control management
- Import and export functions for source phrases
- Translation source language designation

In addition, there are several quality-of-life features that are highly desirable. These account for the various approaches to managing language data, offering flexibility to the user. For example, it is helpful if a solution provides support for:

- Central administration
- Trial-specific phrase sets
- Grouped phrases (e.g., dosage phrases)
- Ability to filter languages to those required for a specific trial

Potential pitfalls

There are considerable risks when using a manual system or a phrase library solution that is not tightly integrated into the labeling workflow. Many organizations are currently reliant on Word or Excel documents, or archaic custom software solutions that operate independently of the labeling solution. Organizations that use translation management systems independent of their labeling workflow will often encounter the following issues:

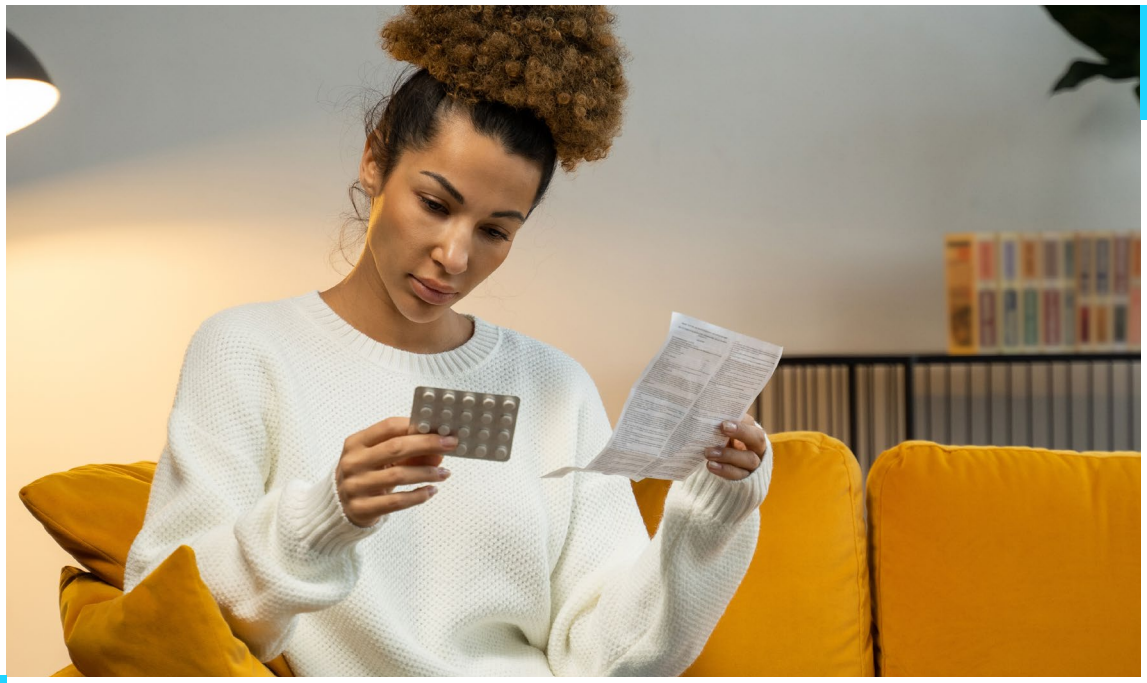
Some of the regulatory requirements that need to be printed include:

- **Manual keying**

  The label creation process is reliant on users moving information between different systems by copying and pasting or retyping. In addition to being a slow and cumbersome process, humans are not infallible and manual keying increases risk and introduces the potential for costly mistakes by even the most competent of users. Any uncaught transposition errors have a high likelihood to cause delays or even invalidate the entire results of a trial.

- **Ensuring consistency**

  Regulators across the world have emphasized the importance of providing patients with consistent information about IMPs. It is therefore essential that phrasing remains consistent throughout a trial to reduce the probability of patient confusion. Without an automated workflow, it can be difficult to ensure that once a master-level phrase has been translated and approved for use, it is used across all patient-facing assets.



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Some of the regulatory requirements that need to be printed include:

- **Spotting subtleties**

  Manual processes are always subject to human error; retyping and editing introduce unfortunate opportunities for subtle variations to appear in the text with misspellings, truncation, or poor transposition - potentially altering the meaning of a phrase altogether.

- Formatting changes often occur when copying and pasting information between different systems.
- Changes in pictographic languages such as Chinese can be difficult to spot if the user is not familiar with the character set.
- Widely understood conventions which govern the use of plurals in English are not always applicable in other languages and in some instances, there are different plural forms of the same phrase for use that are dependent on the context.

- **Local revisions**

  Without a centralized and automated approved phrase library, teams and individuals have significant scope for interpretation. Locally managed spreadsheets or other systems are at risk of revision to reflect personal subjective interpretations and preferences.

- **Auditing challenges**

  The lack of a centralized electronic audit log means delays with audit requests and when using a paper-based system, the loss of a single piece of paper could derail a trial or lead to a product being pulled from the market. Furthermore, paper approval processes frequently involve re-scanning proofs after each wet ink signature indicating approval has been acquired. The image is degraded every time that it is scanned, making it difficult to decipher some elements of the label, and responsible persons end up being asked to assess a label that is different from how it will appear in production.

Embracing automation and creating a streamlined workflow with Loftware Prisym 360

Designed specifically for clinical trials, Loftware Prisym 360 is an end-to-end labeling solution. The software has unique features and capabilities to build and maintain an integrated phrase library which allows an organization to significantly reduce the amount of time it takes to create, approve and print labels. The platform can also easily collate multiple labels to generate artwork PDFs of single -panel and multi-page label booklets ready for printing.

The whole labeling process can be achieved in days rather than months, with the generation of country-specific labels based on a master-level template, complete with translations, at the push of a button. This allows for quick and accurate updates in response to changes in the trial protocol or alterations to the study locations with little notice.

Alongside a model GxP-compliant phrase library, the platform supports the creation of translated country-specific labels through:

- An electronic approvals process for labels with automated pathing and reminders, with all amendments and signoffs collated in a central audit log. Approvals can be conducted in parallel to allow for collaborative working and avoid bottlenecks.
- Genealogy analysis tools that allow users to understand where phrases are used on different assets and provide automated updates when phrases are revised.
- A built-in regulatory rules engine that can be configured with the most up to date rules to prompt users of any country-specific requirements during the artwork design and approval process, including any mandatory phrases or font requirements.
- Ability to automatically collate trial data, randomization data and production data prior to printing through integration with CSM (Clinical Supplies Management), ERP (Enterprise Resource Planning), PLM (Product Lifecycle Management), MES (Manufacturing Execution System) and other tools using validated protocols that allow for the secure flow of data with full traceability. Many of these connectors are also certified with the relevant vendor (e.g., SAP S/4HANA Cloud).

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Prisym 360

in practice

CASE STUDY

How Prisym 360 allowed 48-hour turnaround of trial packs

Clinical trial supplies specialist RxSource needed to find a labeling solution that would allow them to meet increasingly short deadlines for packaging jobs. By implementing Prisym 360 they were able to produce labels for clinical trial products in hours rather than weeks, allowing them to offer a 48-hour express service while reducing their traditional packaging timeline from up to six weeks to only two weeks.

The translation management functionality integrated into Prisym 360 was one of the key reasons that RxSource selected the platform after their team identified that the phrase library could increase the speed of creating country-specific labels while also reducing their reliance on expensive external translation houses.

"As we moved to offer the demand-led approach requested by sponsors we recognized that translation of label content was a consistent roadblock to getting trial packs out of the door at pace,"

said Rhys Evans, Senior Director, CTS and Global Supply at RxSource.

"The Prisym 360 phrase library has been transformative, allowing us to create country-specific labels at the push of a button. Since moving to Prisym 360 we have streamlined many aspects of our operations, allowing us to significantly reduce lead times to the point where we can now package and supply a trial pack in less than 48 hours."

About Loftware

Loftware is the world's largest cloud-based Enterprise Labeling and Artwork Management provider, offering an end-to-end labeling solution platform for companies of all sizes. Maintaining a global presence with offices in the US, UK, Germany, Slovenia and Singapore, Loftware boasts over 35 years of expertise in solving labeling challenges. We help companies improve accuracy, traceability and compliance while improving the quality, speed, and efficiency of their labeling. As the leading global provider of Enterprise Labeling and Artwork Management, along with Clinical Trials Labeling and Regulated Content Management, Loftware enables supply chain agility, supports evolving regulations, and optimizes business operations for a wide range of industries. These include automotive, chemicals, consumer products, electronics, food & beverage, manufacturing, medical device, pharmaceuticals, retail, and apparel.

For more information on Loftware's clinical trial offerings, please go to
Clinical Trials | Barcode labeling software (loftware.com)

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