Counting the Cost of Corrections in Clinical Trials Labelling

Bringing a new drug to market costs millions, so it's highly risky to leave product labelling and packaging to chance. Especially if it's expensive professionals giving hours of their time to these repetitive manual processes, says Peter Muller of Schlafender Hase

The cost of bringing new drugs to market has soared, not least because of rising regulatory requirements. New analysis published earlier this year by Tufts Center for the Study of Drug Development (Tufts CSDD) puts the bill for developing and gaining marketing approval for a new drug at over $2.5 billion, climbing to $2.87 billion when post-approval R&D costs (of $312 million) are factored in[1].

The $2.5+ billion figure (per approved compound) is based on estimated average out-of-pocket costs of $1.4 billion and time costs (expected returns that investors forego while a drug is in development – typically many years) of $1.16 billion. That's before any cost for post-approval studies, required by the US FDA as a condition of approval, to assess new indications, new formulations, and new dosage strengths and regimens, and monitor safety and long-term side-effects in patients.

Maximising Trial Success Despite the Odds

Within all of this, the clinical trials process carries its own particular share of risks and associated costs. If drugs do not pass human testing – and most don't – all of the work that precedes this will have been for nothing: certainly it will not deliver the expected return. So life sciences companies need robust processes in place to ensure that products are taken absolutely correctly, leaving no scope for error in dosage, for example.

The product runs in clinical trials may not be on the same scale as for mass production, but the stakes are enormously high and the authorities and brand owners will be paying close attention to accuracy and results.

In all aspects of product labelling and packaging, relying on manual processes for checks and corrections is inefficient and error-prone, yet the practice is still commonplace in life sciences. This affects all product labelling, from the lab to the pharmacy shelves.

The more regulatory requirements there are, and the more frequently these specifications change, the greater the scope for error. Similarly, the more products, variants and markets a company is dealing with, and the shorter the release cycles, the bigger the chance that something could go awry with the labelling.

The media archives are laden with examples of big names that have fallen foul of regulations, by simply failing to spot a misprint until it's too late, or neglecting to meet new guidelines in a particular market. From children's cough medicines to dietary supplements, the

simplest error in how consumers should store or take the product could result in serious side-effects.

There are all sorts of risks associated with manual proofreading, with the main ones highlighted below.

Exposure to Error
Humans make mistakes. Even with two sets of eyes on a document, proofreaders can develop blind spots – either because they've looked at the same content for too long, or because the task is so repetitive and unstimulating that the brain has become distracted[2]. Yet even the smallest editing or artwork oversight can have serious consequences. In life sciences, the difference between "store this product at *2-8°C*" and "store this product at *28°C*"; "take 1-2 a day" and "take 12 a day"; or "do *not* chew and swallow" and "do *not not* chew and swallow" could be a matter of life and death.

People are Expensive
Manual tasks are unrewarding, demotivating and a poor use of qualified professionals' time. Yet pharmaceutical companies don't typically employ proofreaders; rather they use scientific writers with PhDs to check over content, at great expense.

The cost per hour of work from the employee doing the proofreading doesn't just include the salary, but also tax, benefits, insurance, holidays, office space, training, recruitment costs and so on, which can more than double the gross salary. In the case of graphic designers, there may be additional costs for re-work.

When budgets are tight, and skills in regulatory affairs and quality assurance at a premium[3], it doesn't make commercial sense to use experts to do routine administrative tasks, however vital the outcome. In the worst cases, people who feel un-challenged or under pressure to do extensive manual tasks on top of already demanding workloads, will leave the organisation, and studies suggest that losing a salaried employee can cost as much as twice their annual salary[4], especially for a high-earner. Adding to employees' faltering morale is the stress caused by being at fault for an error – errors that are very easy to make, yet equally easy to avoid.

Lack of Flexibility
Manual proofreading isn't especially flexible. It requires specialist knowledge, native language experts and dedicated, uninterrupted time. It can tie talented people to their desks, and detract from higher-value work.

Where Automation has Traditionally Fallen Short
In the past, attempts to automate proofreading and document comparison – to relieve skilled professionals from mundane tasks – have fallen short. This has been due to technology limitations, language restrictions, and insufficient accuracy to fit the purpose.

Document Conversion Problems
Traditional text comparison tools have clear limitations. They convert content to PDF format and then compare them visually. This option is inadequate for heavily-regulated markets. Converting from one format to another is far from ideal: it can introduce anomalies, and the process doesn't allow teams to work from original documents, which may be important mid-way through a drug approval process. In addition, document conversion for the purposes of comparison is a violation of GMP processes and can lead regulators to question the validity of comparisons, and the entire packaging review process.

Content Corruption
Graphic designers often take the blame for errors caused by conversion errors, because of the different software packages they have to work with. Typically designers will take a Word file, import it into InDesign/QuarkXPress/Illustrator, work on it and then convert it back to a PDF file. The problem is that the various software systems originate from different companies (e.g. Microsoft/Quark/Adobe). The fonts they use may have different names, and even change certain characters (a classic one in pharma is "µg" being changed to "mg" by certain artwork creation software).

Language Limitations
Markets are becoming ever more global, and it isn't just Europe that presents a range of disparate language and regulatory requirements. Asia and Africa bring additional demands.

Relying on software to read and interpret a human language has traditionally been a challenge, despite advances in technology. The issues are similar to those associated with performing the original translation. As specialist agencies note, "MT [machine translation] is not the way to go. Yes it's cheap and there's minimal effort required on your part, but at the end of the day do you really want to lower the value of the high quality content you've created for your home market?"[5]

Inadequate Levels of Accuracy
Where file conversion is taking place, or comparisons rely on certain fonts, language or specialist content knowledge, accuracy starts to suffer. And when teams can't depend on automation for the highest levels of accuracy, their confidence in technology diminishes until they stop using the software, undermining any return on investment. For the users whose necks are on the line, it's better to play safe.[6]

Complexity & Cost
Costs and long deployment cycles have also proved prohibitive. Inflexible licenses can drain capital budgets, while the typical software procurement and implementation cycle is 9-18 months.[7]

Improvements in Automation
Technology has improved a great deal, however, and

there are now new and more robust approaches to text comparison that promise to relieve quality assurance teams of several rounds of manual work – reliably. Better still, these tools can be sourced and run via the cloud now, making them more accessible and affordable than previous options.

A particularly powerful approach to label checking uses text's underlying universal code ('Unicode'), rather than the actual words of a given language. This means that, whatever the format, font or operating system, the software understands what this represents. When it makes document comparisons, it is comparing the code behind the characters – allowing it to compare two files in any language and any font, as long as these support Unicode.

Unicode allows data to be retrievable with a simple keyword search in a database or document management system, and allows documents to be transferred to other applications without content changing or being corrupted.

This offers unprecedented levels of accuracy, and incredible speed, because this kind of text verification approach is able to home straight in on the subtlest changes and anomalies, so that these can be addressed swiftly without the need to painstakingly go through entire documents manually.

It's possible to do the same with images too, allowing teams to compare logos, charts, chemical formulae, etc., and highlight the tiniest discrepancies.

Improved Speed & Productivity

With this kind of automation tool, typical like-for-like document comparison typically takes seconds – versus several hours if done manually – even if the language is unfamiliar. This can free up expert time for frontline regulatory or quality assurance work.

If companies save an estimated five hours per week on manual proofreading/text verification, that could be a $13,500 saving against the salary of a qualified regulatory affairs employee – capacity that could be redeployed to more useful effect.

Growing regulatory demands are increasing the pressure on RA and QA teams, which have never been busier or as overstretched. Unsurprisingly, quality assurance and regulatory affairs are now among the main growth disciplines in life sciences . Yet there is a gap in the available talent pool, and rising concern among life sciences organisations that failure to keep employees stimulated could result in key people moving on. And, of course, service quality is at risk where people's hearts aren't in the task, which is the last thing QA teams need. Reducing reliance on manual processes isn't just a risk-avoidance or insurance strategy. In life sciences, the rise in merger and acquisition activity and the growing trend of smaller batch numbers and increased drug personalisation means label demands are soaring and becoming more complex to manage. Each new demand, each new regulation multiplies the burden on regulatory affairs, quality assurance and marketing to be responsive, accurate and thorough at a time when skilled employees have little or no capacity to spare.

This isn't just a clinical trials requirement, of course, but one with far-reaching application across the life sciences product lifecycle.

As regulatory demands continue to increase, the associated cost and risk can only intensify, so life sciences firms need to find new ways of managing the workload. Find the right solution, and everyone stands to benefit.

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