Transparency and Public Interest: Striking a Balance

Requirements for plain-language summaries of clinical studies, aimed at a broad, non-technical audience, could create new risk for sponsors, warn Pooja Phogat and Vidhi Vashisht of Kinapse

As from next year, life sciences firms will be expected to prepare plain-language summaries (PLSs) for all Phase I-IV interventional trials, to comply with requirements for greater transparency around clinical research, as part of the EU Clinical Trials Regulation 536/2014 (EU CTR Article 37). These summaries need to be intelligible to patients and the general public, as well as experts.

For trial sponsors, this is a significant undertaking. Its perceived magnitude is reflected in the concerns now being raised by study teams and those who will be responsible for delivering the PLSs. These include the fear that, if the summaries are too simplistic in what is included and how it is worded, they could be misleading to some readers – with potentially serious consequences for the organisations responsible.

Most firms can sympathise with the motivation behind plain-language summaries. Once de-identified clinical study reports and lay summaries of trial findings are published on the European Medicines Agency's designated central EU portal, they will be readily available to not only doctors and other researchers, but also subjects who have participated in the trial, any patient affected by the associated medical condition and their care-givers or family members – plus any other member of the general public. Being more open about clinical research will improve external engagement with the work companies are doing and improve public trust, while simultaneously helping to drive greater efficiencies and faster progress – as other teams are better able to build on what's gone before. Meanwhile trial subjects can understand more about the work they have contributed to, and patient advocacy groups can monitor progress with a condition – without having to submit individual requests for firms to respond to.

Balancing Risk Against the Spirit of the PLS

Given the broad spectrum of potential readers, EMA has proposed that the plain-language roundups of the key findings and conclusions are easily digestible and appeal to the lowest common denominator in terms of readers' health literacy. The main reports are inherently very long, detailed and technically complex – i.e. hard to decipher for someone without an industry background and/or prior knowledge of the particular field of study. So the PLS must fill that gap – potentially as the only document that many of its readers will look at to understand the research and its outcomes.

In this context, firms must decide what makes for an optimal summary: what should be included and how best to explain it, as well as what should be left out in order not to lose the least knowledgeable reader. Sponsors are understandably keen to ensure that these documents do justice to the original studies, getting across everything that's important and retaining the original emphasis. Achieving this in an abridged document that uses simpler, non-clinical terminology will be no easy task. During early attempts at these summaries, study teams have been seen to push back against the proposed wording and choice of what to include, worried that it might give the wrong impression, has altered the emphasis, and could be taken out of context or lead to wrong conclusions being drawn. As an example, groups of patients may wrongly infer that the given drug is appropriate and safe for their particular circumstances based on the results of a single study, without considering key information or broader contextual insight which the researchers and the health authorities conclude from multiple studies.

It is important to be aware that EMA has no expressed plans to vet the summaries being published. This places the onus on companies themselves to ensure that the summary documents do their job effectively, without creating new risk for the organisation or to patients. This applies to every market in which the drugs are being sold across the EU too – requiring accurate local-language versions of each document, which again stay true to the original report and do not stray in their emphasis.

When Points of Reference Diverge

The overriding challenge for study teams is not that the EMA's PLS requirement will create a lot of additional work (although it most certainly will), but rather that the task falls outside of their area of skill and experience. Until now, the output these teams have produced has been almost exclusively for a scientific audience; they are not accustomed to presenting their findings to readers who do not share the same base understanding and points of reference. So it presents a risk if the summaries become a weak point and reflect badly on their latest, painstakingly-completed research – by positioning or promoting a drug inappropriately, for instance.

Sponsors are reacting to the situation in a number of ways. Some are creating the summaries to meet the minimum requirements from EMA. They want to avoid being accused of cherry-picking the secondary endpoints they include or skewing the impression the reader takes away from the PLS – compared to the fuller insight a more knowledgeable reader would gain from the comprehensive regulatory and technical disclosure documents. Others instinctively want to add more detail, to cover themselves against potentially being accused of withholding important information. But this could lead to long and unwieldy summaries, which fail to serve their intended purpose.

Finding a Pragmatic Solution

For now, summaries are being produced voluntarily and applied to already-completed clinical studies. Although these scenarios may lack the urgency that will be present when PLSs become a more formal requirement, they do provide a good testing ground. They also present some practical questions, about how these retrospective PLS documents will be distributed to participating subjects, for example.

Other, ongoing logistical challenges include the need to establish standard operating procedures (SOPs) for handling and processing PLSs, and to build templates for forming the content. Designated

teams will need to be trained too, so that they more tangibly appreciate how the summaries will be used, the right balance of what to include and how best to pitch it for a public audience.

To help with this last point, EMA has proposed that, early on in the development of a PLS, sponsors engage with patients who can provide early feedback about the documents and their content, and its framing and wording. In the case of local-language versions for other countries, it is advisable here too to test the translations with local audiences. Although translation tools can help with getting the phrasing right in another language, the only safe way to quality-check local versions and ensure individual dialects and cultural meanings are taken fully into account is to perform bi-directional translations, and confirm that nothing has been lost in the process by asking those on the ground in each target country.

Getting Help

If all of this sounds like a lot of preparation, it's because it is – and sponsors should not underestimate the task in front of them. Certainly, they should not wait until regulation is effective before they start taking action. The transition to producing plain-language summaries of clinical reports as standard will be very intensive and companies will need to be 'ready to go' once PLSs become an actual requirement.

Although the demands of EU CTR Article 37 are considerable, with the right help and advice up front, companies can avoid PLS preparation becoming burdensome. Through ongoing work with life sciences companies of different sizes and at varying states of readiness for PLS production, Kinapse has formulated both effective ways of framing discussions including the author and document reviewers to agree appropriate content, and the best approaches to presenting it for a broad, public readership. Basic measures here might include devices to bring the maths to life (e.g. 0.1% expressed as 1 in 1000 people) supported by simple graphs as illustrated.

It is worth remembering that it is not just the EU that is moving towards greater transparency and public inclusivity. Assuming the US FDA decides to proceed with equivalent measures (the Agency issued a draft document for comment not long ago), companies that do the groundwork now can expect to be able to capitalise on that diligence across other international markets in time.

Pooja Phogat

Pooja Phogat is Head of Development Operations at Kinapse, a provider of complete advisory and operational service across all aspects of EU CTR Article 37 preparation and compliance.

Vidhi Vashisht

Vidhi Vashisht is a Senior Manager for Clinical Trial Disclosure.