

**Managing risk is fundamental to any clinical trial.** Ideally, it's identified and resolved before an experimental therapy is given to patients. But sponsors also need to plan for the risks they cannot predict.

These are the basic principles of risk-based monitoring, which has gained significant traction in clinical research over recent years. Much of the impetus for that trend, explains Chris Simmons, executive director, portfolio management at Covance, comes from regulators. Agencies have recognised that traditional approaches to monitoring – such as 100% verification of source data and visiting sites every six weeks – are no longer sustainable from an outcomes or a cost perspective. As a result, draft guidance from the FDA and a reflection paper from the EMA were published in 2011, with final guidelines emerging in the latter half of 2013.

With the concept still relatively fresh, industry research indicates that risk-based monitoring is applied to approximately 5% of current Phase III trials. The next five-10 years should see many more trial sponsors adopting risk-based approaches, and Covance wants to be ahead of that curve. The company has already rolled out its end-to-end RBM process in a Phase III cardiovascular programme involving more than 10,000 patients across nearly 40 countries. "This is one of the first fully-fledged RBM studies delivered following the approaches conveyed in the final FDA guidance," Simmons says, adding that a series of existing studies will migrate to RBM while new trials will be deployed with full end-to-end RBM processes this year.

Risk identification starts with the trial protocol. And Covance employs quality-by-design principles to eliminate, wherever possible, standard or protocol-specific risks from the outset – avoiding the design component that gives rise to those risks.

One of the most challenging aspects of implementing RBM is ensuring consistent access to study data to support a timely mitigation of risk as and when it surfaces.

# KEEPING RISK IN PROPORTION

CHRIS SIMMONS OF COVANCE EXPLAINS THE IMPORTANCE OF ADOPTING A RISK-BASED APPROACH TO CLINICAL TRIALS

BY PETER MANSELL EDITED BY JENNY HONE/CLAIRE BOWIE

New technology plays a "massive" role, Simmons notes. Utilising a clinical data repository, Covance employs data integration, standardisation and analytics tools to take the "temperature" of sites over time – a 'closed-loop' process of continuous learning as the study data is collected.

Another challenge is site monitoring, particularly where trial sites may have relied on a monitor to manage quality control. "This will require change management to understand the concerns raised by sites and ensure that everyone fully understands RBM," Simmons explains.

What Covance offers is an end-to-end approach to RBM that depends on upfront site-by-site assessment as well as applying data analytics once the trial is underway.

RBM principles apply globally and are growing exponentially throughout the clinical development lifecycle. As Simmons observes, most applications to date have been in high volume, lower-risk studies, where there are better opportunities for delivering return on investment. In the future, though, he sees a broader focus on delivering efficiencies in the lower-volume, higher-risk segment. And, he notes, today's varying interpretations of RBM are likely to be brought together over time.

Covance's own approach, which it began to develop nearly three years ago, is "very much

aligned" with both regulatory guidance and TransCelerate's position paper, Simmons says. The cardiovascular trial with end-to-end RBM has another two or three years left to run. But the strategy is already generating value in terms of client and internal team satisfaction as well as study delivery.

With broader adoption of RBM looming, Covance is comfortable being a pioneer. "I think our processes are proving to be robust yet flexible," Simmons comments.

The common misconception, he notes, is that the primary objective of RBM is cost reduction. In contrast, a principal aim of risk-based management is an output of RBM quality improvement leading to cost effectiveness. So the key, Simmons emphasises – and ground level for Covance's holistic approach to RBM – is "not to do less but to do it smarter". ■

For further information go to [www.covance.com/RBM](http://www.covance.com/RBM)

