Going All In on eCOA

An Interview with:

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Ron Sullivan, Executive Vice President and eCOA Product Line Executive, ERT

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Cameron Robertson, Director – Business Operations at Exco InTouch

Mika Lindroos, Director of Product Management at CRF Health

Steve Young, Senior Vice President of US Operations at CluePoints

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Going All In on eCOA

Significant growth opportunities in the eCAO field mean the industry is calling out for solutions, advice and guidance that can help deliver on its promises. Here, nine experts from organisations across the sector share their insights on some of the industry's most pressing questions surrounding this expanding market.

Why, in this day and age, are some clinical trials still clinging on to the use of paper to capture patient-reported outcomes?

Adam Butler, Senior Vice President, Strategic Development & Corporate Marketing, Bracket Global

In today's age of rapid digitisation across industries spanning banking, retail, healthcare and countless others, clinical trials has been relatively slow to adopt electronic methods and instead, reverts to traditional paper approaches for capturing patient-reported outcomes. Attributed to the industry's stringent regulations that make it difficult to wholly rely on electronic methods, the slow adoption can also be ascribed to clinicians' requirements for maintaining reporting flexibility during data capture.

Often, it is difficult to fully predict the breadth of information and level of specificity that will need to be captured during a study session and the connotation that technology cannot rapidly adapt to such evolving needs is still perceived. On the contrary, electronic clinical outcomes assessments (eCOA) offer myriad benefits that not only meet clinicians' requirements of adaptability, but have also been proven to increase patient compliance, reduce site monitoring costs and limit data variances – a challenge that paper records have long produced. The streamlined functionality of electronic methods is actually increasing data quality by capturing categorical and statistical information, not unstructured text.

In fact, digitisation in clinical trials is driving the "Blockbuster Drug of the Century" movement, which refers to patient engagement's ability to drive better outcomes and lower healthcare costs. As such, as digitisation continues to reveal quantifiable benefits, the movement will soon outweigh any traditional, unstructured data capture needs, and ultimately move clinical research into the twenty-first century.

In your opinion, what major hurdles still exist in the industry when it comes to ePRO adoption?

Ron Sullivan, Executive Vice President and eCOA Product Line Executive, ERT

As global adoption of eCOA continues to grow, so does our understanding of the benefits delivered as well as stakeholders' needs when implementing technology in clinical trials. Research has repeatedly shown that patients prefer electronic collection methods over paper, trial sponsors continue to see improved data quality, and global regulators have issued guidelines for eCOA data collection in clinical trials.

Any hurdles remaining for even greater eCOA adoption likely stem from sponsors' and CROs' study teams' perceptions of operational obstacles that could disrupt their internal processes. For example, the perception may be that eCOA data capture would require earlier decisions and process changes than paper COA collection. While programming an eCOA study requires more time than printing paper copies at study start, there is considerable time saved with eCOA throughout study execution via electronic scale measurement, transcriptions, data entry, data queries and source data verifications.

Another perception may lie within the implementation of eCOA – specifically that electronic solutions may interfere with the normal patient rapport that is required during the clinical assessment process. Does eCOA present a physical barrier to the clinical interview process? Quite the contrary. Well-established literature provides evidence that eCOA improves patient/clinician communication and candour, while mitigating site rater variability and enabling better care.

Despite these lingering (mis)perceptions, eCOA adoption is projected to grow three times faster than COA within clinical research, even before the accelerator of BYOD that is working its way into the equation. Clinical trial sponsors looking to adopt and implement an eCOA strategy can do so successfully by collaborating with clinical trial teams, eCOA providers and COA experts familiar with transitions from paper-based COA data collection.

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How is ePRO driving more responsive study designs?

John Sage, Senior Vice President, Respiratory & eCOA at iCardiac Technologies, Inc.

ePRO enables more responsive clinical study designs, primarily from two perspectives: speed of data exchange and expansion into new modes of patient monitoring.

ePRO designs are integrating predictive algorithms that measure if a patient is experiencing a worsening of conditions. These algorithms combine inputs from the patient responses to the patient-reported outcome (PRO) instrument, and from the deployed patient measurement device to assess changes in the patient's condition. Specifically in the respiratory space, the combination of PRO input and daily pulmonary function data are utilised to alert both the research site and the patient, if the patient is trending towards a potential exacerbation. Simple reminders are sent to patients to perform routine cleaning of devices like metered dose inhalers (MDIs) and peak flow meters, thus supporting continuity of data accuracy during the treatment period.

In addition, real-time compliance monitoring allows the site and the clinical research associate (CRA) to be very responsive in working with the patient to stay current on their diary submissions. Rapid response helps with patient retention. Study designs are now able to take advantage of new modes of quality of life (QOL) monitoring with the integration of physical activity monitors and new exploratory endpoints being written into protocols to capture the patient's activity levels. These data can then be correlated with standardised PRO instruments to gain more insight into how the patient is performing daily routines during the course of the trial.

The benefits of BYOD are well understood for late-phase studies. How are we likely to see BYOD impacting earlier phases?

Jeff Lee, CEO at mProve Health

It is common to equate BYOD with reduced hardware costs on large studies. I'm not convinced that cost-saving is the only, or even the primary, advantage of BYOD. BYOD offers greater convenience for patients, a strong case for a higher completion rate, as well as access to the onboard sensors of modern smartphones. Arguably, these elements constitute a more patient-friendly approach to data collection, which is very applicable to early-phase research.

Let's examine the relevance of each of these BYOD advantages:

- Convenience for patients: Even in an inpatient, Phase I study, with a small number of participants, allowing the patients to utilise their personal phones creates a more inviting environment for their stay in the study. Asking them to turn off their personal device, in favour of a dedicated device, is becoming increasingly problematic in our smartphone-centric world.
- Higher completion rate: This advantage is greater in outpatient studies (such as a large Phase I or Phase II study), since the patient is not at risk of forgetting to bring that dedicated device. Furthermore, critical reminders that enhance participation are more likely to be received when using the patient's native phone.
- Access to onboard sensors: While still in the early stage of market acceptance, utilising the patient's onboard sensors creates the opportunity to reduce the burden of active patient reporting/data collection, to passively collected information from their native phone, thereby reducing burden.

For these reasons, our clients enjoy meaningful value from BYOD in early-phase settings.

With the continuous emergence of front-end and back-end systems, are we likely to see more collaboration and consolidation with a greater focus on eClinical integration?

Cameron Robertson, Director – Business Operations at Exco InTouch

There is little doubt of the value of eClinical integration. Data is king in clinical research and historically, systems such as EDC and eCOA have been deployed to collect clean, reliable data for evaluating drug development. In recent years, eClinical has evolved to encompass additional technologies such as wearables, EHRs and eConsent. Integration of these systems ranges from simple data transfers between databases, to real-time consolidation of data from various sources into one database accessed via a single customised web portal.

Standardised data formats are essential for eClinical integration. Likewise, integration is crucial in order to maximise the process and cost-efficiency gains afforded by standardisation. The biggest challenge to integration is the standardisation of the metadata that flows between systems, which is evidenced by the increased prominence of organisations such as CDISC (Clinical Data Interchange Standards Consortium). A business case by CDISC in 2014 suggests using data standards saves 70-90 % of time and resources during study start-up and ~75 % of time during study conduct. For regulatory eSubmissions, standardising data saves ~$180m per submission and a 12-year clinical programme can be reduced by two years. In addition, regulators will soon require CDISC standards for eSubmissions in the US (FDA) and in Japan (PMDA) as they enable higher quality reviews.

eClinical integration has other significant challenges, including the need to replace entrenched non-compatible legacy systems and nervousness around displacing

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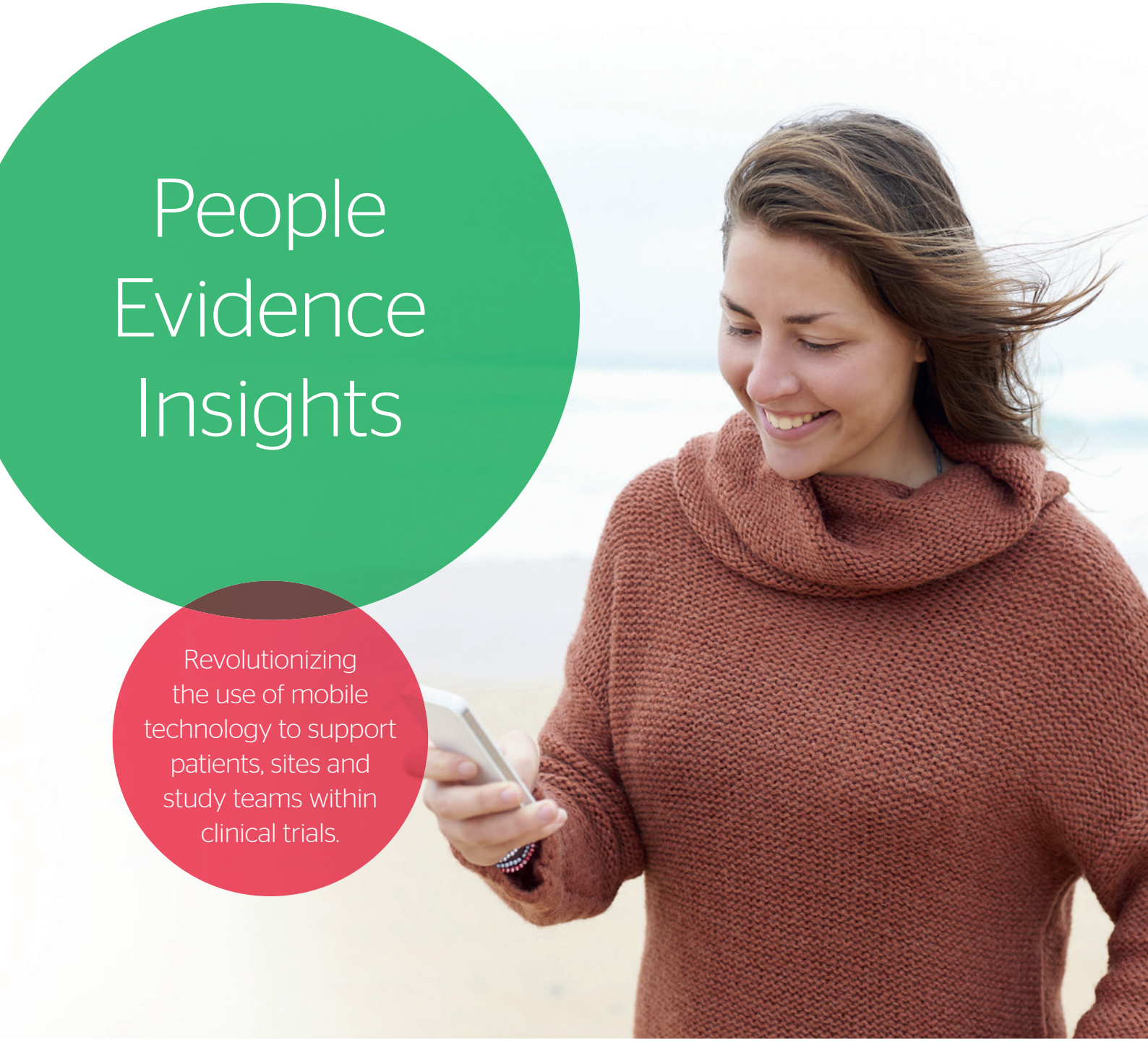

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tried and tested methodologies; however as with other eClinical technologies, we can only expect to see greater adoption in coming years as the industry drives further efficiency to decrease the time and cost of conducting clinical research.

What impact are eConsent technologies having on the industry?

Mika Lindroos, Director of Product Management at CRF Health

Emerging eConsent solutions hold the promise of improving participant comprehension in the onboarding stages of clinical trials while eliminating many of the regulatory deficiencies common to the informed consent process. The availability of innovative new technology is driving sponsors to explore how best to implement an electronic consent approach into their studies, but also leaving many understandably cautious of the potential complexity that adoption might bring. Similarly, investigative sites are also likely to be wary of the integration of yet another technology platform into their study management, and all the training and process adaptions that come along with it.

A seamless approach is on the horizon. Integrating ePRO and eConsent solutions so that they can be delivered on a single device and as part of a single data collection platform, enabling sponsors and study teams to gain all the benefits associated with both, without adding layers of additional technology, could represent the most investigator- and participant-friendly option. While better supporting the process for development, approval and management of informed consent content, a single-platform solution holds the potential to enhance patient understanding, increase regulatory compliance and reduce quality risks, as well as remove the additional burden for sites and participants that would go hand-in-hand with the use of a separate platform.

At a point when we are seeing an influx of new technology across clinical trials, getting systems to work together as much as possible, so that the end user has the experience of a single platform, is key. For today's investigators and sponsors, integrating ePRO with eConsent represents a welcome step.

How are ePRO technologies supporting the surge towards risk-based monitoring?

Steve Young, Senior Vice President of US Operations at CluePoints

ePRO is a form of direct electronic source data entry, and as such there is no separate source residing at each site requiring on-site monitoring review or transcription into an eCRF and subsequent on-site SDV. This therefore reduces the overall on-site monitoring effort which very much supports the RBM paradigm.

Beyond this, and perhaps more importantly, use of ePRO technologies enables pro-active, ongoing, centralised access to patient diary data for study team review and assessment. ePRO data includes audit trail information (such as the date-time stamps associated with each entry), which supports deeper assessment of diary data reliability that is impossible using paper diaries. Central statistical monitoring (CSM) techniques – which are a key component of RBM – can be applied to this ePRO data to detect anomalous patterns in both diary answers and audit information. These anomalies can then be investigated and action taken.

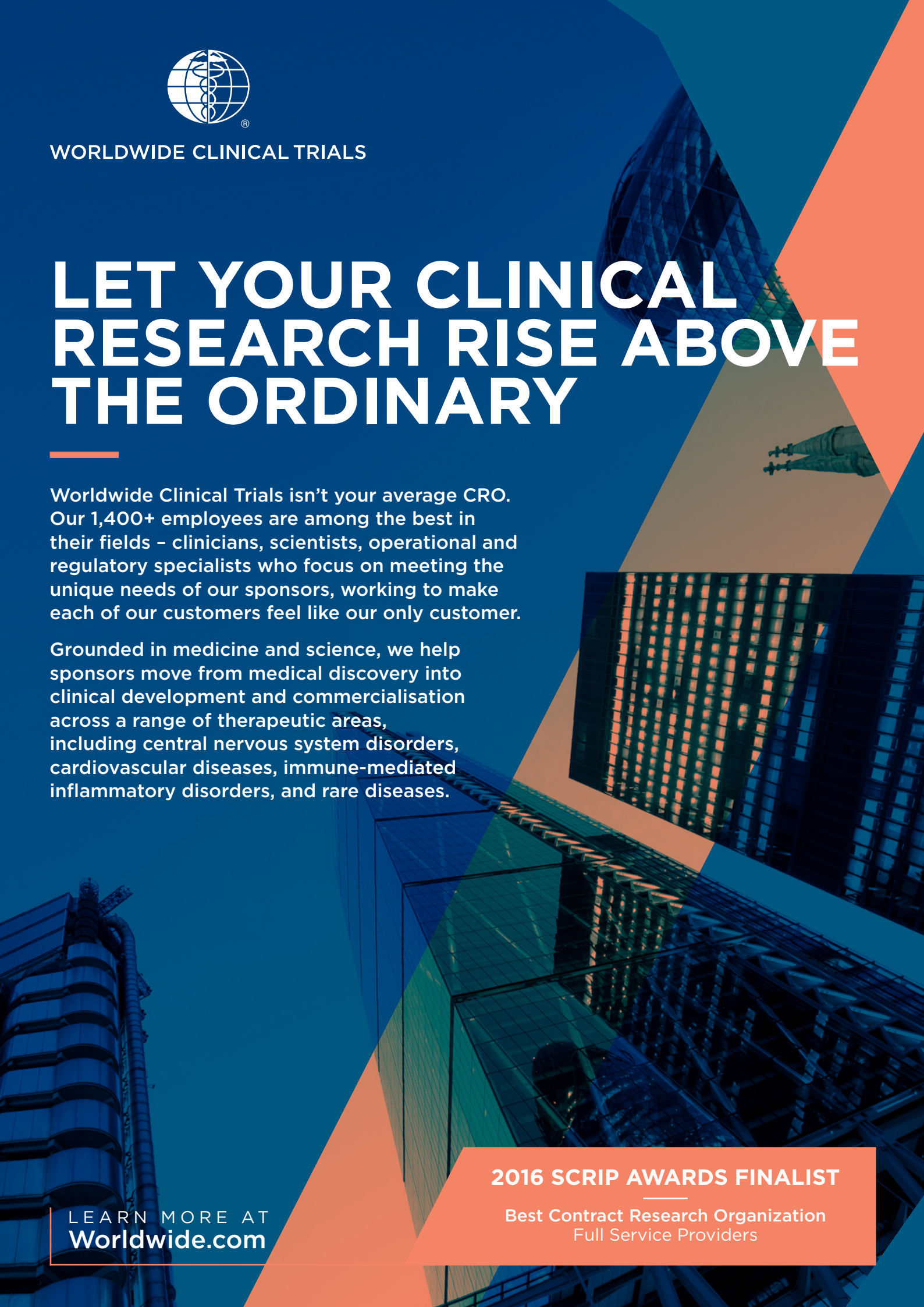
Indeed, remarkable findings of misuse of ePRO devices have been made in ongoing clinical trials analysed using CSM. In one trial, the unusual timing of entries from different patients raised red flags and revealed a case of fraud at a site that would have been nearly impossible to detect using traditional monitoring and data management checks – and completely impossible if the diaries were paper-based with no accompanying audit trail. In this case, it was ultimately found that ePRO devices had not even been distributed to patients, and instead the diary entries had been fabricated by site staff! CSM techniques were applied to the ePRO data and revealed that a preponderance of entries at one site were being made between 6pm and 7pm local time, which was a unique pattern when compared with data from other sites. Only the use of ePRO could enable this type of robust statistical monitoring which is core to an RBM approach.

Advances in wearable device technology are creating new opportunities across the life sciences sector. How can pharma integrate these tools in a more impactful way in the clinical trial space?

Tom Evans, R&D Director at CamNtech

Wearable devices must be looked at in the context of an intended use and what measurable results can be captured from them. Some systems carry exciting promises and visualisations, but may only reach a fraction of the intended population, not measure what is needed today and be unreproducible in three years' time. Consideration must be given to exactly what underlying feature will be measured and whether the system as a whole is designed with that in mind. Using resources to collect large-scale data without precise planning in the hope that "data mining" will produce the desired results is optimistic at best. Similarly, some ePRO options will limit themselves to sections of the population, or produce distortions as participants more or less familiar with a device family are forced to operate it.

Used correctly, wearable devices can reliably collect data which would be inaccessible by other means, and make it cheaper and easier to process than ever before. They can be integrated into the design at an early stage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to capture precisely the important measures, or they can also be "added in" to a trial without impacting the core. But in either case a clear idea must be maintained of the intended value and use of the data.

From an ePRO perspective, what do you think clinical trials will look like in 10 years' time?

Jeffrey Zucker, MS, Vice President, Feasibility, Recruitment Optimization, and Clinical Assessment Technologies at Worldwide Clinical Trials.

ePRO technologies will continue to transform how clinical trials are delivered, especially in studies where they can demonstrate real value in increased accuracy of data and improvements in patient convenience. In 10 years' time there will still be paper-based patient-reported outcomes (PRO) being collected, largely due to patient preference and the nature of the PRO itself. However, I am confident we will see these technologies used to collect the routine daily diary entries, such as those relating to pain scores, glucose readings and values for concomitant medication information, in nearly 100 % of the trials taking place.

For some patients who struggle to use devices, particularly those with neurological conditions, there will still be the need for paper-based tools. However, in the coming years we will see ePRO span more and more indications and grow in all phases of research, from Phase I through to post-marketing. While this wider adoption will no doubt be spurred by costs being driven down as a result of broader take-up, the growth of BYOD – and its further validation – will also serve to bring costs down.

The last decade has seen the birth and growth of the ePRO field and I fully expect the next 10 years to bring significant further growth – especially with more BYOD options. With the continued focus on patient-centricity in clinical trials, the evolution and maturity of the technology will really lead to widespread adoption; this will further drive increased reliability of the data, spurring a self-sustaining cycle and driving more sponsors and research sites to adopt ePRO-based solutions.

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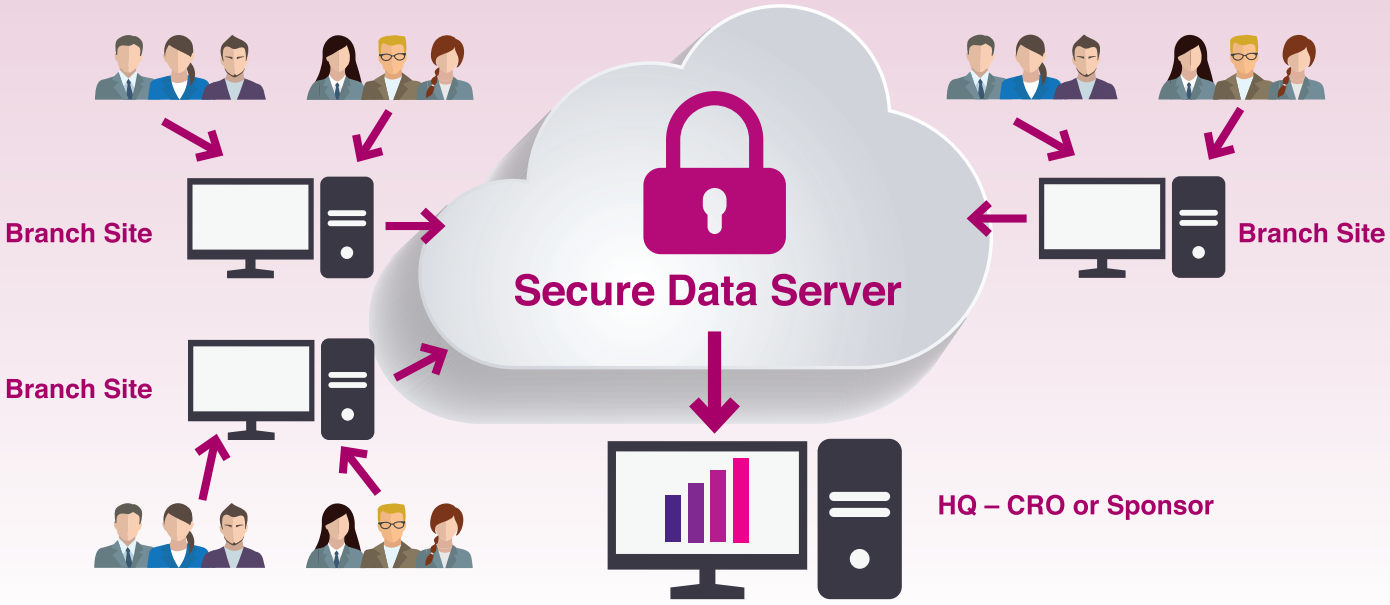

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