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## PROactive patient reporting

Electronic patient diaries provide real-time access to accurate and reliable patient reported outcome data. **Tanya Hair** explains how clinical trial teams can use information obtained from e-diaries to inform their decision-making and optimise trial management

Over the past five years biopharmaceutical companies have begun to realise the benefits of electronic patient diaries (e-diaries) and they are rapidly adopting this technology to help manage their clinical trials. For example, in 2004, a CDISC survey on the attitudes, adoption and use of data collection technologies found that 30% of biopharma companies and CROs were using e-source data in their trials.

E-diaries are now recognised as an effective alternative to traditional paper methods. They provide real-time access to accurate and reliable patient reported outcome (e-PRO) data. They are also gaining regulatory acceptance (see Box page 28). Since the first product to gain FDA NDA approval based on e-diary data in 2003 (Allergan's ACULAR LS for ocular pain), the momentum for using e-PRO will only gather pace.

The use of e-diaries enables clinical trial teams to make informed decisions throughout a trial. E-diaries help optimise trial management in four key areas: patient selection; protocol and data compliance; patient safety; and data collection and analysis.

### Patient selection

Initial screening of trial participants is crucial to the success of any trial. Any screening process that includes false-positive patients and excludes false-negative patients has

serious implications for a trial – from erroneous data and higher patient dropout rates to wasted time, resources and medication.

Researchers have greater control over the patient selection process if they use e-diaries to validate their initial screening. After the first patient visit, the trial team can send patients home with an e-diary to record their daily activities and assess their eligibility for a trial. The diary can be used to record anything from pain scores to daily eating habits. This information is transmitted wirelessly to a central database and a web-based tool is used to compare the patient's responses to the eligibility criteria. Based on the results, the team can move eligible patients onto the next stage of the trial and release ineligible patients – ensuring a high-quality study population.

Between November, 2002, and February, 2004, one of the world's leading pharmaceutical companies used e-diary technology to manage a Phase III trial for irritable bowel syndrome (IBS).<sup>1</sup> As part of the screening process, the e-diary data alerted the trial team to an unusually high level of screening failures. The researchers took a closer look at the inclusion criteria and realised that one of the measures was inappropriate for this patient population.

Using the online protocol amendment, the researchers were able to intervene and immediately correct the problem. As a result,

the level of randomised patients increased and the trial was able to proceed as planned.

### Patient safety

Patient safety in clinical trials is of utmost concern for all trial teams and sponsors. In 1999, the death of Jesse Gelsinger in a gene transfer trial sparked a comprehensive investigation of research sites across the US. The Office for Human Research Protections (OHRP) found evidence of non-compliance with human subject regulations and shut down human research at major medical centres. Following this investigation, several agencies, including the Department of Health and Human Services (DHHS) Office of Inspector General (OIG), published reports and made recommendations in an effort to improve research subject safety.<sup>2</sup>

Using e-diaries is one way sponsors can improve patient safety. With traditional paper collection methods, researchers must wait until a patient's site visit before they can evaluate self-reported outcomes data and address any potential problems. Researchers can then only practise reactive trial management – responding to problems after they happen. With e-PRO, the team can monitor patients' responses in real-time through a web-based portal. This means the researchers can intervene immediately if a patient appears to be experiencing complications. This allows the teams to be proactive – identifying and addressing issues in their early stages before serious complications arise.

### Data compliance and quality

Patient compliance with traditional paper diaries is notoriously low, especially as there is



no way for researchers to monitor when data are being recorded. As a result, paper diaries are often incomplete, irrelevant, illogical, or even fabricated – jeopardising study results.

In a study published in the *British Medical Journal* in May, 2002, patients who were assigned paper diaries reported 90% compliance, but their actual compliance rate (recorded secretly via electronic methods) was found to be only 11%.<sup>3</sup> In addition, the practice of ‘diary hoarding’ was a significant problem – patients failed to open the diary for days and then filled in multiple diary entries at once. Moreover, 75% of patients using paper diaries had at least one day of hoarding and 32% of the study days contained no diary openings at all.

Several features in e-diaries ensure that patients enter the right data at the right time. Alarms and reminders prompt patients to enter data at specified times throughout the day. Time-stamped entries ensure that patients are entering data in real-time, rather than recalling symptoms from memory, thereby improving data quality. In addition, edit checks prevent patients from entering incomplete or illogical data.

Recent studies have shown that e-diaries significantly improve patient compliance and data accuracy compared with traditional paper diaries. In the IBS study mentioned already, the researchers used e-diaries to collect an estimated two million pages of real-time, primary efficacy data from 5,000 patients in 23 countries in the Americas, Europe, Africa, and Australia. The data compliance level for this study was 97%.<sup>1</sup>

### Protocol compliance

Unlike paper diaries, e-diaries also help patients comply with study protocols by deliv-

#### Regulatory progress

The FDA announced its intention to provide a new patient reported outcome (PRO) guidance document more than two years ago, but it has not been published as yet. Even so, the focus of the guidance will be on PRO as a whole and only a short section devoted to e-PRO. The document is expected after an FDA-sponsored conference (‘FDA Guidance on Patient Reported Outcomes’), 23–25 February, 2006 (see page 32).

E-source data fall under the requirements of CFR 21 Part 11, as well as the FDA’s Guidance for Industry Computerized Systems Used in Clinical Trials. The latter does not include a specific reference to e-diaries, however, and only exists as a draft version at present.

CDISC is also in the process of drafting a document about EDC via its e-source data interchange (e-SDI) group.

ering helpful reminders, such as telling them not to eat or drink before a blood test, or prompting them to take their medications.

In addition, some e-diary technologies feature online protocol amendments that can be transmitted directly to a patient’s e-diary, enabling researchers to proactively manage trials and make adjustments based on real-time patient reported outcomes data.

### Data collection and analysis

With paper diaries, clinical trial teams waste hours or even days entering hand-written diary entries into a database. This manual entry process jeopardises data quality as it poses a high risk for transcription errors. E-diaries streamline the data collection and analysis process and trial sponsors can achieve database lock days or even weeks sooner than studies using paper diaries.

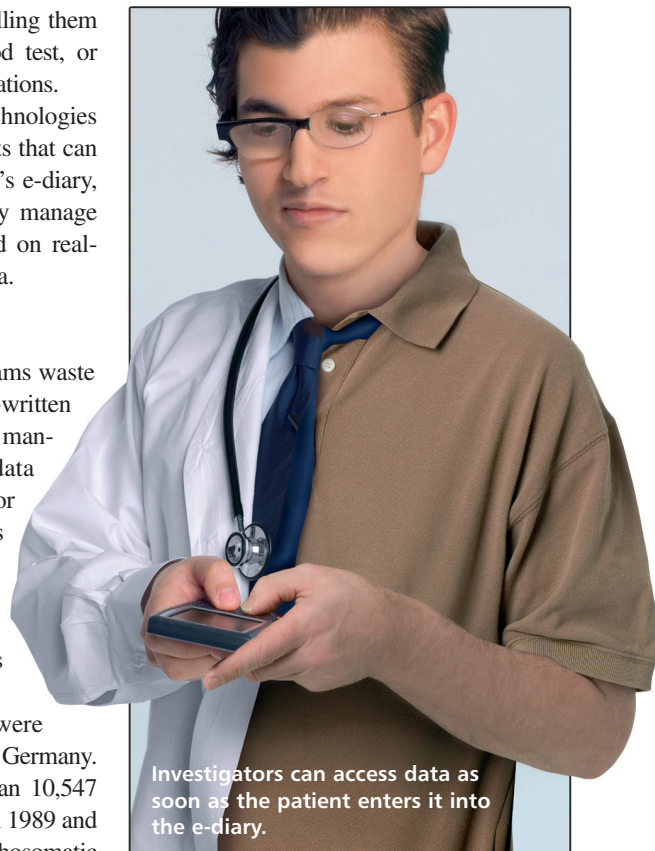
The benefits of e-diaries were clearly seen in a study conducted in Germany. Data were collected from more than 10,547 in-patients and out-patients between 1989 and 2003 at the Department of Psychosomatic Medicine Charite, Humbolt University, Berlin. Participants either used paper or e-diaries to record their experiences (2,892 used paper diaries while 7,655 used e-diaries). Subjects were asked to input data on six psychometric scales: anger, elevated mood, anxious depression, involvement, apathy, and tiredness.

The e-diaries reduced trial preparation time by 67%, they eliminated the need for data entry, and reduced data bank organisation and patient report time by 78%. As a result, one working day per 100 questionnaires was saved compared with paper diaries.<sup>4</sup>


In April, 2004, the IBS study<sup>1</sup>, which is the largest e-diary study to date, achieved database lock for the patient diary data within only five days of the last patient visit – a process that takes an average of 30 days with paper diaries.

### Real-time results

While a paper diary is a static, inflexible means of acquiring patient data, an e-diary is an interactive, comprehensive trial management tool that is more than just a questionnaire in a box. E-diaries provide real-time access to valuable patient reported outcome data, allowing researchers to proactively manage trials and intervene when necessary



Investigators can access data as soon as the patient enters it into the e-diary.

to adjust protocols and protect patients from potential harm. They also offer researchers greater control over trial and patient management and ultimately improve the safety and effectiveness of medical treatments. 

### References

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