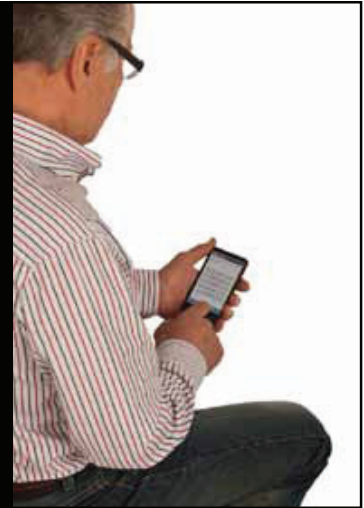


# Data Matters and so does Compliance



Careful design of eDiaries leads to higher rates of compliance in studies that require patient-reported outcome data – and compliance matters to both sponsors and regulators.

*CRF Health kindly provided their handheld devices to collect live feedback from the conference delegates at this year's annual ACDM conference, as discussed in the article by Tracy Fells on behalf of the conference committee. The following article discusses the use of these devices within Clinical Trials. The following article has been edited to fit the constraints of publishing; a full text article is available upon request.*

*Ali Green, Editor, Data Matters.*

A study team spends a great deal of time, care, resources and attention on the design of a clinical trial. The trial design is subjected to rigorous checking and a number of approval processes. Only until the study team is confident that the protocol meets all good clinical practice (GCP) requirements, primary endpoints, and in many cases, agency approval, does a sponsor finalise a protocol and prepare it to send to an Institutional Review Board (IRB), Ethics Committee and Investigators.

When a protocol calls for patient-reported outcome (PRO) measures, the study team pays close attention to the way in which they will capture such patient outcome data. After all the careful planning and meticulous trial design, the study teams and investigators must then rely on unsupervised patient data entry to collect what is often pivotal data. Because trial subjects are not research professionals, the design and number of questions in an eDiary must strike a careful balance. Many study teams would want as much data as possible to be collected. And although unsupervised data

entry is an essential part of some trials, the questionnaires utilised must elicit responses that meet the protocol design needs and not place too great a burden on the trial subjects. Electronic Patient Reported Outcome (ePRO) devices can not only facilitate data collection and analysis, but also provide important control over the data recorded.

### **Key Ideas to Consider for eDiary Data Collection**

Keep it simple. That's the key to compliance. Unsupervised data collection should not rely on expecting clinical trial subjects to remember precisely what to do every day within a clinical trial. The eDiary acts as a personal assistant, and essentially guides the patient through the clinical trial and minimises patient burden by providing features such as portability, audible alarms, questionnaire navigation, and privacy for the patient. When subjects hear the alarm, for example, they can log-in to the eDiary (using their password) and respond to easy-to-read questions in their own language. They simply touch the

screen to answer those questions. This puts the subjects' experience at the centre of the design, which makes it easy to use and easy to comply.

Keep it reliable. That's the key to good data collection. To prevent bias and to provide the same experience across the study, ensure that every subject receives the same device, one that is suitable for the therapeutic area. And choose a device that can display the languages of every country where the trial is to be conducted. This is important as some devices lack the capability to accept programming in complex Indian, Hebrew, or Japanese languages. Plan ahead. Complex languages might not be required in the early stages of the clinical trial, but an expansion to other countries/languages might be necessary for a variety of reasons; i.e. slow recruitment or changes in study parameters. Adding additional countries not originally planned for can affect the eDiary Design (i.e. screen size limitation or operating system incompatibility due to the addition of complex languages), so it is good to know

the capabilities of your ePRO service provider upfront.

### Keep it flexible

That's the key to skillful/proficient eDiary development. With these eDiaries, study teams are able to build in smart branching logic to limit the number of question pages to be viewed. However, here, it is important to remember some diary design rules. For example, when complete answers are not displayed on the screen, it has been shown that some diary users fail to scroll and read all options before entering a response. Smart design can improve compliance rates. Also, study teams should be mindful of the subject's condition when building in certain criteria. You would not necessarily want the alarm to go off if a subject does not enter information exactly on time. You may build in a certain entry time window to allow for subjects that are at work or just need a moment of privacy to enter the data. Since there is a cost to transmitting data, be sure to match the data sending frequency to only meet the actual need of the study team to see the data. The study population and the therapeutic indication under the study drive the timing of diary entries. Diary entries may be event-driven, such as each time a person with asthma uses a rescue inhaler. Also, a study design

may require a diary entry at a special time each day (e.g. after taking medication or just before bedtime), or a specific day each week. Some studies may require only completing a questionnaire at each visit to the investigator site. Whatever the criteria, creating a simple experience requires expertise and flexibility in the design and development of a successful ePRO solution.

### Keep it strong

A knowledgeable, experienced ePRO service provider team and a solid system behind them is key to a smooth and positive project. The ePRO service provider team helps the study team through the device selection process by reviewing protocol complexity and diary performance requirements. Diary performance is important to achieving high compliance rates, especially for daily diaries. A collaborative design approach is favourable, working with the study team in interactive design meetings and using real-time simulations and prototypes of the eDiary. That kind of collaboration allows the team to visualise what study subjects would face on the eDiary as they work to develop the finalised questionnaire together. This provides a unique opportunity to evaluate the patient experience in real time as the eDiary is designed and built. If screen changes or other diary functionality take too much time, the subject is likely to become frustrated and compliance will suffer. Fast response times have a very strong, positive correlation with assessments of usability of computer systems, and such systems will keep a subject engaged throughout the course of lengthy and/or frequently-administered questionnaires. High quality project management and systems provided by the service provider, gives a study team a great deal of assurance that the data collected is consistent, accurate and reliable.

### Why Is Compliance So Important?

The FDA's recently published Guidance for Industry on Patient-Reported Outcome Measures emphasises that the agency's focus is on compliance with the protocol. It states, "If a patient diary or some other form of unsupervised data entry is used, we plan to review the clinical trial protocol to determine what steps are taken to ensure that patients make entries according to the clinical trial design and not, for example, just before a clinic visit when their reports will be collected." ([www.crfhealth.com/FDA\\_Guidance\\_PRO\\_Dec2009\\_Final.pdf](http://www.crfhealth.com/FDA_Guidance_PRO_Dec2009_Final.pdf))

With an electronic solution, every patient-reported outcome entry is created with a date/time stamp. That provides important documentation that the data was entered in accordance with the study design. A paper-based approach makes it impossible to know when the subject actually entered the data. Paper lets you see how much data was collected, but there is no way to know when it was collected. That dilutes its value.

As shown above, ePRO can reduce the burden on trial subjects. It can also ease burdens on sites by eliminating the need for double data entry and source data verification. Those reasons plus the lack of extraneous or superfluous data with ePRO solutions (that you may still get with paper), also significantly minimises errors and variability, making overall data cleaner. ePRO provides cleaner data which enhances the scientific decision-making process. Increasingly, it can be integrated into EDC systems. It can shorten the time to database lock. From the early days of the historic Palm-based devices to the now fully wireless slim-designed Windows Mobile® technology, ePRO has evolved during the past 10 years, and as the technology has improved, so have the ePRO solutions.

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