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# Why Paper Diaries Should Be Banned in Clinical Trials

**By Dr Valdo Arnera**

Every now and then, a shift in technology revolutionizes an entire industry. Consider the advent of email and automatic banking machines. Once the mainstream adopts these processes, it is difficult to imagine how we managed without them. Today a similar transformation is taking place in the pharmaceutical world, as more companies worldwide replace paper diaries with electronic patient diaries in clinical research.

Electronic patient reported outcome (ePRO) solutions capture self-reported data directly from patients at home or at investigator sites around the world. Most often patients use PDA devices which transmit these data to a central server. An ePRO system provides sponsors with higher quality data than paper, accurate timestamps and real-time access to vital compliance, enrollment and safety information.

If market adoption continues at its current pace, in ten years paper diaries no longer will exist for studies using PRO as primary or secondary endpoint data. I propose that we accelerate the pace and call for paper diaries to be banned.

If your study depends on what patients tell you, you have no choice but to use electronic diaries. It very well could be the difference between making your study a huge success or a failure.

## It is impossible to get high quality data from paper

Paper diaries offer no controls over timeliness or quality. Subjects make entries that are incomplete (skipped items), illegible (poor handwriting), and illogical (inappropriate responses). Further, patients respond days later, complete diaries in batches, invent data, forward-fill, and mark multiple responses in the same question. All these situations present serious data analysis problems.

We are all familiar with "parking lot syndrome," in which patients retrospectively complete days or weeks of diaries just prior to a site visit. Patients also forward fill paper diaries. A study published in the British Medical Journal showed that 45 percent of

subjects in a pain study invented data by forward filling at least once.

With paper, the burden is placed on patients to remember diary response times. Paper diaries can be confusing for patients to understand and accurately answer. In many studies, the questionnaires branch into different paths depending on the patient's responses. The burden is on the patient to understand which set of questions to answer based on their reactions or symptoms.

Electronic diaries allow sites to obtain accurate, real time information on patients' reactions during a trial. They are the best way to collect both objective and subjective assessments of patient experiences.

## Paper is slow

If a patient is not performing well in a study by failing to complete diaries regularly — or more importantly, because of worsening symptoms — it can take weeks or months for sites to notice. Site personnel have to spend time reviewing paper diaries and making manual, error-prone calculations and measurements where needed. These activities detract from time that could be spent caring for patients — one of the reasons site investigators become study coordinators in the first place.

Electronic patient diaries allow responses only during the appropriate times specified by the protocol. They use controls to ensure complete, legible and logical reports; encourage compliance through alarms; reduce respondent burden; and provide real-time site management of patient performance. In short, electronic diaries solve the problems of paper diaries.

## Electronic diaries promote a fast, honest response

In a Merck Research Laboratories insomnia study comparing paper and electronic diaries, one patient reported that he enjoyed using the paper diary because he only had to play catch-up about 60 percent of the time. This kind of statement that should convince all of us involved in data quality that paper diaries are nightmares.

Studies prove that electronic diaries motivate subjects to complete their diaries. It is much more efficacious to be able to ask patients how they feel at a precise moment and get an immediate, accurate answer.

## Electronic diaries empower subjects to be more compliant

An elderly female fibromyalgia patient in the UK once reported that her electronic diary alert sounded during a wedding reception. She simply laughed, excused herself, and took five minutes to complete and send her diary. It did not occur to her that this activity was a burden. It is highly unlikely that she would have carried a paper diary with her to the wedding. History tells us that she would have completed her diary retrospectively, or not at all.

Patients using electronic diaries enjoy a much higher degree of privacy. They can respond more freely than on a piece of paper that will be read by others. In a study on female sexual dysfunction using a cross-over design, patients reported 80 percent more sexual episodes on the electronic diary than they reported on paper.

Electronic diary patients say that they are encouraged to comply because they feel that someone is paying attention to their symptoms whenever they transmit their data. They are aware also that their study coordinators are supposed to review their data, which compels them to complete reports as expected.

Patients in a year-long lower back pain trial showed 90 percent compliance because they could hold the electronic diaries in any position they pleased. One man said he would not have been able to fill in detailed responses with paper because he was too uncomfortable to write. These patients completed electronic diaries six times a day, seven days a week because they could use the device even when lying down. And they felt encouraged because they were actively involved in managing their pain and health.

## Electronic diaries enable more reliable, smaller, faster, safer trials

One of the major advantages of ePRO solutions is that they have been shown to reduce data variance as compared to paper. This enables smaller, more conclusive studies.

Biostatisticians could adjust and lower estimates on how many patients are needed to prove efficacy in Phase II studies, based on the expected variance of paper data at hand. This can create a significant savings in money and time. In Phase III studies, such high quality data provide more reliable scientific conclusions. Instant access to up-to-the-minute ePRO data allows adaptive trial designs which are almost impossible with paper.

## Electronic diaries are the future, today

Paper might do well enough in rare exceptions, such as when time sensitivity is not an issue and a question relates to patient experiences over a week. But when it matters if a subject completes the diary on Monday instead of next Thursday, it is certain that paper data ultimately will fail.

Despite continued increasing adoption in the ePRO industry, some companies still are reluctant to change. Managers may worry that if there is a problem with electronic diaries it will hurt their careers, because no one was ever reprimanded for using paper — yet. The real danger lies in spending millions on trials that failed because of outdated, inaccurate paper diaries.

If the primary efficacy endpoint is coming from the patient it makes no sense to use paper diaries. Trials are all about data. It is the only thing they produce.

For efficacy and faster, smaller, less expensive trials it is time to put away the paper and pick up what has proven to be extremely effective technology: the electronic diary.

**Dr Valdo Arnera**

Dr Valdo Arnera has more than 18 years of experience in the pharmaceutical industry. He is skilled in both science and management, and speaks frequently on these topics. Dr Arnera has been an active co-chair of the DIA's Special Interest Area Communities (SIAC) eClinical and Standards committee.