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# Delivering on the eDiary Promise

**F**DA's Critical Path Initiative (CPI) is an important milestone in drug regulation and drug development. It represents FDA's interest, on behalf of the public health, to more quickly bring safe and effective medicines to the American public. Since clinical testing is the longest step in the clinical development timeline, anything that improves the efficiency and quality of clinical trials can play an important role in facilitating clinical development, as recognized by FDA's CPI. We believe that well-designed electronic diaries (eDiaries) can play just such a role, making clinical trials more efficient, more sensitive to medication effects, and more accurate.

Patient reported outcomes (PROs) are an integral and critical part of clinical testing: As of 1994, over three quarters of Phase I-IV trials collected some PRO data. PROs are becoming more important as drugs target important end-points such as pain, and as improving well-being and quality of life becomes more important to approval and marketing of therapeutic agents. An increasing proportion of PRO data are collected using diaries, because investigators recognize the need to get real-time data in patients' natural environments, avoiding the biases that creep into PRO data when patients are asked to retrospect and summarize past experience. Traditionally, paper diaries have been used. Yet, because of problems of legibility, out-of-range values, poor compliance with timely completion (hoarding, back-filling, and forward-filling), paper diaries have not yielded the expected improvement in assessment of patient experience.

## Real data from the real world

eDiaries can and do deliver on the premise and promise of diaries for collecting reliable PRO data. eDiaries improve efficiency by delivering data without the need for error-prone transcription and keying. eDiaries deliver higher-integrity data, by providing for skip patterns and range-checking at the time of entry. Most importantly, eDiaries deliver data that really was collected in real time in the real world: Research from multiple studies has shown that timely completion rates of 90% or better can be reliably achieved. eDiaries represent an important advance in how investigators collect PROs.

How does real-time data on PROs facilitate clinical development? A small gain in efficiency comes from the operational efficiencies arising from capturing cleaner data, computerized at the point of entry. The greater benefit comes from improved study sensitivity, which translates into smaller, more efficient and more informative studies. The methodological improvements attending an eDiary solution can help squeeze out "noise" that pervades paper diary data. Reduced noise translates into increased statistical power—the ability to detect real drug effects. A recent study of treatment for over-active bladder demonstrated this dramatically. Compared to a similar study conducted with paper diaries, an

eDiary solution reduced noise (error variance) by 33%. Similar results have been reported in a sleep-quality study.

What is the benefit of reduced noise? Studies can be smaller; the 33% drop in error variance translates into a 50% decrease in the number of patients that are needed to detect drug effects. A smaller study can be completed faster and cheaper. Studies can be more sensitive and definitive; with the same number of patients in the study, the reduced noise can dramatically reduce the rate of false-negative findings, which can require repeat studies or even lead the sponsor to drop a promising drug. On the flip side, by providing more definitive information, more sensitive studies can provide the information a sponsor needs to "kill" an unpromising drug earlier in development: sponsors are recognizing that resources consumed by candidate drugs that are killed later in development are a major resource drain.



Thoughtful application of eDiaries can make clinical development much more efficient.

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## Re-engineering the clinical trials process

In other words, thoughtful application of eDiary methods can make clinical development much more efficient, consistent with the CPI's aim of applying new tools to better evaluate safety and efficacy. Thus, encouraging the use of eDiary in PRO research represents just the sort of collaboration between FDA, academia, and industry that is envisioned by the CPI. We have been pleased at the FDA's openness to these new scientific developments and honored to have had the opportunity to confer and cooperate with FDA and with sponsors on issues related to eDiary. eDiary methods can play a role in the re-engineering of the clinical trials process to achieve increased accuracy and efficiency in producing safe, effective medications. □

Note: References for research studies mentioned are available from [www.invivodata.com](http://www.invivodata.com).

