

Paper vs. Web

A Tale of Three Trials

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A comparison of a paper-based study with two Web-based ones shows how Web technology can save sponsors money.

As we enter the 21st century, Internet-based data collection, retrieval, and management are becoming the norm in drug and device clinical research. By increasing data quality as well as reducing the time to database lock, companies can reduce both time to market and development costs.

There is little question that implementing a Web-based clinical trial involves a new paradigm for clinical research. Table 1 summarizes some of the differences between a paper trial and a Web-based trial.

The process of converting from paper to Web-based systems involves many stakeholders, including sponsors, independent clinical study sites, site maintenance organizations (SMOs), contract research organizations (CROs), and regulatory authorities. But in our experience as a CRO, the greatest challenge to the implementation of Web-based trials lies within the sponsor company's organization. Some clinical research personnel question efforts to move away from the use of tried-and-true tools such as paper-

based case report forms (CRFs), and point out that such tools have worked well for a significant span of time.

Web-based clinical trials, however, can offer advantages in cost, quality, and speed over paper-based trials. This article reviews these advantages, then compares three clinical studies that were part of a larger infertility drug clinical development program. The comparison pits a traditional paper-based study against two studies of the same type conducted using different sets of Web-based tools. In this case, the advantages of Web technology were clear.

Barriers to conversion

Setting up a Web-based clinical trial involves several costs. The most significant costs are incurred in hiring a team of programmers to write source code, in assigning clinical and data management experts to interface with the programming group, and in setting up internal computer systems, including the purchase of hardware and software. Alternatively, the programming involved in the Web-based aspect of the system can be subcontracted to companies with clinical trials expertise. Following the initial setup costs, there will be marginal costs for each additional clinical trial as well as fixed annual fees for system maintenance.

Although new technologies are in development, the basic technology necessary to execute Web-based trials has existed for some time. As a result, there are no fundamental structural or technological barriers to the implementation of Web-based clinical trials. Ideally, a Web-based system should not require software installation, modem upgrades, or high-speed Internet access. However, certain issues specific to particular clinical study sites can arise, including old personal computers and Internet browsers, small

computer screens, browser incompatibilities, old network systems, and corporate Internet access policies. To solve these problems, the IT department must carry out an in-depth survey of a confirmed study site's computer-related equipment and provide in-house consultation to resolve all technical issues.

Savings in Web-based trials

The cost-saving potential offered by Web-based trials is substantial, and can grow exponentially as a trial's size grows. The following are estimated cost savings for a 40-center study with 1000 subjects and a 100-page CRF.

Printing the CRF. CRF printing costs can run as high as \$100 per book. For 1000 subjects, this can represent a cost savings of \$100,000 before considering the staffing resources necessary to ship the CRFs and the direct shipping costs themselves.

Double-key data entry. This cost can be as high as \$3 per page—doubled. For a 100-page case book and 1000 subjects, this can represent a cost savings of \$600,000.

Query management. In the case study that follows, comparing a paper query management system with an electronic online system using edit and logic checks, there was a 65% reduction in queries. For the hypothetical study being discussed here, 3000 paper queries could be reduced to approximately 1000. Using an estimated in-house cost of query management of \$50 per query, the savings would be approximately \$100,000.

Monitoring. Because many monitoring problems can be identified in advance, at least one monitoring trip can be eliminated, and the monitor time spent at the site during the remaining visits can be minimized. Even saving just one trip and one additional day of monitoring for each of the 40 study sites in our hypothetical case, the savings for one day of travel, one

TABLE 1 Comparison of tasks in paper-based and Web-based trials

Task	Paper-based trial	Web-based trial
Paper CRFs	Yes	No
Printing of CRFs	Yes	No
Data entry	Double-key by sponsor	Entered once by site
Edit and logic checks	Using statistical software	At time of data entry
Query management	Paper forms	Electronic record
Data management	Paper forms	Instantaneous audit trail
Monitoring	All done in field	In field and in office
Problems identified	At site	In advance
Problems resolved	After site visit	Before site visit

day of monitoring, and travel costs could run up to \$3000/site. The total savings in this case would be \$120,000.

Return on investment

To develop a Web-based system, it is best to hire at least three experienced programmers familiar with Internet architecture, programming language, and database design. It is also vital to have clinical and statistical experts involved to assure

tured. We were able to share the development costs with our client sponsors so that our direct out-of-pocket costs were relatively small. If one builds a large infrastructure of programmers, salespeople, and executives, it could take at least two to three years to be profitable.

A case study

Three identical infertility clinical trials, involving a total of 349 subjects at 31 cen-

ated 1109 queries, consisting primarily of missing and illegible data. The monitoring group generated an additional 1826 queries, about half of which simply acknowledged that the data was truly missing or correct. Although the monitoring group generated a similar number of queries per page (all causes) in Study 2, the data entry group generated no queries because data entry occurred at the study site (with no edit or logic checks). For Study 3, there was a 65.5% reduction in all-cause queries generated by the monitoring group and a 63% decrease in queries at the time of data entry compared with the all-paper CRF program.

Diffusion of Web-based technology

Within two years, we believe, most companies will be using Web-based systems to perform clinical trials. Three likely developments will make this possible.

- The prices for Web-based systems will fall as competition increases.
- Confidence in the use of electronic data will increase.
- Economies of scale will develop as studies with similar designs, architectures, and business rules are implemented.

Although homegrown systems will be feasible, outside suppliers may be better positioned, given rapidly evolving Internet technologies, to develop applications for the new technologies and seamlessly provide them to pharmaceutical companies.

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usability and functionality of the system.

In the short term, the sponsors should be very close to break-even after the initial study and have significant direct savings for each subsequent study. Additionally, products should get to the market sooner. A one-month-accelerated approval on a New Drug Application (NDA) of a drug with annual sales of \$600 million would represent additional revenue to the sponsor of \$50 million. From the developer's point of view, the return on investment depends on how the business is struc-

ters, were performed to support two NDA submissions. Study 1 was performed with traditional paper CRFs and a data clarification system. Study 2 used our Web-based data collection system with no edit or logic check functions. Study 3 used our Web-based data collection system with full edit and logic check functions. For each study, our company calculated the total number of queries and the queries generated per page.

The results are summarized in Table 2. For Study 1, the data entry group gener-

TABLE 2 Query management in Web-based and paper-based clinical trials^a

Study	Number of subjects	Number of pages reviewed	Queries, all causes ^b	Queries per page	Queries at data entry	Queries per page
Traditional paper (Study 1)	192	11,130	2935	0.264	1109	0.100
Web-based, no edit or logic checks (Study 2)	66	2475	900	0.364	0	0
Web-based, with edit and logic checks (Study 3)	191	7908	937	0.118	612	0.037

^aData is incomplete.

^bQueries at data entry plus queries from monitoring group.