

**Cost Effectiveness:
TARGET E*CRF™ Query
Management System**

*Internet-Based Clinical
Trials*



**The New Paradigm In Electronic
Drug Development**

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INTRODUCTION

There are many stakeholders involved in the process of converting from paper to web-based systems, including sponsors, independent clinical study sites, site maintenance organizations (SMO's), contract research organizations (CRO's) and the FDA.

Costs

There are several costs involved in setting up a web-based clinical trial. The most significant costs are incurred in:

- hiring a team of programmers to write source code
- assigning clinical and data management experts to interface with the programming group
- 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 set-up costs, there will be marginal costs for each additional clinical trial as well as fixed annual fees for system maintenance.

Benefits

The benefits of web-based clinical trials, however, can be invaluable for a company seeking to expedite the clinical development process. They can include:

- more rapid access to trial data and trial progress
- higher-quality data entry due to edit and logic checks at the time of data entry
- elimination of double-key entry
- elimination of commercial paper case report forms (CRF)
- alerts to safety and enrollment issues at the time of data entry
- faster time to data lock
- seamless integration with electronic NDA submissions

Technical Issues

Although there are new technologies in development, the basic technology necessary to execute web 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 clinical study site-specific issues can arise that, when identified, can usually be easily addressed, including old personal computers and internet browsers, small computer screens, browser incompatibilities, old network systems, and corporate Internet access policies.



To address these issues, an in-depth survey of a confirmed study site's computer-related equipment is carried out and consultations provided to each site to resolve any and all technical issues. This is a global advantage to the site as it helps to fine-tune/update their computer system.

Main Challenge

In our experience, the greatest challenge to the implementation of Internet-based trials lies within the sponsoring company's organization. Some clinical research personnel question efforts to move away from the use of tried-and-true tools such as paper-based CRF's, and point out that such tools have worked well for a significant span of time.

There is little question that implementing a web-based clinical trial involves a new paradigm for clinical research. Some of the similarities and differences between a "paper" trial and an Internet-based trial are highlighted in the exhibit below.

Table 1. Paper-Based Versus Internet-Based Trials: Various Tasks

Task	Paper-Based Trial	Internet-Based Trial
Paper Case Report Forms	YES	NO
Printing of Case Report Forms	YES	NO
Data Entry	Double-Key by Sponsor	Entered by Site Once
Edit and Logic Checks	SAS Program	Time of Data Entry
Query Management	Paper Forms	Electronic Record
Data Management	Paper Forms	Instantaneous Audit Trail
Data Quality Assurance	After In-House Data Entry	Monitoring Function
Monitoring	All Done in Field	Combination Field and Office
	Problems Identified at Site	Many Problems Identified in Advance
	Problem Resolution After Site Visit	Problem Resolution Prior to Site Visit

AREAS OF DIRECT COST SAVINGS IN WEB-BASED TRIALS

Tasks

1. Printing of the CRF

This cost can be as high as \$100/book. For 1,000 patients, this represents a cost elimination of \$100,000 plus resources to ship and direct shipping costs.



2. Double-Key Data Entry

This cost can be as high as \$3/page x 2. For a 100 page case book and 1,000 patients, this represents a cost elimination of \$600,000.

3. Query Management

In a case study 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 current hypothetical study, there would be a reduction from 3,000 paper queries to approximately 1,000. Using an estimated in-house cost of query management of \$50/query, there would be a savings of approximately \$100,000.

4. Monitoring

Since many monitoring problems can be identified in advance, there can be a reduction of at least one monitoring trip, as well as a reduction of time spent at the study site. Even if just one trip and an additional one day of monitoring is saved for each study site, for a multicenter study with 40 sites, the savings for one day of travel, one day of monitoring and travel costs could run up to \$3,000/site. The total savings in this case would be \$120,000.

Table 2. Summary of the Minimum Estimated Cost Savings of a Multicenter Study

Number of Centers	40
Number of Patients	1,000
CRF Pages	100

Tasks	Paper	Electronic	Net Savings
Printing of CRF's (\$100/Book)	\$ 100,000	0	\$ -100,000
Double-Key Data Entry (\$3/Page x 2)	600,000	0	-600,000
Data QA (\$3/Page))	300,000	0	-300,000
Query Management (\$50/Query)	150,000	50,000	-100,000
Monitoring Savings (One Trip, \$3,000/Trip)	120,000	0	-120,000
Total Cost	\$ 1,170,000	\$ 50,000	\$ -1,120,000



TARGET e*CRF[®]

Target e*CRF[®] is an Internet-based, proprietary, data and project management system created exclusively by **TARGET HEALTH INC.** to collect clinical trial data over the Internet. Operationally, data are entered and submitted directly to a remote central database through a web-based data entry interface. Benefits include real time data availability, elimination of traditional paper CRF books, and minimization of data transcription and logic errors.

Table 3. Internet-Based Data and Project Collection/Management System

Description	Key Features
Is 100% developed and managed by TARGET HEALTH INC.	Comes with either the sponsor's or a customized database
Is a customized application with a web user interface	Comes with data warehousing
Requires NO software installation and NO high speed internet connections	Runs on all computer systems
Runs off regular modem phone lines	Has customized pages and data entry screens
Is housed at a secure website and utilizes secure encrypted communication	Can provide pre-assigned patient and pin numbers
Provides unique websites and domain name	Has built-in encryption
Is fully compatible with SAS	Has a sophisticated, thorough user-friendly, query management system
Benefits include:	Can provide E-mail notifications
1. real time data availability	Has customized edit/logic checks
2. elimination of traditional paper CRF's	Has customized range checks
3. less transcription and logic errors	Has a friendly customized navigation system
	Can deliver customized management reports



AN INTERNET-BASED TRIAL CASE STUDY

Methods

Three identical clinical trials, involving a total of 349 patients at 31 centers, were performed in the area of infertility to support two NDA submissions. Study 1 was performed with traditional paper CRF's and a data clarification system. Study 2 utilized the Target e*CRF™ Internet-based data collection with no edit or logic check functions. Study 3 utilized the Target e*CRF™ Internet-based data collection tool with full edit and logic check functions. For each study, the total number of queries and the queries generated by page were calculated.

Results

For Study 1, the data entry group generated 1,109 queries, consisting primarily of missing and illegible data. The monitoring group generated an additional 1,826 queries, about half of which were acknowledgment that the data were truly missing and/or correct. Although there was a similar number of queries/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 to the all-paper CRF program.

Table 4. Metrics of Paper Versus Electronic Systems

Study	N (Patients)	Pages Reviewed	Queries, All Causes	Queries/Page	Queries at Data Entry	Queries/Page
1. Traditional Paper	192	11,130	2,935	0.264	1,109	0.100
2. Internet Based - No Edit or Logic Checks	66	2,475	900	0.364	0	0
3. Internet Based – With Edit and Logic Checks	191	7,908	937	0.118	612	0.037*

*At the time of this analysis, 16,494 pages were entered into the database and 7,908 pages were reviewed by the monitoring group.

CONCLUSION

Within two years, in our opinion, most companies will be using Internet-based systems to perform clinical trials. This will occur as: (1) the prices for Internet-based systems fall with more competition; (2) there is increasing confidence in the use of electronic data; and (3) economies of scale develop as studies with similar designs, architectures and business rules are implemented.

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

