



261 Madison Avenue, 24th Floor, New York, NY 10016

The Economic Impact of Using a Paperless Trial Master File (TMF) in a 80-Center Study in Ulcerative Colitis

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Executive Summary

Target Health Inc., a full service eCRO, has developed Target Document®, a web-based document management and sharing system, which allows companies to augment, or even replace, their paper-based filing system with a transparent, cost-effective, system for users within a company as well for their customers and vendors. Currently, pharmaceutical companies and CROs spend millions to manage the vast amount of paperwork during the drug and device development process. The Sponsor, or CRO, if delegated, and each clinical research site must separately maintain a Trial Master File (TMF) which creates a major overlap of duplicate documents in multiple locations, and the large potential for error.

This report documents the financial impact of Target Document® to a CRO and Sponsor when substituted for a paper TMF system, in an 80-center study in ulcerative colitis. While conducting in-depth interviews with employees of Target Health Inc. and the Sponsor, it was found that implementing Target Document® achieved significant productivity improvements among project management, regulatory and document management staff in the clinical research department. Large financial benefits were also achieved by reducing costs for physical storage space for TMF binders, overnight mail and associated labor costs, project management meetings and paper and photocopying supplies.

One of the key aims of the project was to optimize the workflow that is inherently clumsy in a paper-based document system. By enabling easy access to the web-based documents, the project expanded the communication workflow among the CRO, sponsor, CRAs and vendors. It eliminated loss of important documents, enabled more efficient filing of new documents and provided a test case for other uses of the system within the company, among these: 1) legal, 2) finance, 3) procurement, and 4) quality assurance/control .

In the financial analysis, it was found that for this project there was a major reduction in overnight mail costs and the elimination of 0.5 FTE previously required to manage documents. QA/QC review time was dropped by 50% as review of documents could be done seamlessly at the desktop. There was no need to send documents to the Sponsor as all final documents resided on the web.



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1. Introduction

Pharmaceutical companies, CROs and clinical sites spend millions to manage the vast amount of paperwork that regulatory agencies require during the drug and device development process. Currently, each clinical research site must maintain documents specific for their site as well as for the clinical trial at large. Each Sponsor also must maintain most of the same documents stored at the clinical sites, with additional documents required for Sponsors. If a CRO is involved, they often have to send a copy of all of their files to the Sponsor at the end of the clinical trial. This system is costly and prone to errors. Not only is there a major overlap of duplicate documents, there is the potential for confusion about versions and signatures. In addition to the often large shipping and handling costs, the associated reconciliation tasks are time consuming and expensive.

In today's world, with nearly universal access to computers and the Internet, it is inefficient and risky to maintain multiple paper copies of documents at multiple sites. There is a need for reasonably priced systems for managing, organizing, and sharing electronic documents.

Currently, systems exist that provide pharmaceutical and device companies an organizational framework for multiple users to collaborate on a single document in a regulated environment. While some document systems provide a comprehensive and all-encompassing solution to enable users to manage, organize, and share electronic documents, they require users to undergo significant training. In addition, these systems can be quite expensive. As a result, adoption is low, use is limited, and the clinical sites and contract clinical research associates (CRAs) often do not have access to a common document system and, therefore, need to email or send documents through overnight mail. Systems are needed that can easily integrate the internal operations of the pharmaceutical companies with outside contractors and clinical sites, who need to create and share documents.

2. What Is Target Document®?

Target Document® is a secure, **USER FRIENDLY**, web-based, 21 CFR Part 11 compliant, document sharing, distribution, and management system that allows authorized users, depending on their roles and permissions, to post, share, electronically sign, and archive any electronic document using a Web browser, without the need to install software. Target Document® can **eliminate** the distribute of critical documents via email and is ideal for companies wanting their own system to communicate with vendors, CROs, study sites, CRAs, etc. Target Document® is also ideal for CROs needing to collaborate with many sponsors. Target Document® can be used in any industry and is multi-functional.



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2.1 Advantages

- Friendly user interface without any clutter or useless features.
- Completely web-based, so there is no need to install software.
- Eliminates the need to send expensive document packages.
- Keeps an electronic audit trail of document download by users; no more “I didn’t get it” excuses.
- Speeds up document distribution and signoff.

2.2 Features

- Web-based solution
- Login ID/password security (also used for electronic signatures)
- User creation/management
- Role and permissions creation/management
- User self-registration with administrator approval
- Template folder management
- Folder and/or document access controllable by authorized users
- Locking/unlocking restricts unauthorized changes to folders/documents
- Upload/download any document type deliverable across the web: PDF, Word, Excel, text, audio, video, etc.
- Document check-in/check-out
- Document renewal notification
- Communication tool for projects and documents
- Automatic To-Do list for document review and FDA-compliant electronic sign-off
- Document history/routing status
- Tracking of all versions of uploaded documents
- Automatic activity/change history (audit trail) for folders and documents
- Restriction to delete signed documents, or folders with signed documents
- Status reports
- And more

2.3 Administrator Features

- Automatic notification informs administrator when system error occurs
- Department creation/management
- Generate system/session logs by specified date range
- Password reset
- Password expiration configuration



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3. Purpose

This report provides a framework to evaluate the financial impact of Target Document® on organizations. Readers should use this study to understand the business case for investing in Target Document®.

4. Methodology

Each aspect of implementation of Target Document® was assessed, including software costs and training, cost savings of overnight mail and associated labor costs, document storage costs as well as the overall productivity benefits to the sponsor and CRO. Risks were also assessed including likelihood of software failure and the inability to access documents via the web.

5. Key Findings

The study yielded a number of key findings:

- **ROI** - Based on the associated ROI analysis of the Target Document® implementation, the ROI for this implementation is 198% with a breakeven point (payback period) of approximately 6 months after deployment.
- **Benefits** - The main benefit has been rapid document access, workflow transparency and productivity improvements. After implementing Target Document®, paper files have been largely eliminated except certain document containing original signatures. Additional cost savings include reduction 1) of space required for paper file storage, 2) in paper and binders supplies, 3) in photocopying labor and supplies, and 4) of direct and labor costs associated with sending documents by overnight mail. Total cost savings within 1 year for this one study are estimated to be \$73,100, which represented about 7% of study startup and monitoring costs.
- **Risks** - Key risks associated with Target Document® are the complete crash of the system and inappropriate deletion of documents. To address these risks, the system is backed up daily and a backup tape sent off site weekly. If a document is inappropriately deleted, it can be recovered by the administrator through a built-in interface.
- **Costs** - The largest initial cost for this implementation was \$25,000 for the software and a hosting fee of \$10,000. Since this was a single study, it was not possible to amortize hosting fees or for multiple studies to be performed under a renegotiated software license. Professional services and internal labor costs for implementation and training approximated \$2,000.



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6. Results

See Table 1 for a detailed assessment of costs.

The cost of Target Document® for this study of 80 sites was \$35,000; \$25,000 for software plus \$10,000 for software hosting. There was no need to spend \$20 for 80 3" binders or store them in archives, which generated a savings of \$1,600 plus \$8,000 respectively. There was additional savings of overnight mail transactions of \$15,000. There were approximately 300 documents that could be signed and processed electronically for an additional savings of \$30,000. Signing documents only required document review and reentry of the user's password. While the sign-off process takes the same amount of time whether electronic or paper, what is different is that there is no longer the need to print a hard copy, for example, of a monitoring report, and then file it in a binder in a file cabinet, which also takes up space in a busy office.

Since there was no need to photocopy and store documents in binders, there was an additional savings of \$35,000 which represents full-loaded labor of a 0.5 FTE. One vendor who provided contract CRA support was able to save about \$2,000 in overnight mail costs since all invoices were posted directly into Target Document®. This also facilitated payment to the vendor. As a result there were \$110,100 worth of costs that were replaced with a document system costing \$37,000. This represented a cost savings of \$73,100 and a ROI of 198%.

Not only was there an excellent return on investment, all users of Target Document® were pleased with both the speed that documents were processed and the transparency of the system. Each training session took approximately 1 hour, and through WebEx, multiple users could be trained at one time. Additional training was available as needed.

Another way that the sites and Sponsor were able to save additional monies was, instead of shipping paper documents via overnight mail, was to fax these documents directly to a dedicated electronic fax account. When this occurred, documents were easily converted to a .PDF format, and loaded directly into Target Document® without the need to print the document first.



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Table 1. Costs, Cost Savings and ROI When Using a Web-Based Document System for Clinical Trials

EVENT	N	FREQ.	UNIT COST	TOTAL	SUMMARY
Software License	1		\$25,000	\$25,000	
Hosting	1		\$10,000	\$10,000	
Training	5		\$400	\$2,000	
TOTAL COSTS					\$37,000
Overnight Mail					
CRO/Sponsor Document Transfers	1	20	\$50	\$1,000	
Site Contract Approvals to Sponsor	80	1	\$50	\$4,000	
IRB Approvals to Sponsor	80	3	\$50	\$12,000	
Contract CRA Invoices	5	10	\$50	\$2,500	
Sub-Total					\$19,500
Trial Master File					
Binders	80		\$20	\$1,600	
Photocopy and filing of Essential Documents (FTE)	0.5		\$70,000	\$35,000	
Storage of Binders (5 years)	80	5	\$20	\$8,000	
QC review	80		\$200	\$16,000	
Sub-Total					\$60,600
Document Signoffs					
Documents Requiring Signoff	300		\$100	\$30,000	
					\$30,000
Sub-Total					
TOTAL SAVINGS					\$110,100
ROI					198%



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7. Discussion

Target Document® was shown to be a user-friendly, 21 CFR Part 11 compliant, web-based, document sharing solution that was used to share information about any document within and between the sponsor and CRO. Target Document®'s rich toolset provided users with the ability to download/upload, manage, and share and store any type of document. Users were able to add and organize folders, download/upload and manage documents, notify document owners and subscribers of changes made to a document and expiration dates, track document history, create document routing maps for distribution to document subscribers, electronically sign or reject documents, search for documents based on search keywords, work with document revisions, and more. Target Document® was able to house and manage a paperless TMF and replace a paper management system.

Vendors were able to upload invoices and supportive documentation rather than overnight these documents and there was no need to print, sign and overnight documents requiring hand written signatures. Invoices could be approved with electronic signatures with full transparency to the sponsor.

Although the cost of paper savings was minimal relative to other costs, the savings to the environment by reducing the use of paper, toner and electricity contributed to a reduced carbon footprint. Multiply these savings across thousands of clinical trials, in aggregate, electronic document systems can provide for a lower environmental impact.

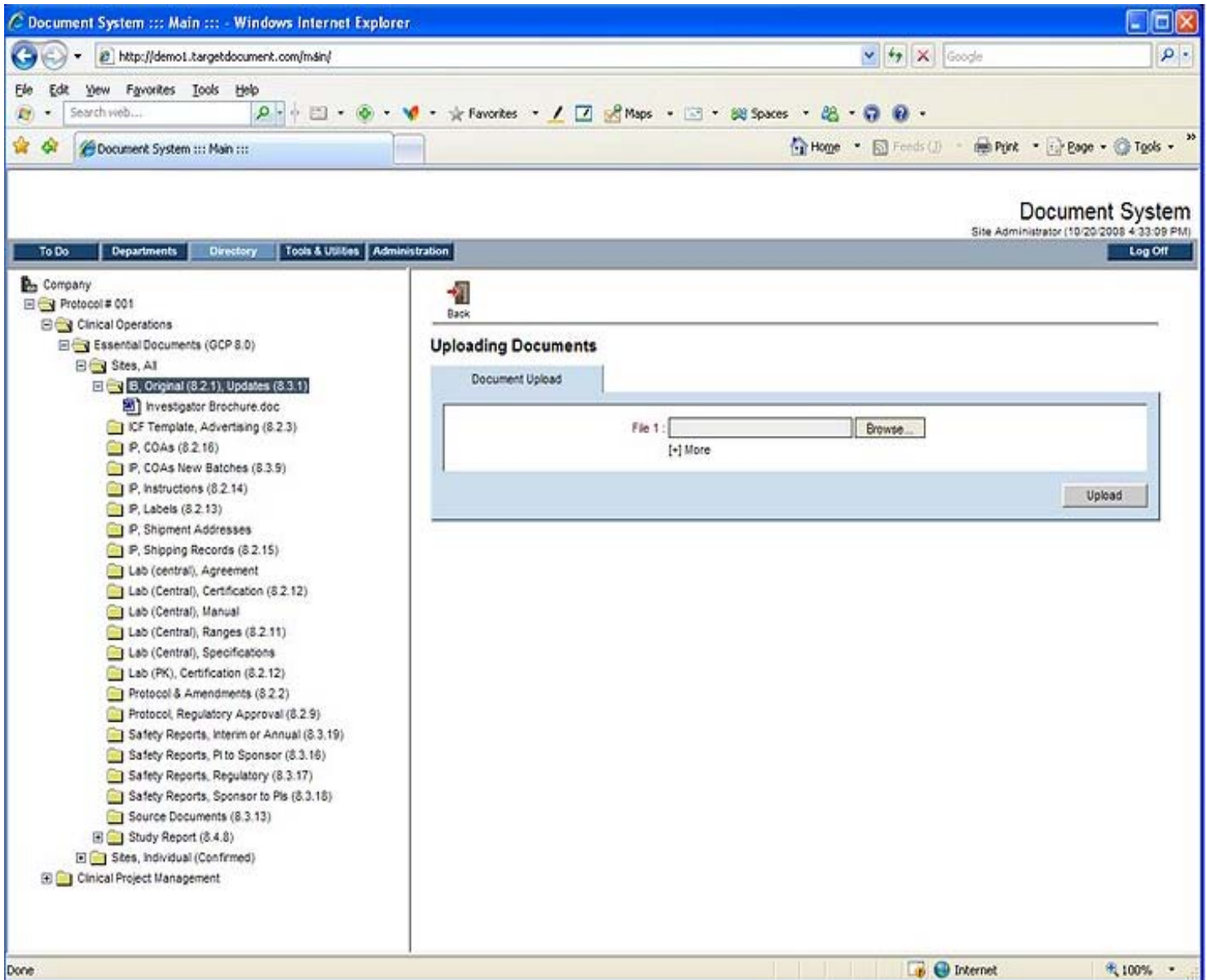
8. Conclusion

It is time for the pharmaceutical industry to embrace current technology tools to optimize the clinical trial process for drugs, biologics and devices. We all store documents electronically but it is time to centralize the process so that all interested parties, whether they are clinical research sites, pharmaceutical companies, CROs, auditors and regulators can be assured that we are all, literally, on the same page, at least electronically. The advantages of using a document sharing system can change and improve the way we conduct clinical trials. If we could only give up our reliance on paper, we would help save our planet.

9. References

1. Mitchel, J., Moncrieffe, A., Kim, Y.J., et al. The Paperless Trial, Past, Present and Future. *European Pharmaceutical Contractor*, Autumn 2007.
2. Mitchel, J. Ghilezan, I., Y. Kim, Y.J., et al., "The End of the Paper Trail," *European Pharmaceutical Contractor* Winter 2008; 72-75.

Figure 1. Browsing For Document Upload





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Figure 2. Managing Documents Within the TMF

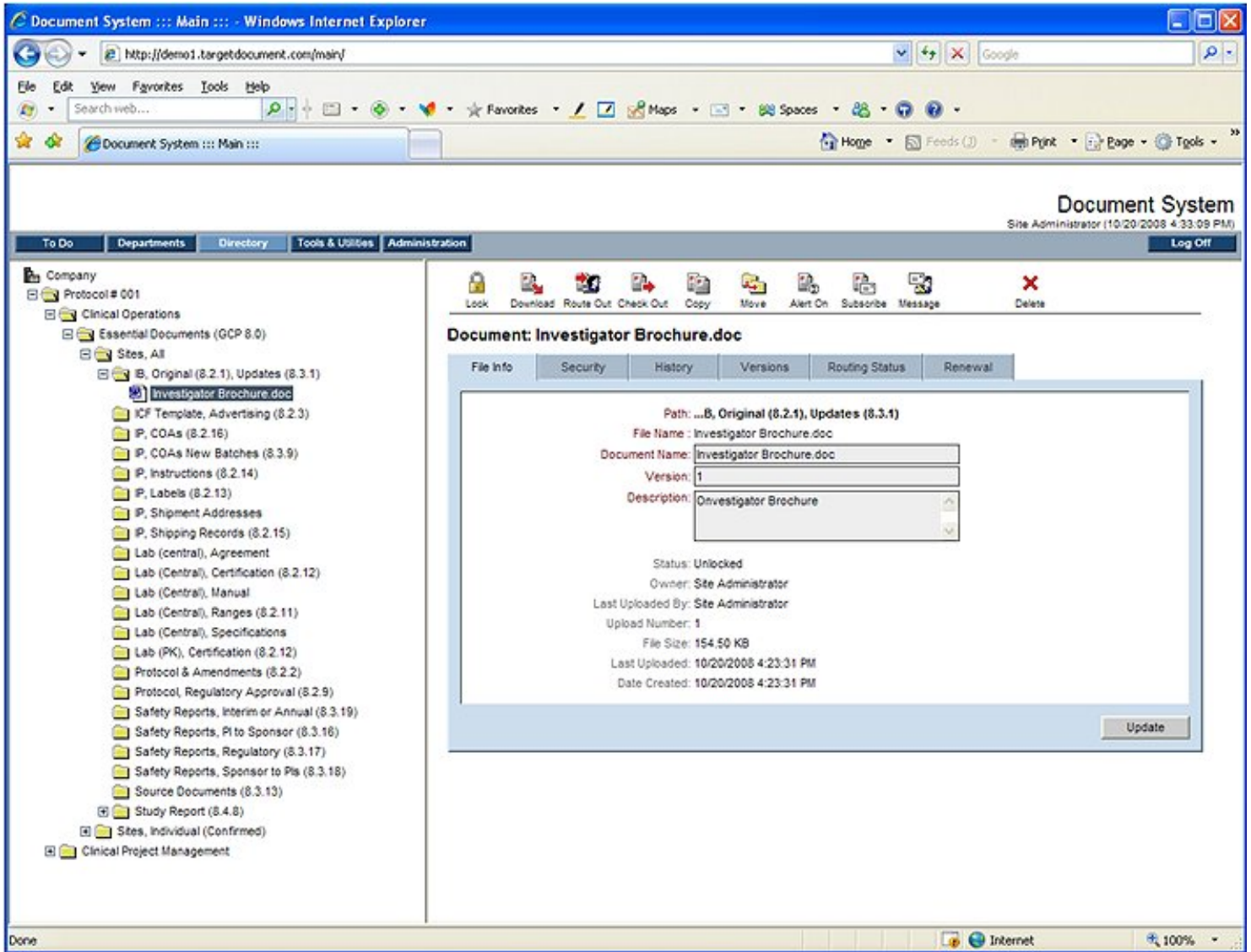


Figure 3. Signing Electronically

