

A Comparison of Accuracy, Speed, and Task Satisfaction between Paper-Based and Image-Based Data Entry of Case Report Forms

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MSc in Clinical Research

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ABSTRACT

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A Comparison of Accuracy, Speed, and Task Satisfaction between Paper-Based and Image-Based Data Entry of Case Report Forms.

MSc Research Report submitted in accordance with the requirements of the Liverpool John Moores University MSc in Clinical Research.

Objectives—To compare the accuracy, speed, and data processor task satisfaction between data entry from CRF images, and data entry from paper CRFs.

Design—A randomised, unblinded study. Volunteers entered two CRF booklets viewing CRF images as source documents. Based in part on their accuracy and speed entering the first two booklets, the volunteers were randomised into either the image group ($n = 11$) or the paper group ($n = 10$). Four more CRF booklets were entered after randomisation, and a task satisfaction questionnaire was completed.

Setting—The study was conducted at the Charlottesville Trials Management Center of PRA International.

Subjects—PRA employees who volunteered to participate in the study.

Main Outcome Measures—Mean error rates (number of errors per 100 fields) for both groups were calculated for the four randomised CRF booklets and compared. Mean entry speed in minutes per booklet for both groups was calculated for the four randomised booklets and

compared. Mean task satisfaction scores were calculated for both groups from the questionnaires and compared.

Results—The mean number of errors per 100 fields for the image group was 1.31, and for the paper group was 1.04, resulting in a difference of 0.27 ([95%CI] –0.29 to 0.84) more errors per 100 fields for the image group. The mean entry speed for the image group was 9.47 minutes per booklet, and for the paper group was 9.57 minutes per booklet, showing a difference of .09 minutes per booklet less ([95%CI] –1.85 to 1.66) for the image group. The mean task satisfaction scores for the image group was 11.82, and for the paper group was 12.30, resulting in a difference of 0.48 lower ([95%CI] –1.84 to 0.87) for the image group.

Conclusion—The null hypothesis for the primary objective, that there is no difference in data entry accuracy between using CRF images and paper CRFs can not be rejected based on these results. Analysing pooled data from this study and an earlier study ($n = 14$ per group) showed 0.51 more errors per 100 fields ([95%CI] 0.02 to 1.00) for the image group. A detailed review of the entry errors suggests that if double data entry methods are maintained, there is no significant impact on the overall database quality with the use of CRF images.

Based on the entry speed results, entry speed from CRF images can be considered non-inferior to entry speed from paper CRFs at the 5% significance level. There is potential for overall data entry productivity improvements when workflow and logistics factors are included.

Based on the task satisfaction results, the null hypothesis of no difference between the groups can not be rejected.

AIMS AND OBJECTIVES

The aim of this project was to analyse the impact of using imaged case report forms (CRFs) during data entry. Working with displayed images throughout the clinical data management process, instead of using paper CRFs, offers many advantages discussed later in this paper. This project examined the effect on data entry accuracy, data entry speed, and the task satisfaction of data processing personnel when paper CRFs were replaced with images for data entry.

The primary objective of the study was to determine if data processors entering data from CRFs displayed on a monitor would display an average error rate that was higher than the average error rate that would be realised by entering data into a database from traditional paper CRFs.¹

The project had two secondary objectives. The first was to determine if data processors could enter data from CRFs displayed on a monitor with a speed of entry no slower than the speed of entry seen when data processors enter data from paper CRFs. The second was to analyse, by use of a questionnaire, if the task satisfaction of data processors performing data entry with CRFs displayed on a monitor was lower than the task satisfaction of data processors performing data entry with paper-based CRFs.²

¹ This objective is phrased reflecting the assumption, based on previous works, that a higher error rate would be found in the image group. In the statistical treatment of this question, however, it was intended to test for any difference, therefore a two-tailed approach was used. This is reflected in the methods and results sections.

² Analogous to the note above, task satisfaction scores were tested for any difference using a two-tailed approach.

INTRODUCTION

BACKGROUND

Overview

In order to provide context for the comparison of image-based and paper-based data entry of CRFs, a brief discussion of clinical data management, double data entry, quality control of clinical databases, and alternative data collection models would be useful.

Clinical Data Management

Clinical Data Management has been called “the art, and the science, of creating a computer database of clinical trial data (1).” Because Clinical Data Management represents a significant portion of the drug development process—estimated to be as much as 30-40% of the overall cycle time from protocol development to integrated clinical report (2)—there is competitive pressure to reduce the time, and hence the cost, of performing data management.

Appendix A displays a flow chart of a typical data management process. The traditional data management process involves creating data tables or files, and data entry screens, based on the content of the CRF used in the study. When CRFs are received from investigator sites into the data management unit, they are typically logged into a CRF tracking system. Some form of manual review for completeness and accuracy may then take place. Then data processing personnel enter data from the CRFs into the database, using the data entry screens. This is normally followed by a review of the data in the database by personnel with a clinical background, usually assisted by computer programs, to identify inconsistent, potentially erroneous or unusual data, and to code text fields such as adverse events and concomitant medications. This review step typically involves generating queries, or questions about the

data, which are returned to the investigative site for clarification. When this review, or data cleaning process, is completed, there is customarily a quality control step, which involves comparing the contents of the database with the data on the CRFs. There may also be a separate quality assurance review of the database at this point.

Double Data Entry

Data entry of trial data into the electronic database is a key step in this process. Most data management groups perform some method of double data entry, involving two different operators, with the differences between the two passes of entry compared within the computer. There is a continuing debate on the value of double data entry (3, 4, 5, 6, 7). Some parties believe that in some cases the errors that are detected during double data entry could also be detected by techniques such as range checks, and that many of the errors that might go undetected with range checks would have little or no impact on the statistical analysis of the database (5). Others have suggested that a continuous sampling approach might be preferable (7). However, double data entry of paper CRFs remains the most common method of entering data into the clinical trial database (1, 3, 8). This data will eventually form the basis for the statistical evaluation of the trial, so it is important that the transfer of data from the paper CRF to the electronic database is performed accurately.

Database Quality Control

While some sources suggest that the step of comparing the database to CRFs is less useful than the use of thorough validation programs in some circumstances (9), most companies perform some review of this type (9, 10). The method of selecting which data will undergo a quality review, and what constitutes an acceptable error rate has received a great deal of discussion (10, 11). Methods range from performing quality control on 100% of fields

designated as critical fields, to performing checks on 100% of all fields for randomly selected patients, to some combination of these approaches. In random selection, the portion of patients selected may be based on a fixed percentage such as 10%, or on a formula (e.g., $\sqrt{n} + 1$). Acceptable error rates may be expressed in terms such as zero errors in critical fields, and fewer than 5 errors per 10,000 fields checked overall. Alternatively, a statistical model based on the likelihood of accepting a data set with an acceptable quality level and rejecting a data set with an unacceptable level may be employed (11).

Alternative Data Collection Models

This project is limited to examining the model of scanning a paper CRF and using the electronic image within the framework of classic centralised data management. There are, however, alternate methods of data collection available.

For many years, the use of remote data entry (RDE) systems has been discussed as a method to speed data collection, collect data closer to the source, and eliminate data problems earlier in the process. However, few companies have embraced RDE as their primary method of data capture (12). One reason may be the high cost of RDE (1). Some experts have gone so far as to pronounce that “Remote data entry, in the conventional sense, has failed” and that “no more than 5% of all trials will ever use RDE as the primary method of data collection (13).”

Current discussion has moved from RDE to web-based data capture (13, 14). According to one proponent, “Internet technologies are already maturing, and further improvements will make future generations of web-based CRF systems even more attractive (14).”

The traditional data capture process involving hand completion of CRFs remains the primary method in use (1). It is estimated that up to 95% of all clinical data is still captured using paper-based collection methods (12, 15).

IMAGING CRFS

Paper CRFs remain the most common data collection tool at the investigator site. The tools to scan those CRFs and create electronic images are readily available. There are several reasons why a data management group might perceive an advantage to scanning paper CRFs on receipt, and performing data management activities using the electronic image of the CRF.

Using an image instead of paper simplifies the implementation of electronic document management and automated workflow tools.

Logistical advantages may be anticipated. These include eliminating the need to store large numbers of CRFs in a secure and controlled yet readily accessible location near the data management group, reducing the physical handling of the CRFs, and making the image of the CRFs available to multiple data management personnel simultaneously and regardless of location (16, 17, 18).

Additionally, scanning the CRFs upon receipt may further an overall goal of creating an electronic submission to a regulatory authority.

Workflow Process Management

There are many commercial document management systems available that enable the use of CRF images in place of paper CRFs. The use of these tools can allow for integration and

coordination of study team activities, provide for improved CRF tracking, and increase workflow efficiency (16).

A white paper produced by one pharmaceutical company together with a workflow system vendor (19) reports that the company “cut the time to close a clinical trial” and that this was “as a direct result of imaging and workflow.” The workflow system led to improvements in several areas with “an immediate impact on quality, productivity, and cycle time.”

With consistent pressure to reduce the cycle time that data management contributes to the drug development process, there is obvious interest in “electronic document management systems [that] can offer savings in time for clinical studies (16).”

Electronic Submissions

Submissions to regulatory agencies have traditionally been paper-based. However, one author estimates global registration of a single product could exceed seven million pages of paper submitted to the various countries involved, and notes that “Pharmaceutical companies and regulatory agencies are drowning in paper (20).”

The FDA is committed to “...develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of [Investigational New Drug] INDs and human drug applications...(21).” In support of legal mandates stemming from the Prescription Drug User Fee Act (PDUFA), the FDA has developed an Electronic Regulatory Submission and Review (ERSR) program strategy to support the transition from paper-based submissions to an electronic review environment. The FDA has produced numerous guidance documents detailing the requirements for electronic submissions (22, 23, 24, 25, 26).

There have been a number of other electronic standards initiatives (DAMOS, MERS, SEDAMM) which have the same basic goal of developing standards for transferring electronic data to regulatory agencies (20). The International Conference on Harmonisation (ICH) through the ICH Multidisciplinary Group 2 (M2) Expert Working Group (EWG) is engaged in the recommendation of standards for electronic transfer of regulatory information (20, 27).

Both the FDA and the ICH M2 EWG group have identified Portable Document Format (PDF) as a standard for electronic transfer of documents (23, 24, 28).

The need to submit data to regulatory agencies electronically does not require that data processing personnel also work with images. However, the various electronic submission guidelines require indexing and bookmarking of CRF booklets (23, 24). The data needed for this index is similar to the data which would normally be used as part of the CRF tracking during the data management process. There would be an advantage to entering this index information once, rather than duplicating this effort at different points in the study process. Having established a need to scan CRFs as images, and index them with key study information, it could be considered desirable to utilise these images and this data during the full data management process.

PREVIOUS STUDIES

PRA Pilot Study

PRA International, Inc. (PRA) performed a data imaging pilot project, which was reported by Lawson, Brown, and Shostak in the Drug Information Journal in 1997 (17). The pilot was performed with the objectives of reducing the physical storage requirements of CRFs,

preserving the integrity of the CRFs, and increasing the ability of multiple functional areas to simultaneously access the imaged CRFs.

The team developed a VAX-based imaging system using current processes and technology. A pilot study that was small in scale and of limited scope was identified. Although no formal controls were used to compare processing times, the team generally found that data processing activities were more difficult and less time efficient in the pilot study. Some of these shortcomings were attributed to limitations inherent to the technology that was used. The team specifically cited problems with the visualisation of the form on the screen. Nonetheless, the team concluded that imaging could be a useful tool in the CRF industry.

Hopkins Fax Study

Personnel at Johns Hopkins University performed a feasibility assessment comparing the reliability of data entered from CRFs that were transmitted by fax directly to computer images, with the reliability of data entered from paper forms. This assessment was reported by Deiner-West, Connor, Newhouse, and Hawkins in *Controlled Clinical Trials* in 1998 (18). The purpose of the assessment was to test the feasibility of an alternative fax-based system using existing paper forms, without changing the current data management system. All forms were entered initially from paper source. Second pass data entry was performed on 50% of the forms with paper source, and on 50% with image source. The forms that were entered on second pass from image source, were also keyed a third time, again from image source.

This allowed for discrepancy rates to be compared three ways: paper vs. paper, paper vs. image, and image vs. image. Error rates were low for all data source comparisons. Error rates were two to three times higher from image source than from paper source. The study did not record entry times, and makes no comparisons in this area.

The assessment discusses several difficulties that were encountered. Several of these were specific to the fax-based model that was used. The need for monitors large enough to display full-page images was noted.

Swansea Pilot Study

An unreported pilot study was performed in February, 1999, at PRA International in Swansea, Wales. Involving seven volunteers, this study was exploratory in nature, and designed to collect information that could be used to better construct this project (PACCRM030 Project). All seven volunteers performed data entry using a set of CRFs and a database designed specifically for the pilot study. Each volunteer first entered a test patient for familiarisation with the database and the CRF. Each volunteer then completed a brief questionnaire that included demography data, and a self-estimate of personal computer and data entry experience. Then all seven volunteers entered two CRF booklets using CRFs that had been scanned and were presented as images. At this point, each volunteer completed a brief questionnaire designed to assess individual reaction to the experience of entering those two patients. Then the seven were randomised into paper ($n = 4$) and image ($n = 3$) groups. Both groups then entered four additional CRF booklets. At this point the same brief individual reaction questionnaire was completed again. The number of data entry errors and the speed of data entry were then analysed, as well as the results of the questionnaire. This data is presented in tabular format in Appendix B, but the small sample size must be considered when reviewing the data.

The primary purpose of the Swansea Pilot Study was to test the methods that would be used to collect data in this project, and to explore the initial results prior to finalising the plan for this project. The data collected in the Swansea Pilot Study also helped to provide a basis for determining the sample size to be used in this project.

An analysis of the data from the Swansea Pilot Study suggested that data processors entering data from CRF images made more entry errors than those entering data from traditional paper CRFs. The mean number of errors for the image group was 1.26 errors per 100 fields greater than the mean number of errors for the paper group ($p = 0.035$; [95%CI] 0.13 to 2.38).

No difference in data entry speed was demonstrated, with the image group averaging 0.29 minutes per booklet less than the paper group ($p = 0.791$; [95%CI] -2.98 to 2.39).

The task satisfaction score using an unvalidated measurement instrument averaged 2.67 points lower for the image group ($p = 0.045$; [95%CI] -0.08 to -5.25) suggesting lower end-user satisfaction in the image group.

RATIONALE OF STUDY

Basis of Study Objectives

Three issues were examined in this project.

- The accuracy of data entry using CRFs displayed on a monitor as compared to data entry from paper CRFs.
- The speed of data entry using CRFs displayed on a monitor as compared to data entry from paper CRFs.
- Data processors' task satisfaction from performing data entry using CRFs displayed on a monitor as compared to data entry from paper CRFs.

The Methods section details the approach used for assessing these three items.

Data Entry Accuracy

The primary objective of this project was to determine if the average error rate for data entered from CRF images was higher than the average error rate for data entered from paper CRFs. Understanding the potential impact on accuracy is important for several reasons. It is an industry axiom that “no study is better than the quality of its data (8).” The transfer of data to the computer database is a critical step, with accuracy of data entry being essential (3). Ultimately, errors in the data could expose clinical patients to risk, or prevent approval of important new therapies.

There is a wealth of regulatory guidance that requires assessing the impact of computerised systems on quality. European Union (EU) Good Manufacturing Practices (GMP) Guide Annex 11 on Computerised Systems states: “Principle: Product quality and quality assurance should not decrease when computerised system replaces a manual operation (29).” This has been extended by others to: “Principle: Data quality and quality assurance should not decrease when a computerised system replaces a paper operation (30).”

ICH Good Clinical Practices (ICH-E6) echo the same theme in section 5.1.3, “Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly (31)” and in section 5.5.3,

“When using electronic trial data handling and/or remote electronic trial data systems the sponsor should: Ensure and document that the electronic data processing system(s) conforms to the sponsor’s established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e., validation) (31).”

This concept is repeated in section 5.8 of the ICH Statistical Principles for Clinical Trials (ICH-E9) (32).

FDA guidance documents are consistent in their message. According to the Guidance for Industry: Computerized Systems Used in Clinical Trials,

“The design of a computerized system should ensure that all applicable regulatory requirements for record keeping and record retention in clinical trials are met with the same degree of confidence as is provided with paper systems (33).”

It is also important to know that the imaged CRF is in general legible, for later use as part of an electronic submission. The FDA guidance for providing New Drug Application (NDA) submissions in electronic format states, “If a paper CRF was used in the clinical trial, the electronically submitted CRF should be an exact image or series of images of the paper CRF (23).”

Readability of retrieved images is specifically mentioned as requiring validation consideration in the optical imaging section (9.9.1) of the Computer Systems Validation guide published by the Association for Clinical Data Management (ACDM) and the Statisticians in the Pharmaceutical Industry (PSI) (34).

The issue of accuracy of data entry from images compared to paper CRFs was analysed in the Hopkins Fax Study, in the context of comparing forms transmitted by facsimile machines directly to computer images, with those entered from paper CRFs. That project concluded that error rates for entry from the CRF images was significantly higher than the error rates from the paper CRFs (18). This result was consistent with an earlier study which was cited in

the Hopkins Fax Study (35). Additionally, the Swansea Pilot Study suggested that higher error rates were seen when entering from images.

This critical issue was examined further in this study by comparing data entry accuracy from images to data entry accuracy from paper, and determining if the mean number of errors per 100 fields for data entry from images is higher than the mean number of errors per 100 fields for data entry from paper CRFs.

Data Entry Speed

Improving the speed of data entry is not central to the major perceived advantages of imaging CRFs. However, data entry personnel take pride in being able to enter data quickly from the CRFs, with clearly legible CRFs being a factor in their entry speed (1). In the PRA Pilot Study it was reported that data entry speed decreased with the use of the imaging process (17). While this problem was attributed primarily to technical issues with the specific imaging retrieval system used in that study, it bears further examination. Data entry speed from images was measured and compared to data entry speed from paper, and tested for non-inferiority.

Data Processor Task Satisfaction

Moving from paper-based CRFs to image-based CRFs has a significant impact on the data processors performing data entry. In the PRA Pilot Study it was noted that staff found the images often harder to work with than paper CRFs, partly for process specific reasons, but partly from difficulty in viewing the form on the screen (17). The questionnaires completed in the Swansea Pilot Study also indicated a much higher level of user acceptance for paper-based entry, although the small sample size limits the usefulness of that information. The data

from these questionnaires is shown in Appendix B. These factors have led to the desire to research the end-user acceptance of image-based entry in more detail. A better instrument for collecting that information was used in this study, as described in the Methods section.

Context of Study Objectives

There are many reasons why imaging of CRFs can be considered desirable as discussed above. This study did not evaluate the overall benefit of working with CRF images, but instead focused on the impact of images on specific data entry activities.

The increasingly widespread availability of electronic image and document management systems, coupled with greater acceptance of the use of these systems, will lead to more situations where paper CRFs are replaced by CRF images. The purpose of this study was to gain further understanding of how this will impact data entry personnel.

METHODS

GENERAL DESIGN

The study was designed as an unblinded comparison between data entry of a set of CRF booklets performed using images, and data entry performed using paper versions of the same set of CRF booklets.

Study Subjects

Study subjects were PRA employees who volunteered to take part in this research. Study participants received a gift certificate of nominal value to compensate them for their time. Subjects were made aware of the general purpose of the study, with each participant reading and signing the Volunteer Consent Form shown in Appendix C. Subjects were informed that their individual study results would remain confidential, and that they would be referred to only by subject identifiers. Subjects were told that they could withdraw from participation at any point.

Randomisation Scheme

People who perform skilled but repetitive tasks typically become faster and more accurate as those tasks are repeated. Clinical data processors performing data entry are initially less accurate and slower when presented with new CRFs and new data entry screens, but they become faster and more accurate as they continue to enter patients into the database. This learning curve is most dramatic during the entry of the first few CRF booklets during any new study. Therefore, one of the most significant trends to be expected when analysing data entry accuracy and speed, is improvement over time within a single entry operator. Additionally, there can be a wide variability between individual data processors, particularly during the

early phase of this learning curve. In order to minimise these effects, all subjects first entered two patients from CRF images prior to being randomised into two groups.

Subjects were randomised using a stratified scheme. Two factors were considered when placing a subject into a group, error rate and entry speed. Subjects who completed data entry of the first two patients with more than 3 errors per 100 data items were classified as less accurate, and those who made 3 or fewer errors per 100 fields were classified as more accurate. Subjects who completed the entry of the first two patients averaging more than 12 minutes per CRF booklet were classified as slow, and those averaging 12 minutes or less per CRF booklet were classified as fast. Based on these two criteria, equally weighted, subjects were dynamically allocated to a group. The randomisation was designed to result in an 80% chance of the subject being randomised to the “correct” group, so as to maintain a random element to the assignment step. This is consistent with the ICH E9 Guidelines on dynamic allocation, which note that “Deterministic dynamic allocation procedures should be avoided and an appropriate element of randomisation should be incorporated for each treatment allocation (32).” This stratified randomisation was performed in Microsoft Excel.

Task Satisfaction Questionnaire

Based on the results of the previous studies discussed in the introduction, it was determined that an improved instrument for measuring task satisfaction should be developed to test the difference in data processor reaction to entering data from CRF images versus paper CRFs.

The questionnaire was designed after reviewing methods used in the design and administration of quality of life questionnaires (36, 37, 38) and techniques used with educational and psychological test design (39, 40, 41).

The first step in designing a questionnaire is to determine what the instrument should measure (36). The goal in this project was to determine task satisfaction based on the volunteers' assessment of task difficulty, legibility of the CRF data, and impact on their job satisfaction. Three questions were developed to collect this information.

The questionnaire was designed to be self-administered. Self-administered forms give respondents more time to think carefully about their answers, and eliminate the need for an interviewer (38). The use of an interviewer in an unblinded study would be a source of potential bias.

Closed-form questions (those that require selecting from a list of responses) were chosen to enable analysis. Open-ended questions elicit more personal responses, but are difficult to quantify (37). A five-point Likert scale was selected. Four- and five-point scales are most frequently recommended (40), with a five-point scale being chosen here because "neutral" was considered a valid response. Likert scales (or summative scales) provide subjects with a limited selection of clearly defined responses (37), and are frequently used to assess attitudes (42).

The validity of the questionnaire was then examined. Validity can be defined as "the degree to which accumulated evidence and theory support specific interpretations of test scores entailed by proposed uses of the test (39)." An assessment of whether the questionnaire is actually measuring what it is intended to measure is part of such an evaluation (36).

Validity can be discussed in three main areas—content validity, criterion-related validity, and construct validity (41). Some standards view validity as a unitary concept, and refer to types of validity evidence, rather than distinct types of validity (39).

Content validity (or evidence based on content) involves clearly defining what is being measured, and judging whether the items on the questionnaire are representative of the topic (39, 41). Questions need to be easily understood, and they need to be answerable (38). Review of content validity for this questionnaire included analysis of the questions by the author and industry supervisor, as well as pre-testing the questions as described below.

Criterion-related validity, which involves correlating questionnaire items with another known measure (41) is typically used when there is a gold standard against which to measure (36). No appropriate gold standard was found with which to perform such a comparison.

Construct validity, which involves a systematic attempt to understand the relationships between the characteristics that a test is intended to measure (41), is employed to examine a new instrument when no gold standard exists (36). The Standards for Educational and Psychological Testing consider construct validity to be redundant with validity, preferring to view the validity argument as establishing the construct validity of a test (39).

In an attempt to investigate the validity of the questionnaire, it was piloted with eight volunteers. The volunteers were randomised into two groups ($n = 4$), half of whom were given a simple 5-page CRF booklet. The other half were given a 5-page CRF booklet that had been scanned and saved as an image, intentionally blurred, skewed, slightly distorted, and with the contrast reduced. These CRF pages were then reprinted. The volunteers were asked to transcribe the contents onto a blank CRF booklet. At the end of this exercise each volunteer was asked to complete the three questions on the piloted questionnaire. The group working with the lower quality pages completed the questionnaire with scores that were distinctly lower than those working with the higher quality pages. Using a five-point scale (5 = Strongly Agree, 1 = Strongly Disagree) for each of the three questions, the group using the

higher quality pages had a score averaging 5.75 points higher than the group working with known poor CRF booklets ($p = 0.020$; [95%CI] 1.30 to 10.20). Additionally, there was a correlation between the overall score on the questionnaire and the number of errors made doing the transcription. The data for this questionnaire pilot is shown in Appendix D.

Based on this testing, it was felt that this questionnaire would be an improvement over the instrument used in the Swansea Pilot Study.

Study Preparation

Subject Information Forms, Task Satisfaction Forms, CRF booklets, and data entry screens were created in preparation for performing this study.

The Subject Information Form, shown in Appendix E, was designed to collect basic information about the subject. Data collected included gender, date of birth, data entry experience, and computer skills self-assessment. The Task Satisfaction Form is shown in Appendix F.

Six CRF booklets, consisting of ten pages each, were created for this project. The booklets, shown in Appendix G, were designed to meet several criteria. They were designed to be similar to typical clinical trial CRFs, although shorter than most study CRFs, and feature inclusion/exclusion pages, demographic pages, vital signs pages, concomitant medication pages, and adverse event pages. They also contain pages that feature entirely numerical data, and pages that feature entirely textual data. The booklets were intended to be simple to enter, to minimise the need for special instructions, and reduce the learning curve as much as reasonable. The six CRF booklets were completed by three different authors.

Each page of these paper CRFs was scanned, and converted into an electronic image. The electronic images were combined into a single file for each case booklet. These files were used to display the CRF images on the computer screen when data processors were entering from images.

Data entry screens were created to match the CRF booklets. These screens, and their underlying data tables, were created using DLB Recorder 3.1, a commercial clinical data management system.

Technical Information

The study was performed at the PRA Charlottesville Trials Management Center. A test environment was set up, consisting of two identical PC work stations, each configured with two 17-inch monitors. Data entry was performed using DLB Recorder 3.1. Images that had been saved using Adobe Acrobat 3.0 were displayed as PDF files. The method of storing and displaying the image is not central to the issues being examined in this project, but PDF files are the *de facto* standard for electronic submissions as discussed in the Introduction. A full technical specification of the hardware and software used in the project can be found in Appendix H.

Study Conduct

One or two subjects were evaluated per session. Each subject followed the same protocol (shown in Appendix I). This involved first receiving an explanation of the project and the volunteer's role in the study, completing a Subject Information Form, and getting a brief introduction to the sample CRF and data entry screens. The subject then completed data entry of Booklets 101 and 102, with the CRFs presented as images on the computer monitor. Start

and stop times for these were recorded automatically. Before continuing, the subject was randomised into either the image group or the paper group. The subject then completed data entry for Booklets 103, 104, 105, and 106. Start and stop times were recorded automatically. The subject completed the task satisfaction questionnaire as the final step.

SAMPLE SIZE

Study sample size was calculated for the primary objective, and the two secondary objectives. These calculations were based on expectations derived from the Swansea Pilot Study, previous research described in the Introduction, and industry experience.

Primary Objective

The study sample size calculations for the primary objective assumed no difference in the means between the two groups as the null hypothesis, with the alternate hypothesis assuming 1.25 or greater additional errors per 100 fields on average for the image group.

$$H_0: \bar{x}_{\text{paper}} = \bar{x}_{\text{image}}$$

$$H_A: \bar{x}_{\text{paper}} - 1.25 \geq \bar{x}_{\text{image}}$$

The standard deviation was estimated to be 0.85. An alpha of .05 and a power of .9 was used for the calculation. A power of .9 was selected because it is desirable to limit the likelihood of a Type II error for the primary objective. Based on these assumptions each group required a minimum of 10 subjects.

The estimated difference in the mean used as the alternate hypothesis was based on the results reported in the Hopkins Feasibility Assessment and those observed in the Swansea Pilot Study. The Hopkins Feasibility Assessment noted error rates in the image group as two-to-

three times higher than those in the paper group. The Swansea Pilot Study resulted in 1.26 more errors per 100 fields in the image group.

The standard deviation was estimated as 0.85. The standard deviation in the Swansea Pilot Study was 0.853. Several refinements were made in the subject instructions for this project, in an attempt to reduce one source of variability.

Secondary Objectives

Data Entry Speed

The sample size for the data entry speed comparison was calculated for testing non-inferiority. The null hypothesis was that the mean entry speed for the image group (based on each volunteer's entry speed calculated as average number of minutes per CRF booklet) was 2.0 minutes per booklet slower than the mean entry speed for the paper group. The alternate hypothesis was that entry speed was equal between the two groups.

$$H_0: \bar{x}_{\text{image}} - 2 \geq \bar{x}_{\text{paper}}$$

$$H_A: \bar{x}_{\text{image}} = \bar{x}_{\text{paper}}$$

The sample size was calculated using an alpha of .05, and a power of .8. A power of .8 was considered acceptable for the secondary objectives. Sample size was calculated by treating this as a superiority study and reversing the error probabilities, which is a valid approach for handling equivalence studies (43, 44). (In other words, $H_0: \theta = 0$, $H_A: \theta = -2$, where θ is difference in means, and using a 20% significance level and a 95% power.) This results in a sample size of 10 per group. It is acknowledged that 2 minutes per booklet is a substantial

difference in speed, when testing for non-inferiority, and this is addressed in the Discussion section.

Task Satisfaction

The sample size selected for the primary objective is also suitable for the task satisfaction measurement. The sample size was estimated as adequate to show a difference of 2.0 or greater in the means of the two groups with the standard deviation estimated as 1.35.

$$H_0: \bar{x}_{\text{paper}} = \bar{x}_{\text{image}}$$

$$H_A: \bar{x}_{\text{paper}} - 2 \geq \bar{x}_{\text{image}}$$

This calculation reflects an alpha of .05 and a power of .9. Although a power of .8 was considered acceptable for the secondary objectives, the size of the anticipated difference in task satisfaction means allowed for a power of .9, based on the sample size which was already required for the primary objective. In the Swansea Pilot Study the difference between the two means was 2.67, and the standard deviation was 1.31.

PLANNED ANALYSIS

Data to be Included in Analysis

Data from all study volunteers who were randomised was to be evaluated. For the analysis of data entry accuracy, an average error rate was to be established for each study volunteer. An average error rate for those booklets completed was to be calculated in the event a volunteer who was randomised failed to complete the entry of all four CRF booklets

For the analysis of data entry speed, it was stipulated that the entry time for a CRF booklet could be omitted if the volunteer experienced exceptional computer system problems (e.g., was booted out of the system and had to reinitialise the entry application). Average entry speed was to be calculated from the remaining booklets that were entered. Average entry speed would also be calculated including the booklet in question, with results that were statistically significant in both scenarios considered to be more robust.

For the analysis of task satisfaction, data was to be analysed for all volunteers who completed the questionnaire.

The Results section describes the disposition for all volunteers who completed a consent form, including any issues which were encountered during the conduct of the study.

Analysis of Data Entry Accuracy

Data entry accuracy was analysed as the primary study objective. The analysis was performed by comparing the mean error rate of the image group (based on each volunteer's number of errors per 100 data fields), with the mean error rate of the paper group (based on each volunteer's number of errors per 100 fields). The comparison was made by calculating the *t* ratio (or Student's *t*) of the two samples. The difference in means would be considered statistically significant if the *t*-test generated a *p*-value < 0.05. The difference would be considered to have practical significance if the point estimate was 1.25 errors per 100 fields or greater.

The data was also to be examined in the following subgroups:

- Gender
 - Age
-

- Data entry experience
- Baseline error rate
- Baseline entry speed
- Error rates for text pages
- Error rates for numeric pages

It is important to note that these analyses were to be treated as exploratory in nature, intended to look at trends and possibly determine areas bearing future analysis. The conclusion regarding the impact of imaging on the accuracy of data entry was to be based on the single primary objective. This is important to control against the effects of multiplicity (45, 46), and to maintain credibility.

David Morgan described the issue of multiplicity in Applied Clinical Trials:

...if 10 different variables are analysed at the end of a study, then there is a much higher chance of spuriously positive results...if many different subgroups are examined, the chance of a false positive would again be inflated...To avoid this inflation of Type I error, it is important to specify in advance the variable, time point, and subject population to be analysed (46).”

ICH Guideline E9 (Statistical Principles for Clinical Trials) discusses the importance of relying on pre-defined analyses in section 5.1, noting that “principal features of the proposed confirmatory analysis of the primary variables” should be clearly specified in advance, and “only results analyses envisaged in the protocol can be regarded as confirmatory (32).”

Analysis of Data Entry Speed

The data for entry speed was analysed by calculating the mean entry time for the four CRF booklets entered after randomisation for the two groups, and comparing the means, again by calculating the t ratio. Results were presented as confidence intervals rather than as p -values. Probabilities associated with Student's t -test (and most statistical tests) are relevant to testing the null hypothesis that the groups are equal (44). While it is possible to calculate significance levels based on the lower confidence bound that are appropriate to non-inferiority tests, this can cause confusion with p -values as they are normally presented (44). If the difference in the mean between the image group and the paper group can be described with a confidence interval, which has an upper bound at the 95% level of 2 minutes per booklet or less, then the speed of entry from images will be considered non-inferior to the speed of entry from paper CRF booklets.

Analysis of Data Processor Task Satisfaction

The data from the task satisfaction questionnaire was analysed by totalling the score for all three questions (Strongly Agree = 5, Strongly Disagree = 1) for each volunteer, and then calculating the difference between the mean score of the image group with the mean score of the paper group. The comparison was made by calculating the t ratio of the two samples. The difference in means would be considered statistically significant if the t -test generated a p -value < 0.05 . The difference would be considered to have practical significance if the point estimate was 2 or greater.

RESULTS

VOLUNTEER DISPOSITION

Twenty-one volunteers participated in this study. All volunteers completed the entry of all six required CRF booklets, and every volunteer completed the Task Satisfaction Form. Volunteers were randomised into two groups, image ($n = 11$) and paper ($n = 10$). Two incidents occurred during the performance of the study that merit discussion.

Subject 4 (image group) did not stop after entering the first two patients from CRF images to receive instructions regarding which group she would be randomised into. Instead she continued to enter the following four CRF booklets also from images. When the volunteer's parameters were entered into the randomisation program belatedly, the resulting randomisation code indicated that she should have been assigned to the paper group. The volunteer was the fourth participant to be randomised into the study, so this error did not contribute to any balance problems between the group baselines. Consideration went into conducting the main analyses for the project once with this subject included in the group in which she actually participated, and once with this subject in the group to which she should have been assigned. Given that the dynamic allocation for the remaining 17 subjects was carried out based on her actual participation, this alternate analysis was felt to have little value, and was not performed.

Subject 2 (paper group) made nine errors entering the vital signs page during Visit 1 of Booklet 105. This was caused by jumping from the first vital signs record to the second during entry of that page. This resulted in three errors for the first record, and the omission of the entire second record. By comparison, no other volunteer made more than two errors entering both vital signs pages for any one booklet. For 70 of the 84 booklets that were

entered after the volunteers were randomised, no errors were made on the vital signs pages. The impact of this mistake is clear, with vital signs being the only page type where several more errors were made during entry from paper CRFs than from CRF images (see Figure 40). Despite this entry mistake, it was decided to include the results from Booklet 105 for Subject 2 as part of the main analysis data set. It can not be assumed that an error of this type is unaffected by the choice of entering from paper CRFs versus CRF images. A second calculation omitting this booklet was also made to show the impact of excluding this data.

BASELINE DATA

Group	Average	Gender		Experience	
	Age	M	F	Data Entry	Medical Data
Image Group	33	4	7	1.8	2.8
Paper Group	36	4	6	3.1	4.3
All Volunteers	35	8	13	2.4	3.5

Average age in years
 Count by gender, M=male, F=female
 Years of data entry experience
 Years of working with medical data

Computer Skills Self Assessment	
Image Group	Average = 3, Above Average = 6, Excellent = 2
Paper Group	Average = 5, Above Average = 4, Excellent = 1
All Volunteers	Average = 8, Above Average = 10, Excellent = 3

No volunteers assessed their skills as Poor or Below Average

Figure 1: Table Summarising Demographic Data

The image and paper groups were well-balanced in age and gender. On average, the paper group had more data entry experience. The image group included four volunteers with 3.5 years or more experience performing data entry, and six volunteers with no experience performing production data entry. The paper group had three volunteers with 3.5 years or more experience performing data entry, and four volunteers with no production data entry experience.

Computer skills self-assessment scores were similar between the two groups, but this measurement was not considered useful as explained in the Discussion section.

Baseline data entry accuracy and baseline data entry speed are shown below in the tables analysing the accuracy and speed data.

CONFIRMATORY ANALYSES

Data Entry Accuracy

Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Image Group	5.04	1.15	3.09	0.98	1.76	2.09	0.41	1.31
Paper Group	4.64	1.62	3.13	1.08	0.68	1.58	0.81	1.04

Number of Errors per 100 Fields

Difference in the Means 0.27
 (Image - Paper, for Randomised Booklets)
 ($p=0.322$; [95%CI] -0.29 to 0.84)

Figure 2: Table Summarising Accuracy Data

The mean number of errors per 100 fields for the image group was 0.27 greater ($p = 0.322$; [95%CI] -0.29 to 0.84) than the mean number of errors per 100 fields for the paper group. Based on this result, the null hypothesis can not be rejected at the 5% significance level.

This calculation was also performed excluding Booklet 105 for Subject 2, for the reasons explained in the Volunteer Disposition section. Using the amended data, the mean number of errors per 100 fields for the image group was 0.41 greater ($p = 0.107$; [95%CI] -0.10 to 0.93) than the mean number of errors per 100 fields for the paper group.

Data Entry Speed

Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Image Group	13.94	10.06	12.00	10.06	9.50	9.37	8.97	9.47
Paper Group	15.31	10.52	12.91	10.08	9.38	9.63	9.18	9.57

Minutes per CRF Booklet Entered

Difference in the Means -0.09
 (Image - Paper, for Randomised Booklets)
 ([95%CI] -1.85 to 1.66)

Figure 3: Table Summarizing Entry Speed

The mean entry speed for the image group was 0.09 minutes per booklet faster than the mean speed for the image group ([95%CI] -1.85 to 1.66). The upper bound of the confidence interval is less than 2, therefore the entry speed of the image group is considered non-inferior to the paper group at the 95% confidence level.

Data Processor Task Satisfaction

Question	Q1	Q2	Q3	Mean
Image Group	4.27	3.73	3.82	11.82
Paper Group	4.40	4.10	3.80	12.30

Scores based on Strongly Agree = 5, Strongly Disagree = 1.

Difference in the Means -0.48
 (Image - Paper)
 (p=0.466; [95%CI] -1.84 to 0.87)

Figure 4: Table Summarizing Task Satisfaction

The mean satisfaction score for the image group was 0.48 lower than the mean satisfaction score for the paper group ($p = 0.466$; [95%CI] -1.84 to 0.87). The null hypothesis can not be rejected at the 5% significance level.

EXPLORATORY ANALYSES

Data Entry Accuracy

Data Entry Accuracy by Subgroups

Image Group	Baseline			Randomised				
Booklet	101	102	Mean	103	104	105	106	Mean
Male (n=4)	4.39	1.24	2.82	1.58	1.01	1.80	0.34	1.18
Female (n=7)	5.41	1.09	3.25	0.64	2.19	2.25	0.45	1.38
Group Mean	5.04	1.15	3.09	0.98	1.76	2.09	0.41	1.31

Paper Group	Baseline			Randomised				
Booklet	101	102	Mean	103	104	105	106	Mean
Male (n=4)	4.50	1.46	2.98	1.01	0.56	2.48	0.45	1.13
Female (n=6)	4.73	1.73	3.23	1.13	0.75	0.98	1.05	0.98
Group Mean	4.64	1.62	3.13	1.08	0.68	1.58	0.81	1.04

Number of Errors per 100 Fields

Figure 5: Table Summarising Accuracy by Gender

There was little difference in the accuracy measurements when summarised by gender (Figure 5). The difference in the means for males (image - paper) was less than the difference in the means for females, but this was largely attributable to Subject 2 (male, paper group) whose inflated error rate on Booklet 105 has been discussed.

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
37+ (n=4)	3.72	1.46	2.59	1.01	2.03	2.36	0.56	1.49
<37 (n=7)	5.79	0.97	3.38	0.97	1.61	1.93	0.32	1.21
Group Mean	5.04	1.15	3.09	0.98	1.76	2.09	0.41	1.31

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
37+ (n=5)	5.05	1.89	3.47	1.26	0.45	2.34	0.99	1.26
<37 (n=5)	4.23	1.35	2.79	0.90	0.90	0.81	0.63	0.81
Group Mean	4.64	1.62	3.13	1.08	0.68	1.58	0.81	1.04

Number of Errors per 100 Fields
Age in years

Figure 6: Table Summarizing Accuracy by Age

The most noticeable characteristic when summarising the accuracy measurements by age (Figure 6) was not the difference in the means between the image and paper groups by subgroup, but the overall difference in the two age groups. Although not statistically significant, the higher error rate for the volunteers over the age of 37 (0.40 errors per 100 fields greater, $p = 0.31$; [95%CI] -0.43 to 1.22) encourages speculation about the role of eyesight in data entry accuracy.

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Exp = 0 (n=6)	5.86	1.58	3.72	1.05	1.95	1.95	0.53	1.37
Exp<3.5 (n=1)	3.15	0.00	1.58	0.90	3.60	4.05	0.45	2.25
Exp>3.5 (n=4)	4.28	0.79	2.53	0.90	1.01	1.80	0.23	0.99
Group Mean	5.04	1.15	3.09	0.98	1.76	2.09	0.41	1.31

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Exp = 0 (n=4)	4.84	1.58	3.21	0.90	0.68	2.48	0.90	1.24
Exp<3.5 (n=3)	4.05	1.65	2.85	1.20	0.60	1.35	0.60	0.94
Exp>3.5 (n=3)	4.95	1.65	3.30	1.20	0.75	0.60	0.90	0.86
Group Mean	4.64	1.62	3.13	1.08	0.68	1.58	0.81	1.04

Number of Errors per 100 Fields
Experience in years

Figure 7: Table Summarising Accuracy by Experience

The summary of accuracy measurements by experience level (Figure 7) shows no significant impact on the difference in means between the image and paper group. Not surprisingly, the most experienced data entry personnel in both groups exhibited lower error rates than those volunteers with less data processing experience. The image group does not follow this trend with the middle tier, but that case only involves a single volunteer.

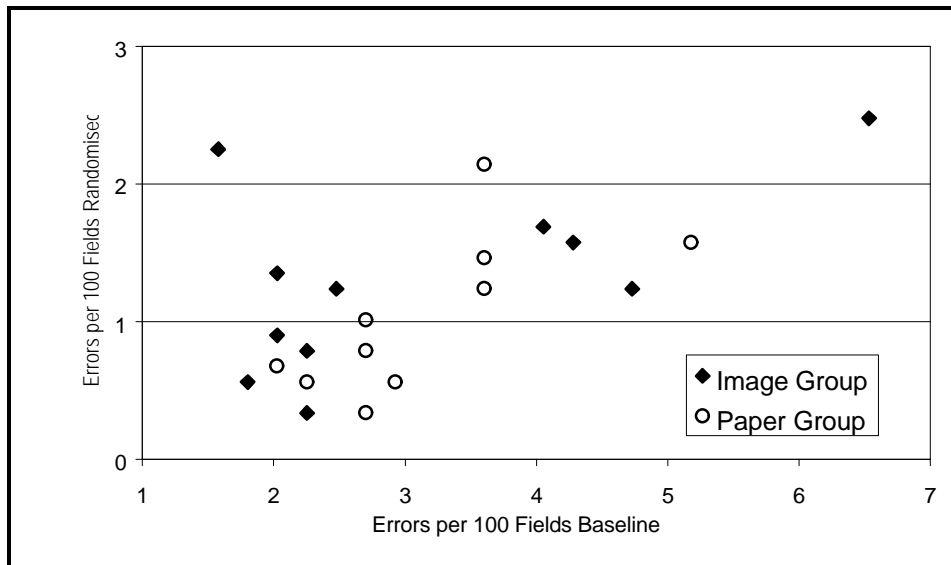
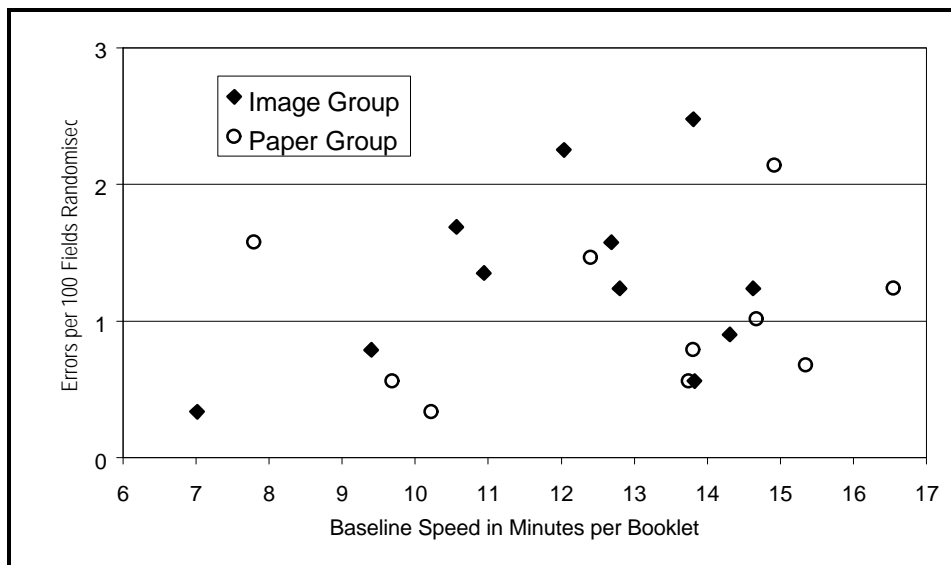
Data Entry Accuracy by Baseline Measurements*Figure 8: Scatterplot Summarising Accuracy by Baseline Accuracy**Figure 9: Scatterplot Summarising Accuracy by Baseline Speed*

Figure 8 and Figure 9 display as scatterplots the relationship between data entry accuracy for the randomised booklets compared with baseline data accuracy and baseline data entry speed respectively. The randomised groups were well balanced because of the dynamic allocation approach based on initial data entry error rates and speed. No trends are shown here to

challenge the conclusions reached analysing the overall difference in the means between the two groups.

Data Entry Accuracy by CRF Page Type

Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Image Group	1.56	0.20	0.88	0.29	0.49	1.02	0.04	0.46
Paper Group	1.98	0.18	1.08	0.23	0.14	0.41	0.27	0.26

Number of Errors per 100 Fields

Difference in the Means 0.20
 (Image - Paper, for Randomised Booklets)
 (p=0.083; [95%CI] -0.03 to 0.43)

Figure 10: Table Summarising Data Entry Accuracy for Text Pages

Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Image Group	0.70	0.49	0.59	0.20	0.49	0.16	0.08	0.24
Paper Group	0.59	0.63	0.61	0.32	0.18	0.09	0.09	0.17

Number of Errors per 100 Fields

Difference in the Means 0.07
 (Image - Paper, for Randomised Booklets)
 (p=0.435; [95%CI] -0.11 to 0.24)

Figure 11: Table Summarising Data Entry Accuracy for Numeric Pages

Data entry accuracy was also analysed specifically for the pages in the CRF booklets labelled as Text pages and Numeric pages. This data is summarised in Figure 10 and in Figure 11. (Full detail data listings for all page types are included in Appendix J.) The difference in the mean accuracy rates for Text pages was greater than the overall difference in the means for complete booklets. The mean error rate for the image group from Text pages was 0.20 per 100 fields greater than that for the paper group ($p = 0.083$; [95%CI] -0.03 to 0.43).

Data Entry Speed

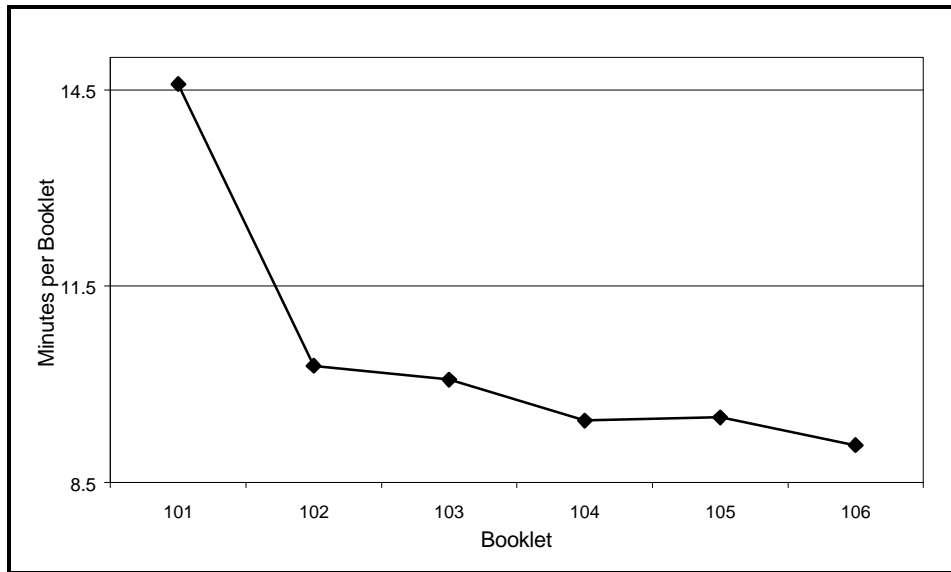


Figure 12: Line Graph Summarising Overall Entry Speed Trend

Figure 12 shows the overall data entry speed trend data for the combined paper and image groups. The trend shows an increase in entry speed with experience with the specific CRF booklet and data entry screens. The greatest increase occurred during the initial two booklets, demonstrating the value of having the volunteers enter two booklets prior to being randomised.

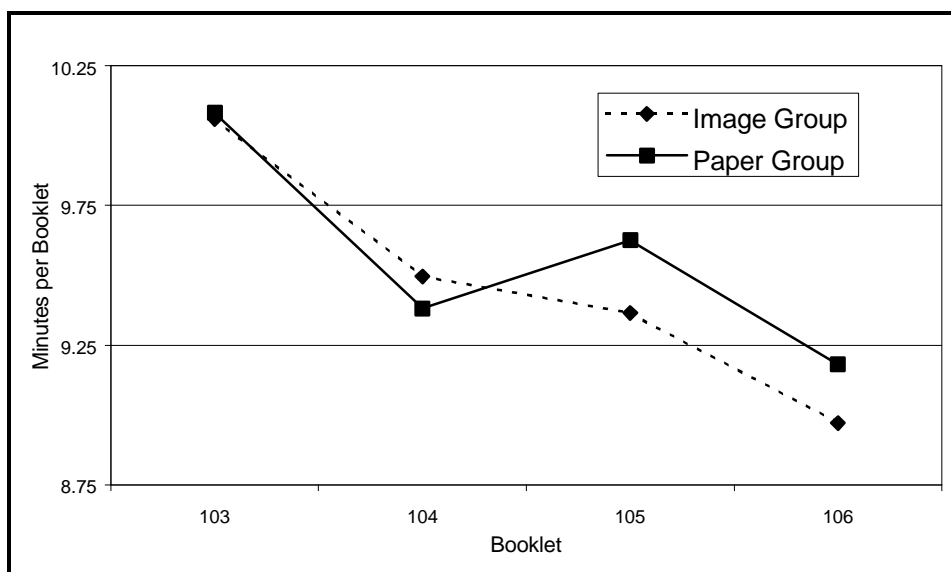


Figure 13: Line Graph Comparing Image and Paper Entry Speed Trend

Figure 13 shows the data entry speed trend for the four post-randomisation booklets, by image and paper groups. The increase in entry speed for the image group is slightly greater than the increase in speed for the paper group, providing reinforcement to the confirmatory analysis for data entry speed, that entry speed from CRF images is non-inferior to entry speed from paper CRFs.

Data Processor Task Satisfaction

Question	Q1	Q2	Q3	Mean
Image Group	4.3	3.5	3.5	11.3
Paper Group	4.7	4.3	4.0	13.0

Scores based on Strongly Agree = 5, Strongly Disagree = 1.

Difference in the Means **-1.75**
 (Image - Paper)
 (p=0.312; [95%CI] -5.75 to 2.25)

Figure 14: Table Summarising Task Satisfaction Scores for Experienced Data Processors

Figure 14 summarises the task satisfaction questionnaire, limited to the volunteers with the most data entry experience (more than 3.5 years of entry experience). The difference in the mean task satisfaction scores between the image group and the paper group for this subgroup was -1.75 ($p = 0.312$; [95%CI] -5.75 to 2.25).

DISCUSSION

DATA ENTRY ACCURACY

Comparison to Previous Studies

The Hopkins Fax Study noted error rates from data entered from CRF images which were two to three times greater than the error rate for data entered from paper CRFs. The Swansea Pilot Study accuracy results showed a difference in the mean error rate between the image group and the paper group of 1.26 errors per 100 fields. This project did not demonstrate a difference between the image and paper groups as dramatic as the previous results.

The Hopkins Fax Study relied on faxed transmission of the CRF to generate the CRF image, which would typically result in a lower quality image, and required data processors to operate two separate terminals to perform data entry from the image. The image was displayed on a 16-inch monitor and data processors had limited tools for manipulating the image view. By comparison, this project used a high-end scanner to create the CRF images from the paper CRFs. Data processors viewed the image on one of the two 17-inch monitors with which their PC was configured. They had the full suite of PDF viewing tools available. Technical improvements could account for some of the difference in results between the Hopkins Fax Study and this project.

The only technical difference between this project and the Swansea Pilot Study that might be relevant is the difference in computer monitors employed. The Swansea Pilot Study presented both the CRF image and the database entry screen on a single 21-inch monitor. This project presented the CRF image on one 17-inch monitor, with the database entry screen on an adjacent monitor. The authors of the summary of the Hopkins Fax Study, however, suggested

that a single large monitor would be better than small dual monitors. It is not likely that the difference in results between this project and the Swansea Pilot Study can be attributed to any technical improvements.

One possible explanation for the difference in the results of this study compared with the Hopkins Fax Study and the Swansea Pilot Study may be related to the degree of difficulty of the CRF data. The Hopkins Fax Study used CRFs from an ongoing clinical trial in melanoma. Those CRFs would have been more complex and more difficult to read than the CRFs created for this project, because oncology trials typically involve large quantities of complex clinical information. The Swansea Pilot Study made use of the exact same set of CRF booklets as this project. The data in the CRF booklets was handwritten by three Americans. Six of the volunteers in the Swansea Pilot Study were European. The single American volunteer in the Swansea Pilot Study (Subject 3) had a much lower error rate than the other volunteers. All 21 volunteers in this PACCRM030 project were American, and may have found the handwriting easier to read.

It could be argued that the more difficult the CRF source data is to read, the more clearly the difference in error rates between paper CRFs and CRF images is manifested. This trend is not clear when looking at the data from the four randomised booklets in this project. Additionally, the error rate for the paper group in the Swansea Pilot Study, even excluding Subject 3, is lower than the error rate for the paper group for this project, so this explanation can not be considered satisfactory.

Pooled Analysis

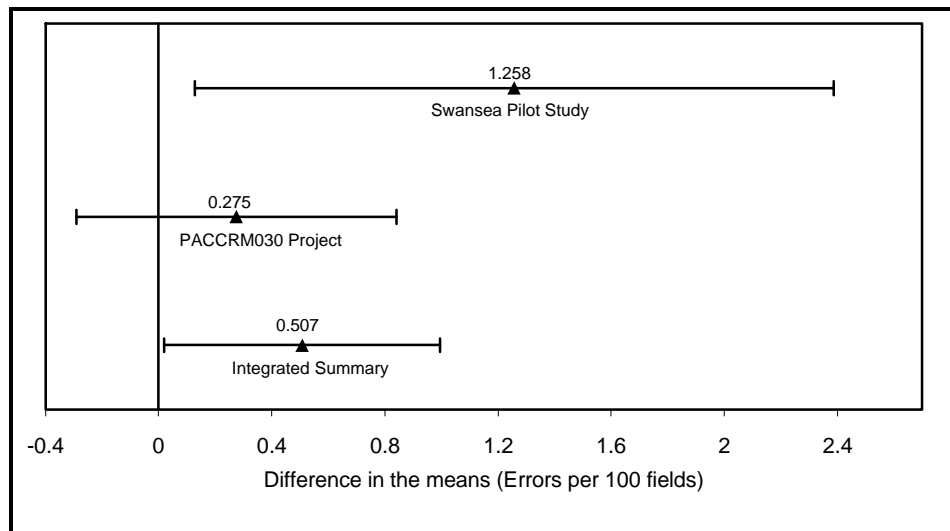


Figure 15: Integrated Summary of Accuracy Data

Combining the data from the Swansea Pilot Study with the data from this project, and performing an integrated analysis of the pooled data suggests another explanation. The difference in the mean error rates between the image group (1.46 per 100 fields) and the paper group (.95 per 100 fields) for the pooled data is 0.51 more errors per 100 fields ($p = 0.043$; [95%CI] 0.02 to 1.00). Figure 15 displays the 95% confidence intervals for the Swansea Pilot Study, this project, and the pooled data. The full detail listing for the integrated summary can be found in Figure 42 in Appendix J. It may be that the true difference in the means is smaller than the figure upon which the sample size for this project was calculated.

Overall Impact on Quality of Data Management

The integrated summary of accuracy data suggests that the use of CRF images for data entry may result in an increase in the raw error rate. This does not necessarily translate into a clinical database with a higher error rate. Most data management groups employ some form of double data entry. An increase in the raw error rate may increase the amount of time spent on the reconciliation of entry differences, but it only directly increases the database error rate

if both the first and second data processors enter the same incorrect value for the same data field.

There were a total of 888 enterable fields in the randomised portion of this study, 222 fields per patient. There were 23 fields out of these 888 (2.6%) where at least two of the 21 volunteers entered the same incorrect data. These 23 fields contain 108 errors (69 image, 39 paper) out of the total 220 errors made during the randomised portion of the study, or 49.1% of all errors. In other words, about half of the total errors are concentrated in less than 3% of the fields. The remaining errors are evenly balanced, 59 in the image group (.62 per 100 fields), and 53 in the paper group (.61 per 100 fields). It makes sense to focus more closely on these 23 fields, because these are the fields where double data entry could lead directly to an error in the final clinical database.

Double data entry yields one of three results. Both entry operators may enter the correct value, and this correct value is automatically reconciled as a verified record in the clinical database. Both entry operators may enter the identical incorrect value, and this incorrect value is automatically reconciled as a verified record in the clinical database. Or, both operators may enter different values, and an operator will manually review the two entries and select what is believed to be the correct value.

These 23 fields were analysed considering these three possible outcomes, and applying basic probability. It was assumed that in those cases where an operator needed to manually review a field, because two different values had been initially entered, the correct value would be selected 95% of the time. This manual reconciliation is a focused, heads-up task. Given that the correct value was entered during heads-down data entry nearly 99% of the time, and that a

majority of the 21 volunteers entered the correct value for 221 out of the 222 fields, this is a conservative assumption.

Consider a field which was entered by 11 volunteers. Assume seven volunteers entered the correct value, three volunteers entered a common incorrect value, and one volunteer entered a different incorrect value. There are 55 possible pairs of these 11 volunteers. In three pairs, both parties entered the identical incorrect value, and this incorrect value would then be the value recorded in the clinical database. In 21 pairs, both parties entered the identical correct value, and the correct value would then be the value recorded in the clinical database. In the remaining 31 pairs, two different values are present and a manual review of the values would take place. Using the assumption of a 95% correct manual resolution, 5% of these 31 pairs will result in an incorrect value in the clinical database. 5% of these 31 pairs and 100% of the three pairs above will produce an overall 8.27% chance of this field being incorrect after double data entry.

Raw Error Rates							
	Image Group			Paper Group			
	Errors	Fields	Err/100	Errors	Fields	Err/100	
23 Problem Fields	69	253	27.27	39	230	16.96	
865 Other Fields	59	9515	0.62	53	8650	0.61	
All Fields	128	9768	1.31	92	8880	1.04	

Errors = Total errors for all volunteers
Fields = Total number of fields
Err/100 = Errors per 100 fields

Average Errors Adjusted for Double Data Entry							
	Image Group			Paper Group			
	Errors	Fields	Err/100	Errors	Fields	Err/100	
23 Problem Fields	1.92	23	8.37	1.24	23	5.41	
865 Other Fields	0.53	865	0.06	0.53	865	0.06	
All Fields	2.45	888	0.28	1.77	888	0.20	

Errors = Average number of errors using double data entry analysis
Fields = Number of fields
Err/100 = Errors per 100 fields

Figure 16: Table Summarising Impact of Adjusting for Double Data Entry

Figure 43 in Appendix J displays detailed data concerning these 23 fields, applying this methodology to analyse them. Figure 16 summarises the results of this analysis. The raw error rate of the image group is 1.31 errors per 100 fields, compared to 1.04 errors per 100 fields for the paper group. There are .27 more errors per 100 fields for the image group, or 26% more than the paper group.

When the effect of double data entry is factored in, the result has less practical significance. The error rate for the image group is 0.28 errors per 100 double-data-entered fields, compared to 0.20 errors per 100 double-data-entered fields for the paper group. There are 0.08 more errors per 100 double-data-entered fields for the image group, or 39% more than the paper group. The ratio between the two groups is magnified, but the difference in error rates is reduced from .27 more errors per 100 fields, to .08 more errors per 100 double-data-entered fields.

This overall error rate would typically be further reduced during various data review and quality control steps. Studies vary in complexity, and data processors realise improved accuracy with additional training on specific CRF booklets and database entry screens. It is not useful to apply this error rate as a benchmark for other studies.

Based on this analysis, data entry from CRF images would not result in a dramatic increase in database error rates, when double data entry is employed. This project did not demonstrate, at the 5% significance level, that the raw data entry error rate was higher for CRF images than for paper CRFs. If the data from the integrated summary is used to suggest that more errors will be seen when using CRF images, the anticipated impact would be largely limited to slightly increased time for reconciliation of the entry errors.

The data from this study might also be used to suggest that CRF pages containing large amounts of free text may be the most likely to result in increased raw error rates when paper CRFs are replaced with CRF images. Limiting the amount of free text collected on a CRF might reduce any potential negative impact on accuracy found in moving to CRF images.

DATA ENTRY SPEED

Comparison to Previous Studies

The Hopkins Fax Study did not calculate data entry speed. The PRA Pilot Study reported that data entry speed decreased with the use of CRF images, but suggested that technical shortcomings of the image system contributed to this problem. The Swansea Pilot Study resulted in the image group having a faster average entry time than the paper group, but was not constructed to test non-inferiority.

The results of this project are consistent with the results of the Swansea Pilot Study. The results of this study are different than would be suggested by the PRA Pilot Study, and this difference can be attributed to the use of improved technology.

Pooled Analysis

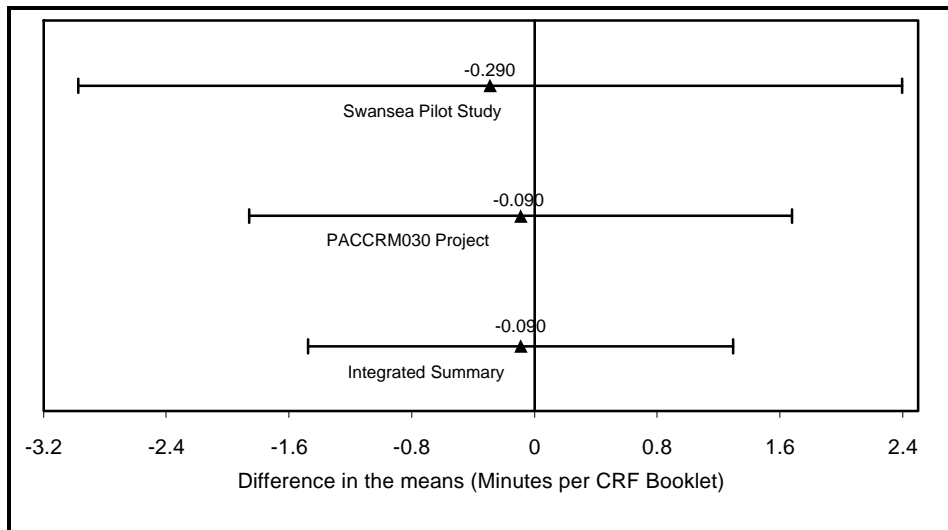


Figure 17: Integrated Summary of Speed Data

Combining the data from the Swansea Pilot Study with the data from this project, and performing an integrated analysis of this pooled data, strengthens the overall conclusion of non-inferiority. The difference in the mean entry speed of the image group compared to the paper group is .09 minutes per booklet less for the image group (or 1.0% faster) with the 95% confidence interval narrowing to (-1.47 to 1.30). Figure 17 shows the 95% confidence intervals for the Swansea Pilot Study, this project, and the pooled data. The full detail listing for the integrated summary can be found in Figure 44 in Appendix J.

Overall Impact on Data Processing Productivity

The data from this project suggests that data entry speed from CRF images is non-inferior to data entry speed from paper CRFs. The upper confidence bound for this test was set at 2

minutes per CRF booklet. This is a generous allowance for non-inferiority. Consideration must also be given to the additional time savings which would be anticipated from improved logistics and workflow factors when CRF images replace paper CRFs.

CRF images allow data processors direct and immediate access to the CRFs they require for data entry. Paper CRFs must be stored in a secure and controlled location. By eliminating the time-consuming tasks of retrieving and returning paper CRFs to and from their secure storage, and eliminating the accompanying check-out and check-in procedures, significant process efficiencies can be realized. In addition, further time savings would be anticipated from automated workflow processes which are possible when working with images.

The purpose of testing data entry speed using CRF images for non-inferiority, compared to data entry speed from paper CRFs, was to ensure that there were no factors affecting data processors which would erode the inherent speed advantages that CRF images are felt to hold. The confidence bound of 2 was felt appropriate given this context. The actual 95%CI upper bound of 1.66 for this project (and 1.30 for the integrated summary) reinforces the belief that the overall impact of using images on data processing would be an increase in productivity.

TASK SATISFACTION

Comparison to Previous Studies

The PRA Pilot Study reported anecdotal evidence that data processors experienced some frustration when working with CRF images. The Swansea Pilot Study found a large difference in questionnaire results attempting to measure task satisfaction. This project used a specially developed questionnaire, and had each volunteer complete the form only once. The results from this project found a difference in mean task satisfaction scores which was much

smaller than the Swansea Pilot Study. Based on this data, it can not be concluded that data processors were less satisfied with the task of entering data from CRF images than with the task of entering data from paper CRFs.

The results of this project might fail to verify the anecdotal evidence from the PRA Pilot Study, in part, because of the improved technology employed in this project. The results of this project may differ from the Swansea Pilot Study, because of the different instrument used to measure task satisfaction. The task satisfaction questionnaire was an imperfect instrument, for the reasons described in the Study Design Shortcomings section below. The questionnaire used in this project was designed following the techniques described in the Methods section, and was considered an improvement over the questionnaire used in the Swansea Pilot Study.

Pooled Analysis

The questionnaire used in this project was not consistent with the questionnaire used in the Swansea Pilot Study. Combining the data from these different questionnaires for an integrated summary was not considered appropriate.

Overall Impact on Data Processor Satisfaction

The data from this project does not support any firm conclusions about the overall impact of using CRF images on the task satisfaction of data processors. The change from using paper CRFs to CRF images is a major paradigm shift. Despite the lack of a clear result in comparing task satisfaction scores between the two groups in this project, a plan to move a data processing group from paper CRFs to CRF images should include a consideration of change management issues.

STUDY DESIGN SHORTCOMINGS

Computer Skills Self-Assessment

The computer skills self-assessment question on the Subject Information Form did not collect reliable data. This became clear when mapping responses against objective data for some volunteers. In some cases, entry level data processors selected assessments that were higher than certified systems engineers selected for themselves. The question was poorly formed, giving the respondent no fixed item with which to compare.

The Subject Information Form was tested in the Swansea Pilot Study. This problem was not identified at that time. In the Swansea Pilot Study, all seven volunteers completed this form simultaneously. This gave the volunteers a natural frame of reference, the other volunteers, with which to compare their skills. This project, by contrast, was completed one or two volunteers at a time, removing this frame of reference.

A better construction would have been “I consider my computer skills, when compared to a typical data processor with three years of experience, to be:,” providing the volunteer with an objective reference.

The data collected in response to this question for this project is not considered reliable, and was not used in the analysis.

Task Satisfaction Questionnaire

The questionnaire used in this study to assess task satisfaction was designed and tested as described in the Methods section. The final item on this questionnaire, “Entering the last few CRF booklets did not decrease my job satisfaction:” resulted in questions from many of the

volunteers. They were instructed to respond to this item “from the point of view of a data processor performing production data entry.” It is possible that difficulty understanding this item affected the task satisfaction scores. This problem was not encountered when pilot testing the questionnaire.

Sample Size Calculations

The difference in data entry accuracy between the image group and the paper group in the integrated summary was found to be 0.51 more errors per 100 fields for the image group. If this is a representation of the true difference in the means, then a much larger sample size (59 per group) would be required to correctly power the study, using the same criteria as this project ($\alpha = .05$, $\text{power} = .90$, $\text{standard deviation} = 0.85$) if the practical significance of this smaller difference was considered consequential.

FURTHER RESEARCH

Several areas of further research might be interesting. Naturally, it would be useful to attempt to correct the identified shortcomings from this project. Improvements to the Task Satisfaction Form would allow for more accurate assessment of the data processors' attitude toward the use of CRF images.

Additionally, it might be informative to assess the relationship between eyesight and entry from images, to see if those with less than perfect vision are better able to work with CRF images or paper CRFs. It would also be interesting to compare entry from CRF images using a single 21-inch monitor, with entry from CRF images using two 17-inch monitors.

CONCLUSION

The data entry accuracy data from this project does not support rejecting the null hypothesis for the primary objective at the 5% significance level. Analysis of the integrated summary of accuracy data from this project and the Swansea Pilot Study provides some suggestion that the error rate for data entry from images may be higher than the error rate for data entry from paper. The practical significance of the difference is inconsequential.

Detailed review of the data entry errors suggests that if this difference in error rates exists, its impact on database accuracy is marginal, when double data entry methods are used. There might be some additional effort required to reconcile differences between the two passes of data entry.

The data entry speed data from this study supports a claim of non-inferiority for entry from CRF images at the 5% significance level. Data entry from CRF images is not expected to be slower than data entry from paper CRFs, and when logistic and workflow factors are considered, it is anticipated that replacing paper CRFs with CRF images will result in improved data entry productivity.

The task satisfaction data from this project does not support, nor disprove, a claim of reduced satisfaction for data processors using CRF images when compared to data processors using paper CRFs.

There are no obstacles to implementing an image management and workflow system based on this comparison of the accuracy, speed, and task satisfaction between paper-based and image-based data entry of case report forms.

APPENDICES

- A. Typical Data Management Process Flowchart
 - B. Swansea Pilot Study Data
 - C. Volunteer Consent Form
 - D. Questionnaire Pilot
 - E. Subject Information Form
 - F. Task Satisfaction Form
 - G. CRF Booklets
 - H. Technical Description of Hardware and Software
 - I. Data Entry Protocol
 - J. Study Data Detail Tables
-

A. Typical Data Management Process Flowchart

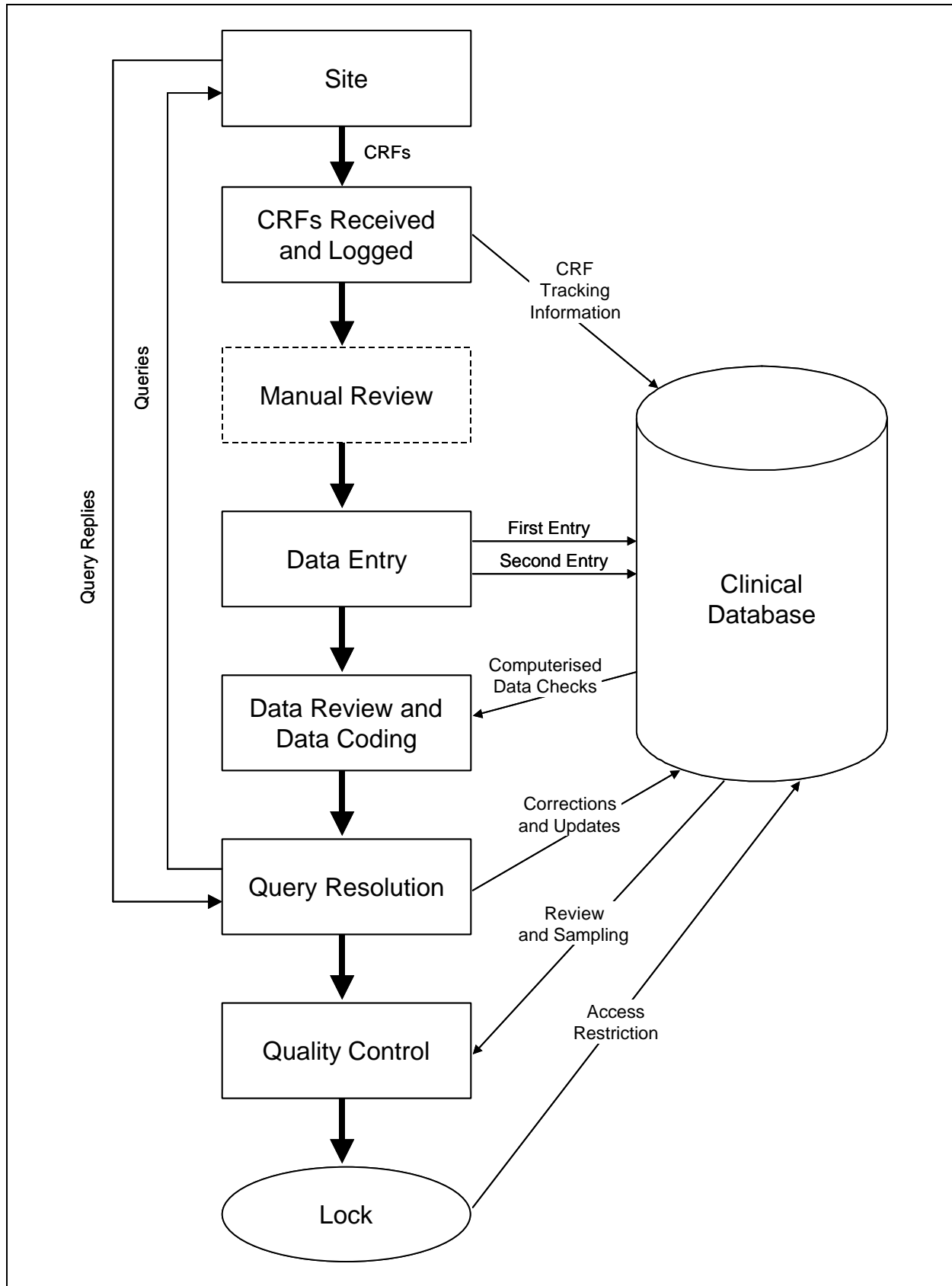


Figure 18: Typical Data Management Process

B. Swansea Pilot Study Data

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	5.86	0.45	3.15	0.45	1.80	2.70	0.45	1.35
Subject 2	5.86	0.90	3.38	3.15	3.60	1.35	0.00	2.03
Subject 6	7.66	1.80	4.73	1.80	2.70	1.80	4.05	2.59
Mean	6.46	1.05	3.75	1.80	2.70	1.95	1.50	1.99

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 3	3.15	0.45	1.80	0.00	0.00	0.45	0.00	0.11
Subject 4	2.70	0.45	1.58	0.00	0.45	0.90	0.45	0.45
Subject 5	5.41	0.45	2.93	0.00	0.45	4.50	0.00	1.24
Subject 7	13.06	12.16	12.61	1.80	0.45	1.80	0.45	1.13
Mean	6.08	3.38	4.73	0.45	0.34	1.91	0.23	0.73

Number of Errors per 100 Fields

Difference in the Means 1.26
 (Image - Paper, for Randomised Booklets)
 (p=0.035; [95%CI] 0.13 to 2.38)

Figure 19: Swansea Pilot Study Accuracy

Image Group	Baseline	Randomised
Subject 1	10.50	7.75
Subject 2	9.50	9.50
Subject 6	11.50	8.50
Mean	10.50	8.58

Paper Group	Baseline	Randomised
Subject 3	12.00	10.00
Subject 4	7.50	6.50
Subject 5	11.50	9.75
Subject 7	12.50	9.25
Mean	10.88	8.88

Minutes per CRF Booklet Entered

Difference in the Means -0.29
(Image - Paper, for Randomised Booklets)
($p=0.791$; [95%CI] -2.98 to 2.39)

Figure 20: Swansea Pilot Study Speed

Image Group Question	Baseline				Randomised			
	Q1	Q2	Q3	Total	Q1	Q2	Q3	Total
Subject 1	4	4	4	12	4	4	4	12
Subject 2	3	4	3	10	4	4	4	12
Subject 6	4	2	3	9	5	2	3	10
Mean	3.67	3.33	3.33	10.33	4.33	3.33	3.67	11.33

Paper Group Question	Baseline				Randomised			
	Q1	Q2	Q3	Total	Q1	Q2	Q3	Total
Subject 3	3	2	3	8	5	4	5	14
Subject 4	5	3	3	11	5	5	5	15
Subject 5	3	3	2	8	4	4	4	12
Subject 7	5	4	3	12	5	5	5	15
Mean	4.00	3.00	2.75	9.75	4.75	4.50	4.75	14.00

Question Scores

(Very Difficult/Very Unpleasant/Very Hard to Read = 1)

(Very Easy/Very Pleasant/Very Easy to Read = 5)

Difference in the Means -2.67

(Image - Paper, for Randomised Booklets)

(p=0.045; [95%CI] -0.08 to -5.25)

Question #1

I found the act of entering the last two patients to be:

(Very Difficult, Difficult, Average, Easy, Very Easy)

Question #2

I found the act of entering the last two patients to be:

(Very Unpleasant, Unpleasant, Average, Pleasant, Very Pleasant)

Question #3

I found the last two patients' CRFs to be:

(Very Hard to Read, Hard to Read, Average, Easy to Read, Very Easy to Read)

Figure 21: Swansea Pilot Study Questionnaire

C. Volunteer Consent Form

Volunteer Consent Form

I acknowledge by my signature below that:

1. The Protocol for Study Volunteers has been reviewed with me. The general purpose of the study and my role as a volunteer were explained to me. I understand that I will be asked to:
 - Receive instructions on CRF Entry and the Entry Database
 - Complete a Subject Information Form
 - Perform data entry of booklets 101 and 102 from CRF images
 - Be randomised into a study group (either paper or image)
 - Perform data entry of booklets 103, 104, 105 and 106
 - Complete a questionnaire about this experience

2. I am participating in the study voluntarily, and understand that I may withdraw my consent at any point.

SIGNATURE

PRINT NAME

DATE (DD-MON-YYYY)

Figure 22: Volunteer Consent Form

D. Questionnaire Pilot

Control Group Question	Q1	Q2	Q3	Total	Errors
Subject 4	5	5	5	15	0
Subject 6	5	5	5	15	0
Subject 7	4	4	4	12	0
Subject 8	5	5	5	15	0
Mean	4.75	4.75	4.75	14.25	0.00

Blurry Group Question	Q1	Q2	Q3	Total	Errors
Subject 1	2	1	1	4	3
Subject 2	4	2	3	9	3
Subject 3	5	2	5	12	0
Subject 5	3	3	3	9	1
Mean	3.50	2.00	3.00	8.50	1.75

Scores based on Strongly Agree = 5, Strongly Disagree = 1.

Difference in the Means 5.75
(Control - Blurry)
(p=0.020; [95%CI] 1.30 to 10.20)

	Mean Difference	significance	[95%CI]
Question 1	1.25	0.121	(-0.44 2.94)
Question 2	2.75	0.001	(1.58 3.92)
Question 3	1.75	0.086	(-0.34 3.84)

Figure 23: Table Summarising Data from Questionnaire Validation

E. Subject Information Form

PACCRM030 Project

Personal Information

Initials:

Date of Birth:

DD MON YYYY

Sex: (M or F)

Nationality: _____

Experience

Years of Data Entry Experience:

Total: .

Medical Data: .

I consider my computer skills to be:

Poor

Below Average

Average

Above Average

Excellent

Figure 24: Subject Information Form

F. Task Satisfaction Form**Subject Initials**

Initials:

--	--	--

Questionnaire

Entering the last four CRF booklets was simple to do:

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree

It was easy to read the data for the last four CRF booklets:

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree

Entering the last four CRF booklets did not decrease my job satisfaction:

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree

Thank you for your assistance in completing this form.

Figure 25: Task Satisfaction Form

G. CRF Booklets

Screening Visit

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Inclusion Criteria

YES	NO	
<input type="checkbox"/>	<input type="checkbox"/>	1. Inclusion Criteria number one.
<input type="checkbox"/>	<input type="checkbox"/>	2. Inclusion Criteria number two.
<input type="checkbox"/>	<input type="checkbox"/>	3. Inclusion Criteria number three.
<input type="checkbox"/>	<input type="checkbox"/>	4. Inclusion Criteria number four.
<input type="checkbox"/>	<input type="checkbox"/>	5. Inclusion Criteria number five.
<input type="checkbox"/>	<input type="checkbox"/>	6. Inclusion Criteria number six.
<input type="checkbox"/>	<input type="checkbox"/>	7. Inclusion Criteria number seven.
<input type="checkbox"/>	<input type="checkbox"/>	8. Inclusion Criteria number eight.
<input type="checkbox"/>	<input type="checkbox"/>	9. Inclusion Criteria number nine.

Exclusion Criteria

YES	NO	
<input type="checkbox"/>	<input type="checkbox"/>	1. Exclusion Criteria number one.
<input type="checkbox"/>	<input type="checkbox"/>	2. Exclusion Criteria number two.
<input type="checkbox"/>	<input type="checkbox"/>	3. Exclusion Criteria number three.
<input type="checkbox"/>	<input type="checkbox"/>	4. Exclusion Criteria number four.
<input type="checkbox"/>	<input type="checkbox"/>	5. Exclusion Criteria number five.
<input type="checkbox"/>	<input type="checkbox"/>	6. Exclusion Criteria number six.
<input type="checkbox"/>	<input type="checkbox"/>	7. Exclusion Criteria number seven.
<input type="checkbox"/>	<input type="checkbox"/>	8. Exclusion Criteria number eight.

Screening Visit

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Demography

Gender 1 Male
 2 Female

Ethnic Origin 1 White 3 Oriental 5 Hispanic
 2 Black 4 Other

Date of Birth / /

DD MM YYYY

Height . inches

Weight . pounds

Visit 1

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Vital Signs #1

Time of Exam : :

HH MM

Blood Pressure / mmHg

(systolic) (diastolic)

Heart Rate beats/min

Temperature . °F

Vital Signs #2

Time of Exam : :

HH MM

Blood Pressure / mmHg

(systolic) (diastolic)

Heart Rate beats/min

Temperature . °F

Visit 1

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Numeric Data

One .

Two .

Three .

Four .

Five .

Six .

Seven .

Eight .

Nine .

Ten .

Eleven .

Twelve .

Figure 26: Pages 1-4 of CRF Booklets

Visit 1

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Text Data

One _____

Two _____

Three _____

Four _____

Five _____

Six _____

Seven _____

Eight _____

Nine _____

Ten _____

Eleven _____

Twelve _____

Visit 2

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Vital Signs #1

Time of Exam :

HH MM

Blood Pressure / mmHg

(systolic) (diastolic)

Heart Rate beats/min

Temperature . °F

Vital Signs #2

Time of Exam :

HH MM

Blood Pressure / mmHg

(systolic) (diastolic)

Heart Rate beats/min

Temperature . °F

Visit 2

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Numeric Data

One	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Two	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Three	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Four	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Five	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Six	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Seven	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Eight	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Nine	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Ten	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Eleven	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Twelve	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Visit 2

Protocol	Subject Initials	Subject Number	Visit Date
PACCRM030			DD MM YYYY

Text Data

One _____

Two _____

Three _____

Four _____

Five _____

Six _____

Seven _____

Eight _____

Nine _____

Ten _____

Eleven _____

Twelve _____

Figure 27: Pages 5-8 of CRF Booklets

End of Study

Protocol PACCRM030	Subject Initials	Subject Number	Visit Date		
			DD	MM	YYYY

Concomitant Medication #1

Medication _____

Date Started

DD MM YYYY

Date Resolved Ongoing

DD MM YYYY

Dose _____ Unit _____

Route _____ Frequency _____

Reason for Medication _____

Concomitant Medication #2

Medication _____

Date Started

DD MM YYYY

Date Resolved Ongoing

DD MM YYYY

Dose _____ Unit _____

Route _____ Frequency _____

Reason for Medication _____

End of Study

Protocol PACCRM030	Subject Initials	Subject Number	Visit Date		
			DD	MM	YYYY

Adverse Event #1

Adverse Event _____

Date Started

DD MM YYYY

Date Resolved Ongoing

DD MM YYYY

Severity 1-mild
 2-moderate
 3-severe

Relationship to Study Drug 0-unlikely
 1-possible
 2-probable

Serious Adverse Event 0-no
 1-yes

Other Drug Treatment Given 0-no
 1-yes

Subject Discontinued from Study 0-no
 1-yes

Adverse Event #2

Adverse Event _____

Date Started

DD MM YYYY

Date Resolved Ongoing

DD MM YYYY

Severity 1-mild
 2-moderate
 3-severe

Relationship to Study Drug 0-unlikely
 1-possible
 2-probable

Serious Adverse Event 0-no
 1-yes

Other Drug Treatment Given 0-no
 1-yes

Subject Discontinued from Study 0-no
 1-yes

Figure 28: Pages 9-10 of CRF Booklets

H. Technical Description of Hardware and Software

Scanner

Fujitsu M3099A Scanner

KOFAX KF 9274 Image Accelerator

WCR KIPP Version 2.12 Software

File Server

Dell PE 4100

2 x 180 MHz processors

256 MB RAM

Windows NT 4.0, Service Pack 5

DLB Recorder 3.1.07

Oracle Server

Digital AlphaServer 4100

2 x 300 MHz processors

512 MB RAM

OpenVMS 7.1 – 1H1

Oracle 7.3.4

Client Machines

Dell Optiplex GXI

400 MHz processor

2 x 17-inch Dell Monitors set to 1024x768 resolution

128 MB RAM

Windows98

I. Data Entry Protocol

Protocol for Study Volunteers

1. Project Objectives

Explain the purpose of the study and what information is expected to be gained. The volunteer should be informed that we will compare the accuracy of data entered from images with the accuracy of data entered from paper as the primary objective. The volunteer should be informed that we will compare the speed with which data is entered from images with the speed with which paper is entered from paper. Additionally, that we will compare task satisfaction scores from the volunteers who performed data entry.

2. Role of Volunteer

Explain what is expected from the study volunteer. The volunteer will be instructed that accuracy is more important than speed, but that a mix of speed and accuracy is most desirable. The Volunteer Consent Form should be signed at the end of this explanation.

3. CRF Entry and Database Instructions

Using a blank CRF instruct the study volunteer in the use of the database. All data entry screens should be reviewed at this time. All coded entry fields (e.g., 1=yes, 0=no) should be explained.

4. Complete Subject Information Form

At this point the volunteer should complete the Subject Information Form.

5. Data Entry of Booklets 101 and 102

The Volunteer should now perform data entry from CRF images using CRF booklets 101 and 102.

6. Randomise Volunteer into Study Group

At this point the volunteer should be randomised into either the paper group or the image group, based in part on the volunteer's error rate and entry speed for CRF booklets 101 and 102.

7. Data Entry of Booklets 103-106

The Volunteer should now perform data entry of CRF booklets 103, 104, 105, and 106 using either CRF images or paper CRFs based on randomisation group.

8. Complete Questionnaire

At this point the volunteer should complete the task satisfaction questionnaire. Volunteers should complete the form from the point of view of a data processor performing production data entry. The volunteer has then completed participation in the project.

Figure 29: Data Entry Protocol

J. Study Data Detail Tables

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	3.60	0.45	2.03	2.25	1.35	1.80	0.00	1.35
Subject 3	3.15	0.45	1.80	0.45	0.45	1.35	0.00	0.56
Subject 4	10.81	2.25	6.53	1.35	4.95	3.15	0.45	2.48
Subject 6	8.56	0.90	4.73	1.80	0.90	1.80	0.45	1.24
Subject 7	4.05	0.90	2.48	1.35	0.45	2.70	0.45	1.24
Subject 10	3.15	0.00	1.58	0.90	3.60	4.05	0.45	2.25
Subject 14	6.76	1.35	4.05	0.45	1.80	3.60	0.90	1.69
Subject 15	4.05	0.45	2.25	0.00	1.35	1.35	0.45	0.79
Subject 16	6.31	2.25	4.28	0.90	2.70	1.80	0.90	1.58
Subject 17	1.35	2.70	2.03	0.90	1.35	0.90	0.45	0.90
Subject 21	3.60	0.90	2.25	0.45	0.45	0.45	0.00	0.34
Mean	5.04	1.15	3.09	0.98	1.76	2.09	0.41	1.31

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	5.86	1.35	3.60	0.90	0.45	6.31	0.90	2.14
Subject 5	3.15	1.35	2.25	0.45	0.00	1.35	0.45	0.56
Subject 8	3.15	0.90	2.03	0.45	0.90	0.90	0.45	0.68
Subject 9	4.05	1.35	2.70	0.45	0.45	0.00	0.45	0.34
Subject 11	5.86	1.35	3.60	1.35	1.80	0.90	1.80	1.46
Subject 12	3.60	2.25	2.93	0.45	0.00	1.35	0.45	0.56
Subject 13	4.50	0.90	2.70	1.80	1.35	0.90	0.00	1.01
Subject 18	4.05	1.35	2.70	0.90	0.45	1.35	0.45	0.79
Subject 19	4.50	2.70	3.60	1.35	0.45	1.80	1.35	1.24
Subject 20	7.66	2.70	5.18	2.70	0.90	0.90	1.80	1.58
Mean	4.64	1.62	3.13	1.08	0.68	1.58	0.81	1.04

Number of Errors per 100 Fields

Difference in the Means 0.27
(Image - Paper, for Randomised Booklets)
(p=0.322; [95%CI] -0.29 to 0.84)

Figure 30: Accuracy Data Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	12.23	9.65	10.94	9.25	8.07	9.67	8.78	8.94
Subject 3	15.57	12.08	13.83	11.78	10.37	10.55	10.02	10.68
Subject 4	18.18	9.43	13.81	9.55	10.43	8.40	9.12	9.38
Subject 6	14.90	10.70	12.80	11.48	10.93	11.47	10.20	11.02
Subject 7	17.55	11.70	14.63	11.63	11.23	10.57	10.58	11.00
Subject 10	13.12	10.95	12.04	11.87	11.10	11.57	8.38	10.73
Subject 14	12.98	8.15	10.57	7.45	7.43	7.40	7.95	7.56
Subject 15	10.48	8.32	9.40	8.45	8.23	8.05	8.28	8.25
Subject 16	13.22	12.15	12.69	10.58	9.93	9.72	9.83	10.02
Subject 17	16.53	12.08	14.31	12.97	11.20	10.20	10.55	11.23
Subject 21	8.53	5.50	7.02	5.65	5.53	5.43	5.00	5.40
Mean	13.94	10.06	12.00	10.06	9.50	9.37	8.97	9.47

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	17.77	12.07	14.92	11.98	11.17	11.57	10.45	11.29
Subject 5	11.32	8.05	9.69	8.70	8.57	8.05	7.33	8.16
Subject 8	18.97	11.73	15.35	9.05	9.48	9.67	11.43	9.91
Subject 9	13.57	6.87	10.22	6.50	5.12	5.23	5.83	5.67
Subject 11	13.55	11.25	12.40	9.80	9.38	9.15	8.95	9.32
Subject 12	16.50	10.98	13.74	11.35	10.38	12.75	10.78	11.32
Subject 13	16.87	12.48	14.68	10.00	9.73	9.93	9.47	9.78
Subject 18	15.68	11.92	13.80	10.63	11.77	10.25	9.82	10.62
Subject 19	19.60	13.50	16.55	12.93	11.82	13.47	10.98	12.30
Subject 20	9.28	6.30	7.79	9.87	6.40	6.18	6.77	7.31
Mean	15.31	10.52	12.91	10.08	9.38	9.63	9.18	9.57

Minutes per CRF Booklet Entered

Difference in the Means -0.09
(Image - Paper, for Randomised Booklets)
([95%CI] -1.85 to 1.66)

Figure 31: Entry Speed Detail Listing

Image Group				
Subject	Q1	Q2	Q3	Total
Subject 1	5	3	3	11
Subject 3	3	3	2	8
Subject 4	4	4	4	12
Subject 6	4	3	4	11
Subject 7	4	4	4	12
Subject 10	4	4	4	12
Subject 14	5	4	5	14
Subject 15	5	4	4	13
Subject 16	4	4	4	12
Subject 17	5	4	4	13
Subject 21	4	4	4	12
Mean	4.27	3.73	3.82	11.82

Paper Group				
Subject	Q1	Q2	Q3	Total
Subject 2	4	4	4	12
Subject 5	4	3	2	9
Subject 8	4	5	4	13
Subject 9	5	4	5	14
Subject 11	4	4	4	12
Subject 12	4	4	4	12
Subject 13	5	4	4	13
Subject 18	4	4	4	12
Subject 19	5	5	4	14
Subject 20	5	4	3	12
Mean	4.40	4.10	3.80	12.30

Scores based on Strongly Agree = 5, Strongly Disagree = 1.

Difference in the Means -0.48
 (Image - Paper)
 (p=0.466; [95%CI] -1.84 to 0.87)

Figure 32: Task Satisfaction Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	1.35	0.45	0.90	1.80	0.00	1.80	0.00	0.90
Subject 3	1.80	0.00	0.90	0.00	0.00	0.90	0.00	0.23
Subject 4	1.80	0.00	0.90	0.00	2.25	1.35	0.00	0.90
Subject 6	1.80	0.00	0.90	0.90	0.45	0.90	0.00	0.56
Subject 7	1.35	0.45	0.90	0.00	0.00	1.35	0.00	0.34
Subject 10	1.35	0.00	0.68	0.45	0.90	1.80	0.00	0.79
Subject 14	1.80	0.00	0.90	0.00	0.00	0.90	0.00	0.23
Subject 15	0.90	0.00	0.45	0.00	0.90	0.45	0.45	0.45
Subject 16	2.25	0.45	1.35	0.00	0.45	0.45	0.00	0.23
Subject 17	0.90	0.90	0.90	0.00	0.45	0.90	0.00	0.34
Subject 21	1.80	0.00	0.90	0.00	0.00	0.45	0.00	0.11
Mean	1.56	0.20	0.88	0.29	0.49	1.02	0.04	0.46

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	1.80	0.90	1.35	0.00	0.00	1.35	0.90	0.56
Subject 5	1.35	0.45	0.90	0.00	0.00	0.45	0.45	0.23
Subject 8	1.80	0.00	0.90	0.00	0.00	0.00	0.00	0.00
Subject 9	1.35	0.00	0.68	0.00	0.00	0.00	0.00	0.00
Subject 11	3.15	0.00	1.58	0.00	0.45	0.00	0.00	0.11
Subject 12	1.35	0.00	0.68	0.00	0.00	0.45	0.00	0.11
Subject 13	2.25	0.00	1.13	0.00	0.45	0.45	0.00	0.23
Subject 18	0.45	0.00	0.23	0.45	0.45	0.00	0.45	0.34
Subject 19	2.25	0.45	1.35	0.45	0.00	0.90	0.45	0.45
Subject 20	4.05	0.00	2.03	1.35	0.00	0.45	0.45	0.56
Mean	1.98	0.18	1.08	0.23	0.14	0.41	0.27	0.26

Number of Errors per 100 Fields

Difference in the Means 0.20
 (Image - Paper, for Randomised Booklets)
 (p=0.083; [95%CI] -0.03 to 0.43)

Figure 33: Data Entry Accuracy for Text Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.45	0.00	0.23	0.00	0.45	0.00	0.00	0.11
Subject 3	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 4	2.25	0.90	1.58	0.90	0.90	0.45	0.00	0.56
Subject 6	0.00	0.90	0.45	0.45	0.45	0.45	0.00	0.34
Subject 7	0.45	0.00	0.23	0.90	0.45	0.00	0.00	0.34
Subject 10	0.00	0.00	0.00	0.00	0.45	0.45	0.00	0.23
Subject 14	1.35	0.90	1.13	0.00	1.35	0.45	0.90	0.68
Subject 15	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.11
Subject 16	2.25	1.35	1.80	0.00	0.45	0.00	0.00	0.11
Subject 17	0.00	0.90	0.45	0.00	0.00	0.00	0.00	0.00
Subject 21	0.45	0.45	0.45	0.00	0.45	0.00	0.00	0.11
Mean	0.70	0.49	0.59	0.20	0.49	0.16	0.08	0.24

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Subject 5	0.45	0.90	0.68	0.45	0.00	0.00	0.00	0.11
Subject 8	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.11
Subject 9	0.45	1.35	0.90	0.00	0.00	0.00	0.45	0.11
Subject 11	0.45	0.90	0.68	0.45	0.45	0.45	0.00	0.34
Subject 12	0.45	1.35	0.90	0.45	0.00	0.00	0.00	0.11
Subject 13	0.00	0.45	0.23	0.90	0.90	0.00	0.00	0.45
Subject 18	1.35	0.00	0.68	0.00	0.00	0.00	0.00	0.00
Subject 19	0.45	0.90	0.68	0.45	0.00	0.45	0.45	0.34
Subject 20	1.80	0.45	1.13	0.00	0.00	0.00	0.00	0.00
Mean	0.59	0.63	0.61	0.32	0.18	0.09	0.09	0.17

Number of Errors per 100 Fields

Difference in the Means 0.07
 (Image - Paper, for Randomised Booklets)
 (p=0.435; [95%CI] -0.11 to 0.24)

Figure 34: Data Entry Accuracy for Numeric Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 3	0.45	0.00	0.23	0.00	0.45	0.00	0.00	0.11
Subject 4	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 6	5.86	0.00	2.93	0.00	0.00	0.00	0.00	0.00
Subject 7	0.00	0.00	0.00	0.45	0.00	0.00	0.45	0.23
Subject 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 14	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 15	0.90	0.00	0.45	0.00	0.00	0.00	0.00	0.00
Subject 16	0.45	0.00	0.23	0.00	0.90	0.00	0.00	0.23
Subject 17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 21	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Mean	0.86	0.00	0.43	0.04	0.12	0.00	0.04	0.05

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	0.90	0.00	0.45	0.00	0.00	0.00	0.00	0.00
Subject 5	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 8	0.45	0.45	0.45	0.45	0.00	0.00	0.00	0.11
Subject 9	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 11	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 12	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 13	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.11
Subject 18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 19	0.00	0.45	0.23	0.00	0.00	0.00	0.00	0.00
Subject 20	0.45	0.00	0.23	0.00	0.00	0.00	0.45	0.11
Mean	0.36	0.09	0.23	0.09	0.00	0.00	0.05	0.03

Number of Errors per 100 Fields

Difference in the Means 0.02
 (Image - Paper, for Randomised Booklets)
 (p=0.584; [95%CI] -0.05 to 0.09)

Figure 35: Data Entry Accuracy for Adverse Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.90	0.00	0.45	0.00	0.90	0.00	0.00	0.23
Subject 3	0.00	0.45	0.23	0.45	0.00	0.45	0.00	0.23
Subject 4	1.35	0.45	0.90	0.00	0.90	1.35	0.45	0.68
Subject 6	0.45	0.00	0.23	0.00	0.00	0.45	0.00	0.11
Subject 7	0.45	0.45	0.45	0.00	0.00	1.35	0.00	0.34
Subject 10	0.45	0.00	0.23	0.00	1.35	1.80	0.00	0.79
Subject 14	0.90	0.45	0.68	0.00	0.45	0.90	0.00	0.34
Subject 15	0.45	0.00	0.23	0.00	0.00	0.90	0.00	0.23
Subject 16	0.00	0.45	0.23	0.00	0.90	0.45	0.00	0.34
Subject 17	0.00	0.45	0.23	0.45	0.90	0.00	0.00	0.34
Subject 21	0.00	0.45	0.23	0.00	0.00	0.00	0.00	0.00
Mean	0.45	0.29	0.37	0.08	0.49	0.70	0.04	0.33

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	1.35	0.45	0.90	0.00	0.45	0.90	0.00	0.34
Subject 5	0.00	0.00	0.00	0.00	0.00	0.90	0.00	0.23
Subject 8	0.00	0.45	0.23	0.00	0.45	0.45	0.00	0.23
Subject 9	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 11	0.90	0.45	0.68	0.00	0.00	0.45	0.90	0.34
Subject 12	1.35	0.45	0.90	0.00	0.00	0.90	0.45	0.34
Subject 13	0.45	0.45	0.45	0.45	0.00	0.45	0.00	0.23
Subject 18	1.35	0.90	1.13	0.00	0.00	1.35	0.00	0.34
Subject 19	0.45	0.45	0.45	0.00	0.00	0.45	0.00	0.11
Subject 20	0.00	1.35	0.68	0.45	0.90	0.45	0.45	0.56
Mean	0.63	0.50	0.56	0.09	0.18	0.63	0.18	0.27

Number of Errors per 100 Fields

Difference in the Means 0.06
(Image - Paper, for Randomised Booklets)
(p=0.506; [95%CI] -0.12 to 0.24)

Figure 36: Data Entry Accuracy for ConMed Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 6	0.00	0.00	0.00	0.00	0.00	0.00	0.45	0.11
Subject 7	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 16	0.00	0.00	0.00	0.00	0.00	0.00	0.90	0.23
Subject 17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.03

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Number of Errors per 100 Fields

Difference in the Means 0.03
 (Image - Paper, for Randomised Booklets)
 (p=0.199; [95%CI] -0.01 to 0.07)

Figure 37: Data Entry Accuracy for Demog Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.11
Subject 3	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 4	2.70	0.90	1.80	0.00	0.90	0.00	0.00	0.23
Subject 6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 7	0.90	0.00	0.45	0.00	0.00	0.00	0.00	0.00
Subject 10	0.90	0.00	0.45	0.45	0.45	0.00	0.45	0.34
Subject 14	1.80	0.00	0.90	0.00	0.00	1.35	0.00	0.34
Subject 15	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 16	0.45	0.00	0.23	0.00	0.00	0.90	0.00	0.23
Subject 17	0.00	0.45	0.23	0.45	0.00	0.00	0.45	0.23
Subject 21	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Mean	0.74	0.12	0.43	0.12	0.12	0.20	0.08	0.13

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.11
Subject 5	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 8	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 9	0.45	0.00	0.23	0.00	0.45	0.00	0.00	0.11
Subject 11	0.45	0.00	0.23	0.45	0.90	0.00	0.45	0.45
Subject 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 13	1.35	0.00	0.68	0.00	0.00	0.00	0.00	0.00
Subject 18	0.45	0.45	0.45	0.00	0.00	0.00	0.00	0.00
Subject 19	0.45	0.00	0.23	0.00	0.00	0.00	0.45	0.11
Subject 20	0.45	0.90	0.68	0.00	0.00	0.00	0.45	0.11
Mean	0.45	0.14	0.29	0.09	0.14	0.00	0.14	0.09

Number of Errors per 100 Fields

Difference in the Means 0.05
 (Image - Paper, for Randomised Booklets)
 (p=0.467; [95%CI] -0.08 to 0.17)

Figure 38: Data Entry Accuracy for Header Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 7	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 16	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.11
Subject 17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mean	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.01

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 11	0.00	0.00	0.00	0.00	0.00	0.00	0.45	0.11
Subject 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 19	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.11
Subject 20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mean	0.00	0.00	0.00	0.00	0.05	0.00	0.05	0.02

Number of Errors per 100 Fields

Difference in the Means -0.01
 (Image - Paper, for Randomised Booklets)
 (p=0.500; [95%CI] -0.05 to 0.02)

Figure 39: Data Entry Accuracy for Inclusion/Exclusion Pages Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Subject 4	2.25	0.00	1.13	0.45	0.00	0.00	0.00	0.11
Subject 6	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Subject 7	0.90	0.00	0.45	0.00	0.00	0.00	0.00	0.00
Subject 10	0.45	0.00	0.23	0.00	0.45	0.00	0.00	0.11
Subject 14	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Subject 15	1.35	0.45	0.90	0.00	0.00	0.00	0.00	0.00
Subject 16	0.90	0.00	0.45	0.45	0.00	0.00	0.00	0.11
Subject 17	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 21	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Mean	0.74	0.04	0.39	0.20	0.04	0.00	0.00	0.06

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	1.35	0.00	0.68	0.00	0.00	4.05	0.00	1.01
Subject 5	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 8	0.45	0.00	0.23	0.00	0.00	0.45	0.45	0.23
Subject 9	0.90	0.00	0.45	0.45	0.00	0.00	0.00	0.11
Subject 11	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Subject 12	0.00	0.45	0.23	0.00	0.00	0.00	0.00	0.00
Subject 13	0.45	0.00	0.23	0.00	0.00	0.00	0.00	0.00
Subject 18	0.45	0.00	0.23	0.45	0.00	0.00	0.00	0.11
Subject 19	0.90	0.45	0.68	0.45	0.00	0.00	0.00	0.11
Subject 20	0.90	0.00	0.45	0.90	0.00	0.00	0.00	0.23
Mean	0.63	0.09	0.36	0.27	0.00	0.45	0.05	0.19

Number of Errors per 100 Fields

Difference in the Means -0.13
 (Image - Paper, for Randomised Booklets)
 (p=0.171; [95%CI] -0.32 to 0.06)

Figure 40: Data Entry Accuracy for Vital Signs Pages Detail Listing

Image Group				
Subject	Q1	Q2	Q3	Total
Subject 1	5	3	3	11
Subject 3	3	3	2	8
Subject 14	5	4	5	14
Subject 21	4	4	4	12
Mean	4.25	3.50	3.50	11.25

Paper Group				
Subject	Q1	Q2	Q3	Total
Subject 8	4	5	4	13
Subject 9	5	4	5	14
Subject 20	5	4	3	12
Mean	4.67	4.33	4.00	13.00

Scores based on Strongly Agree = 5, Strongly Disagree = 1.

Difference in the Means -1.75
 (Image - Paper)
 (p=0.312; [95%CI] -5.75 to 2.25)

Figure 41: Task Satisfaction Scores for Experienced Data Processors Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	3.60	0.45	2.03	2.25	1.35	1.80	0.00	1.35
Subject 3	3.15	0.45	1.80	0.45	0.45	1.35	0.00	0.56
Subject 4	10.81	2.25	6.53	1.35	4.95	3.15	0.45	2.48
Subject 6	8.56	0.90	4.73	1.80	0.90	1.80	0.45	1.24
Subject 7	4.05	0.90	2.48	1.35	0.45	2.70	0.45	1.24
Subject 10	3.15	0.00	1.58	0.90	3.60	4.05	0.45	2.25
Subject 14	6.76	1.35	4.05	0.45	1.80	3.60	0.90	1.69
Subject 15	4.05	0.45	2.25	0.00	1.35	1.35	0.45	0.79
Subject 16	6.31	2.25	4.28	0.90	2.70	1.80	0.90	1.58
Subject 17	1.35	2.70	2.03	0.90	1.35	0.90	0.45	0.90
Subject 21	3.60	0.90	2.25	0.45	0.45	0.45	0.00	0.34
Subject 1-S	5.86	0.45	3.15	0.45	1.80	2.70	0.45	1.35
Subject 2-S	5.86	0.90	3.38	3.15	3.60	1.35	0.00	2.03
Subject 6-S	7.66	1.80	4.73	1.80	2.70	1.80	4.05	2.59
Mean	5.34	1.13	3.23	1.16	1.96	2.06	0.64	1.46

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	5.86	1.35	3.60	0.90	0.45	6.31	0.90	2.14
Subject 5	3.15	1.35	2.25	0.45	0.00	1.35	0.45	0.56
Subject 8	3.15	0.90	2.03	0.45	0.90	0.90	0.45	0.68
Subject 9	4.05	1.35	2.70	0.45	0.45	0.00	0.45	0.34
Subject 11	5.86	1.35	3.60	1.35	1.80	0.90	1.80	1.46
Subject 12	3.60	2.25	2.93	0.45	0.00	1.35	0.45	0.56
Subject 13	4.50	0.90	2.70	1.80	1.35	0.90	0.00	1.01
Subject 18	4.05	1.35	2.70	0.90	0.45	1.35	0.45	0.79
Subject 19	4.50	2.70	3.60	1.35	0.45	1.80	1.35	1.24
Subject 20	7.66	2.70	5.18	2.70	0.90	0.90	1.80	1.58
Subject 3-S	3.15	0.45	1.80	0.00	0.00	0.45	0.00	0.11
Subject 4-S	2.70	0.45	1.58	0.00	0.45	0.90	0.45	0.45
Subject 5-S	5.41	0.45	2.93	0.00	0.45	4.50	0.00	1.24
Subject 7-S	13.06	12.16	12.61	1.80	0.45	1.80	0.45	1.13
Mean	5.05	2.12	3.59	0.90	0.58	1.67	0.64	0.95

Number of Errors per 100 Fields
Swansea Subjects Identified with -S

Difference in the Means 0.51
(Image - Paper, for Randomised Booklets)
(p=0.043; [95%CI] 0.02 to 1.00)

Figure 42: Integrated Summary of Accuracy Data Detail Listing

	Page Type	Field	Image Group			Error Rate	Paper Group			Error Rate
			RE	UE	CV		RE	UE	CV	
1	ConMed	Medication	2	0	9	0.035	0	0	10	0.000
2	ConMed	Medication	4	1	6	0.140	1	0	9	0.010
3	ConMed	Medication	5	1	5	0.214	7	0	3	0.490
4	ConMed	Frequency	4	3	4	0.148	3	1	6	0.097
5	ConMed	Route	2	0	9	0.035	2	0	8	0.040
6	Demog	Month	2	0	9	0.035	0	0	10	0.000
7	Numeric	Number	1	0	10	0.009	1	0	9	0.010
8	Numeric	Number	1	0	10	0.009	1	0	9	0.010
9	Numeric	Number	0	1	10	0.009	2	1	7	0.048
10	Numeric	Number	7	0	4	0.407	0	0	10	0.000
11	Numeric	Number	3	0	8	0.076	1	0	9	0.010
12	Numeric	Number	2	0	9	0.035	2	0	8	0.040
13	Numeric	Number	1	0	10	0.009	1	0	9	0.010
14	Text	Text	1	0	10	0.009	1	1	8	0.019
15	Text	Text	3	0	8	0.076	0	0	10	0.000
16	Text	Text	5	1	5	0.214	4	0	6	0.160
17	Text	Text	3	0	8	0.076	1	0	9	0.010
18	Text	Text	2	0	9	0.035	3	0	7	0.090
19	Text	Text	2	0	9	0.035	0	0	10	0.000
20	Text	Text	2	0	9	0.035	0	0	10	0.000
21	Text	Text	5	0	6	0.209	0	0	10	0.000
22	Vitals	Year	2	1	8	0.042	2	0	8	0.040
23	Vitals	Systolic	2	0	9	0.035	4	0	6	0.160
			Average Errors			1.925	Average Errors			1.243

RE = Repeated Error, i.e., more than one identical error
UE = Unique Error, errors not in common with other entries
CV = Correct Value

$((RE*(RE-1))/2)$ represents the number of possible pairs with identical incorrect values, which will be automatically recorded in the clinical database with an incorrect value

$((UE*(UE-1))/2)$ represents the number of possible pairs with different values for each pass of data entry which will require manual reconciliation

.05 represents the percentage of pairs requiring manual review which will be recorded in the clinical database with an incorrect value, assuming the manual review selects the correct value in 95% of these cases

$((RE+UE+CV)*(RE+UE+CV-1))/2$ represents the total pool of potential pairs

The error rate, which is the likelihood of the field being recorded in the clinical database with the incorrect value is then calculated as:
 $((RE*(RE-1))/2 + ((UE*(UE-1))/2)*.05) / (((RE+UE+CV)*(RE+UE+CV-1))/2)$

Figure 43: Impact of Adjusting for Double Data Entry Detail Listing

Image Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 1	12.23	9.65	10.94	9.25	8.07	9.67	8.78	8.94
Subject 3	15.57	12.08	13.83	11.78	10.37	10.55	10.02	10.68
Subject 4	18.18	9.43	13.81	9.55	10.43	8.40	9.12	9.38
Subject 6	14.90	10.70	12.80	11.48	10.93	11.47	10.20	11.02
Subject 7	17.55	11.70	14.63	11.63	11.23	10.57	10.58	11.00
Subject 10	13.12	10.95	12.04	11.87	11.10	11.57	8.38	10.73
Subject 14	12.98	8.15	10.57	7.45	7.43	7.40	7.95	7.56
Subject 15	10.48	8.32	9.40	8.45	8.23	8.05	8.28	8.25
Subject 16	13.22	12.15	12.69	10.58	9.93	9.72	9.83	10.02
Subject 17	16.53	12.08	14.31	12.97	11.20	10.20	10.55	11.23
Subject 21	8.53	5.50	7.02	5.65	5.53	5.43	5.00	5.40
Subject 1-S			10.50					7.75
Subject 2-S			9.50					9.50
Subject 6-S			11.50					8.50
Mean			11.68					9.28

Paper Group Booklet	Baseline			Randomised				
	101	102	Mean	103	104	105	106	Mean
Subject 2	17.77	12.07	14.92	11.98	11.17	11.57	10.45	11.29
Subject 5	11.32	8.05	9.69	8.70	8.57	8.05	7.33	8.16
Subject 8	18.97	11.73	15.35	9.05	9.48	9.67	11.43	9.91
Subject 9	13.57	6.87	10.22	6.50	5.12	5.23	5.83	5.67
Subject 11	13.55	11.25	12.40	9.80	9.38	9.15	8.95	9.32
Subject 12	16.50	10.98	13.74	11.35	10.38	12.75	10.78	11.32
Subject 13	16.87	12.48	14.68	10.00	9.73	9.93	9.47	9.78
Subject 18	15.68	11.92	13.80	10.63	11.77	10.25	9.82	10.62
Subject 19	19.60	13.50	16.55	12.93	11.82	13.47	10.98	12.30
Subject 20	9.28	6.30	7.79	9.87	6.40	6.18	6.77	7.31
Subject 3-S			12.00					10.00
Subject 4-S			7.50					6.50
Subject 5-S			11.50					9.75
Subject 7-S			12.50					9.25
Mean			12.33					9.37

Minutes per CRF Booklet Entered
Swansea Subjects Identified with -S
Individual Booklet Times not captured in Swansea Pilot Study

Difference in the Means -0.09
(Image - Paper, for Randomised Booklets)
[95%CI] -1.47 to 1.30)

Figure 44: Integrated Summary of Speed Data Detail Listing

TABLE OF ABBREVIATIONS AND ACRONYMS

ACDM	Association for Clinical Data Management
CRF	Case Report Form
DAMOS	Drug Application Methodology with Optical Storage
ERSR	Electronic Regulatory Submission and Review
EU	European Union
EWG	Expert Working Group
FDA	United States Food and Drug Administration
GMP	Good Manufacturing Practices
ICH	International Conference on Harmonisation
IND	Investigational New Drug
M2	Multidisciplinary Group 2
MERS	Multi Agency Electronic Regulatory Submission
NDA	New Drug Application
PDF	Portable Document Format
PDUFA	Prescription Drug User Fee Act
PRA	PRA International, Inc.
PSI	Statisticians in the Pharmaceutical Industry
RDE	Remote Data Entry
SEDAMM	<i>Soumission Electronique Des Dossiers D'Amm</i>

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