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(54) Title: METHOD AND APPARATUS OF ASSURING INFORMED CONSENT WHILE CONDUCTING SECURE CLINICAL TRIALS
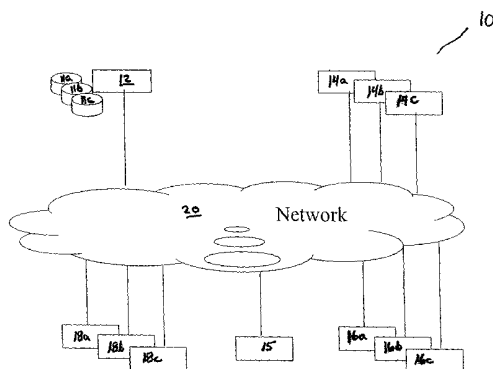
(57) Abstract: The present invention is a method of conducting clinical trials. Each clinical trial includes members comprising trial administratros, trial monitors, trial investigators, and trial participants or patients. The trial administrator selects the trial monitors and the trial investigators and defines procedural guidelines for the performance of the clinical trials. The trial investigators in turn select the trial participants to be enrolled in the clinical trials. The trial monitors observe the conduct of the clinical trials to detect any deviations from the procedural guidelines previously established by the trial administrator. The present invention allows the conduct of the clinical trial to take place over a network, e.g., the Internet or the telephone grid. The participants use computing devices connected to the network to perform transactions of the clinical trial. Each of these tests comprises one or more periods of execution or intervals, test elements, and a plurality of exception limits. All the trial participants arelisted in a database and are assigned access and validation levels. The clinical trial is performed according to the procedural guidelines by carrying out all of the transactions of the clinical trial. The executed transactions are stored in a database. Any time during the performance of the clinical trial the stored transactions can be queried at random to assure veracity of the clinical trial and to notify the trial administrator if any discrepancy is fount to prevent fraud.

METHOD AND APPARATUS OF ASSURING INFORMED CONSENT WHILE CONDUCTING SECURE CLINICAL TRIALS

FIELD OF THE INVENTION

This invention relates to authenticating that a recorded event occurred in a

5   proscribed manner and was performed by authorized personnel. More specifically, this

invention relates to assuring that the recorded event occurred with an informed consent.

Background of the Invention

Companies in the pharmaceutical and biotechnology industries annually funnel

huge monetary investments into research and development (R&D) of new medical

10   technology, i.e., drugs, medical devices, and new methods or techniques to diagnose and

treat medical disorders. The life cycle of any new medical technology generally

originates in a laboratory, after which the new medical technology undergoes several

phases of investigation to prove its safety and efficacy. Once a sufficient body of

evidence has been amassed to assure such safety and efficacy, the new medical

15   technology is sent before a regulatory committee for review. If the medical technology is

subsequently approved, it can then be marketed for sale and sold, enabling the companies

investing in that new medical technology to begin to realize the return on their investment

in the development of the new technology. The life cycle for most of the new medical

technology is lengthy; for example, as of 1997 the process of developing a new medical

20   technology from laboratory to marketing took an average of 10 to 12 years.

Over the past decade a new industry has arisen as an adjunct to the clinical

research process of developing new medical technologies. R&D service providing

organizations, known as Contract Research Organizations (CROs) arose out of a growing

need among the pharmaceutical and biotechnology companies to curb costs. Rather than

25   hiring full-time research staff, companies turned to CROs as a resource for these

companies to outsource the administrative and coordinating responsibilities for clinical

research. Over time CROs compounded other value-added services to encompass a

spectrum of services, including clinical trial coordination, monitoring of data collection,

identification of quality research trial investigators and sites, and centralized laboratory

testing. The development of the CROs was also logical for other reasons, including the favorable implications for the pharmaceutical and biotechnology companies to have their new medical technology tested under the unbiased eye of a third-party organization.

5   One of the greatest claims made by the CROs is the ability of their trained staff professionals to shorten the amount of time required to complete a research project, which would in turn shorten the amount of time required to pass regulatory scrutiny. As can be recognized from the protracted 10 to 12 year development period described above, such shortening of the life cycle time is very desirable for most pharmaceutical and biotechnology companies. This is especially true because while a newly invented drug or

10   medical device may be patented upon discovery, with the 20 year patent term commencing on the date of filing of the patent application, such new medical technology does not become profitable until it is approved, marketed, and sold. Thus, if as described above, it can take 10 to 12 years for the new technology to become profitable, there will only be a limited portion of the patent term remaining.

15   It is not inconceivable that after spending millions on R&D and after facing a tough regulatory approval process, a pharmaceutical or biotechnology company would have but 2 to 5 years of exclusivity to exploit the exclusion sale of the new medical technology. Such outcome is ultimately detrimental: it discourages R&D in the medical field, encourages hasty clinical research to expedite the regulatory process, and places

20   smaller to mid-sized companies at a distinct disadvantage to the established "health care giants." The protracted pre-marketing time, particularly in the United States, has also been criticized as being a barrier to the passage of vital new medical technologies. In many cases, life-saving drugs can only be obtained in settings of research or in markets outside the control of the United States government.

25   Despite the emergence of the CROs, their services are still severely under utilized. It is estimated that in the United States less then 20% of the medical R&D market is captured by the CROs. These figures are far smaller outside of the United States, particularly in Europe and Japan.

Life Cycle

Typically, a clinical trial is carried out in the following manner: At the initiation of a clinical trial, the company sponsoring the trial or the CRO contracted for the trial (the "sponsor") will select a number of trial investigators. These trial investigators are usually

5   doctors who specialize in the area of medicine relevant to the new medical technology under study. The trial investigators are chosen based upon several criteria, including:

1) The number of trial participants seen and the ability of the trial investigator to accrue trial participants into the study.

2) The facility and support staff available to the trial investigator.

10   3) The trial investigator's ability to collect and maintain data in a secure fashion without compromising trial participant confidentiality or care.

A trial protocol will be formulated to achieve the desired goals of the trial, and the protocol will be presented for review and approval before an Institutional Review Board (IRB). The IRB is a committee consisting of peers and people with experience in the

15   research field. It may consist of physicians, nurses, PhD's, bio-statisticians, bio-ethicists, and/or others qualified to evaluate research on human. The IRB evaluates research protocols to assure scientific integrity while maintaining the trial participants' safety and privacy within a standard of ethics acceptable for human experimentation. Once a clinical trial is under way, the trial investigators do the following:

20   1) Begin recruiting trial participants that fit the inclusion/exclusion criteria of the protocol.

2) Explain the risks and benefits of the trial to the trial participants.

3) Ask the trial participants to give an informed consent.

4) Apply new medical technology, i.e., administer medical treatments.

25   5) Initiate and continue trial data collection.

The trial data is collected by the trial investigators in the form of reports that are then forwarded to the sponsor. Reporting generally takes the form of paper sheets that are handwritten and transmitted via fax or placed into digital form with the use of an

electronic scanner. These reports generally serve as the data collection vehicle with various parameters studied as outlined in the particular protocol. The parameters studied in a clinical trial may include subjective findings such as trial participants' complaints, satisfaction, or symptoms. Objective parameters may also be studied, which parameters

5   include physical examination, laboratory or radiological tests, and other measured findings. Finally, a separate parameter followed in almost all trials is incidence of adverse events or complications from the treatment.

In the course of a clinical trial, an important responsibility is that of a trial monitor. The trial monitor is a person who is usually hired by a CRO to verify that the

10   data reported by the trial investigators corresponds to the source documentation, i.e., the trial participants' clinic records. The trial monitor serves as an auditor of the trial investigators to police the integrity of the data collected. The trial monitor also assures that all documentation, such as each trial participant's informed consent, is properly signed and that the trial investigators stay true to the procedure set forth in the trial

15   protocol. The trial monitor also checks to assure that the reports forwarded to the sponsor correspond to the actual medical records documented by a trial investigator in a trial participant's chart.

As the clinical trial progresses, the sponsor is made cognizant of the overall status of the trial. For example, if an inordinate number of complications arise from the medical

20   treatment, it is the sponsor's responsibility to know of the problem and to react. Sometimes such reactions may prematurely halt the trial. Conversely, it is not uncommon for the new medical technology to be so effective that the reaction and the responsibility of the sponsor is to offer the new medical technology to more trial participants.

At the end of the trial, a stage of trial "closing" is conducted. During this stage all

25   reports are finalized and any missing data is reconciled by the trial investigators. After this, the sponsor consolidates the data collected during the trial for statistical analysis. The results of such analysis are then made available for reporting to the regulatory bodies and/or academic publishing.

Detriments

There are many instances where the life cycle described above falls short of its optimal potential. In fact, negative reports and issues of the shortcomings of medical R&D are in the news daily. In January 2000, all human gene therapy experiments carried

5   out at an Ivy League university and sponsored by the United States government was halted after the death of a trial participant. After further review, there was evidence that the trial participant was not provided proper informed consent. In addition to simple human error, there are ample situations where monetary pressure may lead to potential fraud by the trial investigator and/or the sponsor. Such fraud may include the falsification

10   of the trial data, loose interpretation of the trial protocols to allow into a study trial participants who may not be proper candidates, statistical manipulation to allow results to appear better than actual, under-reporting of adverse events, etc. There have even been situations where an entire group of trial participants reported upon in the trial, did not even exist.

15   In the early 1990's the National Surgical Adjuvant Breast and Bowel Project ran a clinical trial evaluating benefits of performing mastectomy for trial participants with breast cancer versus lumpectomy with or without radiation. During this trial, one of the site directors, the equivalent of the trial investigator, falsified the dates of certain events of the trial, in order to allow ineligible trial participants to appear eligible for the research.

20   This ultimately resulted in a massive government investigation costing millions of dollars, a delay in the availability of the trial results affecting thousands of patients with breast cancer, skepticism concerning the trial results, loss of the trial investigator credibility, and the derailment of the careers of several prominent academic figures.

The potential for similar situations to recur forces the increased stringency of

25   regulatory processes, thus adding to the already long life cycle period required before marketing and sale of the new medical technology.

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Consent

It should be noted that in the life cycle of performing clinical research, the solicitation of the proper informed consent from the patient is a critical part of meeting ethical and legal standards. Informed consent is a major area of fraud and error during

5   the clinical research process. These errors and instances of fraud relate to several major areas which include episodes where:

1) The research investigator (typically the doctor responsible for the trial) does not explain the content of the informed consent document for which the patient's signature is solicited;

10   2) The occurrence of informed consent is backdated;

3) The patient's or investigator's signature is forged on the informed consent.

Recently the U.S. government has initiated steps to assure better patient safety for enrollees in clinical research projects. At the forefront of this initiative is the implementation of strict guidelines for the execution of informed consents. These

15   guidelines would include intervals during the clinical trial for which the informed consent would be required, or triggering events during the clinical trial process that might alter the implications of trial enrollment for the patient, i.e., the occurrence of adverse events. Additionally, the government will enforce serious penalties for failures to obtain the proper informed consent, including fines of $250,000 per individual and $1 million per

20   institution.

In another governmental initiative the Food and Drug Administration (FDA) laid out guidelines that clearly define the manner in which electronic records can be signed using at least two distinct tokens, such as a user name and password 21 C.F.R. § 11.200(1) (2000). The prerequisite to the use of an electronic signature, however, is that

25   the organization assigning the electronic signature has verified the identity of the individual 21 C.F.R. § 11.100.(b) (2000).

With the proliferation of electronic data collection in clinical research there is and will continue to be an exponentially increasing need for the use of electronic signatures. This increase makes the collection of physical signatures and verification processes

unrealistic, especially in cases where geographically broad populations of users must be quickly granted access to a particular system

Evolution

In view of the pressures placed upon the sponsors in terms of time expenditure

5   while sustaining the scientific rigor, several CROs and industry specialists have begun implementing digital formats for data collection. Digital data collection and collaboration of research over digital networks have the potential for multiple advantages. These advantages include the ability to consolidate the trial data into a single database as the trial data is being collected, thus allowing for the analysis of data in real time. In

10   addition, data can be validated upon entry, ultimately resulting in less time spent at the end of the trial to reconcile "loose ends" in the data collection process. These and other advantages of electronic data collection are clearly superior to conventional methods of handwritten forms, scanning, and faxing. However, many concerns still exist over issues of data security, trial participant privacy, and veracity of the collected data.

15   Furthermore, while electronic data collection has the potential to improve upon the time expenditure in the clinical trial process, it does not resolve the need to vigorously monitor the trial for fraud. In other words, while the electronic data collection makes the clinical trial process faster, it does not improve the scientific rigor with which the trial investigators collect and report upon the trial data.

20   In any clinical research setting the key event leading to the generation of data is that between two individuals: the trial participant, e.g., a patient, and the trial investigator, e.g., a doctor. In conventional methods, this interaction is the event that is documented in the trial participant's medical records and is a reflection of the trial participant's physical examination, reports of subjective complaints, interpretations of objective testing, and a

25   synthesized analysis of the trial participant's information as a function of the trial investigator's professional training.

The conventional methods of clinical research rely upon a trial investigator's signature on a paper document. This creates ample of opportunity for fraud and an obvious need for strict monitoring. As the clinical research field looks more to digital

30   data capture and transmission, there is a greater need to authenticate the information.

While various methods have been proposed for digital authentication of individuals, what is needed is the authentication that a recorded event occurred in a proscribed manner and was performed by authorized personnel. This event may include the interaction between two or more authorized personnel, such as the doctor and patient. Moreover, such

5   authentication must lead to the acceptance or rejection of the trial data in a clinical study or trial.

SUMMARY OF THE INVENTION

The present invention is a method of conducting clinical trials. Each clinical trial includes members comprising trial administrators, trial monitors, trial investigators, and

10   trial participants or patients. Additionally, these members may include reporters, scientists, and others interested in sampling the results of the study as it progresses. The trial administrator selects the trial monitors, persons responsible with assuring the veracity of the study, and the trial investigators, persons such as nurses and doctors who will actually administer the study or trial. The trial administrator will further define

15   procedural guidelines for the performance of the clinical trial. The trial investigators in turn will select the trial participants or patients to be enrolled in the clinical trial. The trial monitors observe the conduct of the clinical trials to detect any deviations from the procedural guidelines previously established by the trial administrator.

The present invention allows the clinical trial to be conducted over a network, e.g.,

20   the Internet or a telephone grid. The participants use computing devices connected to the network to perform transactions of the clinical trial. Each of the tests comprises one or more periods of execution or intervals, test elements, and a plurality of exception limits. All the trial participants are listed in a database and are assigned access and validation levels. The clinical trial is performed according to the procedural guidelines by carrying

25   out all of the transactions of the clinical trial. The executed transactions are stored in a database. Any time during the performance of the clinical trial the stored transactions can be queried at random to assure veracity of the clinical trial and to notify the trial administrator if any discrepancy is found to prevent fraud.

Each transaction of the inventive method is performed by one of the members initiating a session by establishing a data path from a computing device equipped with various authentication hardware and/or software, to the computing device on which the inventive method is implemented. As the connection is established and the member has

5   logged in, the invention determines what level of access is allowed and what level of authentication is required for the logged-in member. After performing the required authentication method, the members who are the trial participants and the trial investigators are shown a plurality of tests to choose from. When the required test is selected, the trial data entry may begin.

10   The trial participants and the trial investigators are asked to reply to a plurality of questions or enter information corresponding to various elements of the test. Each of the entered values is immediately evaluated to determine if values entered are outside of the exception limits. The exception limits may be default or custom set by the trial administrator. If the exception limits are exceeded, the trial participants and the trial

15   investigators are asked to verify if the values are correct.

The login authentication process initiates or starts the clock running on a time range within which data entry or the current session must conclude. In situations where the interaction of the members of the clinical trial is authenticated, the login authentication process may include the input of more than one authorized personnel or

20   member of the clinical trial during the established time range. Regardless of the number of authenticated parties or members of the clinical trial, the data entry may occur as follows:

1) before the authentication of all necessary parties or members of the clinical trial;

2) sandwiched in between authentications, e.g., at least one authentication followed by

25   data entry which is followed by at least one authentication or re-authentication, and so
           on; and/or

3) after the authentication of all necessary parties or members of the clinical trial.

Transactions failing that test may not be committed to the database, i.e., the results will be discarded.

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After logging in, the members who are the trial monitors and the trial administrators may be allowed to execute various reports and queries on the information collected by the clinical trial up to date. Such reports and queries may assist these members in assuring that the clinical trial adheres to its procedural guidelines and

5   therefore the data collected is beyond reproach.

BRIEF DESCRIPTION OF DRAWINGS

The foregoing objects and advantages of the present invention may be more readily understood by one skilled in the art with reference being had to the following detailed description of a preferred embodiment thereof, taken in conjunction with the

10   accompanying drawings wherein like elements are designated by identical reference numerals throughout the several views, and in which:

Figure 1 is a network topology diagram, showing connectivity of various parts of the system of the present invention.

Figure 2 is a diagram of the hardware components of computing devices used by

15   the system of the present invention.

Figure 3a is a flow diagram of a database entry program of the present invention, used to populate the application database.

Figure 3b is a logical relationship design diagram of elements comprising the records of the application database.

20   Figure 4a is a sample login screen for gaining access to the clinical trial management program of the present invention.

Figures 4b-4f are a sample screen of the clinical trial management program listing various test and intervals at which these tests are to be performed.

Figure 4g is a sample report screen of the clinical trial management program

25   listing for the trial monitor various information indicating test performance status.

Figure 5 is a flow diagram of the clinical trial management program of the present invention.

Figure 6 is a logical relationship design diagram of elements comprising the records of the trial database and their relationship to elements of the application database.

Figure 7 is a flow diagram of the informed consent with biometric authentication.

Figures 8a-8c is a sample informed consent form.

5   Figure 8d is a display of a log of informed consent use during the execution of the trial.

Figure 9 is a flow diagram for utilizing an electronic signature without the use of the paper signature.

DETAILED DESCRIPTION OF THE INVENTION

10   As shown in Figure 1, the inventive system 10 comprises computing devices 14, i.e., 14a, 14b, 14c, for use by trial participants and trial investigators, computing devices 16, i.e., 16,a, 16b, 16c, for use by trial monitors, a computing device 15 for use by a trial administrator, and computing devices 18, i.e., 18a, 18b, 18c, for use by laboratories to connect via the network 20 to a computing device 12, where the trial management program of the present invention is executed. Computing device 12 maintains and

15   utilizes databases 11 which include an application database 11a for defining trials, i.e., scopes of studies, a personnel database 11b for defining persons authorized to access the inventive system residing on computing device 12, and a trial database 11c for saving and maintaining information collected with reference to the trials of the applications database

20   11a. The databases 11 do not have to be physically distinct, any distinction is made herein only for the purpose of clarity of description; in fact these databases 11 may be subdivided into more discreet units. Computing device 12 gathers the trial data submitted through computing devices 14 and 16 for the purpose of collecting that information in the trial's database 11c. The network 20 may be any type of a network, including a telephone

25   network, a local area network, e.g., the Intranet, and a wide area network, e.g., the Internet.

The computing devices 12, 14, 15, 16, and 18 may take the configuration of any computer ranging from mainframes and personal computers (PCs) to digital telephones

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and hand held devices, e.g., PALM PILOT™ personal assistance devices. In one illustrative embodiment of this invention shown in Figure 2, such a computing device may comprise a bus 30, which is connected directly to each of the following: a central processing unit (CPU) 32; a memory 34; a system clock 36; a peripheral interface 38; a

5 video interface 40; an input/output (I/O) interface 42; a communications interface 44; and a multimedia interface 46.

The common bus 30 is further connected by the video interface 40 to a display 50; by the I/O interface 42 to a storage device 52, which may illustratively take the form of memory gates, disks, diskettes, compact disks (CD), digital video disks (DVD), etc.; by

10 the multimedia interface 46 to any multimedia component 56; by peripheral interface 38 to the peripherals 58, such as the keyboard, the mouse, navigational buttons, e.g., on a digital phone, a touch screen, and/or writing screen on full size and hand held devices, e.g., a PALM PILOT device™; by the communications interface 44, e.g., a plurality of modems, to a network connection 60, e.g., an Internet Service Provider (ISP) and to other

15 services, which is, or are, in turn connected to the network 20, whereby a data path is provided between the network 20 and the computing devices 12, 14, 15, 16, and 18 (Figure 1) and, in particular, the common bus 30 of these computing devices; and furthermore, by the communications interface 44 to the wired and/or the wireless telephone system 54.

20 **Defining Trial Data**

Before clinical trials are carried out they are defined by values that may be placed into the application database 11a (Figure 1). The entity, person, or persons creating, authoring, or instigating the trial driven by the inquiry into the hypothesis under study in a particular clinical trial is (or are) called the trial administrator. The trial administrator

25 defines every aspect of any clinical trial, which may be administered by the inventive system.

Each aspect of the clinical trial of the inventive system is defined by one of a series of database tables 70, shown in Figure 3b. These tables 70 may be developed and managed with the help of any modern database management software, such as ORACLE,

30 SYBASE, MICROSOFT ACCESS™, and others. After being defined, the tables 70 are

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stored in the application database 11a (Figure 1). Each of these tables 70 references other tables 70 by the virtue of a relational architecture.

The inventive system provides a method to enable the creation of the tables 70 to define the anticipated application data. The hierarchical sequence of the method is shown

5   in Figure 3a. There, in step 172, the table defining parts of a clinical trial 72 (Figure 3b) is defined, including the structure of the trial, i.e., randomized, prospective, placebo-controlled, etc.; and the number of patients or trial participants to be enrolled in the trial.

Each of the records entered into the table 72 (Figure 3b) would then be further defined in other related tables in the database 11a (Figure 1). Thus, at step 174 the time

10 intervals table 74 (Figure 3b) comprises timing information regarding individual tests, which may be defined, for example:

1) the actual intervals of the study;

2) the margin of flexibility allowable in defining the time intervals; and

3) the test determinations made at each interval.

15   The tests table 76 (Figure 3b), in turn, is defined in step 176 by listing the tests, e.g., the blood; the urine; the weight; and a quality of life questionnaire, to be performed and replied to. Elements of each test 76 may be further defined in step 178 in the elements table 78 (Figure 3b), which may comprise test parameters such as:

1) test name;

20 2) upper and lower limits of normal;

3) informed consent requirement, i.e., in response to adverse event tests;

4) normal rates of change;

5) optional versus mandatory status of the test;

6) the type of data entry required, i.e., date, number, Boolean, text, etc.; and

25 7) the data entry vehicle used, i.e., checkbox, text field, a pointer to a data file such as a
        music format or a digital image, or an interfaced piece of hardware utilized to obtain
        data.

Each test element 78 (Figure 3b) may be determined to have particular exceptions. Exceptions are values or data points entered outside the predefined protocol intervals and tests. They are implemented in order to handle data for patient complications or adverse events, or other points of planned or unplanned data entry. In other words, exceptions are

5   a determination by the trial administrator of what is to be considered abnormal, e.g., body temperature below 96° or above 106° Fahrenheit. In step 180 exceptions 80 (Figure 3b) will be defined for each data element 78 of each test 76 (Figure 3b) calling for such exceptions. Not every element 78 or test 76 may require an exception.

The present application enables each part of one of the clinical trials in tables 72

10   (Figure 3b) as defined by its elements in related tables 78 to be reusable, i.e., may be used to perform multiple clinical trials. In this manner, basic elements commonly found in clinical trials could be made available in a custom generated clinical trial. For example, the trial administrator trying to create a clinical trial may be presented with a panel of trial parts such as patient, doctor, blood test, heart exam, etc. Any trial element may be

15   incorporated into a trial in a "drag-and-drop" or other fashion.

The trial administrators desiring to create or design clinical trials may do so by establishing a data path from the computing device 15 (Figure 1) to the computing device 12, via the network 20 to access the clinical trial management program of the present invention. This can be accomplished by using an Internet-based browser program, e.g.,

20   Microsoft EXPLORER™ or Netscape NAVIGATOR™. After connecting to the computing device 12 (Figure 1), and entering the username/password combination 100, on the login screen 102 of the inventive system as shown in Figure 4a, the trial administrator may create a new trial and begin defining the various elements of the trial. Furthermore, although after the start of the trial modifications may not be accepted, to

25   create new trials the trial administrator may modify and delete any existing trials.

For example, Figures 4b and 4c show the clinical trial 72 comprising intervals 74 and tests 76. When screen buttons 104 are clicked, further components of the trial record 72, e.g., test elements 78 (Figure 3b) and the exceptions 80 (Figure 3b) may be displayed. Description "done" 106 indicates that the particular test 76 for the particular interval 74

30   has been performed.

Defining Personnel Data

As part of development of the clinical trial, the trial administrators will be able to establish or modify an existing list of trial investigators and trial monitors in the personnel database 11b (Figure 1) for the particular trial being developed. Moreover, the trial

5   investigators will be able to enter into the personnel database 11b (Figure 1), lists of names of trial participants/patients selected to participate in the particular study after the trial is developed and is being carried out.

Each entry, i.e., a person's name and pertinent data, of the database 11c (Figure 1) will have an associated set of pre-established permission standards, different permission

10   standards for the trial participants, trial investigators, and trial monitors. These permission standards define the level of access available to each of the trial participants, trial investigators, and trial monitors involved in the trial to the application data in the database 11a (Figure 1), the personnel data in the personnel database 11b (Figure 1), and the trial data in the database 11c (Figure 1). For example:

15   1) The trial participant/patient would have access to subjective questionnaires in the application data in the database 11a (Figure 1) without access to any other data collected by the inventive system.

2) The trial investigator will have access to patient specific information in the database 11c (Figure 1), by patient name and by patient number as well as to summary data

20   within the scope of his or her own results. The trial administrator may also be able to define the type of investigator enrollment, e.g., an open enrollment allowing anyone qualified to act as the trial investigator to sign up or register as the trial investigator in the personnel database 11b (Figure 1).

Alternatively, in an enrollment by invitation only, the trial administrator may choose

25   to develop a trial whereby the trial investigators may have to make a telephone call, e-mail, or mail correspondence to the trial administrator to request and to be furnished the login information. Before furnishing such login information, the trial administrator would update the entries of the personnel database 11b (Figure 1) to give these invited trial investigators access to the inventive system. The receipt of the

30   login information would enable the trial investigator to sign up in the trial investigator

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registration saved in the personnel database 11b (Figure 1) on the computing device 12 (Figure 1).

3) The trial monitor will have access to patient specific information saved in the trial data database 11c (Figure 1) and identified by patient number, i.e., no patient names are revealed.

4) The trial administrator, in addition to full access to the application data database 11c (Figure 1), will have access only to summary data of the trial database 11c (Figure 1) for the entire trial without specific patient information.

Moreover, as shown in Figure 7, all trial participants and all trial investigators are asked, in steps 90 and 92 respectively, to provide a baseline biometric reading, consisting of one or more of voiceprint, fingerprint, iris scan, electronic signature or other biometric modality, along with one or more identifiers such as their name, a user name and password combination, etc. The identifiers may be entered into text boxes on the computer screen. The provided biometric information and identifiers are then permanently recorded into the biometric consent database 94. This information may also be recorded, along with a database identifier that relates the patient's biometric record with other clinical research data, in another data repository or within the biometric consent database 94 itself.

This biometric consent database 94 will be used in step 95, during the performance of the trial, described in detail below, to obtain informed consent verified with biometric authentication from the enrolled trial participants and investigators. The informed consent may be requested at any time during the performance of the trial as dictated by the one or more clinical trials the trial participants are participating in, as well as any food and drug administration's rules regarding informed consent.

Performance of Trial

Once the particular trial has been completely defined or created in the application data database 11a (Figure 1), the trial may commence. After the trial is activated, the parameters defining the trial in the database 11a (Figure 1) can no longer be manipulated.

To facilitate creation of new trials, the entire existing trial may be copied to create a new trial and that trial's parameters may be modified.

To run a trial, the trial administrator contracts the trial investigators to select the trial participants and begin patient enrollment and data collection regarding these trial

5   participants. The trial administrator further contracts the trial monitors to monitor the veracity of the trial data. The trial participants are selected, and lists of names of the trial participants are entered into the personnel database 11b (Figure 1). As shown in Figure 7, in step 90 all trial participants, and in step 92 all trial investigators are asked to provide a baseline biometric reading, consisting of one or more of voiceprint, fingerprint, iris scan,

10   electronic signature or other biometric modality, along with one or more identifiers such as their name, a user name, a password combination, etc. The identifiers may be entered into text boxes on the computer screen. The provided biometric information and identifiers are then permanently recorded into the biometric consent database 94. This information may also be recorded, along with a database identifier that relates the

15   patient's biometric record with other clinical research data, in another data repository or within the biometric consent database 94 itself. This biometric consent database 94 will now be used in step 95 to obtain informed consent verified with biometric authentication from the enrolled trial participants and investigators. The informed consent may be requested at any time, as dictated by the one or more clinical trials the trial participants

20   are participating in, as well as any food and drug administration's rules regarding informed consent.

At this point the clinical trial management program of the present invention, shown in Figure 5, may read in the parameters of the trial established in the application data database 11a (Figure 1) and automatically generate the appropriate questionnaires

25   and forms to allow the trial participants of the trial to fill in the results of tests 77 (Figure 4f).

As shown in Figure 5, the clinical trial management program 200 may be accessed by authorized personnel in step 202 through the login screen 102 (Figure 4a). In step 204, judging by the login and determining the level of access through the use of the personnel

30   database 11b (Figure 1), a determination is made of what level of authentication should

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be performed, or whether authentication is necessary all together. It may be determined
that further or additional authentication is required, such as biometrics authentication of a
single or multiple trial participants, e.g., in situations where the authentication is used to
guarantee the physical interaction between a trial investigator and a trial participant. In
5   such a case authentication steps such as biometrics, e.g., iris or finger print scan, facial
recognition, voice print, retinal scan, facial recognition, etc., and/or DNA authentication,
e.g., the blood, urine, hair, saliva, tissue sampling, etc., in step 206 or other, e.g., entering
social security number, special ID codes, in step 208 may be required before proceeding.
Please note that the authentication may be performed on the individual members of the
10   clinical trials, e.g., the trial investigators and the trial participants; or on the plurality of
members of the clinical trials concurrently, e.g., a plurality of the trial investigators, a
plurality of the trial participants, a combination of the trial investigators and trial
participants.

The concurrent authentication of a plurality of members is utilized by the present
15   invention in situations where the authentication is used to guarantee the physical
interaction between the trial investigators and the trial participants.

The authentication tests may use flexible timeouts defined by the trial
administrator for single and multiple interactive sessions with the trial participant.
Moreover, these sessions are location independent. Each computing device 14, 15, 16,
20   and 18 (Figure 1) used in the authentication may be identified by a unique identification
number, therefore the physical location of such components need not be fixed for the
authentication purposes.

As described above, the preferred embodiment of the present invention
contemplates but is not limited to personnel with predefined purposes. Accommodation
25   of personnel for many diverse purposes, e.g., television, magazine, and newspaper
reporters, colleges, hospitals, competitors, statisticians, insurance companies, etc., not
described in the preferred embodiment may be easily provided by the inventive system
and may be as easily created by these skilled in the art.

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By Participants or Investigators

After logging in step 202 and being authenticated in steps 206 or 208, in step 210 the trial investigators and the trial participants will be shown a list of possible tests 72 (Figure 4c). After selecting a particular entry 76a (Figure 4c) from the screen 72 (Figures

5   4c), the trial investigators and the trial participants are presented with trial data entry screens, e.g., 76a-c (Figures 4d-4f).

However, before allowing the entry of the test result data in step 212, the program 200 may determine in step 211 that an informed consent is required before the trial data for the selected test is accepted. The trial investigators or participants are then presented

10   with the informed consent screen or document in step 95. As shown in Figure 7, the trial investigators and participants will be asked in step 96 to review the consent document along with any necessary supporting documentation. This may be performed by presenting the informed consent document and supplemental information to the patient on the computer screen. A sample Informed Consent Document 300 is shown in Figures 8a-

15   8c.

In step 97 the trial investigators and the trial participants will indicate their agreement with the informed consent document either by typing their agreement into a text box on the computer screen or interacting with the clinical trial management program 200 (Figure 5), for example, by checking a checkbox or clicking a button. In step 98, the

20   trial investigators or the trial participants will then reenter any identifiers entered and saved in the biometric consent database 94 and perform a biometric authentication. The clinical trial management program 200 requires that both the trial investigator's and the trial participant's authentication be performed on the same computing device and within a pre-set period of time, for example, 30 seconds, which insures that the trial investigator

25   and the trial participant have interacted and the consent was given by the trial participant in the presence of the trial investigator. The identifiers and biometric data are compared to the data recorded in the biometric consent database 94 and if they are matched successfully, the successful informed consent agreement is permanently recorded in step 99 in the consent database 94.

Electronic Signature

An additional precaution taken by the inventive system in ascertaining the identity of the trial investigators and participants is the use of the electronic signature 302 (Figure 8c) to verify the consent form 300 electronically. Figure 9 shows a process 310 for

5   providing means to securely grant access via electronic means of communication, to users who are unknown and initially "not trusted", i.e., any information entered by unknown users can not be used for subsequent analysis by a central organization. Thus, all needs for paper document, e.g., informed consent, transmission, subsequent storage, geographic proximity and/or travel are eliminated.

10   Traditionally, the first step in assigning an electronic signature for clinical research that will undergo the FDA approval has been a paper-based signature. In that step the user agrees to the following:

1) To use the electronic system appropriately; and

2) To the fact that their electronic signature will be legally binding and a substitute for

15   their physical signature.

The second step is for a member of the authorized organization that is assigning the electronic signature then physically verifies the identity of this person as well.

In step 312 an unknown user performs the requisite first step by agreeing with a trusted entity by using a single public token. The public token is a unique identifying

20   information associated with the users when they interact with the system, i.e., their username. In step 314 the trusted entity accepts and processes the user provided public token. The trusted entity is a human or electronic system that resides within a trusted and closed area defined by an electronic data collection system, such as the present invention. Furthermore, the public token could be a biometric identification, such as a fingerprint or

25   iris scan. A non-biometric public token may be told to or intercepted by any 3rd party at any time without exposing the trusted system to infiltration.

In step 316, a secret token is then generated by the electronic system from the accepted public token. This secret token may be in the form of a simple text token, e.g., a password, or a more complex secret token, such as an encryption key. This secret token

is then transmitted, by public means, and is received by the user in step 318. The public means may include a telephone line, e-mail, fax, etc. In step 320, the secret token is stored by the trusted entity along with the user's public token.

Having received the secret token, in step 322, the users electronically identify
5   themselves to the system. Their identification includes their public and secret token and any additional information that the organization may require, for example, the user's full name and contact information could be collected at this time.

In step 324, the system confirms that the entered secret token matches the public token. If it does, a notification is sent to the user by either the same or alternate
10   transmission means confirming that they may access the system. This transmission does not contain any public or secret token information.

Having received the notification, in step 326 the users may be requested once again to electronically identify themselves to the system using their public and secret tokens. After one or more such interactions, in step 328 the system may generate a new
15   secret token or automatically prompt the users to create new secret tokens themselves, e.g., "Please choose a new password." This new secret token is then securely stored in the system and becomes the users second or private token for access. The user is now considered trusted and research data can be collected.

As set forth in Figure 5, the trial participants start to enter test result data in step
20   212. The test screens 76a-c (Figures 4d-4f) are dynamically generated by the clinical trial management program 200. In step 210 the actions required, i.e., defined in the application data database 11a (Figure 1), are evaluated and only these required are presented. Furthermore, data entered in response may lead to additional options to be displayed. Actions that have been previously completed are displayed as such, giving
25   instant feedback regarding what was previously entered into the system.

Of course, if after glancing at the list of required actions displayed in step 210 the trial investigator or the trial participant decides not to proceed, in step 214 a logout path may be taken. An in-depth description of the logout procedure will be discussed below.

A transaction of the clinical trial management program 200 begins following the login in step 202 and the authentication in step 204. All the information entered during the session after the login and before the logout is considered a part of this transaction. The transaction will not be committed, i.e., be made a part of the permanent storage 52

5 (Figure 2) until the whole session is completed. As data elements 77 (Figures 4d-4f) are entered in to the test screens 76a-76c (Figures 4d-4f), the clinical trial management program 200 dynamically executes scripts to perform the first level of validation of the data values 77 (Figures 4d-4f) entered. The executed scripts may validate entered data values 77 (Figures 4d-4f) and may be executed by the browser program, e.g., Microsoft

10 EXPLORER or Netscape NAVIGATOR, using its built-in functionality on the computing devices 14, 15, 16, and 18 (Figure 1). Moreover, the executed scripts may validate entered data values 77 (Figures 4d-4f) on the computing device 12 (Figure 1) to provide two levels of data validation.

These scripts compare the values 77 (Figures 4d-4f) entered, with previously set

15 exception limits 80 (Figure 3b) defined in the application data database 11a (Figure 1). In the event where an entered value is outside of these exception limits the inventive clinical trial management program 200 will alert the trial investigator or the trial participant entering the data values 77 (Figures 4d-4f) and may request or require additional data to be entered. For example, a confirmation dialog, to insure that the out-of-range value is in

20 fact correct will be interposed in step 216 and the trial investigators and the trial participants may be asked or forced to reply before proceeding.

After all the test values 77 (Figures 4d-4f) are completely filled in, step 216 saves these values 77 (Figures 4d-4f) in the current transaction, executes the scripts to perform the second level of validation as described above. The values 77 (Figures 4d-4f), entered

25 for each element are once again compared with the exception ranges 80 (Figure 3b) and with the acceptable data change rate. The data change rate is determined by comparing values 77 (Figures 4d-4f) to those entered for the same element at previous intervals. Should the values 77 (Figures 4d-4f) be either out of the exception range 80 (Figure 3b) or change at a rate beyond the preset exception change rate for the given element, an

30 exception record 270 (Figure 6) is added to the current transaction.

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In step 218 it is determined if one or more exceptions are generated at the given

interval for the given element. If exceptions are generated, in step 219 the trial

investigators and participants may be asked to review and sign the consent documents

along with any necessary supporting documentation and indicate their agreement with the

5   informed consent document as described above with reference to step 95 (Figure 7) and

described in detail above. After the consent is given in step 95 or if consent is not

required as determined in step 219, an exception record causes new tests to be added to

the trial participant's complete trial record in step 220 as well as the elements within that

new text that must be completed to close the trial participant's participation in the trial.

10   At this point it is possible to offer an option of completing the exception data immediately

or to queue the exception for completion at a later time.

If in step 222 it is determined that the exception is to be completed now, the test

form for the exception is presented and the data entry loop starting in the step 212 is

repeated. Otherwise, in step 224 the exception is queued, and will then appear in the

15   appropriate data entry options of the step 210.

After values 77 (Figures 4d-4f) in the transaction are saved, and tests generated

from exceptions are completed or queued, the values 77 (Figures 4d-4f) may be stored.

Figure 6b shows the record for storing values 77 (Figures 4d-4f). Each record 270

comprises the following fields:

20   1)   A unique key 270a used to identify the transaction.

2)   A trial key 270b, for pointing to the specific trials table 72 (Figure 6a) of the

application data database 11a (Figure 1) with which the present record 270

identifies or belongs.

3)   An intervals key 270c for identifying the particular interval on the intervals table

25   74 (Figure 6a) of the application data database 11a (Figure 1), which corresponds

to the specific value 77 (Figures 4d-4f) of the present trial identified by the trial

key 270a (Figure 6).

4)   A test key 270d for identifying the particular tests table 76 (Figure 6a) that the

values 77 (Figures 4d-4f) are associated with.

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5)   An element key 270e for identifying or pointing back to the element in the
      elements table 78 (Figure 6a) that the values 77 (Figures 4d-4f) correspond to.

6)   An identification key 270f for identifying the trial personnel who entered the
      values 77 (Figures 4d-4f), such personnel was previously defined in the personnel
5   database 11b (Figure 1) as described above.

7)   A patient identification key 270g associating the values 77 (Figures 4d-4f) with
      the particular trial participant, such trial participant was previously defined in the
      personnel database 11b (Figure 1) as described above.

8)   A date and time created field 270h for storing the year, month, date, hour, minute,
10   second and millisecond that the values 77 (Figures 4d-4f) were recorded.

9)   A data certification code field 270i comprising a plurality of random digits.

The current methods of administering a clinical trial involve monitoring the trial
centers to assure research integrity. The basic role of the trial monitor is to verify that the
data entered by the clinical investigator corresponds to the records taken in the source
15   documentation. The source documentation denotes the trustworthiest record of the data
because it contains records of the interactions between the trial investigator and the trial
participant and the resultant outcome of any tests taken. The source documentation is
held in such high regard because it contains the trial investigator's signature. Usually the
source documentation is regarded as the trial participant's medical chart. The present
20   invention describes a method by which the source documentation can be generated by the
computer application. All new data values entered into the trial database are grouped
according to the date, time, trial participant, computer address, and login episode. For
each and every unit of data entered into the trial database 11c (Figure 1), a multi-digit
unique identification number is generated at random. After each log in episode, the trial
25   investigator's computing device 16 (Figure 1) may print a record of the activities of each
patient handled by the trial investigator during any given login episode. This record will
act as a legal record of the investigator's actions during a log in episode and be clearly
marked with a statement affirming that the investigator has read the record and agrees
with it. The investigator will then be asked to sign the record. The signed record can

then be utilized as the source documentation since it contains a record of patient data with a verifying signature. The document may be appropriately formatted for placement into the trial participant's chart.

Moreover, the inventive method makes the job of the trial monitor considerably

5   easier. Prior to auditing a site where the trial tests are performed, the trial monitor may print out a list of data transactions and corresponding identification numbers. The trial monitor may then make certain that the events documented in the trial investigator's source documentation contains the correct identification numbers.

Since both the investigator source documentation and monitor transaction list are

10   generated from the same server-side database, there is virtually no possibility for fraud or forgery in this. The trial investigator that tries to change the data values or other parameters entered into the database will create a discrepancy between the source documentation and the data transaction list output for the monitor.

10)   A unique identifier field 270j for the identity of the hardware such as the IP

15   address of a network 20 (Figure 1) connection 60 (Figure 2) of the computing

             devices 12, 14, 15, 16, and 18 (Figure 1).

11)   An authentication stamp field 270k generated by the authentication method in

             steps 206 and 208 (Figure 5) for the session in progress.

12)   An actual data record 270l of the 77 (Figures 4d-4f) with data of various types,

20   e.g., text, integer, binary, real, floating, date/time, images, biometrics, etc.,

             keeping their appropriate data type.

13)   Any supplemental data 270m entered along with the values 77 (Figures 4d-4f) as

             defined by the element corresponding to the values 77 (Figures 4d-4f), for

             example, an 'other' field in a multiple-choice question.

25   As shown in Figure 5, in step 216 each record 270 is recorded in the transaction that covers the entire session from login in step 202 to logout in step 214. In step 226 it is determined from the personnel database 11b (Figure 1) or from the application data database 11a (Figure 1) that a logout authentication is required. If authentication is required, in step 228 it is determined which authentication is to be performed, the

biometrics, e.g., iris or fingerprint scan, retinal scan, facial recognition, DNA imprinting

using hair, saliva, etc., in step 230 or other, e.g., entering social security number, special

ID codes, in step 232 may be required before committing the transaction. The

authentication may be performed on the individual members of the clinical trials, e.g., the

5   trial investigators and the trial participants or on the plurality of members of the clinical

trials concurrently, e.g., a plurality of the trial investigators, a plurality of the trial

participants, a combination of the trial investigators and trial participants.

In step 234 it is determined if the required authentication at the end of the session

was properly performed or failed. If the authentication failed, in step 236 the transaction

10   is rolled back and the data does not become a permanent part of the trial data. In the

alternative the transaction may become a permanent part of the trial data with a recorded

indication that the logout authentication failed, or permanently logged outside of the trial

data, however the transaction will be rolled back and the data will not become a part of

the trial data in the trial data database 11c (Figure 1). In step 238, the transaction is

15   committed, i.e., recorded as a permanent record in the trial data database 11c (Figure 1).

Additional determinations may indicate whether transaction comprising the values

77 (Figures 4d-4f) will be rolled back in step 236 or committed in step 238. A session

may end because the timeout period specified for a particular or a group of the trial

participants and trial investigators stored in the personnel database 11b (Figure 1) has

20   been exceeded.

By Laboratories

A particularly useful feature of the present invention is its ability to accept results

for individual trial participants as well as bulk results for groups of trial participants from

laboratories connected by computing devices 18 (Figure 1) to the computing devices 12

25   (Figure 1) via the network 20 (Figure 1) or by a direct digital interface between the

laboratory computing devices 18 (Figure 1) and the computing device 12 (Figure 1).

Where a plurality of samples of the trial participant's specimens, e.g., blood, saliva, or

urine, are tested by a particular laboratory, the results may be securely transferred to the

trial data database 11c (Figure 1). The trial participants' privacy may be maintained by

30   providing the laboratories only with the assigned trial participant unique number. The

laboratory computing device 18 (Figure 1) may then cross-reference the trial database 11c

(Figure 1) using the trial participant unique number and input the appropriate laboratory

test result. This will eliminate the need for human intervention in inputting the test results

and therefore the possibility for human-error or fraud

5   **By Monitors**

As described above, the trial monitor is the entity, person, or persons that

constantly monitor the integrity of the trial insofar as the data entered and the conduct of

the trial investigators and the trial personnel is concerned. The trial administrator often

contracts the trial monitors as part of the CROs or as independent consultants. Typically

10   the trial monitor maintains a record of the activities of the trial investigators and makes

certain that the data submitted by the trial investigator corresponds to the source

documentation, i.e., the patient's medical record. The trial monitor verifies whether the

trial investigator has provided the proper informed consent and that the trial participant's

characteristics conform to the inclusion and exclusion criteria specified in the trial

15   protocol. All consents can be compared with all the exceptions (daily, weekly, monthly,

per trial) to assure that all the consents were accepted when required. Trial monitors will

perform declared and undeclared visits to the trial investigator sites to audit the operations

of the trial investigator in-person.

The inventive system may provide the trial monitor with access to limited

20   information in the trial data database 11c (Figure 1). While the trial monitors may be free

to view all trial participant information from the personnel database 11b (Figure 1), they

may not be able to identify these trial participants except by a unique code assigned to

each trial participant for purposes of the trial. Upon entering the inventive system in step

202, the trial monitor may be asked to authenticate himself or herself in steps 206 or 208.

25   This authentication is accomplished using either a form of biometrics measurement in

step 206 or by username and password method in step 208. Once the trial monitor is

properly logged into the application running on the computing device 12 (Figure 1), they

will have access to the entries of the trial participant related data stored in the personnel

databases 11b (Figure 1) and in the trial data database 11c (Figure 1) referenced

30   according to specific trial investigators. In step 240, the trial monitors will be able to get

complete reports of transactions performed by individual trial investigators, e.g., 84

(Figure 4g), identified by data stamps including the following:

1) date and time of patient visit 86 (Figure 4g);

2) interaction and data entry 88 (Figure 4g);

5   3) Internet protocol address from which data was entered (not shown);

4) trial investigator identification 90 (Figure 4g); and

5) a unique encryption stamp for each transaction 87 (Figure 4g).

These reports may be created for each trial participant according to each time

point, of the intervals 74 (Figure 3b), tracked as per the trial protocol. Furthermore, these

10   reports may enable the trial monitor to verify the trial investigator's source documentation

against the data shown in the report. Separate reports may be generated for data that is

missing, entered late, changed by the trial investigator, or is out of range.

This may allow the trial monitor to address each specific issue with the trial

investigator and to reconcile the problem in the trial data. Separate reports may further be

15   generated for every adverse event reported by the trial investigator. Each report may list

the adverse event and the follow-up necessary to be performed by the trial investigator in

order to document the ultimate consequences to the trial participant.

Summary reports of the trial monitor's verified values 77 (Figures 4c-4f) may be

generate each time a trial monitor completes a review of either a single test element 78

20   (Figure 3b) or group of tests 76 (Figure 3b). The verified values 77 (Figures 4c-4f) will

also be associated with identifying stamps such as date, time, trial monitor's biometrics

authentication, etc. This report may ultimately be printed for approval by the trial

investigator and signature.

By Administrator

25   The trial administrator may be given special access to certain forms of data while

being restricted to others. For example, while the trial administrator may be able to view

overall summary data about a trial, they will be unable to access patient-specific

information in order to maintain patient privacy.

The application will have special functions available to the trial administrator. In general, the trial administrator will be able to have a real-time "bird's eye view" of the ongoing clinical trial. After logging in step 202, the trial administrator will be asked to authenticate himself or herself as described above with reference to steps 204, 206 and

5   208. In step 242 the trial administrator will be enabled to obtain summary data of the trial and application-specific tools to allow manipulation of the summary data.

General functions available to the trial administrator could include summary information, analysis tools, and reporting tools. A summary information area allows the trial administrator access to updates on the status of various trial investigator sites. In

10   doing so, the trial administrator is able to see the performance of each trial investigator via parameters such as the number of patients enrolled or the number of completed patients or the number of delinquencies or the number of adverse events or by the answers to satisfaction-questionnaires about the trial investigators rated by patients/trial participants.

15   Analysis tools may also be available to the trial administrator such that raw summary data representing the current state of the trial will be able to be manipulated. For example, the trial administrator may be able to apply various statistical analysis functions, i.e., averages, standard deviations, control for data variables, etc., to generate graphs and charts. The trial administrator would also be able to use analysis tools to

20   compare two or more trial investigator sites in terms of performance and view the results in graph or chart format.

Reporting tools may be provided such that the trial administrator can generate reports. For example, a pharmaceutical company testing a new drug may want a report that conforms to the outline of a new drug application; the trial administrator, for

25   academic reasons might want a report that is later submitted as a clinical paper to a medical journal. Templates for various kinds of reports will be available to the trial administrator. The trial administrator will be able to customize their own template, which may consist of a series of headings and hierarchical subheadings to format a document. The reports created may be integrated with the analysis tools such that graphs generated

30   dynamically from the trial data will be incorporated into the report. The application will

allow for collaborative authoring and tracking of a document using a system by which parts of a document may be "checked-in" or "checked-out" by multiple trial administrators. The reports created will be able to be output in multiple formats compatible with other word processing software or document readers, i.e., Adobe

5   Acrobat, or Microsoft Word. Ultimately upon completion of the report, the trial administrator may immediately transfer the document electronically to the end viewer such as a peer review committee or a governmental regulatory board.

Reminders

One of the major components of clinical research is the participation of the

10   patients in performing the chore of replying to subjective questionnaires. These questionnaires typically pertain to issues of quality of life, pain scales, and symptom diaries, to name just a few. In addition, subjects involved in clinical research are often asked to take medications that may require strict doses and regimens for route of administration and frequency of consumption.

15   A major area of deficiency in clinical research is the risk that the patients may forget to take the prescribed medications or answer questionnaires at specified times. This ultimately leads to inaccurate results. Moreover, currently there is no method for instantaneous reporting of events adverse to the patient. Patients are often left to their own initiative to report adverse events that may occur before their next visit to a clinic or

20   a discussion with the trial investigators.

The present invention trains the trial participants to use handheld devices and other electronic data entry clients, such as wireless telephones, to answer questions and to report adverse events. In a fashion described above where the questionnaires are formatted electronically to enable entry of subjective data directly from the trial

25   participants' computing devices 14 (Figure 1) over the network 20, the same can be accomplished with the use of wireless technologies where the computing device 14 is connected to the network 20 or even to the computing device 12 itself via wireless means.

The present invention enables the trial participants equipped with handheld devices to participate in clinical research. During that research, the trial participants may

30   be prompted at specified times, through their hand held devices, to initiate certain health

related activities, such as taking medication. Furthermore, the trial participants may be requested to enter data pertaining to health questionnaires.

5   Using a predefined list of trial participants, and network addresses of the handheld devices or the telephone numbers if these devices are telephones, the present invention notifies or reminds the trial participants to perform a trial-related activity at a specified time. If appropriate the trial-related activity through the handheld device, e.g., filling out an informed consent and signing it using the electronic signature as described above. Questionnaire data may be entered in to the handheld device via a keyboard, by writing on a screen with a stylus, using interactive voice response (IVR) or a voice recognition

10   systems.

Simultaneously, messages are routed to the trial administrator's computing devices 15 (Figure 1), which can also be physically or wirelessly connected to the network 20 or an associated health care provider. For example, if the trial participant is unable to be reached, a message, which can be a beep, a voice message, an e-mail, etc., is sent to

15   notify the trial administrator or the associated health care provider to initiate a search for the trial participant. Alternatively, the trial participant can immediately report any form of adverse event, in which case the trial administrator or the associated health care provider will also be notified. This feature of the inventive system adds to improved patient safety during the research process of the trial.

20   While the invention has been particularly shown and described with respect to illustrative and preferred embodiments thereof, it will be understood by those skilled in the art that the foregoing and other changes in form and details may be made therein without departing from the spirit and scope of the invention that should be limited only by the scope of the appended claims.

We Claim:

1.   A method of assuring an informed consent of one or more trial participants, the informed consent signifying an understanding of aspects of a test of a plurality of tests and an agreement to participate in performance of the test, the plurality of tests is carried out during a conduct of a clinical trial by a plurality of members, the plurality of members including the one or more trial participants the clinical trial being conducted on at least one trial computing device connected to a network via one or more data paths, said method comprising the steps of:

conducting the clinical trial according to established procedural guidelines whereby the one or more trial participants perform the plurality of tests by

providing the informed consent when required,

performing the test;

providing test data to the at least one trial computing device.

2.   The method of claim 1, further comprising the steps of:
establishing the clinical trial by scheduling one or more periods of execution for accepting said test data;

assigning the plurality of tests to be performed during said one or more periods; defining a plurality of elements for each of said plurality of tests; and

identifying a plurality of exceptions for setting limits on said test data.

3.   The method of claim 2, further comprising the step of establishing procedural guidelines for conducting the clinical trial, said guidelines identifying which of the plurality of tests require the one or more trial participants to provide the informed consent.

4.   The method of claim 3, further comprising the step of identifying at least one trial administrator and the one or more trial participants for the conduct of the clinical trial.

5.   The method of claim 4, further comprising the steps of:

detecting discrepancies in said provided test data; and

requesting the one or more trial participants who provided said test data in which discrepancy was detected to provide the informed consent.

5   6.   The method of claim 5, further comprising the step of preventing the one or more trial participants from further participation in the clinical trial if the informed consent was not provided.

7.   The method of claim 6, further comprising the steps of:

alerting the one or more trial participants to perform the test scheduled to

10   be performed during a particular period of execution; and

continuously attempting to reach the one or more trial participants if the one or more trial participants fail to reply.

8.   The method of claim 7, wherein the step of alerting further comprising the step of contacting the participant's computing device by sending a message at a network

15   address of the device and displaying a recorded alerting message when the participant reads the message.

9.   The method of claim 7, wherein the step of alerting further comprising the step of contacting the participant's computing device by dialing a telephone number of the device if the participant's computing device is a telephone and playing a recorded alerting

20   message when the participant answers.

10.   The method of claim 7, wherein the step of alerting further comprising the step of contacting the one or more trial participants' pager by dialing a telephone number of the pager and sending a call back number to the pager and playing a recorded alerting message when the participant calls the call back number.

25   11.   A method of assuring informed consent while electronically conducting a clinical trial, the clinical trial having a plurality of members, the plurality of members including at least one trial administrator, at least one trial monitor, at least one trial

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investigator, and one or more trial participants, the plurality of members using one or more computing devices connected to a network to perform a plurality of transactions of the clinical trial, said method comprising the steps of:

(a) establishing procedural guidelines for the clinical trial;

5   (b) performing the clinical trial according to the procedural guidelines by carrying out a plurality of tests;

(c) detecting a discrepancy in said plurality of tests; and

(d) requesting an informed consent if said discrepancy is found.

12.   The method of claim 11, further comprising the steps of:

10   (e) the at least one trial administrator selecting the at least one trial monitor and the at least one trial investigator;

(f) the at least one trial investigator selecting the one or more trial participants to be enrolled in the one or more clinical trial; and

(g) the at lest one trial monitor observing the one or more clinical trial to detect
15 any deviations from the procedural guidelines.

13.   The method of claim 12, further comprising the steps of authenticating said plurality of members and accepting only these of the plurality of transactions that are performed by said plurality of members that are authenticated.

14.   The method of claim 11, wherein the plurality of members comprises at
20 least one trial administrator, at least one trial monitor, at least one trial investigator, and one or more trial participants, the at least one trial administrator selecting the at least one trial monitor and the at least one trial investigator, the at least one trial investigator selecting the one or more trial participants to be enrolled in the one or more clinical trial, the at lest one trial monitor observing the one or more clinical trial to detect any
25 deviations from the procedural guidelines.

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15.   The method of claim 14, wherein the plurality of members further comprises: one or more reporters; one or more scientists, and one or more publishers.

16.   The method of claim 15, wherein the at least one trial administrator selects said at least one trial investigator according to an open enrollment, in said open enrollment anyone qualified to act as a trial investigator is permitted to register as the at least one trial investigator.

17.   The method of claim 16, wherein the at lest one trial administrator selects said at least one trial investigator according to a by-invitation-only enrollment, in said by invitation only enrollment the at least one trial administrator registers said at least one trial investigator.

18.   The method of claim 17, wherein each said one or more clinical trial comprises:

an identification of the at least one trial administrator, and an identification of the one or more trial participants to be enrolled in the clinical trial;

a schedule of a one or more periods of execution during which period a one or more test values are accepted;

a plurality of tests for each of said one or more periods on said schedule;

a plurality of elements for each of said plurality of tests; and

a plurality of exceptions for setting limits on said one or more test values.

19.   The method of claim 18, wherein each of the plurality of members has an associated set of pre-established permission standards, said permission standards define a level of access by each of the plurality of members to said one or more test values.

20.   The method of claim 19, further including a step of allowing access by the at least one trial investigator to said one or more test values through a use of said identification of the one or more trial participants.

35

21.   The method of claim 20, further including a step of allowing access by the at least one trial monitor to said one or more test values through a use of said identification of the one or more trial participants.

22.   The method of claim 21, wherein said carrying out of the plurality of transactions comprises the following steps:

determining a level of access allowed and a level of authentication necessary for a one or more of the plurality of members performing the plurality of transactions;

performing an authentication method corresponding to said determined level of authentication, each of the plurality of transactions comprises steps performed by said one or more of the plurality of members after said performance of said authentication method;

exhibiting said plurality of tests and said plurality of elements and permitting entry of a one or more test values in satisfaction of said exhibited plurality of elements; and

accepting said one or more test values and determining if said accepted one or more test values are outside of said limits.

23.   The method of claim 22, wherein said authentication uses biometrics and non biometrics methods.

24.   The method of claim 23, wherein if said authentication method fails said plurality of transactions is not permanently stored.

25.   The method of claim 24, wherein if said authentication method fails said plurality of transactions is marked as failed and is permanently stored.

26.   The method of claim 25, wherein said authentication method starts the clock running on a time range within which the plurality of transactions must be carried out.

27.   The method of claim 26, wherein the plurality of transactions is prevented from being carried out if said time range is exceeded, said time range is specified by said at lest one trial administrator for each of said plurality of members.

28.   The method of claim 27, wherein said plurality of elements are

5   dynamically generated for said one or more periods of execution, whereby only these of said plurality of elements that require said one or more test values to be entered are exhibited.

29.   The method of claim 28, further comprising steps of exhibiting a confirmation dialog to insure that said entered one or more test values determined to be

10   outside of said limits are correct, and if not correct then insuring that said entered one or more test values be corrected.

30.   The method of claim 29, wherein said entered one or more test values comprise:

a unique key for identifying a transaction;

15   a trial key for identifying the clinical trial;

a test key for identifying said first test of said plurality of tests of the clinical trial identified by said trial key;

an intervals key for identifying each of said one or more periods of execution of said first test;

20   an element key for identifying each of said plurality of elements;

an identification key for identifying said at least one trial investigator and said at least one trial participant who entered said information value;

a patient identification key for identifying each said at least one trial participant;

a date and time created field for storing temporal values of recording of said

25   information value;

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a data certification code field comprising a plurality of random digits;

a unique identifier field to identify the computing devices; and

an authentication field for identifying said authentication method performed.

31.   The method of claim 30, further comprising a step of producing a plurality
of reports of the plurality of transactions, said plurality of reports are created from said
one or more test values and retrieved according to one or more keys comprising:

a date and time of each of said plurality of transactions;

a network address of the computing devices from which information was entered;

an identification of the at least one trial investigator;

an identification of the computing device on which said plurality of transactions
was entered; and

a unique encryption stamp for each of said plurality of transactions.

32.   The method of claim 31, wherein said step of producing said plurality of
reports enables finding said discrepancy and thereby verify veracity of the one or more
clinical trial.

33.   The method of claim 32, wherein said step of producing said plurality of
reports enables evaluation of performance of the at least one trial investigator.

34.   The method of claim 33, wherein the network is Internet.

35.   The method of claim 33, wherein the network is a telecommunications
network.

36.   A method of authenticating performance of a test and entry of test data
during execution of a clinical trial to guaranty that the test occurred according to
procedural guidelines, included informed consent, and was performed by an authorized
participant, the test being performed and the test data is entered by a plurality of

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authorized participants using a plurality of participant's computing devices into at least one trial computing device executing a trial management program, the at least one trial computing device and the plurality of participant's computing devices are connected to a network, said method comprising the steps of:

5   a)   establishing the clinical trial by

scheduling one or more periods of execution for accepting said test data,

assigning the plurality of tests to be performed during said one or more periods,

defining a plurality of elements for each of said plurality of tests, and

identifying a plurality of exceptions for setting limits on said test data;

10   b)   establishing procedural guidelines for conducting the clinical trial, said guidelines identifying which of the plurality of tests require the one or more trial participants to provide the informed consent; and

      c)   conducting the clinical trial according to established procedural guidelines whereby the one or more trial participants perform the plurality of tests by providing the

15   informed consent when required, performing the test, and providing the test data to the at least one trial computing device.

      37.   The method of claim 36, further comprising the step of assuring authenticity of the informed consent by providing an electronic signature, the electronic signature including a public token and a private token.

20   38.   The method of claim 37, further comprising the steps of:

      examining the test data to detect discrepancies, sufficiency of the informed consent or in the electronic signatures used to guarantee the informed consent;

      requesting a new informed consent to be provided by the authorized participant who provided the test data in which discrepancy was detected; and

25   notifying an administrator in a position to prevent fraud and to determine and prevent danger to the authorized participant.

      39.   A method of authentication of the conduct, recordation, and a plurality of members of one or more clinical trials, the plurality of members including at least one

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trial administrator, at least one trial monitor, at least one trial investigator, and one or more trial participants, the at least one trial administrator selecting the at least one trial monitor and the at least one trial investigator and defining procedural guidelines for the one or more clinical trials, the at least one trial investigator selecting the one or more trial

5   participants to be enrolled in the one or more clinical trials, the at lest one trial monitor observing the one or more clinical trials to detect any deviations from the procedural guidelines, the plurality of members using one or more member computing devices connected to at least one trial computing device via a network to perform a plurality of transactions of the one or more clinical trials, the method comprising the steps of:

10   a)   establishing a plurality of tests and procedural guidelines for each of the one or more clinical trials, each of said plurality of tests comprising a one or more periods of execution, a plurality of elements, and a plurality of exception limits;

        b)   providing to each of the plurality of members a level of access to the test data and an electronic signature, the electronic signature including a public token and a

15   private token;

        c)   performing the one or more clinical trials according to the procedural guidelines and accepting the test data of the one or more clinical trials including informed consent forms, the informed consent forms being signed by the one or more trial participants using electronic signature; and

20   d)   assuring veracity of the one or more clinical trials and notifying the at least one trial administrator if discrepancy is found in the trial data, the informed consent, or in the electronic signatures used to guarantee the informed consent, the at least one trial administrator being in a position to prevent fraud.

        40.   The method of claim 39, wherein the step of providing the electronic

25   signature further comprising the steps of:

                accepting a public token selected by a member;
                generating, storing, and providing to the member a secret token;

accepting said public token and said secret token from said member and confirming trustfulness of said member by confirming previously stored identity information of said member; and

said member selecting a new secret token after providing said public token

5   and said secret token.

41.   A method of authenticating performance and recordation of a transaction during execution of a clinical trial to guaranty that the transaction occurred in a proscribed manner and was performed by authorized personnel members, the transaction being performed by the authorized personnel members from a plurality of computing

10   devices connected to a network by using data entry programs, the transaction being recorded on an at least one computing device executing a trial management program, said method comprising the steps of:

a) establishing in the clinical trial a schedule of a plurality periods of execution during which period a plurality of test values are accepted; a plurality of tests for each of

15   said plurality of periods, a plurality of elements for each of said plurality of tests, and a plurality of exceptions for setting limits on said one or more test values;

b) the authorized personnel members accessing the at least one computing device executing the trial management program and identifying themselves;

c) determining a level of access allowed and a level of authentication necessary for

20   the authorized personnel members;

d) presenting said plurality of tests and said plurality of elements and initiating a timer on a time range within which the transaction must be completed;

e) accepting a plurality of test values in satisfaction of said plurality of elements; and

25   f) recording said plurality of test values of the transaction if the transaction was completed with in said time range.

42. The method of claim 41, wherein said authentication uses biometrics and non biometrics methods.

43. The method of claim 42, further comprising a step of determining if said accepted plurality of test values are outside of said limits.

44. The method of claim 43, further comprising steps of exhibiting a confirmation dialog to insure that said plurality of test values determined to be outside of said limits are correct, and if not correct then accepting a new plurality of test values.

45. A method of authenticating the execution and recordation of at least one clinical trial, said method comprising the steps of:

a) constructing a first database with

a set of first records defining the at least one clinical trial to be executed,

a set of second records defining dates on which tests of the at least one clinical trial will be executed,

a set of third records defining respectively said tests executed corresponding to said dates, and

a set of fourth records defining respectively elements of said tests, said elements are parameters to be tested by the corresponding tests,

b) constructing a second database to list only those trial participants that are permitted to enter and access data of the at least one clinical trial;

c) requesting permission to enter trial data by providing identifying information of said trial participant who will enter said trial data and on whose behalf said data is being entered and comparing said identifying information with the list of said trial participants in said second database and authenticating and permitting entry of said trial data if there is a match;

d) accepting said trial data from said authenticated trial participant, said trial data comprising timing information of duration of entry of said trial data and the parameters to which the trial data relates; and

e) testing said accepted trial data by comparing said timing information of duration

5 of entry and the parameters with those timing information of duration and parameters in the first database and, if there is a match, accepting said trial data.

46.   The method of claim 45, wherein said first database is further constructed with a set of fifth records defining value ranges of said elements, and testing whether the trial data related to the parameters falls within said value ranges.

10 47.   The method of claim 46, wherein said accepted trial data is stored in a third database.

48.   A method of authentication of the conduct and recordation of one or more clinical trials, the one or more clinical trials having a plurality of members including at least one trial administrator, at least one trial monitor, at least one trial investigator, and

15 one or more trial participants, the at least one trial administrator selecting the at least one trial monitor and the at least one trial investigator and defining procedural guidelines for the one or more clinical trials, the at least one trial investigator selecting the one or more trial participants to be enrolled in the one or more clinical trials, the at lest one trial monitor observing the one or more clinical trials to detect any deviations from the

20 procedural guidelines, the plurality of members using one or more computing devices connected to a network to perform a plurality of transactions of the one or more clinical trials, the plurality of transactions being stored in a third database, the method comprising the steps of:

a) establishing in a first database a plurality of tests and procedural guidelines for

25 each of the one or more clinical trials, each of said plurality of tests comprising a one or more periods of execution, a plurality of elements, and a plurality of exception limits and defining in a second database the plurality of members;

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b) recruiting and registering the plurality of members in said second database, each of the plurality of members being assigned level of access to a third database;

c) performing the one or more clinical trials according to the procedural guidelines by carrying out all of the plurality of transactions making up the one or more clinical

5   trials; and

d) querying said third database at random to assure veracity of the one or more clinical trials and notifying the at least one trial administrator if discrepancy is found, the at least one trial administrator being in a position to prevent fraud.

49.   A method of authenticating performance of a transaction during execution

10   of a clinical trial to guaranty that the transaction occurred in a proscribed manner, the transaction being entered through a data entry program executing on a first at least one computing device into a third database managed by a trial management program executing on a second at least one computing device, said first at least one computing device and said second at least one computing device are connected to a network, said

15   method comprising the steps of:

a)   establishing in a first database progression of transactions of the clinical trial comprising a schedule of a plurality of periods of execution during which period a plurality of test values are accepted; a plurality of tests for each of said plurality of periods, a plurality of elements for each of said plurality of tests, and a plurality of

20   exceptions for setting limits on said one or more test values;

b)   establishing in a second database a list of a plurality of trial members enrolled to perform said progression of transactions;

c)   said trial members performing said progression of transactions by executing the data entry program, the trial management program identifying said trial

25   members and determining a level of access allowed and performing a level of authentication necessary;

d)   displaying said plurality of elements and accepting a plurality of test values in satisfaction of said plurality of elements; and

f)   recording said plurality of test values if said plurality of test values was received with in a time range within which the transaction must be completed.
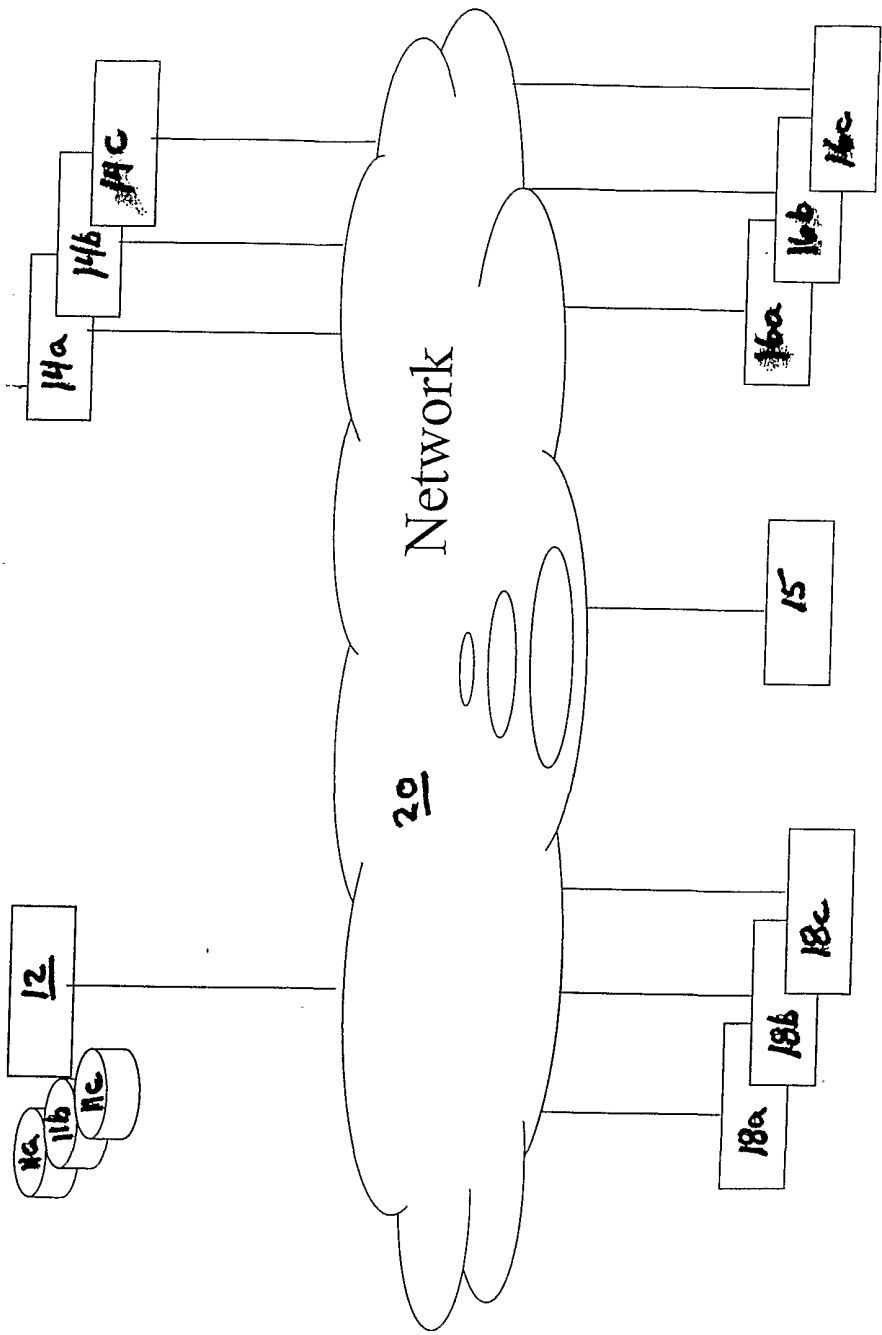
Figure 1

Figure 2

Figure 3b

Figure 3a

File   Edit   View   Favorites   Tools   Help

Back   Forward   Stop   Refresh   Home   Search   Favorites   History   Mail   Print   Edit

Address   http://   medidatasolutions.com/   Go

MediDataSolutions.com

This is a private site for the use of authorized study participants only.

User Name: |

Password:

Enter

Support is available via support@medidatasolutions.com

Done   Internet

_102_

_100_

FiguRe 4a

File   Edit   View   Favorites   Tools   Help

Back   Forward   Stop   Refresh   Home   Search   Favorites   History   Mail   Print   Edit

Address   http://   medidatasolutions.com/example/matrix.htm   Go

You are logged in as H.P. Investigator, M.D.   logout

Patient Record: Doe, John #123456.   close patient record

Baseline
and
Screening   On Study   On Study   Termination

Evaluations   0   3   6   12

Evaluations	Baseline and Screening 0	On Study 3	On Study 6	Termination 12
Eligibility Assessment	done 1/20/00			
Informed Consent	done 1/20/00			
Medical History	X			
Physical Examination	X			
Urinalysis	done 1/20/00			
Blood Chemistry	X	X	X	X
Adverse Experiences		X	X	X
Quality of Life questionaire	X			X

Evaluations   0   3   6   12

Done   Internet

_72_

_76_   _106_   _104_   _74_

FiguRe 4b

Figure 4C

http://dev1.medidatasolutions.com/test.asp?test_id=20&interval_id=1 - Microsoft Internet Explorer

File   Edit   View   Favorites   Tools   Help

Back   Forward   Stop   Refresh   Home   Search   Favorites   History   Mail   Print   Edit   Discuss   Repl.com

Address   http://dev1.medidatasolutions.com/test.asp?test_id=20&interval_id=1   Go

76a

Social History

1. Do you smoke?   No   Yes

2. Do you drink alcohol?   No   Yes

3. Take caffeine drinks?   No   Yes
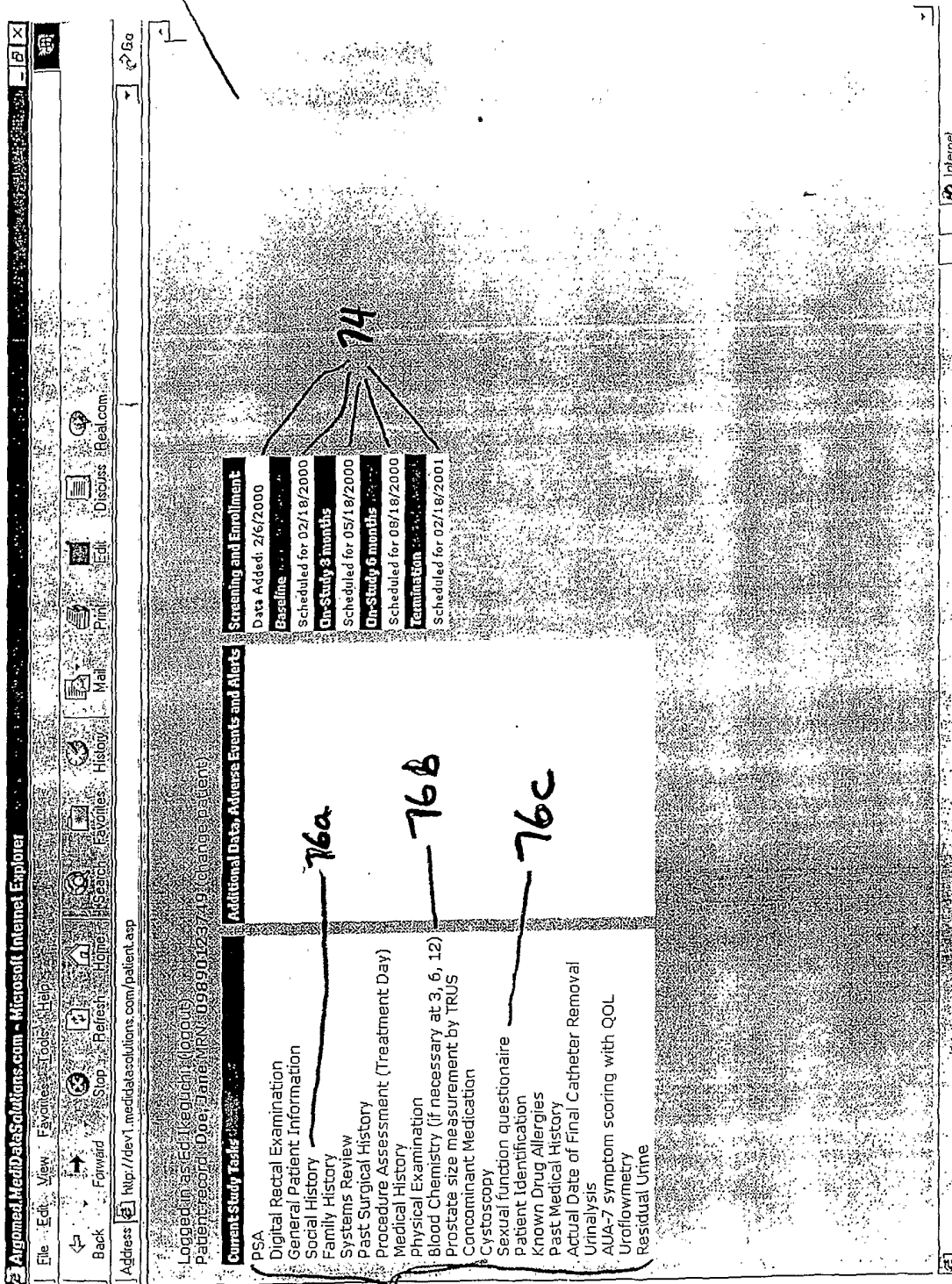
Submit Data

Done   Internet

Figure 4d

Blood Chemistry (if necessary at 3, 6, 12)

1.	White Blood Cell Count	((10)^3/ul)
2.	Hemoglobin	g/dl
3.	Platelets	((10)^3/ul)
4.	Serum Sodium	mmol/L
5.	Serum Potassium	mmol/L
6.	Serum Chloride	mmol/L
7.	Serum Bicarbonate	mEq/L
8.	Blood Urea Nitrogen	mg/dl
9.	Hematocrit	%
10.	Serum Creatine	mg/dl
11.	Serum Glucose	mg/dl
12.	Uric Acid	mg/dl
13.	Calcium	mg/dl
14.	Serum Phosphorous	mg/dl
15.	ALT (SGPT)	U/L
16.	Alkaline Phosphatase	U/L
17.	Total Bilirubin	mg/dl
18.	Total Serum Protein	g/dl
19.	Serum Albumin	g/dl
20.	Serum Cholesterol	mg/dl

Submit Data

Figure 4e

http://dev1.medidatasolutions.com/test.asp?test_id=13&interval_id=1 - Microsoft Internet Explorer
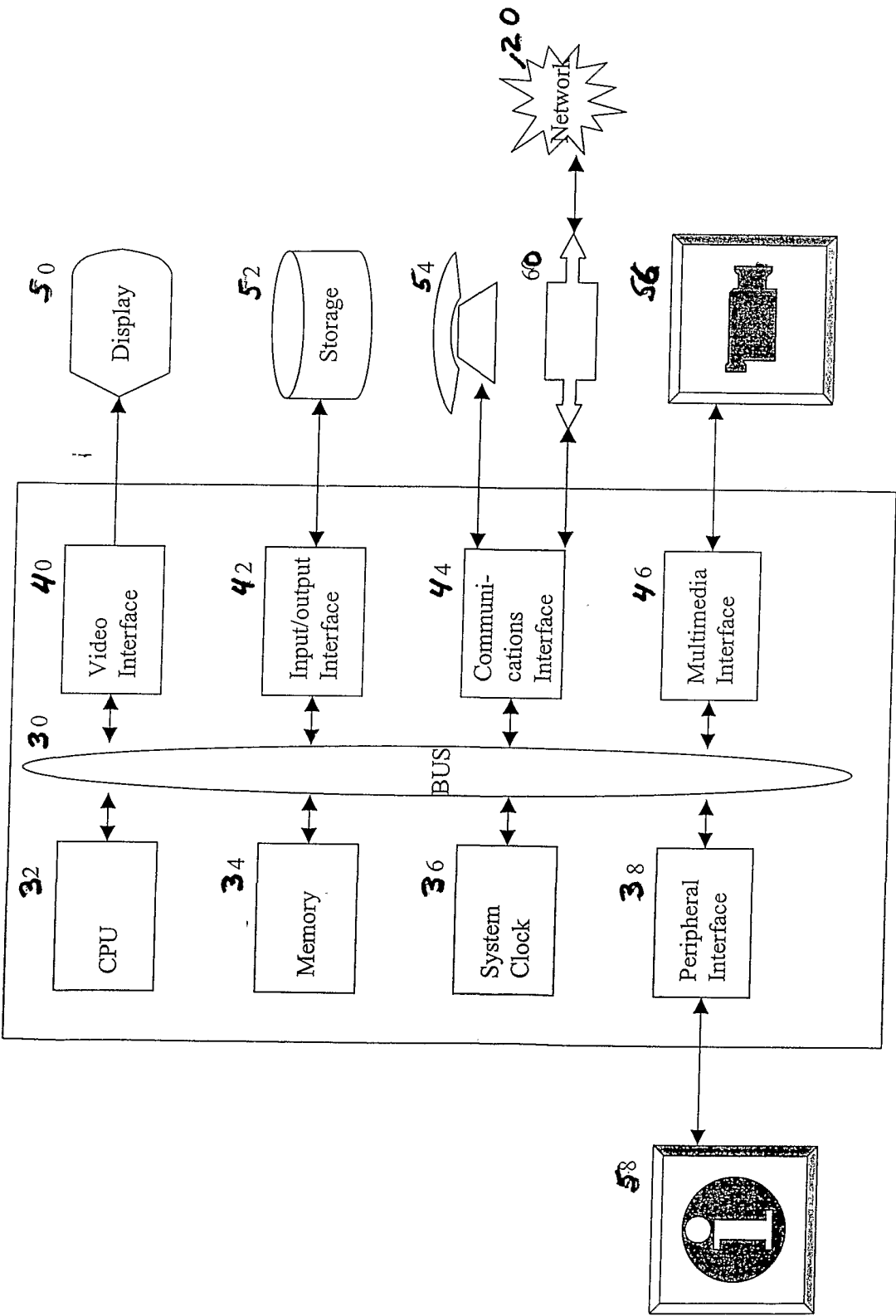
File   Edit   View   Favorites   Tools   Help

Back   Forward   Stop   Refresh   Home   Search   Favorites   History   Mail   Print   Edit   Discuss   Realcom

Address   http://dev1.medidatasolutions.com/test.asp?test_id=13&interval_id=1   Go

Sexual function questionaire

1.   Over the past 4 weeks, how often were you able to get an erection during sexual activity?
    [No sexual activity]

2.   Over the past 4 weeks, when you had erection with sexual stimulation, how often were your erections hard enough for penetration?
    [No sexual activity]

3.   Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?
    [Did not attempt intercourse]

4.   Over the past 4 weeks, during sexual intercourse, how often were you able to maintain an erection after you had penetrated (entered) your partner?
    [Did not attempt intercourse]

5.   Over the past 4 weeks, during sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
    [Did not attempt intercourse]

6.   Over the past 4 weeks, how many times have you attempted sexual intercourse?
    [No attempts]

7.   Over the past 4 weeks, when you attempted sexual intercourse how often was it satisfactory to you?
    [Did not attempt intercourse]

8.   Over the past 4 weeks, how much have you enjoyed sexual intercourse?
    [No intercourse]

9.   Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you ejaculate?
    [No sexual stimulation or intercourse]

10.   Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you have the feeling of orgasm or climax (with or without ejaculation)?
    [No sexual stimulation or intercourse]

11.   Over the past 4 weeks, how often have you felt sexual desire?
    [Almost never or never]

12.   Over the past 4 weeks, how would you rate your sexual desire?
    [Very low]

13.   Over the past 4 weeks, how satisfied have you been with your overall sex life?
    [Very dissatisfied]

Done   Internet

Figure 4B

84

88

86

http://dev1.medidatasolutions.com/chartoutput.asp?month=2&day=6&year=2000 - Microsoft Internet Explorer
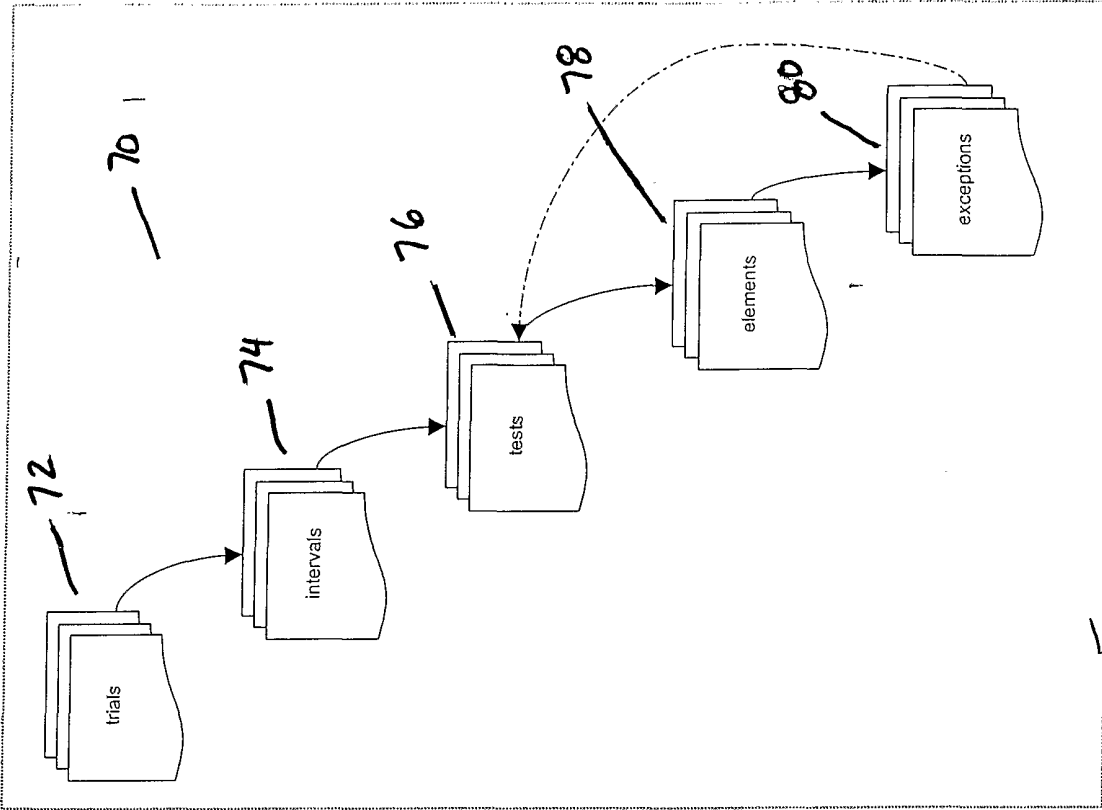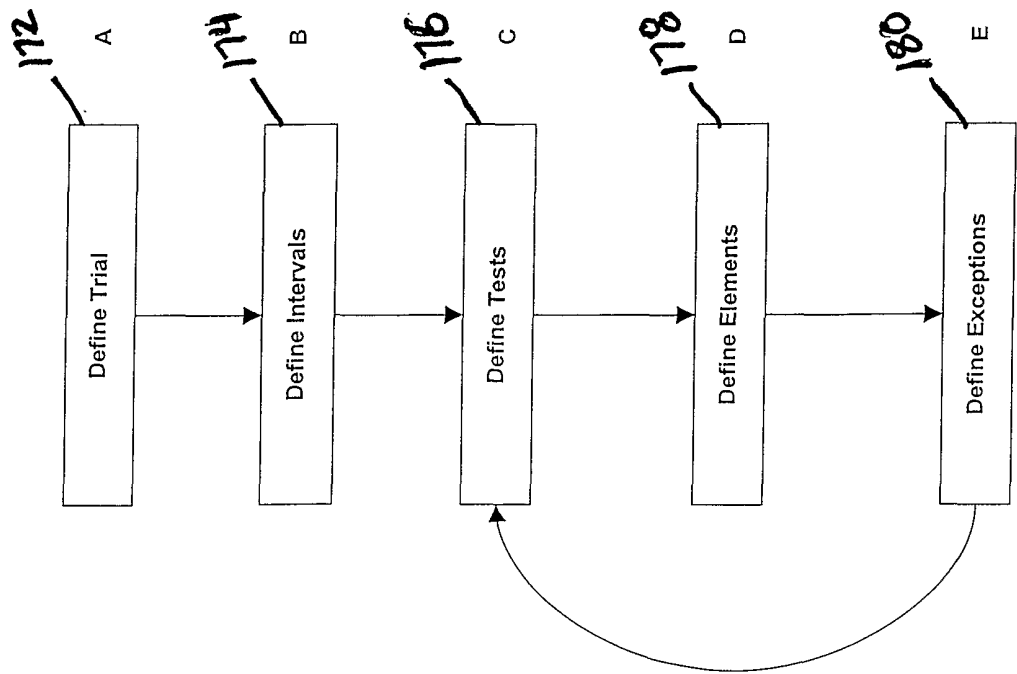
File   Edit   View   Favorites   Tools   Help

Back   Forward   Stop   Refresh   Home   Search   Favorites   History   Mail   Print   Edit   Discuss   Realcom

Address http://dev1.medidatasolutions.com/chartoutput.asp?month=2&day=6&year=2000   Go

Chart Record   90
Doe, Jane
0989123749
Study Activity for 02/06/2000

Each page must be signed after being read and verified.   88

Informed   Please confirm that the patient has read, understands, and has signed an Informed   02/06/2000 14:52 260726
Consent   Consent form.: 1 Informed Consent form is on file.

Patient   Clinical diagnosis of BPH.: 1   02/06/2000 14:53 677987
Inclusion
Criteria
                  Male patient over age 50 who desires to participate in study.: 1   02/06/2000 14:53 202660

                  Prostate size from bladder neck to verumontanum measured cystoscopically between   02/06/2000 14:53 699143
                  20mm to 64mm.: 1

                  AUA-7 score greater than or equal to 13.: 1   02/06/2000 14:53 591937

                  Peak urine flow rate of less than or equal to 12 ml/sec on a voided volume of 125   02/06/2000 14:53 985573
                  ml.: 1

Patient   History of any illness that might confound the results of the study, which produce   02/06/2000 14:53 544228
Exclusion   symptoms that might be confused with those of the disease process under
Criteria   consideration, or which pose additional risk to the patient.: 0

                  PSA greater than 4 ng/ml unless biopsy is negative.: 0   02/06/2000 14:53 435185

                  Confirmed or suspected malignancy of the prostate by digital exam, biopsy, or   02/06/2000 14:53 507817
                  transrectal ultrasound (TRUS).: 0

                  Use of beta blockers, antihistaminics, anticonvulsants, and antispasmodics within 1   02/06/2000 14:53 664558
                  week of treatment unless there is documented evidence that the patient has been on
                  the same drug dose for at least 6 months with a stable voiding pattern: 0 (the drug
                  dose should not be altered or discontinued for entrance into or throughout the
                  study)

                  Use of alpha blockers, anticholinergics, androgens, and gonadotropin-releasing   02/06/2000 14:53 103365
                  hormonal analogs within 1 week of treatment.: 0

                  Use of 5-alpha reductase inhibitors and antidepressants within one month of   02/06/2000 14:53 684521
                  treatment.: 0

                  Residual volume greater than 250 ml measured by ultrasound.: 0   02/06/2000 14:53 167072

                  Compromised renal function (ie - serum creatinine level greater then 1.8 mg/dl or   02/06/2000 14:53 685111
                  upper tract disease).: 0

                  Current urinary retention.: 0   02/06/2000 14:53 602667

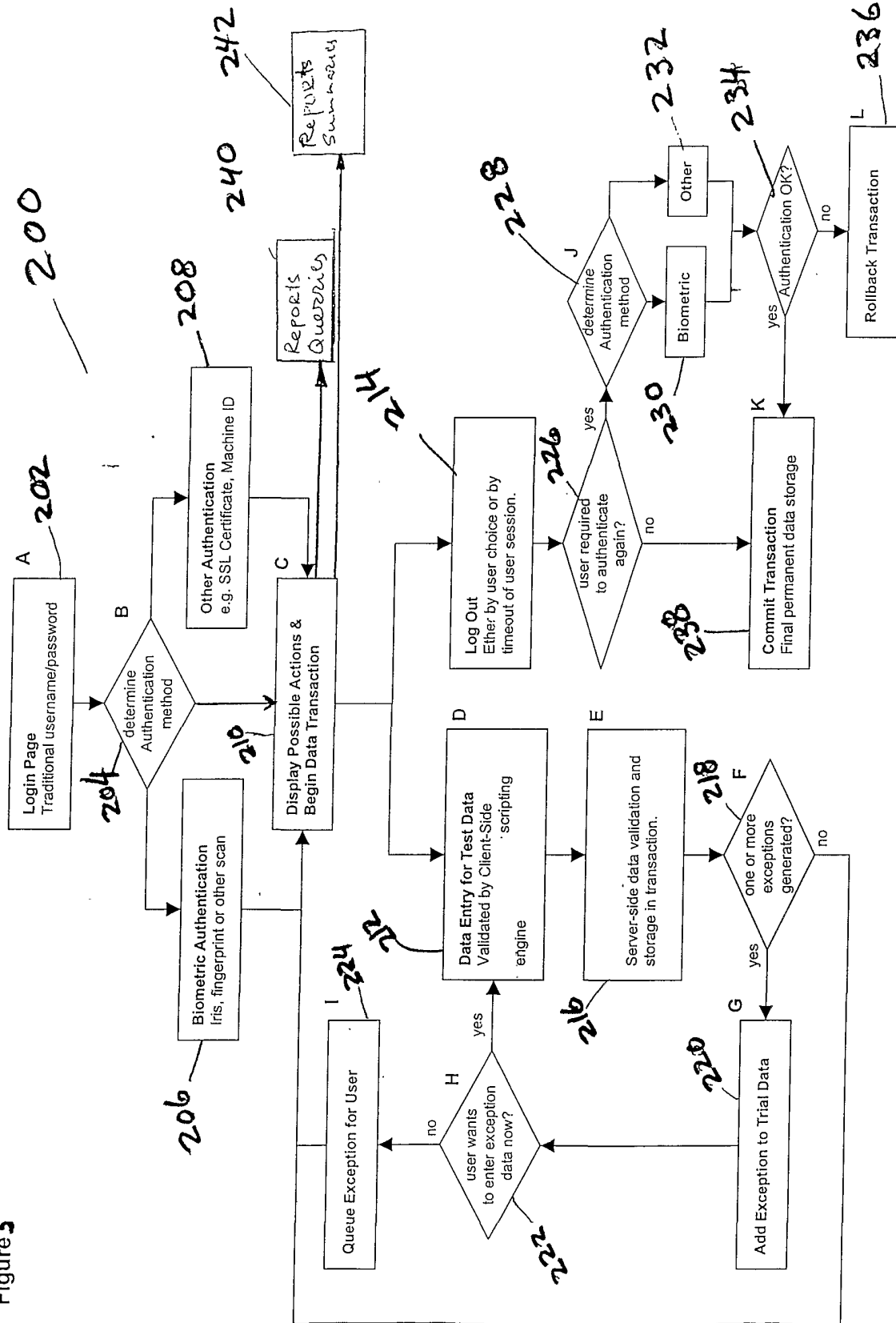Done   Internet

Figure 4g.

Figure 5

200

A — 202
Login Page
Traditional username/password

B
204 — determine Authentication method

208
Other Authentication
e.g. SSL Certificate, Machine ID

206
Biometric Authentication
Iris, fingerprint or other scan

210

C
Display Possible Actions & Begin Data Transaction

214

Reports Queries

240

Reports Summary
242

D — 212
Data Entry for Test Data
Validated by Client-Side scripting engine

E — 216
Server-side data validation and storage in transaction.

F — 218
one or more exceptions generated?

G — 220
Add Exception to Trial Data

H — 222
user wants to enter exception data now?

I — 224
Queue Exception for User

yes

no

no

yes

Log Out
Ether by user choice or by timeout of user session.
228

226
user required to authenticate again?

no

yes

J
determine Authentication method
230

Other
232

Biometric
234

K
238
Commit Transaction
Final permanent data storage

Authentication OK?

yes

no

L — 236
Rollback Transaction

Figure 6

Result key

A — Trial
B — Interval
C — Test
D — Element
E — User
F — Patient
G — Date and time created
H — Certification code
I — Machine identification
J — Authentication information
K — Data record
L — Supplementary text
M — ,

trials

intervals

tests

elements

exceptions

Figure 7