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Diplomarbeit

Alphanet - Clinical Trials Moving Towards Online Solutions

ausgeführt an der
Besonderen Einrichtung für Medizinische Statistik und Informatik,
Institut für Medizinische Bildverarbeitung und Mustererkennung der
Medizinischen Universität Wien

unter der Leitung von
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Abstract

This master's thesis entails a description of a web application with a dynamic central database which allows the creation and management of clinical studies. Over a multi user system, users are able to individually create their own multi-centered clinical studies as well as combine different clinical studies for statistical analysis.

With the latest technology (Ajax and JSF) it is possible to create data entry screens quickly, easily and without any programming. The unique graphical user interface, allows dragging and dropping elements for a high-speed design of electronic case report forms (eCRF). Through the dynamical structure of the database, there are no limitations to the creation of individual clinical studies. These fields can easily be created and managed by the different users. In order to facilitate a clearly laid-out clinical study, the user has the ability to create and integrate categories. The fields can then be associated with the category which provides a clear overview of the clinical study.

By combining the studies in a single web application, the users are able to compare in greater depth the different values from different treatments. In particular, the time and effort required to capture the data should be reduced and duplicate steps, such as duplicate patient information, should be avoided. As a result, the clinical study documentation system, AlphaNet, is in a league of its own.

Kurzfassung

Die vorliegende Diplomarbeit beschäftigt sich mit der Erstellung und Entwicklung von Online-Multicenterstudien, auch Studiendokumentations-systeme genannt. Der Benutzer selbst benötigt keine eigene installierte Desktopapplikation sondern nur einen Webbrowser und Zugriff auf das Studiendokumentationssystem um die Webapplikation laufen lassen zu können.

Durch den Einsatz neuer Techniken wie Ajax als Oberfläche und den Vorteil eines Frameworks wie ICEfaces ergeben sich nicht nur neue Möglichkeiten der Umsetzung, sondern auch eine einfachere Benutzerführung die dem „Look and Feel" einer normalen Desktopapplikation entsprechen. Bestehende Studiendokumentationssysteme sind meist schwer vom Benutzer erweiterbar und die Erstellung von Studien sind für die Benutzer große Hürden.

Durch die dynamische Struktur der Datenbank wird es einem Projektleiter ermöglicht eigene Studien zu erstellen und gleichzeitig zu verwalten. Einzelne Werte einer Studie sowie die Studie selbst können vollständig durch den Projektleiter erstellt werden. Für einen besseren Überblick können Werte in einzelne Kategorien innerhalb einer Studie zusammengefaßt werden. Ein solches System ermöglicht es verschiedensten Studien untereinander zu verknüpfen und statistisch auszuwerten. Durch das Zusammenfassen mehrerer Studien ist es erstmals möglich, Daten untereinander zu vergleichen und statistisch auszuwerten. Insbesondere sollen sich dadurch der Aufwand der Datenerhebung reduzieren und doppelte Arbeitsschritte vermieden werden. Ziel ist es verschiedenste Studien miteinander zu kombinieren und zentral mit einer Webapplikation verwalten zu können. Das Studiendokumentationssystem AlphaNet betritt in dieser Hinsicht absolutes Neuland.

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1 Introduction

"If we knew what we were doing,
it wouldn't be called research, would it?"

Albert Einstein

In recent years, the world of telecommunications has undergone many changes due to the enormous growth of information on the web. Back in the nineteen eighties, digital technology replaced analog technology. In the nineties, mobile phone technology was introduced and in return changed our whole communication behavior. Over the last decade the Internet and the World Wide Web (WWW) have emerged as a significant part of our everyday lives. The WWW has become a powerful tool to share information and not only for regular users, but companies and organizations have recognized the advantage as well. The introduction of the Internet is an enormous confrontation for traditional telecommunication providers. Through the increased interest in sharing data, the providers required an increase of transport speeds and access networks had to be prepared for the customers growing demand for broadband Internet. The Internet became a new marketplace for companies and users as well. Even educational institutions such as schools and universities went onto the internet to share documents and papers or provide training services. Furthermore, countries and governments offer their eGovernment services.

Until now, the field of research for telematics in health care only included future possibilities. Often improvements and advances which are possible through telematics were only discussed, but seldom concrete computer applications were actually implemented (Müller, 2005, p.629ff). However, for most authors it is clear that a need for change is required in this field (Hanika, 2001, p.107-111). The technical possibilities have improved drastically over the past few years (van Eimeren, 1998) creating better and more available global networks opening the doors for distributed medical environments.

Müller (2005, p.629) describes telematics as a technology which combines telecommunication and informatics. One branch of telematics is the health telematics domain, e-Health. Due to the regulations for the distribution of patient information, a major challenge for the telemedicine is the guarantee of patient's privacy.

Clinical studies, also known as clinical trials, face similar challenges. Clinical studies evaluate the effect of medical treatments by comparing the results of a treatment with control groups (who undergo a standard treatment). The clinical studies allow doctors to see if a treatment has achieved its desired effects while providing information on side effects and complications. With the combination of new technologies and the experience of telemedicine over the last 20 years, the opportunity to implement a powerful, effective, secure and user friendly software in the medical field has slowely come into sight.

The main content of this thesis is to take a closer look at the design of our clinical study documentation system, Alphanet. With this system, it is possible to acquire data, link different clinical studies as well as perform statistical analysis between the different studies. The system allows the user to combine the clinical studies, which enables the user to to compare the different values in greater depth with the different treatments. This drastically reduces the time and effort required to capture the data and duplicate steps, such as duplicate patient information, are avoided.

At first, we will look at telemedicine, and in particular, at existing or currently under development clinical study documentation systems. Next, we will discuss the different web technologies, including web 2.0 technologies, which could be used to build a user friendly clinical study documentation system. These include but are not limited to Java Server Pages, Java Server Faces, Struts, and Asynchronous Javascript and XML (AJAX).

Finally, we will discuss the design of our clinical study documentation system, Alphanet. After a brief introduction to Alphanet, we will go into depth on the user interface design and the functional requirements which include the process flow diagrams and use case diagrams. Next we will discuss the technical design which includes the infrastructure and software architecture of the Alphanet clinical study documentation system, and finally we will discuss the database design.

2 Telemedicine

Telemedicine can be described as a combination of telematics and medicine. There are many different common definitions for telematics. Often, telematics is seen as a technology which combines telecommunications and informatics (Wikipedia.org, telematics, 2007). In other words, it is seen as the center piece between telecommunications and informatics. Through this definition, telematics includes a vast number of information and communication technologies as well as system components which can be just as valuable for medicine as for any other area of expertise. The scope of telematics reaches from IT supported solutions that are implemented in medical devices, such as digital signal processing (Electro-Cardiography), image processing (Magnetic Resonance), or pattern recognition (Ultrasound), to system controls or information management systems including a knowledge base or patient information (Angood, 2001, p.1452). Telematic components for communication systems are often open networks like the internet, or can be limited to a specific user group in smaller networks like the intranet. As you can see below, telemedicine has a lot of advantages in many different fields (Hospital of the Ruhr, University of Bochum, Goals and tasks, 2007).

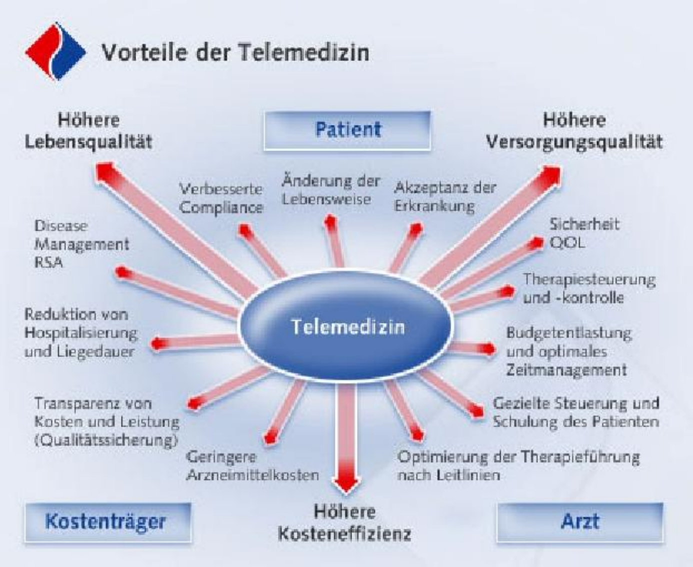

Vorteile der Telemedizin
Höhere Lebensqualität
Patient
Höhere Versorgungsqualität
Verbesserte Compliance
Änderung der Lebensweise
Akzeptanz der Erkrankung
Disease Management RSA
Sicherheit QOL
Therapiesteuerung und -kontrolle
Reduktion von Hospitalisierung und Liegedauer
Telemedizin
Budgetentlastung und optimales Zeitmanagement
Transparenz von Kosten und Leistung (Qualitätssicherung)
Gezielte Steuerung und Schulung des Patienten
Geringere Arzneimittelkosten
Optimierung der Therapieführung nach Leitlinien
Kostenträger
Höhere Kosteneffizienz
Arzt

Diagram 1: Interdisciplinary characters of telemedicine (www.hdz-nrw.de)

The different applications for telematics in medicine can be grouped into three categories (Berger, 1998, 54f):

- **Data-Exchange:** Informational systems which allow the communication and documentation between the doctors as well as the patients. Furthermore, exchange of earnings or other accounting information for health or patient management. The importance is emphasized on the data security and data protection, since it is based on patient specific information.
- **Health Portal:** Information for citizens and patients as well as information for health organizations. Essentially, these do not include patient based data in order to allow data transfer over non secure or open networks. Through this open structure, a comprehensive collection of health data can be collected.
- **Study Documentation Systems:** Information for educational or research purposes. These do not include patient specific information since the information, that is used, is anonymous. In some cases the information requires high security measures and in others no security is required.

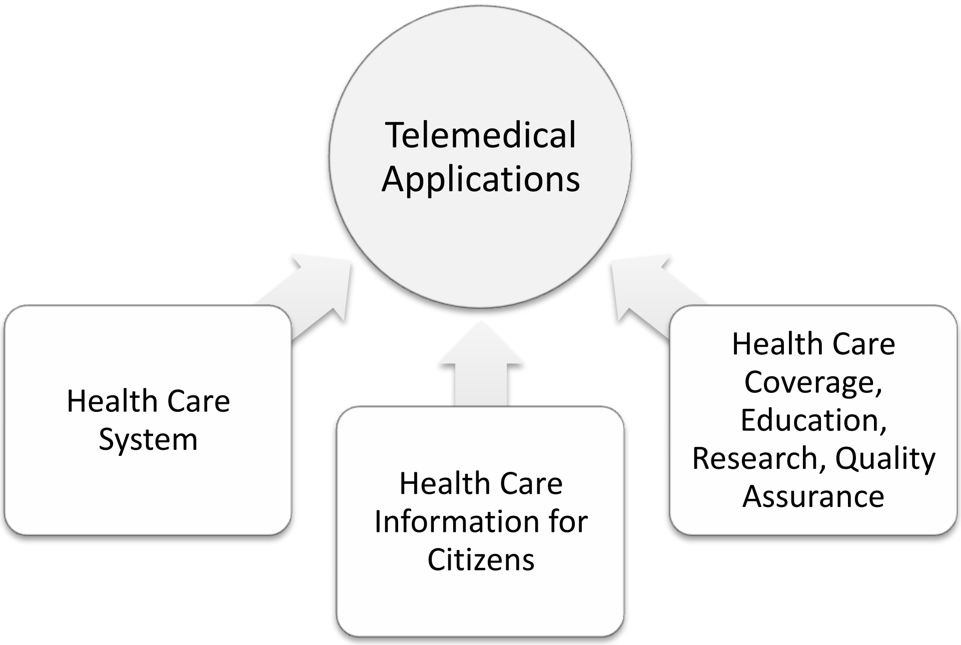

Telemedical Applications
Health Care System
Health Care Information for Citizens
Health Care Coverage, Education, Research, Quality Assurance

Diagram 2: Telemedical Applications

2.1 Why Telematics in Health Care?

Through the internet, for example, users have the possibility to easily access information as well as communicate with others. There are many different types of forums which cover a variety of fields in medicine. The users need to be careful of the authenticity of the information and know if the author has the corresponding qualifications (Huston, Huston, 2000, p.92).

Today, medicine offers a variety of different systems. One includes the electronic medical records. These records allow doctors to receive all relevant information from a patient's previous examinations, instantly, without having to examine the patient again. Furthermore, through consultation systems, registered doctors in private practice are able to receive a second opinion from different locations and make a more qualified diagnosis. Another example would be for specialized hospitals, where doctors can present acute cases to general hospitals. Through the diagnosis of the corresponding medical specialists, the doctors can then decide if the patient is able to be treated in the specialized hospital, if the patient needs to be relocated immediately, or if the patient is not able to be transported and the specialist's team needs to come to the patient (Angood, 2001, 1449ff). Therefore, the patient does not need to undergo unnecessary transportation.

In Germany, there are numerous projects which claim that telemedicine applications improved the medical care for patients, as well as reduce the costs. A study ordered in 1998 from Roland Berger and Partner GmbH, "Telematik im Gesundheitswesen - Perspektiven der Telemedizin in Deutschland", presented the electronic prescription as the first step to the realization of a medical platform.

The following progressions and trends in health care underline the advantages of information and communication technologies:

- New processes for diagnostics and therapy, for example applications in telemedicine.
- The legally anchored use of the electronic health card (e-Card)
- More involvement of the patient in the decision making process.
- More demand from the patient for new services, from scheduling examination dates to intelligent homes for patients requiring nurses at all times.

These examples show the advantages of implementing medical applications. Yet before such a system can insure quality and cost reduction, a vast amount of effort needs to be produced before the implementation. In Europe optimization and quality improvement can only be insured if the European Union is seen as the supply unit in the international context and coordinates a common platform for all projects. The challenge of the committee would be to cooperate with all the European Union states and create a basis or standardization for applications in telemedicine. Important is to define the interfaces and establish standards for the different applications.

2.1.1 Problems in Health Care

The technical considerations for health care systems is a relevant problem in the decision making process. Even though the hardware requirements for a clinical study documentation system are not as high as for other applications in telemedicine, the infrastructure should not be underestimated (Huston, Huston, 2000, p.93f). First of all, clinical study documentation systems require a solid network connection (the bandwidth should not become a bottleneck) and the stability of the system should be warranted. Furthermore, the system should have a high degree of availability and reliability. Through the use of standards and guidelines the complexity of the system can be reduced.

Another important aspect to consider is the legal aspect. Copyright, liability, privacy are all aspects that need to be considered in order to establish a successful system. Yet, it is not enough to only create the technical infrastructure and understand the legal conditions, since the most important aspect in telemedicine is the acceptance of the patients and providers. How the use of technical systems influences the patients confidence towards the doctor's competence has not been investigated yet. The user friendliness of the system is therefore a very important aspect. There needs to be a strong cooperation with the respective departments.

There exists a significant discrepancy between the opportunities and the actual realization of a project. A vast number of ambitious research projects could have succeeded, yet were held back by the clinics, cities or regions once it came to the practical implementation. The reasons for the failed implementation of the applications in telemedicine, next to the failed infrastructure, lies in the incompatibility of the already developed and in-use applications.

So far, no common coordinated strategy has been developed in medical research or within the Austrian health care system. All of the parties involved need to agree on common guidelines, organizational and technical standards, in order to improve the communication between the users of different systems. In Germany a forum for telematics in health care was created called "Aktionsforum für Telematik im Gesundheitswesen" (ATG). This platform allows scientists to collaborate over multiple different locations (Dietzel, 2003, S. 268ff).

Below is a list of the main problems with telematics in health care:

- Failure to recognize the benefit: In today's scenarios, often the users and providers do not recognize the common benefits. The incentives for employees to change their common tasks and take advantage of telematics are still very limited in health care.

- Failure to analyze requirements: The requirements for potential users, doctors and their functions and tasks have not been properly and adequately analyzed.

- Insufficient Legal Foundation: The legal guidelines for the use of telematics in medicine have not been fully specified, especially the liability claims.

- Psychological Barrier: Through the use of telematics in health care, people involved tend to be skeptical about the misuse of data as well as the fear of an even more distant relationship between patients and doctors.

- Poor Evaluations: Due to the difficulty in efficiently evaluating telematic applications, only little reliable information about the effects of such systems could be extracted. Therefore, important basic information is not included when purchasing decisions are met.

2.1.2 Goals and their Advantages

There are many different goals laid out for telematic applications. These goals also bring certain advantages to the field. In the bottom is a list of goals and their advantages in health care:

- An important aspect is the efficient management of medical services. These include the administrative work, data collection and the distribution of work between the employees and different institutes.

- The security and confidentiality with respect to the patient is another goal for telemedicine applications. All exchanges of information, especially personal information, must consider security and confidentiality with careful attention towards the individual patients.

- The access to medical knowledge would be made more available and easier to reach and would create more opportunities for the people involved.

- The availability and the quality of the treatment are not dependent on the location of the patient. Medical expertise of the highest quality can be accessed even in structurally weak regions.

- Availability of Full Patient Data: The quality of the medical decisions are improved through the access of the existing patient information.

- The quality of the medical decisions improves through easier access to existing patient information.

- The patient receives more information and better medical services

The advantages of telematics in health care are the improvements of the diagnosis and therapy through the interdisciplinary exchange of information. As a result, there are reduced costs as well as reduced expenditure of time. Through the acquisition and storing of clinical studies and an improved plan for the diagnostics, unnecessary examinations can be avoided. The most important advantage of the use of new technologies is the improvement of treatments for the patients.

3 Electronic Health Card and e-Card

3.1 The Electronic Health Card in Germany

On the first of January, 2006, the “Law to modernize the compulsory health insurance” (Bundesministerium für Gesundheit, The Electronic Health Card, 2006), replaced the previous insurance cards with the the current health cards. Everybody with an active health insurance in Germany slowly received an electronic health card (eGK). The card eases the access of patient data as well as the administration work. The following functions are implemented with the help of the health card, which exceeds the simple storage of data on Smart-Cards. (Bales 2005, p. 728ff):

- Electronic Prescription
- Emergency Data Records
- Medication Data
- Electronic Patient Records
- Insurance Statement
- Entitlement to medical treatment outside of the European Union (Europäische Krankenversicherungskarte, EKVK)

Not all of these functions are currently available, but the functions will be realized once the efficiency of the system increases. The electronic health cards will not only reduce administrative work, but also medical functions will be eased. In addition, the electronic health card has the European health card (EKVK) on the reverse side (similar to the Austrian e-Card). This allows the claim for treatment in the member countries of the European Union (Bundesministerium für Gesundheit, The Electronic Health Card, 2006).

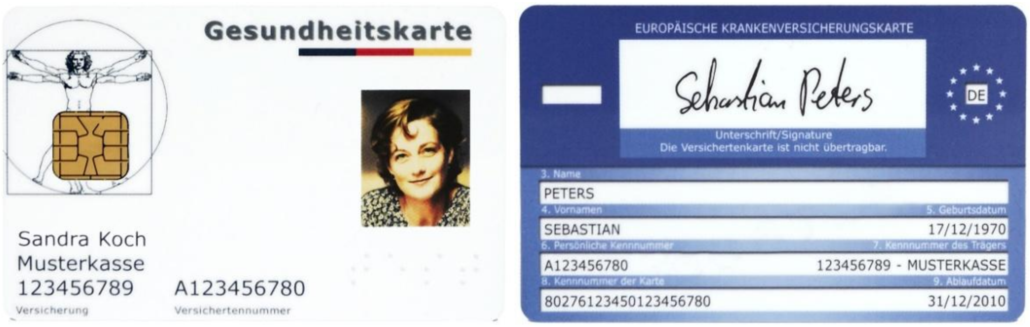


Diagram 3: Electronic Health Card (www.die-gesundheitskarte.de)

Even the simplest functions of the health cards, for example the reading of the insurance information, require a complex infrastructure for the distribution of identifications and passwords. The locations of the certifications require the highest security measures. Furthermore, only the distribution of the 80 million health cards requires a considerable logistical expenditure is required. As a result, the planned date for the introduction of the health cards was postponed numerous of times, since the planning and the realization was far behind the scheduled dates.

Despite all of the problems, one cannot forget the dimensions of the project around the introduction of the electronic health cards. Over 80 million participants in health care were responsible for the establishment of the electronic keys. Through the health cards, around 270,000 doctors, 65,000 dentists, 2,200 hospitals, 21,000 pharmacies and over 300 private hospitals are all connected with each other (Bundesministerium für Gesundheit, The Electronic Health Card, 2006).

3.2 e-Card in Austria

The e-Card is supposed to be the central key for the services of the Austrian social security and health care systems. The first step was to replace the pre-existing health insurance cards. Eight million insurants were provided with chip cards and around 12,000 involved partners with chip card readers and the correspondent software. The goal of the e-Card system was to simplify and improve the administrative work.

The e-Card takes the responsibility of a key card, which allows access to information of the cards owner. On the front side of the e-Card are the social security number, name and title of the patient. On the reverse is the European health card (European Commission, European health card, 2004). The patient's social security signature, birth date and gender are also stored on the card. Once the e-Card is connected to the e-Card server, the information is compared with the information stored on the server. From the e-Card server, the following information can be extracted (Sögner, 2005, p.660f):

- The responsible health insurance bearer
- Information on the costs of prescription, drugs or medical assistance (for example, if prescription is free of charge)
- Information about exemption from costs
- Information of the first consultation (consumed health insurance cards)

3.2.1 Transmission Procedure

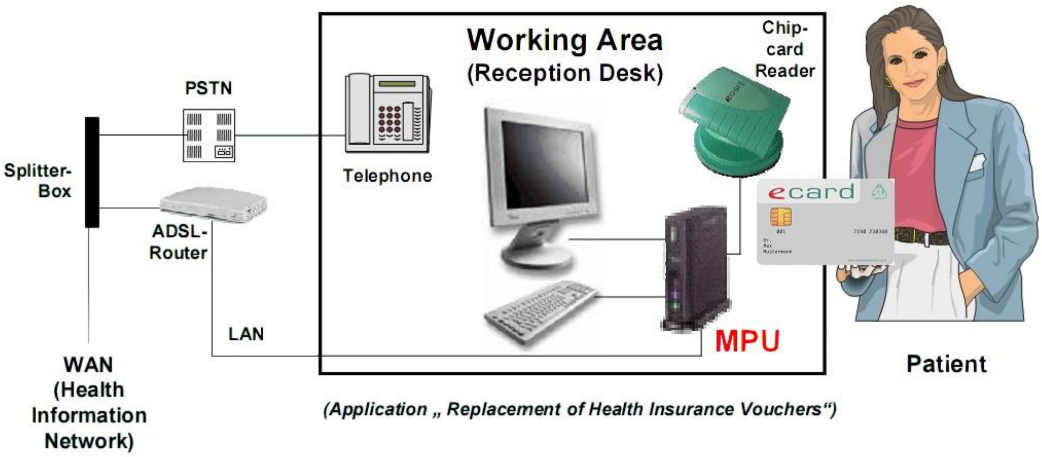


Diagram 4: Medical Practice Unit
(http://www.chipkarte.at/mediaDB/95267.pdf)

In practice, during the transmission only the general information and the date is stored, and not the exact time stamp. The coordinating information includes, the patient data such as the social security number, first name, last name, insurance category, gender, birth date, but not the address or company information. Information on the patients social security status (including information of where and how the patient is insured), is also stored. The system checks if the costs will be handled by the insurance or if the patient is required to deal with the payments. Furthermore, the system checks if the patient is exempted of the costs of prescriptions and services (Sozialversicherungs-Chipkarten Betriebs- und Errichtungsgesellschaft, The Austrian e-card System, 2007).

3.2.2 Peering Point

The Peering Point is the central location, where the GIN-ADSL lines of all participants come together. At this point, the value-added service providers can transfer the respective data. Only when these value-added service providers are used from the other providers over the Peering Point, do the providers have access to the information. The Peering Point is managed through a Peering Point-Association, whereby 50% belongs to the Austrian social security, and 50% to the Austrian state medical board (Sozialversicherungs-Chipkarten Betriebs- und Errichtungsgesellschaft, The Austrian e-card System, 2007). Since the e-Card system is based on the central location of the Peering Point, the system is under constant scrutiny.

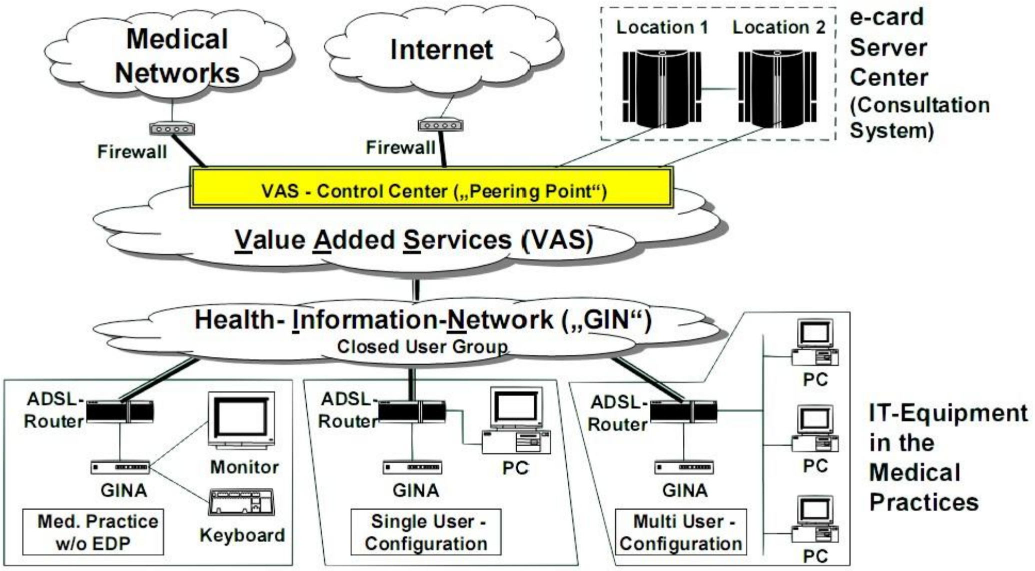

Medical Networks
Internet
Location 1
Location 2
e-card Server Center (Consultation System)
Firewall
Firewall
VAS - Control Center („Peering Point“)
Value Added Services (VAS)
Health- Information-Network („GIN“)
Closed User Group
ADSL-Router
GINA
Monitor
Keyboard
Med. Practice w/o EDP
ADSL-Router
PC
GINA
Single User - Configuration
ADSL-Router
GINA
Multi User - Configuration
PC
PC
PC
IT-Equipment in the Medical Practices

Diagram 5: E-Card System - An Overview
(http://www.chipkarte.at/mediaDB/95267.pdf)

3.2.3 Extended Vision of e-card Usage

In the future the company, “Sozialversicherungs-Chipkarten Betriebs- und Errichtungsgesellschaft”, plans to modify the “Conditions for Claim“- rules for necessary software-updates. For example, new applications have the ability to load and download extended personal information, new data structures and cryptographic key-files to and from the e-card. The following points also show extended features for the future, which resulted in controversial debate in Austria:

- Social Security: Replacement of all paper based health insurance certificates.

- eHealth: Keycard for secure handling of medical transactions
  (Basic token for eHealth telematics).

- E-Government: Signature and encryption card for all fields of the application with corresponding requirements.

- eApplications for Third Parties: By use of access protected storage files („Infoboxes“) through keys and authorization.

- eBusiness: Signature and encryption card with cooperating partners.

4 Data Privacy and Information Security

In the last few years, the directly involved patients and doctors have become more aware of the problems concerning the protection of their personal data. This awareness is not so evident in the public opinion though. Here, disinterest, indifference and resignation are shown towards the requirements of data protection. It is seen more as an obstruction towards the personal data than a helpful resource. Startled are only those, who experience the problem first hand (Müller, 2005, p.630ff).

Information only brings meaning in certain social contexts. Study documentation systems use exactly that idea by using anonymous patient data during the capture of the information. This brings the advantage that the information can never be consolidated with the data stored in the electronic medical records (Dierks, 2005, p.635ff).

4.1 Goals of Data Privacy

Data privacy is the sum of all legal regulations (laws, ordinances, etc.) whose purpose is the protection against improper use of personal data. Data privacy is a fundamental right. Each person is entitled to the fact that their information is not used, processed or seen without their consent. Data privacy protects primarily the person in correspondence with their personal data (Berg, 2004, p.411ff).

The goal of data privacy is to guarantee personal rights, which insures that each individual can determine which information is released under the conditions of the information and communication technology (Hanika, Gansert, 2003, 302ff). Protected information are the personal details, which can only be accessed, processed or used for respective tasks. The departments are responsible for the observance of the data privacy of each individual's personal information (Seibel, Kocher, Landsberg, 2000, p.394ff).

With the formation of a communicative infrastructure, as it is the case for study documentation systems, high standards for data privacy and data security are required. Through the integration of political and economical interests, health care systems (for example, study documentation systems) not only require secure communications in the national realm, but also in the international framework. The different dimensions of data security in health care information are as follows (Ulsenheimer, Heinemann, 2005, p.199ff):

- The integrity of the information
- The confidentiality of the information
- The availability of the information
- The responsibility for the information (reliability and liability)

4.2 Legal Aspects

With respect to clinical study documentation systems, medical data, based on §7 of the Austrian data privacy laws (DSG 2000) (Österreichische Datenschutzkommission, Datenschutzgesetz 2000, 2005), is only allowed to be used or transferred if the respective client holds the responsibility and authority for the content of the medical application. A closer look to our German neighbors shows that their data privacy laws are very similar (Hanika, Gansert, 2003, 305). Furthermore, the leader of the respective study needs to present sufficient legal responsibility and authorization regarding the usage of the medical data. Finally, the guidelines for the planning and realization of medical applications should not violate the patient's right to privacy (Duftschmid, Binder, 2005, p.680ff).

Below are fragments of the Austrian data privacy laws (DSG) and the health care telematic laws (GTelG) (Republik Österreich, Gesundheitsreformgesetz 2005, 2005) both of which are already in use, but not obligatory until 1.1.2008.

- Purpose Binding (§ 6 Abs. 2 DSG): specific restrictions on transfer; may not be disclosed for incompatible purposes; may only be collected for specified purposes. (siehe §§ 46 und 47 DSG).

- Minimization Principle (§ 6 Abs. 3 DSG): The transfer of data is limited to the data required by the medical application. The system is not allowed to transfer more information than required for the application.

- Anonymity (§ 6 Abs. 5 DSG): Patient information needs to be made anonymous at the earliest possible time. At that point, the patient's identifiable features need to be deleted or encrypted. If personal information is required for further processing, based on § 17 DSG, it needs to be reported to the data privacy commission.

- Proof of Identity (§§ 3, 4, 5 GTelG): Data can only be transmitted to health organizations which have proven their identity towards the sender. Electronic certificates should be used, or an inspection through the „eHealth Index". These certificates should be supplied by the Austrian ministry of health by latest July 2006, where the organizations should be registered.

- Confidentiality: Only participants that are involved in the treatment of the patients are allowed to access and use the telemedicine applications (§ 14 Abs. 4, 5 DSG). The transfer of information over a medium that is not exclusively accessible by the sender and receiver (for example, the internet), the data needs to be encrypted (§ 6 GTelG). This can be achieved through the use of the SSL (Secure Socket Layer) and TLS (Transport Layer Security) protocols.

- Integrity: All data needs to be secure against accidental, unexpected or unlawful attacks (§ 14 Abs. 1 DSG). In rule, this should be accomplished through electronic signatures (§ 7 GTelG).

- Documentation (§ 8 GTelG) and Protocols (§ 14 Abs. 7 DSG): All security measures and their controls need to be documented. Furthermore, all data access needs to be recorded.

- International Telemedicine (§§ 12, 13 DSG): The law with respect to data exchange between the member states of the EU, are equivalent to the data privacy laws of the data transfer within Austria. For all other countries, a permit is required from the Austrian data privacy commission. There are a few exceptions, for example Switzerland, where the data privacy laws are similar to the Austrian laws. Here the Austrian laws are considered and only the patient's written consent is required (Duftschmid, Binder, 2005, p.681ff).

5 Clinical Study Systems

„Any sufficient advanced technology is indistinguishable from magic.“

Arthur C. Clarke

Clinical studies evaluate the effect of medical treatments throughout the course of a disease. The clinical studies give an optimal insight to a conclusive result of the treatment. The main point of a clinical study is to compare the results of a therapy from one group with the results of a therapy of one or more control groups. Control groups are groups where the patients are treated with the standard therapy. Clinical trials are the best method to measure if a treatment achieves the desired effects, while at the same time produces a list of side effects and complications of the treatment.

These clinical trials are associated with high financial responsibilities, are very time intensive and require a large amount of organizational effort. In correlation with telematics in medicine or other organizational improvements, costs for resources could be reduced by 15 to 20 percent. Through the use of modern information technologies, the perspective of a more efficient process for clinical multi-centered studies should be possible. Many new organizational concepts are not even feasible without technological interventions. On the other hand, it's important to acknowledge, that appropriate organization and documentation is an important backbone for the success of any system. The setup of the machines and installation of the programs alone, will not guarantee the success.

A number of studies have found that the respective doctors and medical staff (monitors, and study leaders) consume up to 50% of their work for the research, data acquisition, data preparation and relaying of written information. For medical studies, here lies a huge potential for improvements. Depending on the quality of the paper-based studies and the organization of the document flow, alone in the search for information of previous studies and their relationships, up to 20% of the time spent can be reduced. Considering this aspect, problems through information handling can lead to false understandings, as well as require new data acquisition or even neglect potential vital information (Chen, 2000, p.113).

Cost related studies for telematics in medicine have been performed in the United States of America. The studies showed that not in all cases where telematics was implemented in medicine the institute became more profitable. Yet, studies that also considered the quality of the end result, showed that the telematics-backed work produced up to 2 thirds of the costs compared to the same quality of the original procedure. At such a hospital, in case a patient needs to stay for longer periods of time, the hospital is able to save up to 150,000 US Dollars per year (after the costs of the system) (Angood, 2001, S. 1449).

The following sections will discuss the process and the different actors of clinical studies in greater detail.

5.1 Study Protocol

A central point to plan and develop a clinical trial system is the study protocol. A good reference is the Guideline for Good Clinical Practice: Consolidated Guidance from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)[1]. In general, the study protocol contains the background information, the reason for the research, the main goals, the design, the organization, the methodology and and finally the statistical considerations of the clinical study. Not all details of the clinical studies are required for the study protocol on the condition that there is a comprehensive description about the procedure. It is very important that the main points and goals of the protocol are known and understood before recruiting the respective patients (Matthews, 2006. 215ff). Furthermore, the protocol should not change once a clinical study has started.

[1] http://www.fda.gov/cder/guidance/959fnl.pdf; Retrieved on 02.06.2007

5.2 Types of Clinical Studies

There are many different types of clinical studies. In general, there exist controlled trials and uncontrolled trials. Controlled trials require the comparison between the results of the treatment compared to the results of a standard or placebo “control” treatment. Uncontrolled trials only provide treatment over a period of time and measure the value of the treatment, without a comparison to a control group. Below are a list and a more detailed description of the main clinical study types (there are several clinical study designs which are not discussed):

- Controlled Trials
    - Before/After Trials
    - Historical Trials
    - Nonrandomized Trials
    - Randomized Trials
        - Open Trials
        - Blind Trials
- Uncontrolled Trials

5.2.1 Controlled Trials

Controlled clinical studies are studies which require a control group in order to observe and evaluate the treatment. For example in clinical studies, a group of participants is given a new drug, while the control group is given either a standard treatment or a placebo for the illness. There are four main types of controlled trials which are discussed in further detail below.

5.2.1.1 Before/After Trials

This approach is also called Pretest/Posttest. Here, the data of individuals prior to the intervention is compared to the same individual’s data after the intervention. Usually this type of clinical trial is put into practice during the time the data is collected and combined with the previous data.

5.2.1.2 Historical Trials

In historical trials, new interventions are tested on a group of patients and the results are compared with the results of a different group of patients, which were tested previously (Pocock, 1983, p.54 ff). One positive aspect of this method is that all patients will get access to the new therapy.

There are two ways to retrieve the historical control data. One option is to research previous treatments through literature. The problem with this method is that it is very difficult to see if the previous trial actually correlates with the current trial. A common practice in larger hospitals is to preserve the data of clinical studies, in order for the retrieved data to be used for the control group. The second approach is, therefore, to search for data at other clinics which might have these electronic or analog studies stored. Although historical trials have economical advantages and reduce the effort of the treatment, they also have some restrictions. Pocock discuss these problems in detail in chapter 4.2 (1983, p.55 f).

5.2.1.3 Non-Randomized Trials

In the non-randonmized trials the patients are divided into intervention group and control group in a non randomized approach (Pocock, 1983, p.60 ff). The patients are either assigned by the researcher to the group or chose themselves to which of the two groups they want to belong to, control group or intervention group. Both the groups of patients, the intervention group and the control group, are not necessarily tested during the same time period or at the same location. The disadvantage of this approach is that the conditions are not exactly the same between the two groups and therefore make it very difficult to compare the two groups with each other. For more information and as comparison see case-control studies (Lichtenstein, Elwood, Mulrow, 1987, 894ff).

5.2.1.4 Randomized Trials

A randomized trial is an approach where the participants are allocated to a therapy group based on chance. Randomization is a unique type of assigning a patient to a therapy (Pocock, 1983, p.66 ff). It reduces the difference between the patients in the groups by dividing the patients among the groups randomly, which distributes different patient characteristics among all the trial groups. There are two types of procedures. The first procedure is to choose a randomization process to create an accidental and unexpected series of allocations. The second procedure is the hidden allocation, which requires strict regulations in order to garantie that the group's allocation of patients is not discovered by the study investigators (Weil, 1999 140f).

A randomized controlled trial (RCT) is a scientific procedure used in testing participants which are randomly assigned to one of two or more treatment branches of a clinical trial. This is considered the most reliable form of trial confirmation because it eliminates all forms of unauthentic causality. The main idea is that therapy is assigned to subjects at random. This ensures that the different therapy groups are from a statistical standpoint near identical (Pocock, 1983, p.63 ff). RCT is the most powerful and widely used clinical trial design (Pocock, 1983, p.50).

One of the biggest problems in each clinical study is the bias of an appraiser, which is the difference between the expected and the actual value of the parameter being estimated (Matthews, 2006. 25ff). Pocock defines bias as a systematical error, which could occur in different stages of a clinical trial (1983, p.187 f). Randomized trials are engaged to test effectiveness while avoiding these factors. There are two different types open and blind, which are also split into single-blind, double-blind and triple-blind trials (Weil, 1999 141f).

5.2.1.4.1 Open Trials

In an open study, the patient and the scientist know which intervention the patient was allocated to. Both know the full detail of the treatment. The open studies are generally used in biological equivalence studies (Matthews, 2006. 75ff). The problem with open trials is that the placebo effect still plays a role within the patients and therefore produces unwanted results.

5.2.1.4.2 Single-blind Trial

In a single-blind study, only the scientist knows the full treatment of the trial but the patient has no information. Since the patient is unaware to which group he was allocated to, the placebo effect could be reduced and provide more reliable results (Gariballa, Parker, Taub. Castleden, 1998, 316f).

5.2.1.4.3 Double-blind Trial

In a double-blind trial, neither the researcher nor the patient knows something about the therapy. With this approach, two scientists are required. One scientist allocates a number to the group types, while the scientist who is treating the patient is given the number, but not which group the number is allocated to (Bhatia, Karnad, Loak, 1998, 53f). Therefore, the second researcher is unable to tell the patient which treatment is allocated to which patient. Furthermore, within this type of system, the distribution of the ages and sexes of the patients is more widely spread out, providing a more meaningful and accurate result.

5.2.1.4.4 Triple-blind Trial

Triple-blind trials can have more than one meaning depending on the clinical study. In general, it means that three people are so called blinded. The most common approach is to blind the patient, researcher and the scientist which is overseeing the treatment. Another approach is to blind the patient, researcher and statistician. The main goal of all blind trials is to prevent outcome of the treatment to be influenced by anybody directly involved in the study. Triple blind trials just add another layer of security.

5.2.2 Uncontrolled Trials

For uncontrolled trials all participants are given a treatment and are monitored for a period of time to observe the results of a therapy. The main difference between uncontrolled trials and controlled trials is that they do not compare against a control group. Therefore, the results of uncontrolled studies cannot be considered as a confirmation for the success of the therapy (Pocock, 1983, p.51 ff).

5.3 Clinical Study Phases

New medication and treatments are only put into practice after the medication or treatment is tested in a certain sequence in well planned and documented clinical study. Proving of remedies are classified by the pharmaceutical industry into four main phases, after the initial pre-clinical studies and phase 0. The drug-development process will usual proceed through all stages over some years. If it passes the first three Phases, normally the medicine or treatment will be approved for use in the general population.

5.3.1 Pre-Clinical Studies

The pre-clinical studies, also known as laboratory studies, are based on studies or trials on animals or cells (in vitro). The first step is usually the cell study, while the second is to test on lab animals. Different dosages of the medicine and treatment are experimented and tested on the animal subjects before they are introduced to human testing. (American Cancer Society, Clinical Trials: What You Need to Know, 2007).

5.3.2 Phase 0

Phase 0 is the initial test of the medicine or treatment in order to determine if the medicine or treatement behaves in the same way as expected from the pre-clinical studies. This includes a single dose for about 10 to 15 different human subjects (Wikipedia.org, Clinical Trial, 2007).

5.3.3 Phase I

Phase 1 is the first stage in which the full treatment or dosage of the medication is tested on human beings. It is a modality oriented, not a disease oriented, explorative study. Therefore some healthy volunteers will be selected. At this stage the studies are planned to assess the vigilance, tolerability, kinetics and dynamics of a therapy. The volunteers are often employees from the pharmaceutical company, so that they can be observed the whole time by the medical staff. However there are some conditions which require real patients, such as with oncology and HIV drug trials. Phase I usually entails around 15 to 50 patients (American Cancer Society, Clinical Trials: What You Need to Know, 2007).

5.3.4 Phase II

The next step is a disease oriented and confirming trial. At this stage the medication is used by patients, which show the corresponding symptoms. Once the primary safety of the therapy has been confirmed in Phase I, a larger group is required for Phase II (between 25 and 100 patients) (American Cancer Society, Clinical Trials: What You Need to Know, 2007). If the medication effect is positive the next phase can begin.

5.3.5 Phase III

In this phase the medication is compared with a standard therapy. Typically phase III trials are randomized controlled trials on large patient groups (up to 3000 patients). While not required in all trials, it is a conventionally norm that there are at least two successful phase III passes. Only after the treatment or medication passes this stage is it permitted to the general public.

5.3.6 Phase IV

In addition to the introduction to the market, the medication is tested for long-term side effects in a new clinical study. This is necessary to get a full assessment of the drug and to answer the necessary questions of long term effect. These trials usually compare the new drug to the standard therapy being used (American Cancer Society, Clinical Trials: What You Need to Know, 2007).

5.4 Monitoring

Clinical monitoring is the continuous quality control before, after and during a clinical study. The monitoring itself is done by special qualified employees called monitors. A monitor has to know about the clinical trial in general and the individual content for each study as well (Pocock, 1983, p.142). The monitor has the following tasks:

- Verification of the Trial Protocol: The purpose of monitoring is to make sure that the different clinics are following the guidelines set by the clinical study protocol.

- Uncover Therapy Differences and Unwanted Occurrences: Another important aspect of the monitor is to find unwanted occurrences. This helps the doctors react accordingly to the differences found by the monitor (i.e. the doctor could raise the dosage of the drug).

- Control of the Data Collection: The data should be extracted in a well thought out and organized manner. From the beginning, the data should be prepared in order to perform statistical analysis, so that errors, contradictions or missing data can be discovered (Matthews, 2006. 189ff).

- Negotiate General Information: The doctors are interested in the progress of the trial, and the purpose of the monitor is to provide additional information on other clinical studies or events in order to motivate the doctors further.

5.5 Multicenter Trial

Multicenter Trials are clinical studies conducted at several medical centers. Mainly Phase III trials are carried out at more than one clinical center. The main benefits of multicenter trials include (Wikipedia.org, Multicenter Trial, 2007):

- In some studies it is necessary to get a high number of patients The collaboration with multiple medical centers provides the possibility for a wider range of patients in a shorter period of time.

- Through different research centers in different geographic locations, the possibility to get recruit patients with different genetic, environmental, and ethnic or cultural backgrounds is much higher than the research in only one clinic.

- A multicenter study allows doctors and statisticians, with the shared interests and capabilities of different institutes, to work collaborative on one single task.

As specified in the U.S. Food and Drug Administration's Good Clinical Practice (U.S. Food and Drug Administration, ICH E6: Good Clinical Practice, 1996) the following actors should be part of a multicenter trial:

5.5.1 Contract Research Organization

The contract research organization (CRO) is either the organization which was contracted by a sponsor to perform the clinical study or is the sponsor itself. The CRO, or sponsor, is responsible to designate the medical experts to the clinical study.

5.5.2 Coordinating Committee

The coordination committee is assigned by the sponsor or CRO and is responsible for the planning of a clinical trial. This includes the design of the trial, building of the study protocol, patient recruitment, patient randomization, data input and processing, monitoring, periodical analysis, final data evaluation and the drawing-up of manuscripts.

5.5.3 Director of Study

The director of study is responsible and accountable for the entire project. The director is usually involved form the beginning of the project.

5.5.4 Biometrician

Biometricians are responsible for the statistical design of the data, the monitoring of the data, and finally, the statistical analysis and evaluation of the clinical study.

5.5.5 Randomization Control

This position is responsible to check the qualification criteria of the involved patients. Furthermore this position has to control the demographically and clinical data from each single patient and is accountable for the randomization process.

5.5.6 Quality Analyst

Quality analysts are responsible for the quality of the collected data. They also impact the entry form and decide which data should be captured.

5.5.7 Quality Assurance

The quality assurance members assure that the participating research centers fulfill the criteria mentioned in the study protocol. The representative has to verify that the data processing and the monitoring is executed in an appropriate time and manner.

5.5.8 Monitor

In most studies, a monitor controls the recorded data in certain temporal distances and verifies whether the research centers follow the points declared in the study-protocol (see also chapter 5.4 Monitoring).

5.5.9 Staff Members

The staff members are responsible for the treatment and have to take care of the patients involved in the trial. In most cases also the data recording is carried out by a doctor or a nurse. In each participating research center, members who are responsible for the communication with the other research centers should be determined. For the individual research centers, the following personnel are required:

5.5.9.1 Primary Investigator

Professors, doctors or heads of the department usually fulfill the role of the primary investigators. The primary investigator is the negotiating partner of the study sponsor and makes sure that the clinical study follows the good clinical practice regulations.

5.5.9.2 Secondary Investigator

In smaller departments the role of the primary and secondary investigator is taken from one person. The secondary investigator can be regarded as the supervising doctor. This is the person who actually is on the spot and knows about the clinical study plan in detail.

5.5.9.3 Study Coordinator / Study Nurse

The role of the study coordinator or the study nurse is taken by a person from the medical assistance staff. This person is responsible for organizational and administrative work, for example the coordination of appointments.

5.6 Setup of a Clinical Study System

The basic guideline for carrying out clinical studies is specified in the Good Clinical Practice (GCP) document from the U.S. Food and Drug Administration (U.S. Food and Drug Administration, ICH E6: Good Clinical Practice, 1996). The quality of clinical studies in the German speaking realm is defined by the Society of Good Research Practices (Society of Good Research Practices, DGGF, 2007). In order to carry out a clinical study, the

GCP guidelines require extensive documentation that is specified in the studies protocol. The documentation requires different forms. Forms for the acceptance criteria and inclusion criteria assure the unity of the group being treated. Furthermore, certain parameters are documented during the course of the treatment on a timely basis, and the final data acquisition is specified at the end of the document for each individual patient. Depending on the complexity of the study, different forms need to be included for the documentation (Sänger, 2000. p.460).

The data is stored in a central database, whereby, for larger projects, distributed systems are also used. For that purpose, the data for a specific study needs to be consolidated. With the combined data, an analysis through mathematical methods for the study leader is then easily feasible.

Through established software, the data is stored in a rational database, for example an SQL Server. The database is conformed with diverse security measures in order to allow multiple users access to the data stored in the system simultaneously. In addition, the database allows the possibility to apply different user rights to different users. By storing the data in a central location, it simplifies the data security issue (Chen, 2000, p.113).

In order to perform a legitimate medical study, the patient needs to declare his willingness to participate in the study. In this declaration, the different conditions and regulations are specified for the study including the organizational and technical aspects. The data security, in particular the patient’s privacy, is guaranteed by using pseudonym or anonym personal data (Shankar, Martins, O'Connor, Parrish, Das, 2006, p.27). Data acquisition, storage and analysis of the data are usually done through an identification number (ID) or a digital signature (this is only used if it is necessary to backtrack to the personal data, meaning the study is not anonymous). This ID is saved by the corresponding doctor and is used to recall the patient for the continuation of the documentation. It is very important that the patients are not confused with each other during the documentation. In the future, Smart Cards can be used, which is already required by many data security specialists, especially when thinking about merging e-Cards with a clinical study documentation system (Ilg, 2001 p.50ff).

Special internet inputs are necessary for the complexity of the documentations. Complete database solutions are impractical for smaller clinical studies, or for specific questions, due to amount of time required for the conformance of the questions. Therefore, the choice of software should be carefully examined. Object oriented development environments allow the possibility to create a database structure and input mask in a building block system. This system would allow the creation of the necessary input fields and store the required data type into the database. The documentations content can then be dynamically displayed with only the input fields that are required to be filled at that given time being shown. Most of the time, the choice of the development environment, is dependent on the combination of graphical tools and the option of a conventional programming language (Chau, 2004, p.87ff).

In order to allow statistical analysis of the documented material, the study leader, or doctor, should have the possibility to build their own clinical documentation environment. Technically, this can be implemented through the technology AJAX (Asynchronous JavaScript and XML). The client's program would run in the browser, and the user would be able to simply add a clinical study online into the clinical study documentation system. The users only require a functional browser.

Another important aspect in any system is to keep the user interface design as simple as possible. As Weng describes: "[…] their interfaces are often driven by rigorous computable models and are not intuitive to clinical trial experts" (Weng, McDonald, Gennari, 2004, p.1). Using the browser as the interface tool, leaves the developers relatively restricted due to the limitations of HTML (Gillen, Tse, Ide, McCray, 2004, p.1486). Yet, with new technologies, like Ajax, the user interface in browsers is able to have an application-like look and feel (Ajax 13, web-based business and home office applications, 2007).

The hardware configurations for such an application would consist of a database server and a web/application server. Due to the reliability and data security issues, the database should be installed on an individual system. The sensibility of the data requires that the information should be very secure. For that reason, the web server needs to have different sections. First of all, there is a public section. In this section, general information of the clinical studies, for example the clinical study protocols or user documentations, is displayed. In a more closed off section, more selected information for an existing doctor is displayed. Another section is for the study leader or a monitor. Safety concepts like Firewall, encryption and password control prohibits the access to the data by so called trespassers. Addition safety of the data is achieved through the browsers integrated security software with the corresponding encryptions (Wei, 2006, p.50ff).

The forms for the clinical studies should be made available at the doctor's workspace. The main complexity in the conceptualization and implementation of a clinical study documentation system built over the internet is the exact reproduction of the documentation process (Ilg, 1999 p.360ff). The direct access to all the stored data is only possible by the applicable study leader.

During the planning of an internet study, it is important that the doctors have an associate at the central location of the clinical study at any given time. The entire documentation system can be available for all participants at any public location. Redundant information is avoided since the servers will always use the latest version of the studies description. All the information stored through the web-interface will be stored directly onto the database server. The database model is designed in such a way that it allows for easy querying of the stored information (Shankar, Martins, O'Connor, Parrish, Das, 2006, p.25f).

The assistance of a monitor is a very important aspect of a clinical study system (Chau, 2004, p.87ff). For more information read Society of American Gastrointestinal Endoscopic Surgeons (SAGES) „Guidelines for the surgical practice of telemedicine" for a detailed description about the tasks of a Telemonitor and Teleconsultant or see Chapter 5.4 Monitoring. A certain part of the application is only accessible by the monitor, which allows the monitor to process the doctor's entries as well as manage the technical aspects of the system. Furthermore, the monitor is able to view the documentation forms and with a special built in software feature the monitor is allowed to work on request of study-doctors. He is also allowed to urge users.

The centrally stored data is mostly analyzed through standard statistics programs like SPSS. Another possibility would be to allow participating doctors to calculate certain clinical study results at any time. This allows the users to view the constant changes of the newly entered patient data. These results could be displayed in tabular or graphical form. At the same time, forums and communication over email are available, which allow discussion of the results over distance.

The willingness of the participants to take part on such a project can easily be changed to dissatisfaction through disturbances or not repaired software bugs (Ilg, 1999 p.360ff). Therefore it is of high importance to create a secure and solid application. It is vital to have a thorough assessment of the research as well as technology demands necessary for clinical studies (Güler, 2002 p.202ff). The following needs to be considered:

- In regard to the implementation and organizational analysis
- Formulation of context dependant documentation standard for the individual areas is necessary.
- Definition of "constitutional characteristics" of patients that can effect the diagnostic and therapy option at later stages of the treatment (allergies, risk factors, etc.).
- Intelligent search in non-structured data warehouses (medical data mining, navigation systems).
- Logical combination of records
- Presentation Form: Optimization of the Human-Machine Interface.
- Development of an infrastructure, which creates guidelines that incorporates the medical knowledge and database quality security.
- Network security
- Intelligent Human-Machine interface, specifically for data input and output (for i.e., speech input)

5.7 Standards and Guidelines

The main goal of all standards is to assure the quality of the clinical studies and allow the possibility to combine the information between the different studies. According to Ulsenheimer, standards must be realized, especially in the quality of the security and generally in the quality management field (Ulsenheimer, 1998, p.88f). The following diagram depicts the German relationship between the terms, policy, standards, guidelines and recommendations (Hermanek, 1998, p.383ff).

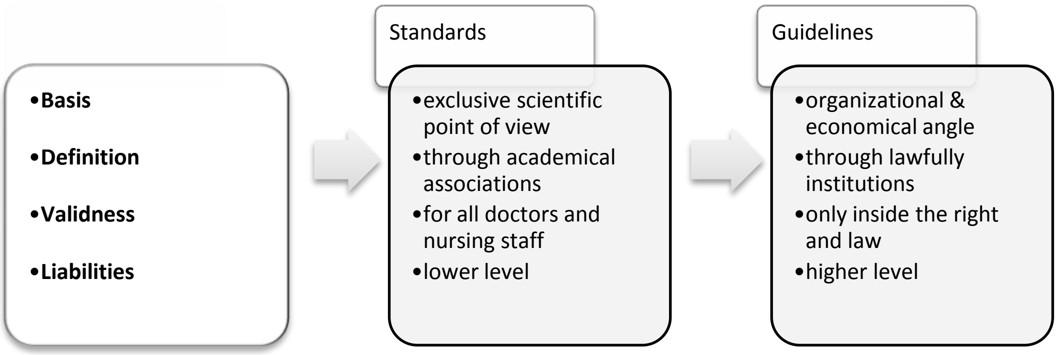

•Basis
•Definition
•Validness
•Liabilities
Standards
•exclusive scientific point of view
•through academical associations
•for all doctors and nursing staff
•lower level
Guidelines
•organizational & economical angle
•through lawfully institutions
•only inside the right and law
•higher level

Diagram 6: Standards vs. Guidelines

The diagram compares the standards versus guidelines. In general, the diagram divides the standards and guidelines into three parts, basic principle, regulation and validity. For the basic principle, the standards interpret mostly scholarly viewpoints, while guidelines look at other considerations like organizational or economical aspects. Standards are regulated through scholarly communities, while guidelines are regulated through legal institutes. The validity of standards is for all doctors and any additional personnel, while for guidelines, it is only valid for the institute which defined the guideline.

Given the advances in diagnostics and therapy, and also in regards to the processing of clinical studies, standards of today can be seen obsolete tomorrow. Therefore, it is essential to update standards in order to allow continuous advancements as well as the alignment towards international developments (Duftschmid, Binder, 2005, p.674ff). The guidelines for telemedicine are independent of a specific medical field, and can therefore be used in any area of telemedicine, especially in those fields, where the guidelines have not been specified yet.The guidelines of the Austrian legal system need to be modified, in order to allow law compliant practices in the Austrian health care system (Eichelberg, Aden, Riesmeier, 2005, p.280ff). The goal of specifying the guidelines is to secure the clinical study participants personal information, to create quality assurance of the clinical study, and to follow the relevant laws and regulations. Therefore, clinical studies need to follow the below mentioned guidelines, principles and conditions (Dietzel, 2003, p.4f):

- The clinical study should follow the corresponding guidelines, policies and laws (Data protection act, ICH Guidelines for Good Clinical Practices, and other relevant ICH Guidelines).

- If it deals with a randomized clinical study, then the study should be registered in the International Standard Randomized Controlled Trial Number Register. Thereby, it deals with the European Meta-Register for controlling clinical studies (International Standard Randomized Controlled Trial Number Register, Controlled-Trials, 2007).

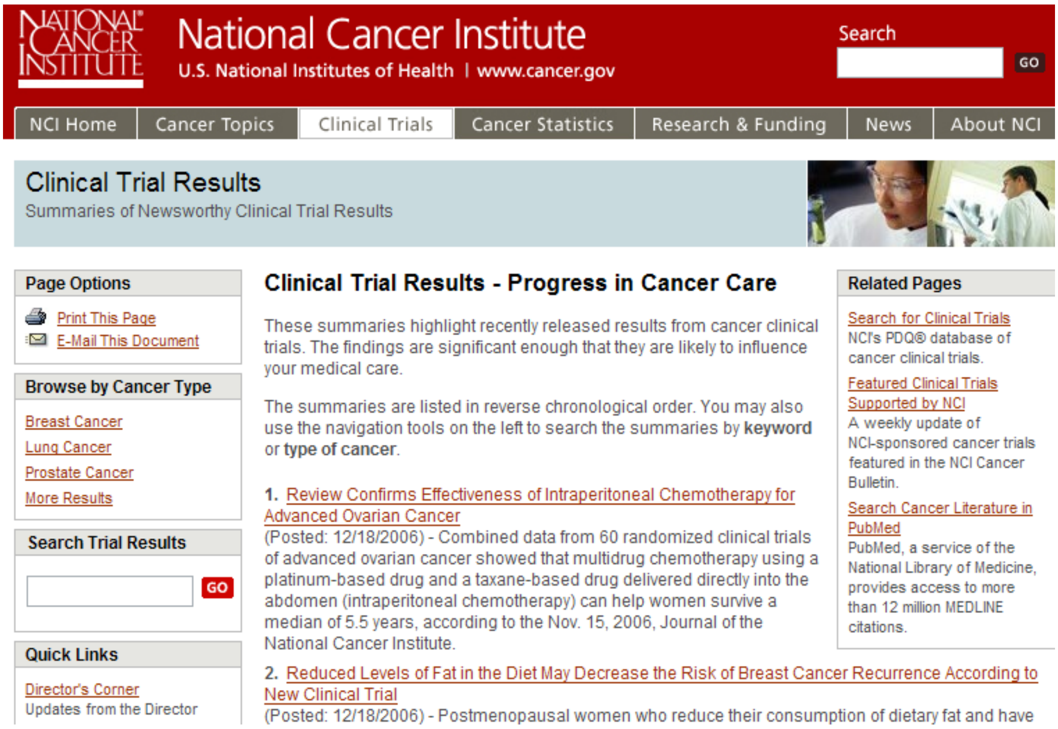
- As mentioned before, the patients must declare their willingness to take part in the clinical studies through a dated signature (and in some cases through a legal partner) (Eichelberg, Aden, Riesmeier, 2005, p.280ff).

5.8 Existing Clinical Study Documentation Systems

This section describes the different clinical study documentation systems which exist, or are under development, in the market today. The systems described below are CancerNet, DOIA, KrebsStudieRegister, PhOSCo, and finally Phase Forward's Clintrial and InForm.

5.8.1 CancerNet

The first clinical study documentation system is the CancerNet system. The use of such informational databases create the opportunity to use clinical studies in a more efficient and simplified manner. This website, which is sponsored by the National Cancer Institute in America, provides guidelines for doctors and information for patients regarding the most recent preventions; diagnosis and therapies of the different types of cancer (see Diagram 7).



Clinical Trial Results

Summaries of Newsworthy Clinical Trial Results

Director's Corner
Updates from the Director

Clinical Trial Results - Progress in Cancer Care

These summaries highlight recently released results from cancer clinical trials. The findings are significant enough that they are likely to influence your medical care.

The summaries are listed in reverse chronological order. You may also use the navigation tools on the left to search the summaries by **keyword** or **type of cancer**.

1. Review Confirms Effectiveness of Intraperitoneal Chemotherapy for Advanced Ovarian Cancer
(Posted: 12/18/2006) - Combined data from 60 randomized clinical trials of advanced ovarian cancer showed that multidrug chemotherapy using a platinum-based drug and a taxane-based drug delivered directly into the abdomen (intraperitoneal chemotherapy) can help women survive a median of 5.5 years, according to the Nov. 15, 2006, Journal of the National Cancer Institute.

2. Reduced Levels of Fat in the Diet May Decrease the Risk of Breast Cancer Recurrence According to New Clinical Trial
(Posted: 12/18/2006) - Postmenopausal women who reduce their consumption of dietary fat and have

Search for Clinical Trials
NCI's PDQ® database of cancer clinical trials.

Featured Clinical Trials Supported by NCI
A weekly update of NCI-sponsored cancer trials featured in the NCI Cancer Bulletin.

Search Cancer Literature in PubMed
PubMed, a service of the National Library of Medicine, provides access to more than 12 million MEDLINE citations.

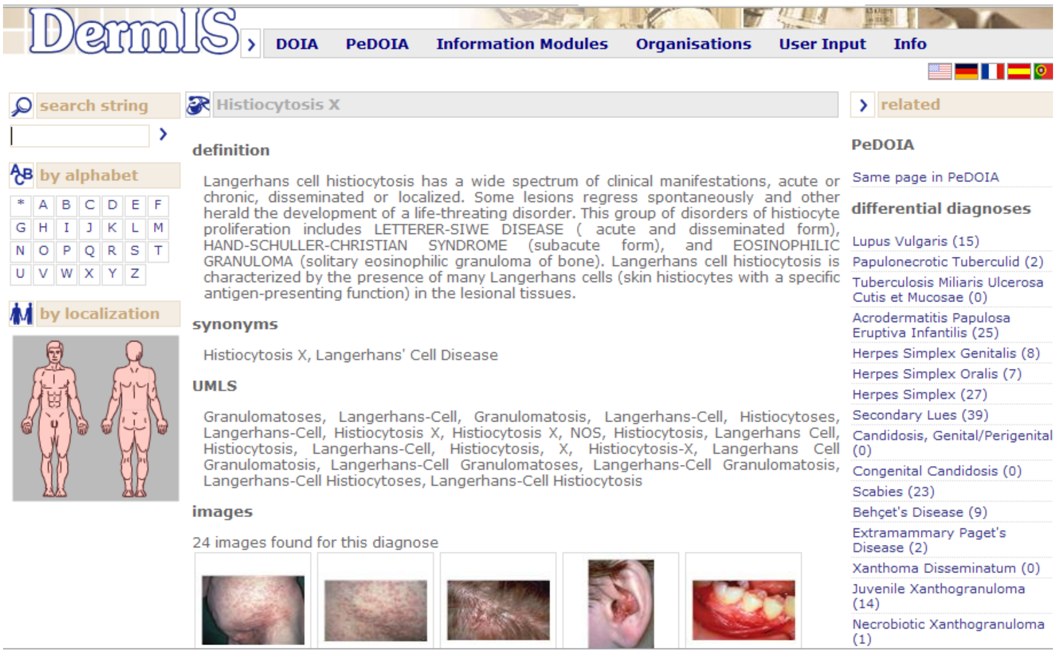
Diagram 7: National Cancer Institute (www.cancer.gov)

Every month different studies are publicized. Access via internet to the information is relatively simple. With over 1,000 users, accessing the site on a daily basis and an information volume of around one million pages, CancerNet is one of the most widely used cancer based medical databases. 80% of the requests come from the USA. CancerNet offers 350,000 new users per year, 600,000 documents yearly, at fifteen cents per document.

Through CancerNet it was proven that the preparation of guidelines and actual studies over the internet, created a higher acceptance for doctors and patients. This is an important prerequisite for the success of any initiatives to better the quality of clinical study preparations (National Cancer Institute, clinical trials, 2007).

5.8.2 Dermatologic Online Image Atlas

Dermatological diagnosis and differential diagnosis is mostly based on the knowledge of the clinical and dermato-histological image of a disease (see Diagram 8).



definition

Langerhans cell histiocytosis has a wide spectrum of clinical manifestations, acute or chronic, disseminated or localized. Some lesions regress spontaneously and other herald the development of a life-threating disorder. This group of disorders of histiocyte proliferation includes LETTERER-SIWE DISEASE (acute and disseminated form), HAND-SCHULLER-CHRISTIAN SYNDROME (subacute form), and EOSINOPHILIC GRANULOMA (solitary eosinophilic granuloma of bone). Langerhans cell histiocytosis is characterized by the presence of many Langerhans cells (skin histiocytes with a specific antigen-presenting function) in the lesional tissues.

synonyms

Histiocytosis X, Langerhans' Cell Disease

UMLS

Granulomatoses, Langerhans-Cell, Granulomatosis, Langerhans-Cell, Histiocytoses, Langerhans-Cell, Histiocytosis X, Histiocytosis X, NOS, Histiocytosis, Langerhans Cell, Histiocytosis, Langerhans-Cell, Histiocytosis, X, Histiocytosis-X, Langerhans Cell Granulomatosis, Langerhans-Cell Granulomatoses, Langerhans-Cell Granulomatosis, Langerhans-Cell Histiocytoses, Langerhans-Cell Histiocytosis

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differential diagnoses

- Lupus Vulgaris (15)
- Papulonecrotic Tuberculid (2)
- Tuberculosis Miliaris Ulcerosa Cutis et Mucosae (0)
- Acrodermatitis Papulosa Eruptiva Infantilis (25)
- Herpes Simplex Genitalis (8)
- Herpes Simplex Oralis (7)
- Herpes Simplex (27)
- Secondary Lues (39)
- Candidosis, Genital/Perigenital (0)
- Congenital Candidosis (0)
- Scabies (23)
- Behçet's Disease (9)
- Extramammary Paget's Disease (2)
- Xanthoma Disseminatum (0)
- Juvenile Xanthogranuloma (14)
- Necrobiotic Xanthogranuloma (1)

Diagram 8: DOIA (www.dermis.net)

The Dermatologic Online Image Atlas consists of a database of dermatological images which have been collected over a number of years and was put online two years ago. The digital images were selected from a 40,000 slide archive and recorded on a photo CD before broadcasting them over the internet. These images not only aid the differential diagnosis, but also provide informational help for patients. In the waiting room, for example, users could access a CD version of the picture database. This application was also created through the help of the National Cancer Institute of the USA (Dept. of Clinical Social Medicine and the Dept. of Dermatology, Dermatology Information Service, 2007).

5.8.3 KrebsStudienRegister

The Deutsche Krebsgesellschaft initiated the establishment of the clinical study register in Germany. Since 1999, the Deutsche Krebsgesellschaft organizes the German KrebsStudienRegister (DKSR) on the internet. This register entails over 400 oncologic therapeutical studies. This clinical study database can be found under www.studien.de. This site also uses a clinical study documentation system (see Diagram 9 and Diagram 10). The site warrants the transparency of the actual research and therefore fulfils the obligation of data privacy for the patients.

Due to the increasing internationalization of the oncological research, the KrebsStudienRegister will follow the global criteria for study registrations (which are formulated by the International Committee of Medical Journals Editors and the WHO). The Deutsche Krebsgesellschaft holds decisive improvements to the efficiency and quality of oncological studies (Deutsche Krebsgesellschaft, Deutschen KrebsStudienRegister, 2007).

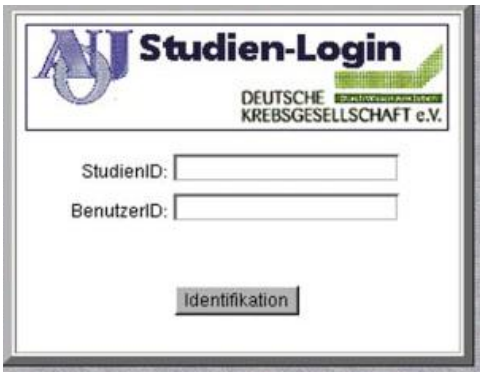


Diagram 9: Studien-Login (www.studien.de)

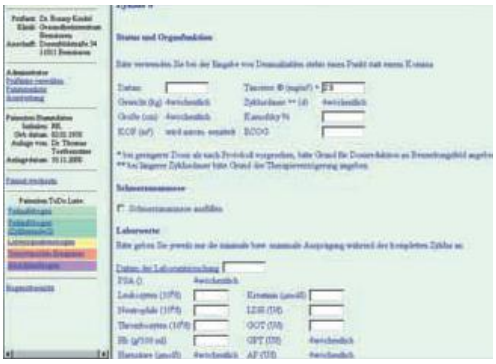


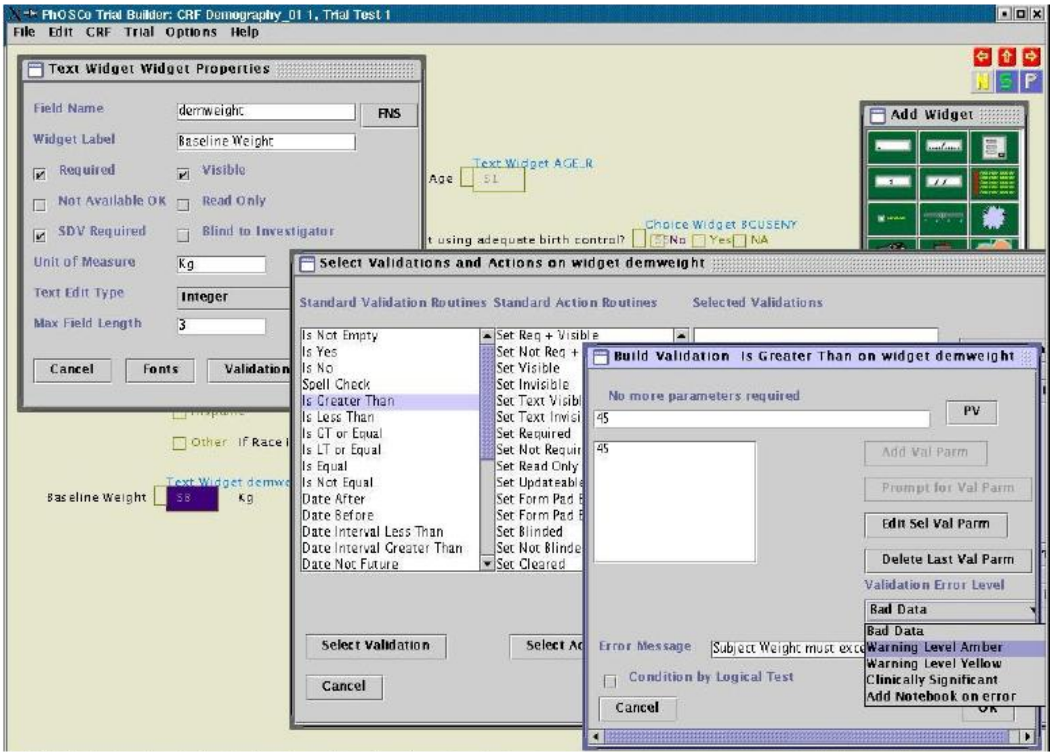
Diagram 10: Clinical Study System (www.studien.de)

5.8.4 Pharma Open Source Community

The Pharma Open Source Community (PhOSCo) project is an open source project which allows the building of clinical trials, the data collection of the clinical trials and the monitoring of clinical trials. The project is designed together with the PhOSCo general License, which not only allows the clients to receive the source code of the program, but also use the software for as many trials as they wish. Furthermore, the code can be customized and new features could added on to it the system depending on the users requirements. The Open Source licensing model of PhOSCo brings a unique and individual approach compared to the tradition vendors. The system is divided into three major modules: the trial builder, the trial recorder and the trial monitor (Venizeleas, GCP-conformable data management, 2006). As of August 6th, 2006, control of PhOSCo is now in the hands of Penguin Trials.

Trial Builder

The Trial Builder is used for specifying and defining the different clinical trials (see Diagram 11). Here the users can decide, what information to display on what page with the type of fields and its validations. The trial builder is used to create the definition of the trial, specifying what pages appear in what order. This information is then stored in a database, which can then be used for the other modules. Below is an image of the Trial Builder (Penguin Trials Ltd. & Co. KG, Pharma Open Source Community, 2007).


PhOSCo Trial Builder: CRF Demography_01 1, Trial Test 1

Text Widget Widget Properties

Field Name: demweight
Widget Label: Baseline Weight
☑ Required ☑ Visible
□ Not Available OK □ Read Only
☑ SDV Required □ Blind to Investigator
Unit of Measure: Kg
Text Edit Type: Integer
Max Field Length: 3

Select Validations and Actions on widget demweight

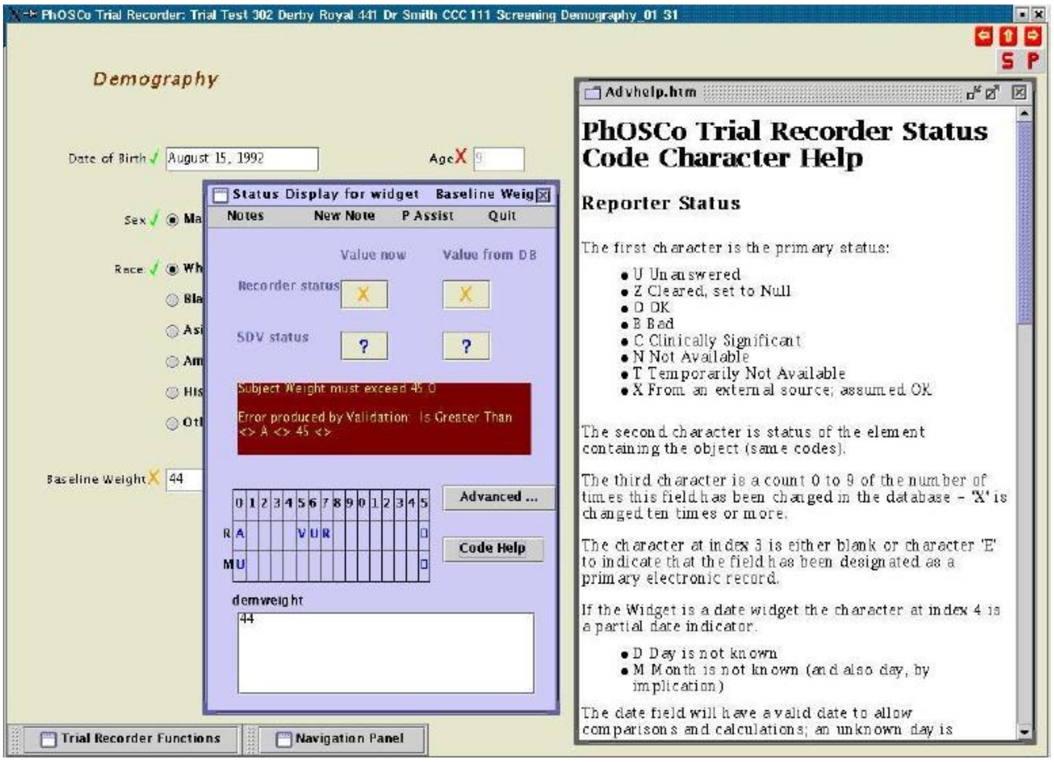
Build Validation Is Greater Than on widget demweight

No more parameters required
45
Validation Error Level: Bad Data
Error Message: Subject Weight must exc
□ Condition by Logical Test

Diagram 11: Trial Builder (www.penguintrials.com)

Trial Recorder

The Trial Recorder is the main application program of PhOSCo (see Diagram 12). This module is used to collect the clinical data information about the patients according to the trial, which was specified in the Trial Builder. Since the Trial Builder also put validation criteria, the trial recorder can be controlled. Once the users entered the clinical trial information, the information is stored into the database. This recorder is mainly used by the clinical trial investigator and its staff. A data manager is also allowed to update certain fields if needed. Below there is an image of the Trial Recorder (Penguin Trials Ltd. & Co. KG, Pharma Open Source Community, 2007).



PhOSCo Trial Recorder: Trial Test 302 Derby Royal 441 Dr Smith CCC 111 Screening Demography_01 31

Demography

Date of Birth ✓ August 15, 1992

Age ✗ 9

Sex ✓ ● Ma

Race ✓ ● Wh

Baseline Weight ✗ 44

Status Display for widget Baseline Weig

	Value now	Value from DB
Recorder status	X	X
SDV status	?	?

Subject Weight must exceed 45.0

Error produced by Validation: Is Greater Than <> A <> 45 <>

	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5
R	A					V	U	R								□
M	U															□

demweight

44

Advhelp.htm

PhOSCo Trial Recorder Status Code Character Help

Reporter Status

The first character is the primary status:

- U Unanswered
- Z Cleared, set to Null
- O OK
- B Bad
- C Clinically Significant
- N Not Available
- T Temporarily Not Available
- X From an external source; assumed OK

The second character is status of the element containing the object (same codes).

The third character is a count 0 to 9 of the number of times this field has been changed in the database - 'X' is changed ten times or more.

The character at index 3 is either blank or character 'E' to indicate that the field has been designated as a primary electronic record.

If the Widget is a date widget the character at index 4 is a partial date indicator.

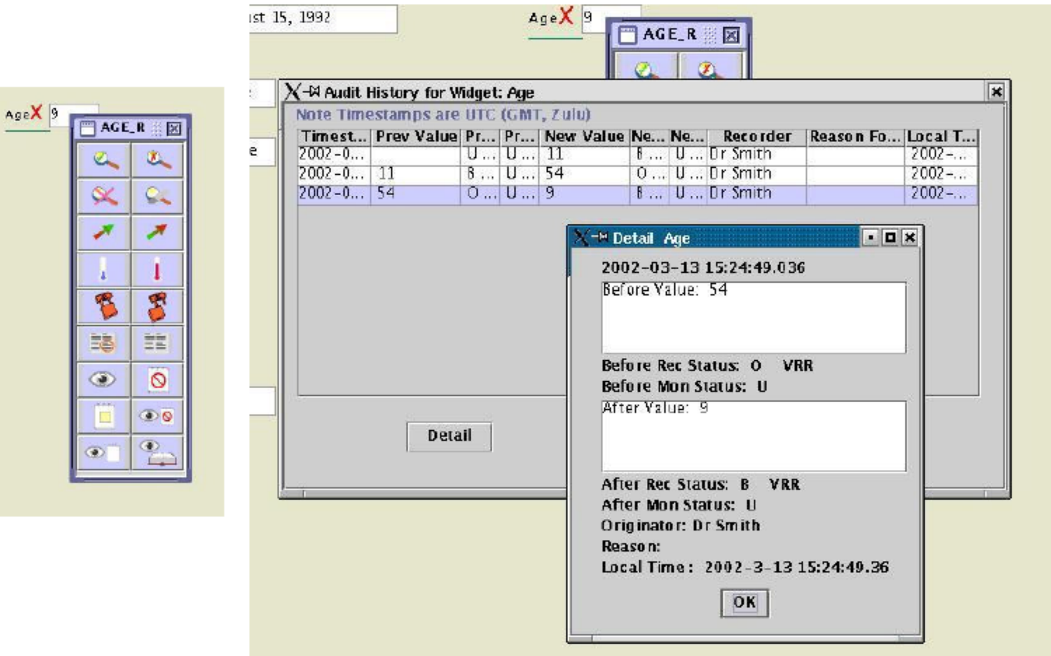
- D Day is not known
- M Month is not known (and also day, by implication)

The date field will have a valid date to allow comparisons and calculations; an unknown day is

Diagram 12: Trial Recorder (www.penguintrials.com)

Trial Monitor

The Trial Monitor allows the monitors to review the collected information from the Trial Recorder (see Diagram 13). The data managers are also able to perform some data management functions, such as updating the status of the clinical trial or adding notational information to specific clinical data. The Trial Monitor cannot be used to change any clinical data, but flags can be set in order to mark certain discrepancies. Below you can see an image of the Trial Monitor (Penguin Trials Ltd. & Co. KG, Pharma Open Source Community, 2007).



Audit History for Widget: Age

Note Timestamps are UTC (GMT, Zulu)

Timest...	Prev Value	Pr...	Pr...	New Value	Ne...	Ne...	Recorder	Reason Fo...	Local T...
2002-0...		U ...	U ...	11	B ...	U ...	Dr Smith		2002-...
2002-0...	11	B ...	U ...	54	O ...	U ...	Dr Smith		2002-...
2002-0...	54	O ...	U ...	9	B ...	U ...	Dr Smith		2002-...

Detail Age

2002-03-13 15:24:49.036

Before Value: 54

Before Rec Status: O VRR

Before Mon Status: U

After Value: 9

After Rec Status: B VRR

After Mon Status: U

Originator: Dr Smith

Reason:

Local Time: 2002-3-13 15:24:49.36

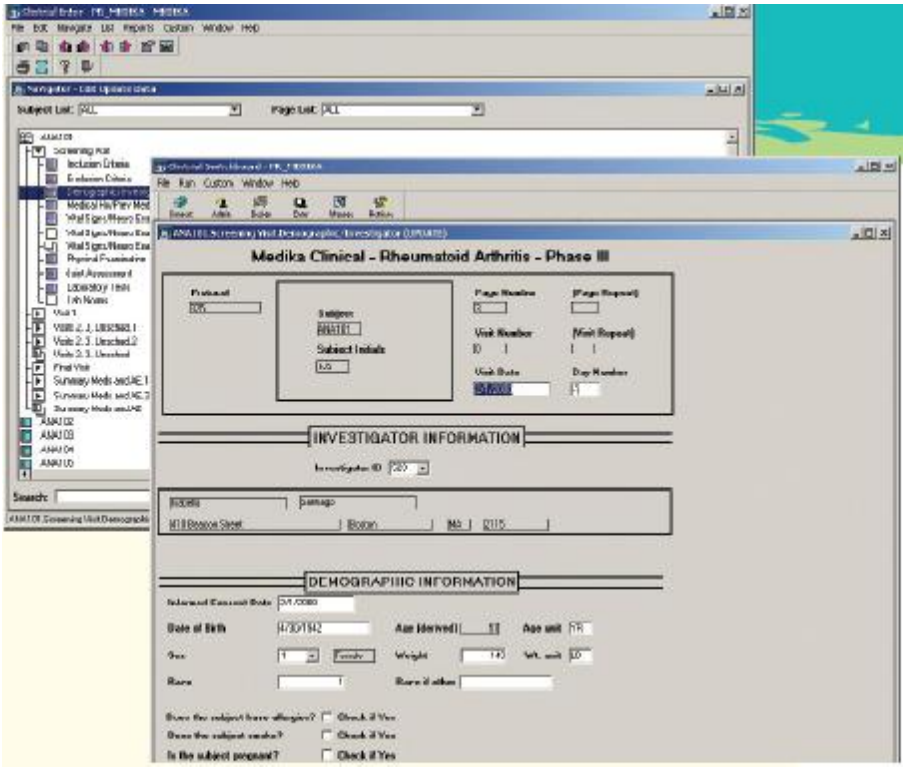
Diagram 13: Trial Monitor (www.penguintrials.com)

5.8.5 Phase Forwards Clintrial and Inform

Phase Forward is one of the leading providers for electronic data management and has slowly moved to more advanced data management solutions for clinical trials with integration of Cognos ReportNet's reporting capabilities. They provide solutions for electronic data capture, clinical data management and even adverse event reporting. The two applications, Clintrial and InForm are described below (Hanover, Julian, 2004, p. 14).

Clintrial

Clintrial is one of the leading clinical data management systems (CDMS). The system allows to create users, access rights and user groups without any database use. The main advantage of Clintrial is that users are able to create their own clinical trials through the system and without any programming (see Diagram 14). Once the forms are created, users can fill the data entry forms, which are provided with validations. With the captured data, users can then export the information to a variety of different file types like SAS, Excel, etc., depending on the users requirements, in order to create the electronic case report forms (eCRF). Below a screenshot of the Clintrial application is shown (Phase Forward, Clinical Data Management – Clintrial, 2007).



Medika Clinical – Rheumatoid Arthritis – Phase III

Subject Initials

Visit Number

(Visit Repeat)

INVESTIGATOR INFORMATION

DEMOGRAPHIC INFORMATION

Date of Birth

Age (derived)

Age unit

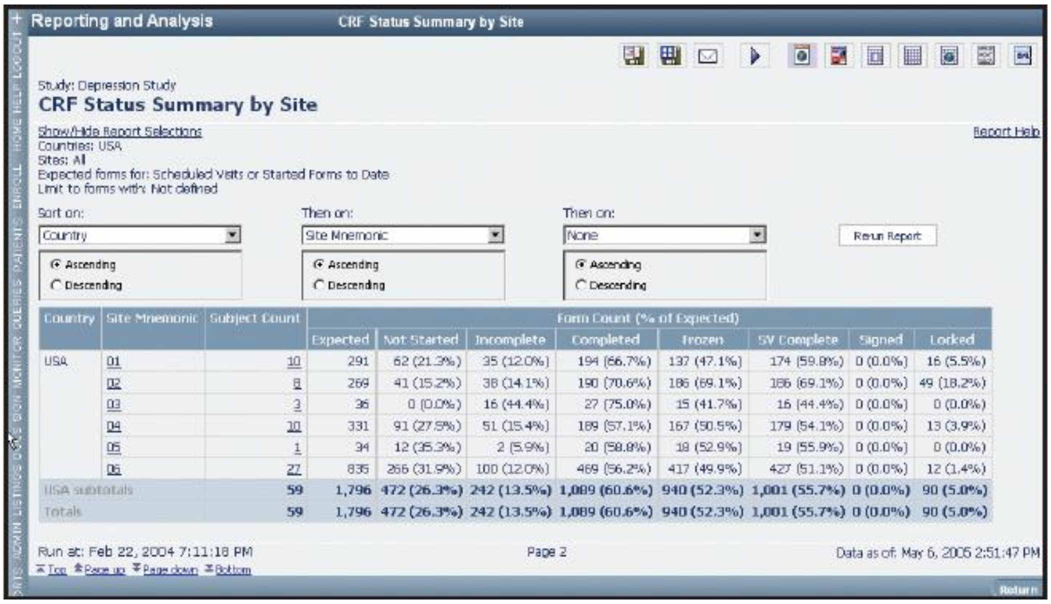
Weight

Is the subject pregnant? □ Check if Yes

Diagram 14: Clintrial in action (www.phaseforward.com)

InForm

An add-on for Clintrial includes the trial management application, InForm (see Diagram 15). It allows creating and administrating of clinical trials, integrating the Clintrial Clinical Data Management System allowing for an effective data management. Another added benefit is the reporting tool used for the eCRF forms, which simplifies the creation of case report forms without requiring any IT assistance. The main feature of InForm includes the web based architecture, creating a scalable option to the Clintrial application. Below you can find an image of the InForm application (Phase Forward, Electronic Data Capture – InForm, 2007).



Study: Depression Study

CRF Status Summary by Site

Show/Hide Report Selections
Countries: USA
Sites: All
Expected forms for: Scheduled Visits or Started Forms to Date
Limit to forms with: Not defined

Sort on: Country
● Ascending
○ Descending

Then on: Site Mnemonic
● Ascending
○ Descending

Then on: None
● Ascending
○ Descending

Country	Site Mnemonic	Subject Count	Form Count (% of Expected)							
			Expected	Not Started	Incomplete	Completed	Frozen	SV Complete	Signed	Locked
USA	01	10	291	62 (21.3%)	35 (12.0%)	194 (66.7%)	137 (47.1%)	174 (59.8%)	0 (0.0%)	16 (5.5%)
	02	8	269	41 (15.2%)	38 (14.1%)	190 (70.6%)	186 (69.1%)	186 (69.1%)	0 (0.0%)	49 (18.2%)
	03	3	36	0 (0.0%)	16 (44.4%)	27 (75.0%)	15 (41.7%)	16 (44.4%)	0 (0.0%)	0 (0.0%)
	04	10	331	91 (27.5%)	51 (15.4%)	189 (57.1%)	167 (50.5%)	179 (54.1%)	0 (0.0%)	13 (3.9%)
	05	1	34	12 (35.3%)	2 (5.9%)	20 (58.8%)	18 (52.9%)	19 (55.9%)	0 (0.0%)	0 (0.0%)
	06	27	835	266 (31.9%)	100 (12.0%)	469 (56.2%)	417 (49.9%)	427 (51.1%)	0 (0.0%)	12 (1.4%)
USA subtotals		59	1,796	472 (26.3%)	242 (13.5%)	1,089 (60.6%)	940 (52.3%)	1,001 (55.7%)	0 (0.0%)	90 (5.0%)
Totals		59	1,796	472 (26.3%)	242 (13.5%)	1,089 (60.6%)	940 (52.3%)	1,001 (55.7%)	0 (0.0%)	90 (5.0%)

Run at: Feb 22, 2004 7:11:18 PM
Page 2
Data as of: May 6, 2005 2:51:47 PM

Top Page up Page down Bottom

Diagram 15: InForm (www.phaseforward.com)

6 Web Technologies

Web interfaces accept input, offer output by generating web pages and provide real time control by eliminating the need to refresh a traditional HTML based web browser. Java Enterprise Edition 5 (Java EE) is a good example of a standard-based approach that works. Ralph Steyer, Chief technical officer at ICEsoft Technologies Inc. appraised in 2005 that there are more than 250,000 Java EE enterprise application deployments, and growing by more than 30,000 per year (Steyer, 2006, p.235ff). Furthermore Ajax-applications enforce the processing on an application server, if you don't want to run the whole business logic on the client.

6.1 Java Enterprise Edition

The Java Platform Enterprise Edition (Java EE) was formerly known as Java 2 Platform Enterprise Edition (J2EE). Java EE is a platform which offers an industrial standard for creating distributed multi-tier applications. The Java EE 5 specification was developed under JSR 244 and the release (Shannon, 2006, p.iii) was finalized on May 11, 2006. Java EE 6 is targeted to ship in 2008[2].

Java EE includes quite a lot of application programming interface (API) specifications, such as Java Database Connectivity (JDBC), Java Remote Method Invocation (Java RMI), Java Message Service (JMS), XML, web services, and more. The platform also includes feature components like JavaBeans, Java Servlets, JavaServer Pages, JavaServer Faces et cetera, which is nicely organized through Java EE (Shannon, 2006, p.6-14). All these techniques are needed to develop our prototype AlphaNet. In addition the Java EE platform has also features such as fail-over, scalability and distribution of load, which are very important for the project. The following chapters describe the main Java EE technologies and services which were used for the prototype implementation.

[2] http://jcp.org/en/jsr/detail?id=313, Retrieved on 30.05.2007

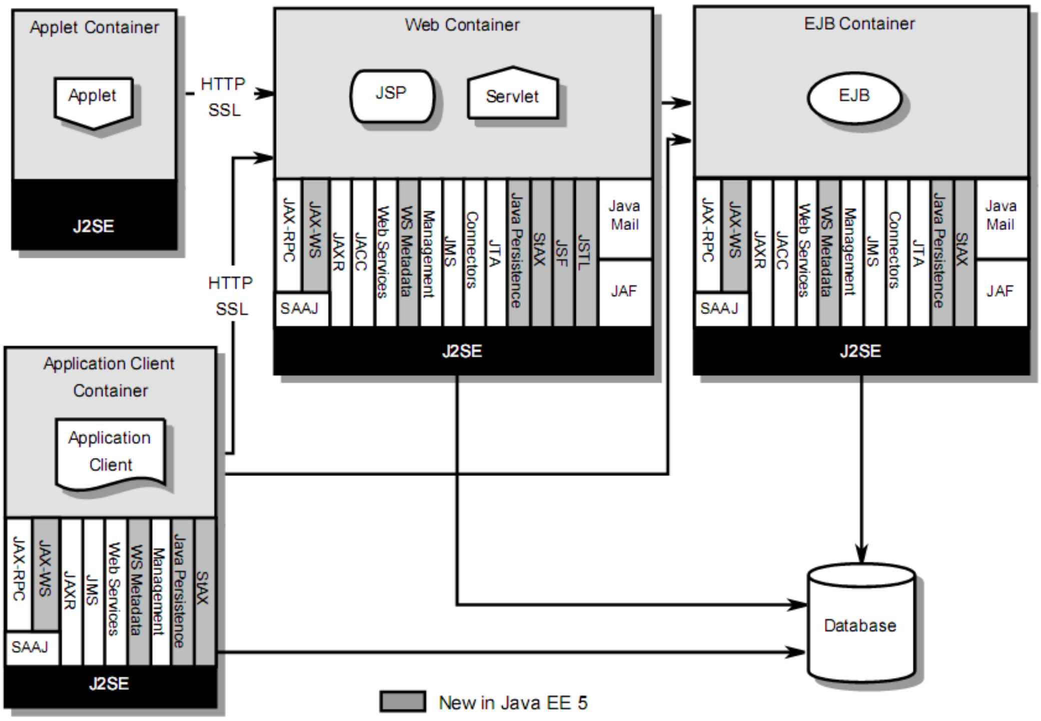


Diagram 16: Java EE Architecture Diagram (Shannon Bill, 2006, p.6)

The architectural elements of the Java EE platform are shown in Diagram 16: Java EE Architecture Diagram (Shannon Bill, 2006, p.6) above. As Sun Microsystems describes in their Specification:

> *"The Containers, denoted by the separate rectangles, are Java EE runtime environments that provide required services to the application components represented in the upper half of the rectangle. The services provided are denoted by the boxes in the lower half of the rectangle. For example, the Application Client Container provides Java Message Service (JMS) APIs to Application Clients, as well as the other services represented. [...] The arrows represent required access to other parts of the Java EE platform. The Application Client Container provides Application Clients with direct access to the Java EE required Database through the Java API for connectivity with database systems, the JDBCAPI. Similar access to databases is provided to JSP pages and Servlets by the Web Container and to enterprise beans by the EJB Container."* (Shannon Bill, 2006, p.5)

6.2 Java Database Connectivity

As soon as Java EE components bring the Java Database Connectivity (JDBC) API into play, the container manages their communications and data sources. In other words Java EE component developers indirectly use the JDBC API's transaction and data source management facilities. See the Java EE Platform Specification for additional details (Shannon, 2006, p.56f). Java EE components used for our implementation, such as JavaServer Pages, JavaServer Faces, and Enterprise Java Beans (EJB) components, require access to our relational data and therefore uses the container JDBC API for the connectivity.

The JDBC API defines how a client may access a relational database. The application programming interface is divided into two interfaces. First of all an application-level interface used by the application components to access a database, and a second service provider interface to connect a JDBC driver to the Java EE platform (Andersen, 2006. p.15).

Common environments for JDBC applications are the two-tier model and the three-tier model. The two-tier model separates functionality into a client layer and a server layer. In this place we won't discuss this model, more details on the two-tier model can be found written by Andersen (2006, p.17f). The three-tier model offers an architecture, which is developed and designed to supply enhanced performance, scalability and availability for enterprise applications. This model introduces a middle-tier server to the business logic and infrastructure. The three main tiers, which are divided into client tier, middle-tier server and the data source, are specified as shown in Diagram 17 on the next page (Andersen, 2006. p.17-20). Within the middle-tier server there are applications to interact with the client and the business logic. T application server is used to provide a management infrastructure for these applications. And a JDBC driver is required to supply connectivity to the primary data sources.

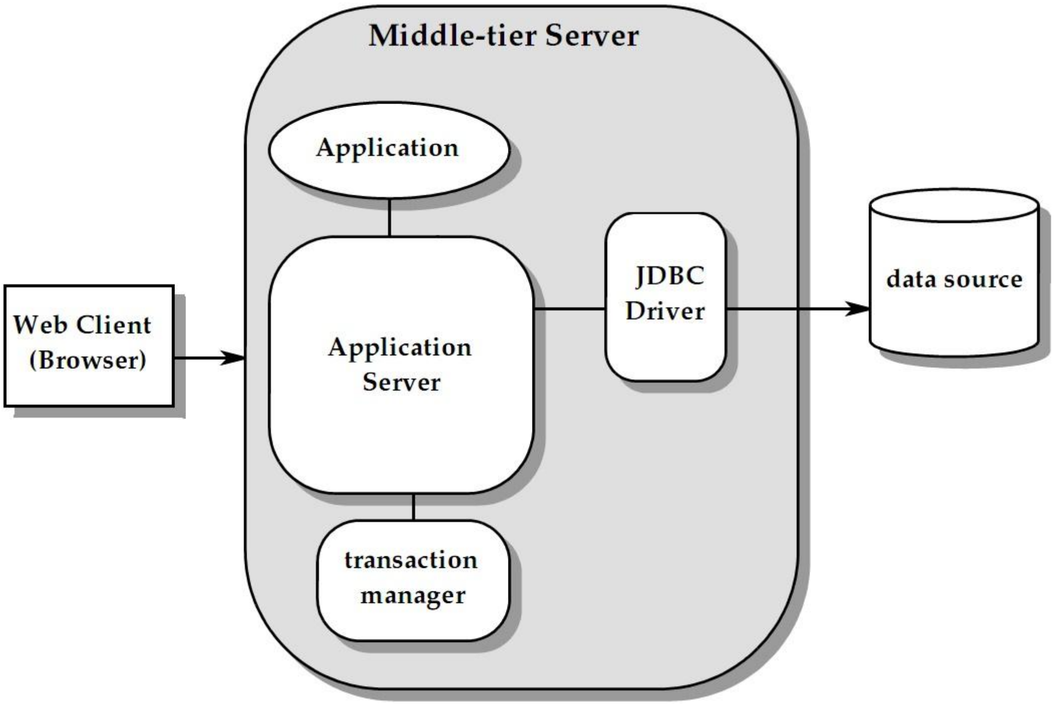


Diagram 17: Three-tier Model (Andersen Lance, 2006. p.19)

The JDBC driver is written in native code and not in Java, and is closed source. An alternative is the Open Database Connectivity (ODBC)[3].

6.3 JavaServer Pages

JavaServer Pages (JSP) platform is a Java Enterprise Edition technology that allows software developers to dynamically generate HTML, DHTML, XHTML, XML or other types of documents, in reaction to a Web client's request. JSP is released by Sun Microsystems.

"JSP technology provides the means for textual specification of the creation of a dynamic response to a request. [...] A JSP page is a text-based document that describes how to process a request to create a response. The description intermixes template data with dynamic actions and leverages the Java Platform."

Delisle Pierre, Luehe Jan, Roth Mark, 2006, p.xxxi, xxxiv

[3] http://msdn.microsoft.com/library/default.asp?url=/library/en-us/odbc/htm/dasdkodbcoverview.asp, Retrieved on 30.05.2007

The technology is built on the concepts of template data, where templates are text or XML fragments which apply dynamic data to the templates and encapsulate different functionality. The JavaBeans component architecture facilitates an access to data and tag libraries providing custom actions, functions and validations. JSP actions are XML-like tags, which are used to invoke built-in functionality. Furthermore, the technology supports the creation of JSP tag libraries that act as extensions to the standard HTML or XML tags. Tag libraries supply a platform independent way to extend the capability of a Web server. JSPs are compiled by a JSP compiler into Java Servlets (Steyer, 2006, p.239ff). The JSP pages specify the basis for the design of web based graphical interfaces for our implementation of AlphaNet.

6.4 JavaServer Faces

JavaServer Faces (JSF) technology is a user interface (UI) framework for server-side applications. JSF made it easier to construct a UI from a set of reusable UI components and simplifies the migration of application data to and from the UI (Burns, Kitain, 2006, p.1-23f).

Before JavaServer Faces, developers often built web applications with HTML UI components, Servlets or JavaServer Pages. This happened because HTML user interface components are the common standard which web browsers support. The problem is that such applications do not have rich UIs, compared to standalone clients, which as a result offers less functionality and reduced usability. There are two main components, which the JSF technology consists of (Jacobi, Fallows, 2006, p.3-15):

1. One component is the Java application programming interfaces (API) to design UI components, manage state, handle events, and validate input. It supports internationalization and openness. (An introduction about JSF APIs you can find in the JavaServer Faces Specification on page 1-27 – 1-30 (Burns, Kitain, 2006).

2. And secondly two JSP tag libraries for expressing UI components within a JSP page, and for linking components to server-side objects. More about the JSF Core Tag Library and the Standard HTML RenderKit Tag Library can be found in Burns, Kitain, 2006, p. 9-13 – 9-57.

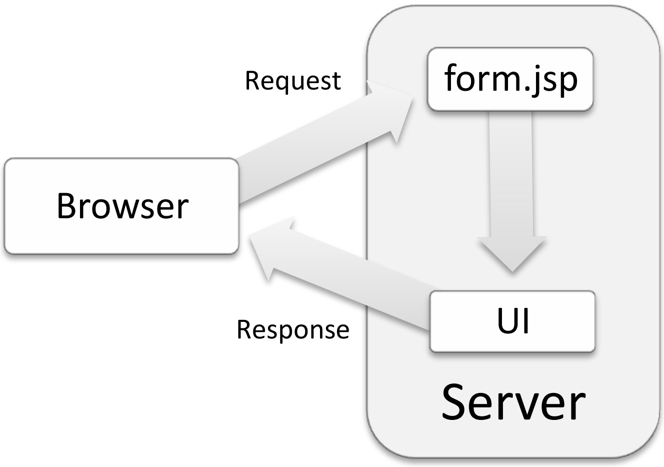


Diagram 18: Shows the relationship between client, server, and JSF

JSF also uses a controller Servlet, which is the only entry point to a JSF application. JSF deploy JSP pages as its view and JavaBeans as its model objects. Unlike Struts, JSF provides ready to use UI components that can be written on JSP pages. Upon a call of a page of a JSF application, FacesServlet constructs a component tree that represents the JSP page being requested. Some components can also trigger events. For page navigation, JSF uses an approach comparable to Struts. What differentiates a JSF application from non JSF Servlet / JSP application is that JSF applications are event-driven. The UI of a JSF application is one or many JSP pages that host Web components such as forms and input boxes. These components are specified by JSF custom tags. Such components can be nested inside another, and it is possible to draw a tree of components. Just as in normal Servlets/JSP applications, JavaBeans is used to store the data the user entered (Kurniawan, Xue, 2004, p.714).

For the implementation of AlphaNet we choose a Model-View-Control (MVC) framework with the support of JSF. For more details see Chapter 7.5.4 Software Architecture.

6.5 Struts

The Struts Framework is an open-source web application developed by Apache, which improves the Model 2 design model. It uses Java Servlet API and JSP technology so that the user does not have to write and compile one. Craig McClanahan created the first version and was donated to the Apache Foundation in the year 2000. Formerly known as Jakarta Struts, it is now an Apache project[4].

The main goal of Struts is to strictly separate the application logic that interacts with a database (model) from the view and the controller. It inherits each feature of MVC, and makes corresponding changes and expansions according to J2EE (Li, Ma, Feng, Ma. 2006, p.1030). The Model is used to design and implement system business logic in a form of Java Beans. Struts provides a Servlet called ActionServlet, which plays the role of the Controller (Kurniawan, Xue, 2004, p.713f).

6.6 Enterprise Java Bean

The Enterprise Java Bean (EJB) technology is one of the Java EE technologies. It is a multipart technology for the implementation of enterprise applications. The specification by Sun Microsystems defines them as "*...an architecture for component-based transaction-oriented enterprise applications*" (DeMichiel, Keith, Enterprise JavaBeans 3.0 – Specification, p. 34).

The creation utilities (version 3.0) simplifies the entire development process. The utility allows the users to add Java comments, create dependencies, as well as add certain suitable components such as EJB Timer, which defines a specific time when it should be activated and perform a defined task. Furthermore it solves serious drawbacks of previous versions, such as creating restore points, which allows the user to return to a previous version (DeMichiel, Keith, Enterprise JavaBeans 3.0 – Specification, p. 34 ff).

[4] http://struts.apache.org/, Retrieved on 13.06.2007

6.7 Asynchronous JavaScript and XML

Asynchronous JavaScript and XML also known as Ajax, is a web development technique for creating interactive web applications with the look and feel of a normal desktop application. The intention is that the web page does not have to be reloaded each time the user requests a change. This increases the web page's interactivity, speed and usability (Jacobi, Fallows, 2006, p 173 - 211).

The term web 2.0 has become more and more popular in recent months. Often these are social network applications which are perfectly suitable to provide background information on people (Wikipedia.org, Web 2.0, 2007). Examples are del.icio.us[5], flickr[6], 43things[7], writely[8], num sum[9] or ajax13[10]. Generally, the technologies and services that comprise web 2.0 regularly include Ajax (Adler, 2005, p.19ff).

One group of web 2.0 applications can be described as web-based applications. Those include word processing, spreadsheet and slide-show presentation offering simple online clones of offline office products. Typically, these Web 2.0 applications work with the “What You See Is What You Get” (WYSIWYG) concept, often supported by Ajax and Java technologies (Reichinger, 2006, p.55ff). This Rich Internet applications are built with similar techniques like Ajax, Adobe Flash or Flex, that allow web pages to partly update content without refreshing the whole page (Treese, 2006, p.15ff).

[5] http://del.icio.us/, Retrieved on 02.06.2007

[6] http://www.flickr.com/, Retrieved on 02.06.2007

[7] http://www.43things.com/, Retrieved on 02.06.2007

[8] http://docs.google.com/, Retrieved on 02.06.2007

[9] http://www.numsum.com/, Retrieved on 02.06.2007

[10] http://us.ajax13.com/en/, Retrieved on 02.06.2007

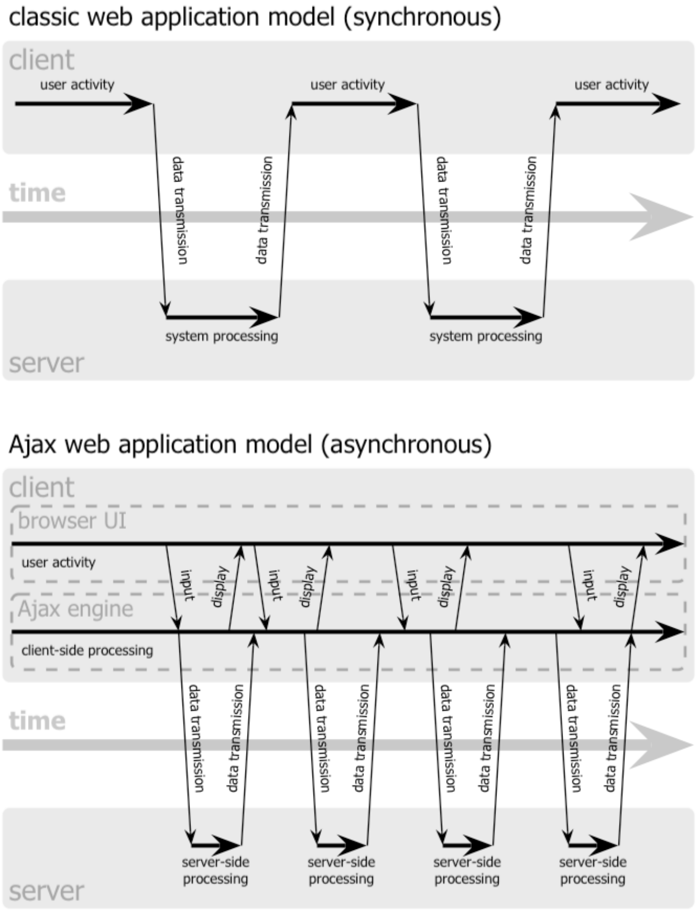


Diagram 19: Synchronous vs. Asynchronous (Garret Jesse, Ajax, 2005)

Diagram 18 above shows the synchronous interaction pattern of a traditional web application (top) compared with the asynchronous pattern of an Ajax application (bottom). But Ajax isn't really a new technology (Garret, Ajax: A New Approach to Web Applications, 2005). It combines a number of existing technologies in powerful new ways. In general, Ajax uses XHTML and CSS for a standard-based presentation. The communication is done by the Document Object Model (DOM). For Data exchange and operations often XML and XSLT is used, but you can also use other techniques like JavaScript Object Notation (Jason). To maintain the asynchronous data retrieval, XMLHttpRequest is used, whereas JavaScript binds everything together. As described before Ajax does more than only loading a simple webpage. At the beginning of the session, the browser loads an Ajax engine, often written in JavaScript. This engine is responsible for both rendering the interface the user sees and communicating with the server on the user's behalf. The Ajax engine allows the user's interaction with the application to happen asynchronously which is independent of communication with the server. So the user is never staring at a blank browser window and an hourglass icon, waiting around for the server to do something. That's how the look and feel of a desktop application reaches the web.

6.8 Ajax Frameworks

"*A framework eases the work of the Ajax programmer at two levels: on the client side, it offers JavaScript functions to send requests to the server. On the server side, it processes the requests, searches for the data, and transmits them to the browser.*"

(Wikipedia.org, Ajax Frameworks, 2007)

The big problem with Ajax is that there are more than a hundred different frameworks. Some frameworks are very complex and provide complete libraries to build web applications. On Ajax Patterns (Ajax Patterns, Frameworks, 2007) you can find a great list with almost all frameworks which are available. They divide the frameworks into two big groups "JavaScript toolkits" and "server-side and hybrid frameworks". Furthermore JavaScript frameworks are mostly JavaScript toolkits. This group could be divided into these subcategories: Ajax dynamic graphical maps and diagrams, visual effects, Flash integration, logging, dealing with XML and widget libraries. The second group can be separated in C++, C#, Java, ColdFusion, Perl, PHP, Python, Ruby and multi language.

6.8.1 Client Side Frameworks

Client side frameworks are mostly toolkits using the XMLHTTPRequest object in a JavaScript file and providing some callbacks to do the asynchronous requests. A toolkit is generally used in reference to graphical user interface (GUI) toolkits. As described in the chapter above, there are many different toolkits, which makes it very difficult to decide on the right one (AjaxPatterns, Frameworks, 2007). Since our condition was the drag and drop element, the number of quality libraries and toolkits were drastically reduced. As a result, we tried a few frameworks with which we tested and implemented small parts of our application in order to decide on the final framework.

6.8.1.1 Prototype

Prototype is an open source JavaScript Framework that aims to simplify development of dynamic web applications. Prototype is freely distributable by Sam Stephenson under the terms of an MIT-style license[11]. The project is run in union with Ruby on Rails, but can be used independently as well. The framework enables to use object oriented concepts like classes and inheritance within JavaScript. Basic Ajax functionality such as web remoting is also supported. On the Prototype website (Stephenson, Prototype is a JavaScript Framework, 2007) one of the features that is promoted is the part of the Prototype framework, DOM extensions. Prototype adds many convenience methods to elements returned by the `$()` function. For example, through `$('example').addClassName('active').show()` the element with the ID `'example'`, adds a class name to it and is displayed if it was invisible before. The `'example'` element did not have those methods in originally JavaScript. For a quick entrance into the world of Prototype Ryan Campbell's "Quick Guide to Prototype"[12] is recommendable.

6.8.1.2 Open Rico

Open Rico is another open source JavaScript framework which supports Ajax infrastructure and user interaction. An XMLHttpRequest response can be routed to one or more callback operations, DOM objects, or JavaScript objects and the framework includes the drag-and-drop functionality. It also supports simple Ajax animation such as scaling and transitions. Rico offers a JavaScript object named AjaxEngine that makes it simple with Ajax to update the contents inside a page. It provides a very straightforward way to change the HTML content of any HTML element. But it also provides an open ended way to respond to more complex data sets returned via a JavaScript object. Rico is released under the Apache License[13], and is based on the Prototype JavaScript Framework (Bill and others, Open Rico, 2006).

[11] http://en.wikipedia.org/wiki/MIT_License, Retrieved on 11.06.2007

[12] http://particletree.com/features/quick-guide-to-prototype/, Retrieved on 11.06.2007

[13] http://www.apache.org/licenses/LICENSE-2.0.html, Retrieved on 11.06.2007

6.8.1.3 Dojo

Dojo is an Open Source DHTML toolkit written in JavaScript. Dojo aims to solve some long-standing historical problems with DHTML which prevented mass adoption of dynamic web application development. Main features are the drag and drop and the SVG-operation support, but Dojo comes with a lot more widgets. The Dojo Foundation is supported through IBM, Sun, AOL, OpenLaszlo and more (Dojo Foundation, Dojo – the JavaScript Toolkit, 2007). Some demos of the Dojo toolkit can be found on their website[14].

6.8.1.4 Script.aculo.us

Script.aculo.us provides a cross-browser interface with diverse JavaScript libraries with an animation framework, the drag and drop feature, some Ajax controls, DOM utilities, and unit testing. The visual effects framework for (X)HTML/CSS includes a series of expandable core effects. Script.aculo.us also applies auto completion for text fields and in-place editing (Fuchs, Script.aculo.us – JavaScript Toolkit, 2007). You can also find some demos on webpage of Script.aculo.us[15].

6.8.2 Server Side Frameworks

As the name Server side frameworks indicates, they are constituted on the server side. The big distinction to client side frameworks is that the Programmer does not need to code any JavaScript. Therefore you have to operate with a language which the API supplies through the framework. As a result, the developer can easily implement client side activities which get converted into normal AJAX functionalities when called-up (Maryka, 2006, p.3).

[14] http://dojotoolkit.org/demos, Retrieved on 11.06.2007

[15] http://wiki.script.aculo.us/scriptaculous/show/Demos, Retrieved on 11.06.2007

6.8.2.1 Google Web Toolkit

Google Web Toolkit (GWT) can be specified as a server side framework. GWT is an open-source toolkit by Google as part of the Google Code initiative, which is used for normal Java Swing programming on the server side in web pages using the GWT API. The GWT tools help developers during the implementation of a web application, so that the written Java code is interpreted to the relevant AJAX code on the client side. GWT emphasizes reusable, efficient solutions to reoccurring Ajax challenges, namely asynchronous remote procedure calls, history management, bookmarking, and cross-browser portability (Google, GWT - Build AJAX apps in the Java language, 2007). The Google Web Toolkit software is developed by Google under the Apache License, v. 2.0 (see chapter 6.8.1.2 Introduction).

6.8.2.2 Echo2

Echo 2 uses pure Java to code Ajax applications. The Java compiler automatically generates HTML and JavaScript in real time. Furthermore Echo2 coordinates messages between browser and server, whereas the messages were transmitted in XML. There is also the possibility to hand-write custom JavaScript components if desired. Echo2 has an Open-source license (Mozilla Public License[16] (MPL) or GNU LGPL) and is published by Next App, Inc. An online demo[17] can by found on their webpage (NextApp Inc., Echo2, 2007).

6.8.2.3 ZK

ZK is an open-source Ajax Web framework that enables rich user interface (UI) for Web applications with Java instead of JavaScript programming (Potix Corporation, ZK Framework, 2007). The framework is advertised as one of the most active projects in SourceForge.net. There is no need of compilation or proprietary expressions or scripts, just Java and EL expressions ZK includes an Ajax-based event-driven engine, sets of XUL and XHTML components. The markup language, called ZUML makes the design of user interfaces as simple as authorizing a HTML page. ZK also includes a

[16] http://www.nextapp.com/products/mpl_license.html, Retrieved on 12.06.2007

[17] http://demo.nextapp.com/Demo/app, Retrieved on 12.06.2007

lot of widget components and components in XUL and XHTML to enhance a web application. Among them are Grids, combo boxes, trees, list boxes, tab boxes, popup, menus, audio, timer and the drag and drop feature. Programming and design of new components is also possible. You can also add JavaScript Toolkits like DOJO or FCKeditor[18]. Through the server centric processing, the visual representations and contents are synchronized automatically between clients and servers. Cross browsers are supported, by rendering XUL and XHTML components into HTML tags and JavaScript. ZK is under an open-source license GNU General Public License[19] (GPL) and is published by Potix Corporation.

6.8.2.4 OpenLaszlo

OpenLaszlo is an open source platform for web applications (rich Internet applications) with a friendly user interface. The technology architecture connects client and server design with the administrative benefits and cost saving of web applications. OpenLaszlo 4.0 applications are written in a language called LZX[20] which originate from XML and JavaScript. LZX enables a declarative, text-based development that supports quick prototyping and software development best practices. LZX is similar to XUL[21], MXML[22], and XAML[23]. Through the technology's design it is easy to use for developers who are familiar with HTML and JavaScript (Laszlo Systems, OpenLaszlo, 2007). The technology compiles to several runtimes, such as Shockwave 7, 8, and DHTML with JavaScript (similar to native Ajax applications). Web Applications compiled to Shockwave Flash (SWF) 7 or 8 run in the Flash 9 player and DHTML code will run in any standard browser. OpenLaszlo is published under the open source Common Public License[24] (CPL).

[18] http://www.zkoss.org/zkdemo/userguide/, Retrieved on 10.06.2007

[19] http://www.gnu.org/copyleft/gpl.html, Retrieved on 12.06.2007

[20] http://www.openlaszlo.org/lps/docs/reference/, Retrieved on 10.06.2007

[21] http://www.mozilla.org/projects/xul/, Retrieved on 10.06.2007

[22] http://www.adobe.com/devnet/flex/articles/paradigm.html, Retrieved on 10.06.2007

[23] http://msdn2.microsoft.com/en-us/library/ms752059.aspx, Retrieved on 10.06.2007

[24] http://www.opensource.org/licenses/cpl1.0.php, Retrieved on 12.06.2007

6.8.2.5 JBoss Ajax4JSF

JBoss Ajax4jsf is an open source component framework which supports JSF, by adding Ajax technology to it. Ajax4jsf forces the full set of JSF advantages. As we previously described, we decided to implement AlphaNet using JSF/JSP and through our search first came across the JSF supporting library Ajax4jsf. With this technology it is possible to develop web applications without JavaScript. Ajax4jsf has rich components with the look-and-feel of a desktop application through the Ajax technology which can easily be combined into JSF applications. The following Diagram 20 shows the Ajax4jsf request processing flow.

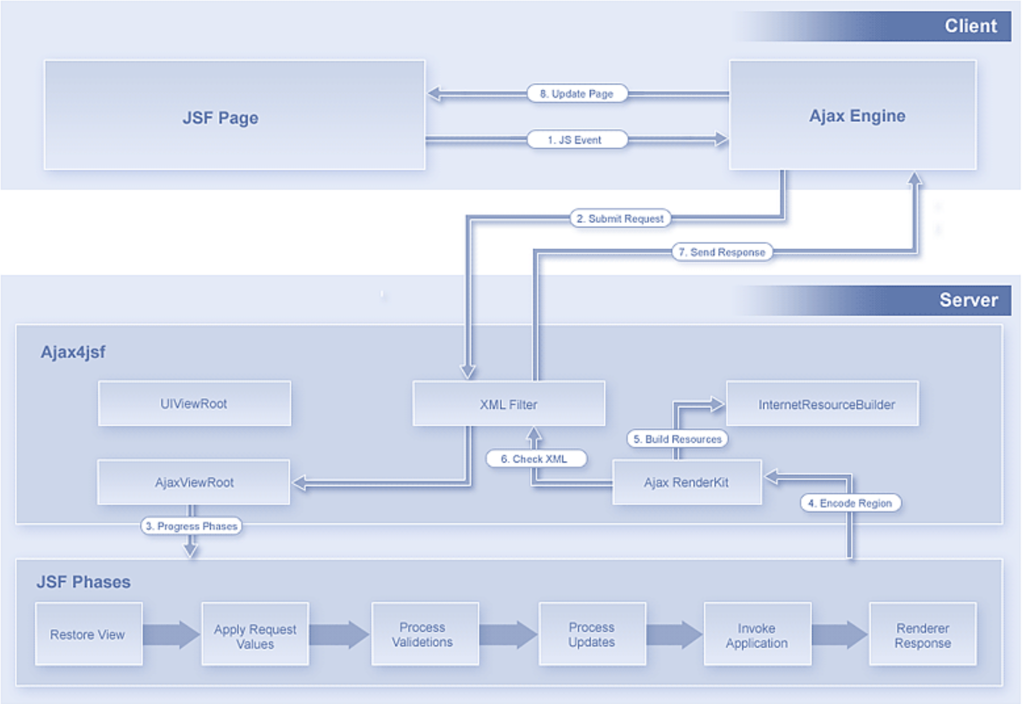


Diagram 20: Ajax4jsf request processing flow (Exadel, 2006, p.6)

The Ajax4jsf JavaScript engine runs on the client-side. The component development kit (CDK) contains a code-generation and a pattern facility using syntax similar to JSP. These resources help to minimize the usual creation of components. JBoss Ajax4jsf is developed under the Lesser General Public License[25] (LGPL) through JBoss a division of Red Hat (Red Hat Middleware, Ajax4jsf Developer Guide, 2007).

[25] http://www.gnu.org/licenses/lgpl.html, Retrieved on 12.06.2007

6.8.2.6 ICEfaces

ICEfaces is also an Ajax based solution for rich internet applications with pure Java. ICEfaces offer IDE Tool Integration – Bundles for BEA Workshop Studio, Sun Java Studio Creator 2, Eclipse, Oracle JDeveloper 10g, NetBeans v5.5 with Visual Web Pack (VWP) and BM Rational Application Developer v6.0 under the CE licence[26] (ICEsoft Technologies, ICEfaces, 2007). The Framework is also ready for use as a standalone bundle under the MPL (compared to Echo2). As Ajax4jsf, ICEfaces provides an environment for JSF, which replaces the regular HTML based JSF renderers with Direct-to-DOM (D2D) renderers. ICEfaces also has an integrated component suite. The technology also integrates a bridge to deliver presentation changes to the client browser and to communicate user interaction events back to the server. The basic architecture is shown in the Diagram 21 below.

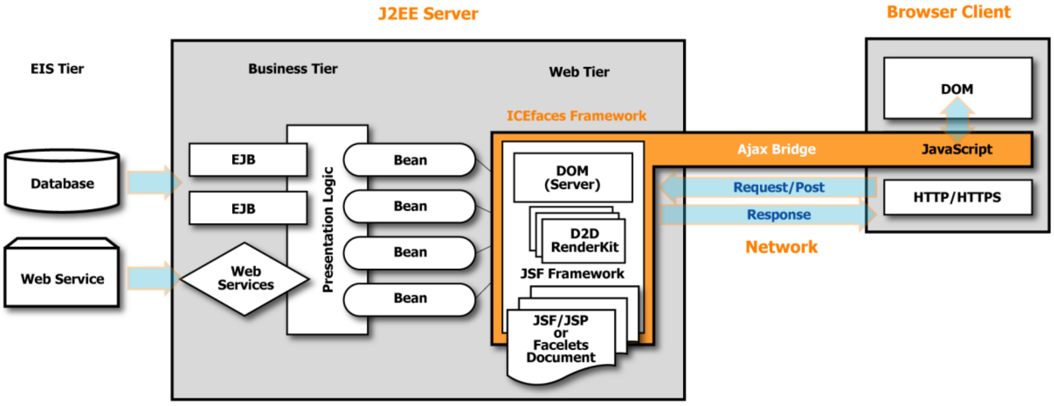


Diagram 21: Basic architecture of an ICEfaces enabled application (ICEsoft Technologies, ICEfaces - Developer's Guide, 2007)

The Ajax Bridge has server and client elements that organize the communication between browser (client) and server application. The Bridge is responsible for delivering growing presentation changes from the renderer to the browser, and collecting those changes in the browser DOM to affect the presentation changes. The Bridge is also responsible for detecting user interaction with the presentation, and delivering user events back to the application for processing through the standard JSF lifecycle (ICEsoft Technologies, ICEfaces – Developer's Guide, 2007). After a thorough analysis of the different frameworks, and with our decision to use JSF, we decided to take advantage of the features of ICEfaces for our application.

[26] http://www.icesoft.ca/downloads/license_community.html, Retrieved on 11.06.2007

7 AlphaNet - Implementation

> *"The killer app will not be a shrink-wrapped program that sells millions. The killer app will be a Web site that touches millions of people and helps them to do what they want to do."*
>
> Lou Gerstner

AlphaNet is comprised of a web application with a dynamic central database which allows the creation and management of clinical studies. Over a multi user system, users are able to individually create their own clinical studies as well as combine different clinical studies for statistical analysis. The right to modify, create or view the clinical studies is strictly regulated with the user management system. This hierarchical system assures the security of clinical studies and, more importantly, of the patient's anonymity

With the latest technology (Ajax and JSF) it is possible to create data entry screens quickly, easily and without any programming. The unique graphical user interface, allows dragging and dropping elements for a high-speed design of electronic case report forms (eCRF).

Through the dynamical structure of the database, there are no limitations to the creation of individual clinical studies. These studies can therefore entail data from wound analysis, bacteriological reports, nutritional data or even laboratory reports. These fields can easily be created and managed by the different users. In order to facilitate a clearly laid-out clinical study, the user also has the ability to create and integrate categories. The fields can then be associated with the category which provides a clear overview of the trials. In general, the user is able to set up study default parameters for the database, protocols, users, access rights and user groups without requiring any database knowledge.

For the safety and reliability of the application, data security is present throughout the entire system. First of all, the information stored in the database is protected with the high standard SHA-256 encryption. Secondly, the data transmission is secured through SSL (Secure Sockets Layer) encryption which allows safe communication between the server and the client. Finally, the unique user management system enables simplified yet secure data management. Clinical study creation, modification, view and data entry are all regulated depending on the user's rights.

The following sections will first describe the general user interface design and then discuss in detail the functionality of the clinical study documentation system. Once the functional requirements have been explained, the system's architecture will be discussed, followed by the description of the database model and all of its elements.

7.1 Project Overview

Presently for clinical studies, the user is required to manually create a clinical study form, print the form out, have the employees fill them according to the patient and send it to a secretary or a study assistant who then inputs the data into the computer. The main aspect of AlphaNet is to reduce this administrative work effort. AlphaNet entails the following business case:

- One stop for Clinical Study information
- Forecasting visibility
- Reduces duplicate processes across regions
- Improves ability to effectively manage multiple jobs while reducing time spent per job
- Consolidates operation meetings

The mission of AlphaNet is to proactively identify and manage different studies with unique input requirements while maintaining awareness between the different studies.

The AlphaNet system will be comprised of two main parts, the creation of clinical studies, and the management of the clinical studies. The creation of clinical studies includes field management and category management. The field management system allows different fields of different types to be created and managed by the users within a clinical study. For the purpose of creating a clearly laid-out clinical study, the user will also have the ability to create and integrate categories. The fields can then be associated with the category which in return provides a clear overview of the clinical study.

Once the clinical study has been created, the management of clinical studies comes into play. This includes managing the patients and capturing the patient's data for the respective clinical study. Furthermore, a scheduler will be implemented, which allows the user to schedule the capture dates for the individual patients. The right to modify, create, view or manage the clinical studies will be strictly regulated with the user management system. The main purpose of the user management system is to provide privacy and security for the different clinical studies and, more importantly, for the patient's anonymity. The sections below describe the user interface design and the functional specifications for the creation of clinical studies.

7.2 User Profile

There are five different types of users, which will access the application. Below is the list of all the user types in the AlphaNet application. The table also contains a general description of the user roles, which are then mentioned in the individual use cases. Furthermore, primary language is given, even though the systems locale will be altered. Additionally, the table entails information in the expected usage of the user roles and the access limitations. Finally, the table states if the given user role is required to be familiar with the subject matter or the interface.

#	User Type	Description of User	Language	Expected System Usage	Unrestricted access to system?	Familiar with subject matter and interface?
1	Admin	Person who has access to change and/or create all or any entries	English	Daily	Yes	Yes
2	Project Leader	Person who has access to create a clinical study and change only the studies he has created.	English	Weekly	No	Yes
3	Monitor	Person who has access to unlock a project or close a project.	English	Weekly	No	Yes
4	Investigator	Person who can view and enter patient information to the clinical studies that the Project Lead or Admin have assigned the user to.	English	Daily	No	Yes

5	Trial Nurse	Person who can only input patient information for specific patients	English	Daily	No	No

Table 1: System Users

7.3 User Interface Design

The following section provides a brief description of the user interface design which is necessary for general information of the AlphaNet system. The purpose of this section is to describe the general functionality of AlphaNet and describe the user interface design. This information is then used to describe the functional specifications in greater detail.

7.3.1 Login

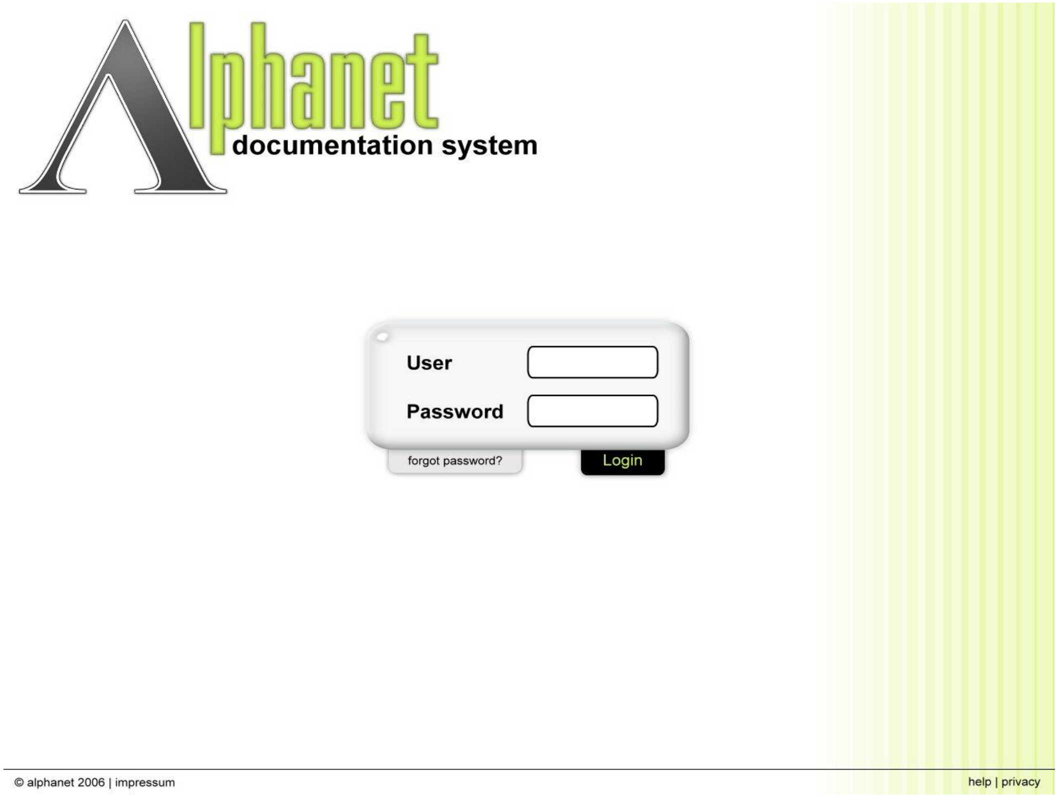
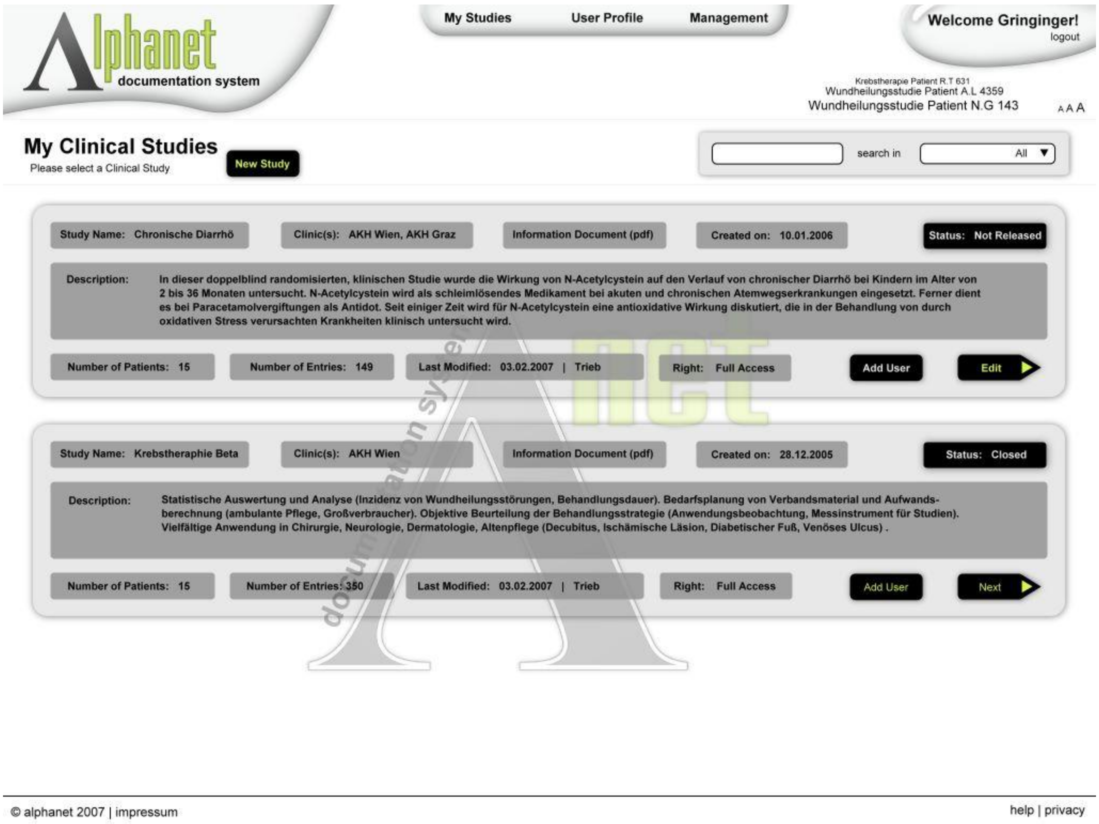


Diagram 22: Login: User Interface Design

The goal of the login is for the users to log onto the AlphaNet Application. This use case is designed for all user roles. The login page entails two text fields for the username and password and a login button, as well as a “forgot password” button, which is used to email the password to the mentioned username. Once the user enters the username and password, the system validates the credentials. If the user enters the wrong password or username, the page is refreshed stating the same. If the user is a valid user, then the page is forwarded to the homepage.

7.3.1 Homepage



My Clinical Studies
Please select a Clinical Study

Study Name: Chronische Diarrhö | Clinic(s): AKH Wien, AKH Graz | Information Document (pdf) | Created on: 10.01.2006 | Status: Not Released

Description: In dieser doppelblind randomisierten, klinischen Studie wurde die Wirkung von N-Acetylcystein auf den Verlauf von chronischer Diarrhö bei Kindern im Alter von 2 bis 36 Monaten untersucht. N-Acetylcystein wird als schleimlösendes Medikament bei akuten und chronischen Atemwegserkrankungen eingesetzt. Ferner dient es bei Paracetamolvergiftungen als Antidot. Seit einiger Zeit wird für N-Acetylcystein eine antioxidative Wirkung diskutiert, die in der Behandlung von durch oxidativen Stress verursachten Krankheiten klinisch untersucht wird.

Number of Patients: 15 | Number of Entries: 149 | Last Modified: 03.02.2007 | Trieb | Right: Full Access

Study Name: Krebstheraphie Beta | Clinic(s): AKH Wien | Information Document (pdf) | Created on: 28.12.2005 | Status: Closed

Description: Statistische Auswertung und Analyse (Inzidenz von Wundheilungsstörungen, Behandlungsdauer). Bedarfsplanung von Verbandsmaterial und Aufwandsberechnung (ambulante Pflege, Großverbraucher). Objektive Beurteilung der Behandlungsstrategie (Anwendungsbeobachtung, Messinstrument für Studien). Vielfältige Anwendung in Chirurgie, Neurologie, Dermatologie, Altenpflege (Decubitus, Ischämische Läsion, Diabetischer Fuß, Venöses Ulcus) .

Number of Patients: 15 | Number of Entries: 350 | Last Modified: 03.02.2007 | Trieb | Right: Full Access

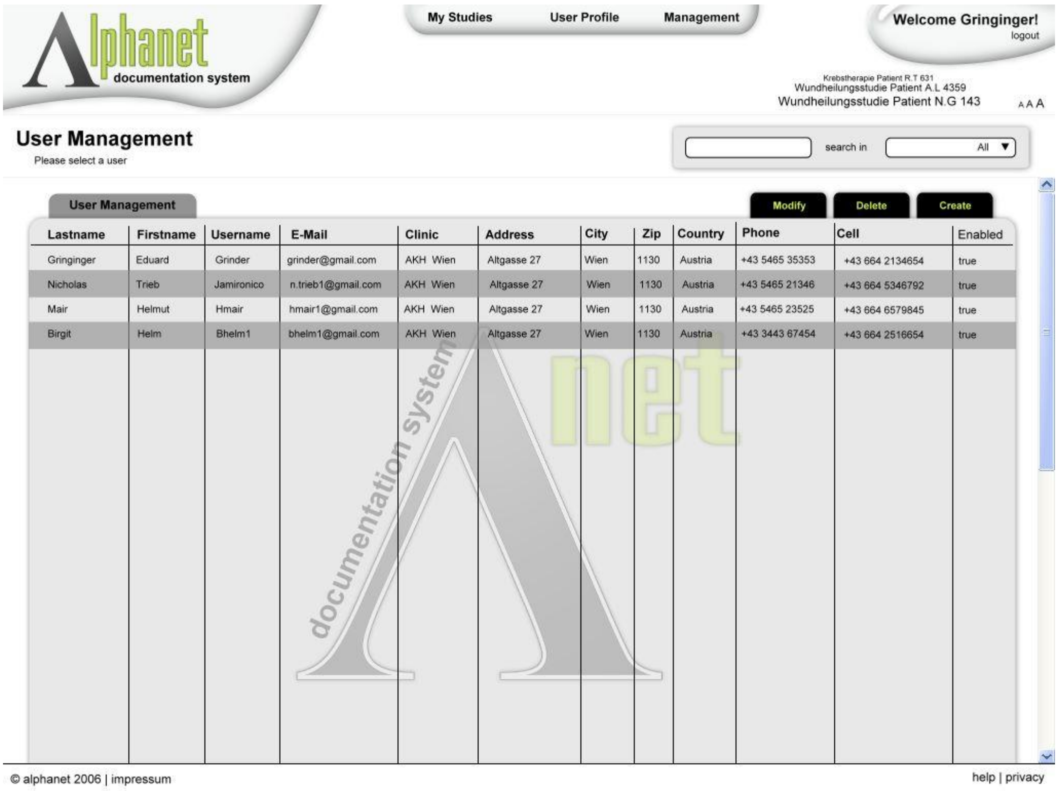
© alphanet 2007 | impressum

Diagram 23: Homepage: User Interface Design

The homepage is designed for all users, but depending on the user’s type and rights different functionalities are available. The page displays a list of clinical studies, which are associated to the user. In case a user is not part of a clinical study, the page displays a link to the administrator or project leader. The item in the list displays the clinical study name, the location, a link to the informational PDF document, the date it was created, the status, the number of patients and entries associated with the clinical study, the last modified date and finally the right the user has for the clinical study. If the user is a project leader or administrator, then the user can add another user to the clinical study.

Furthermore, depending on the status of the clinical study (i.e. Released, Not Released or Closed) a different button is displayed. In case the clinical study has not been released for entries, the clinical study has an edit button displayed for users with full access. This allows the user to modify the clinical study. Once the clinical study has been released, the clinical study can not be modified anymore, and patients and entries can be added to the clinical study. Therefore, a button called “Next” is displayed for the clinical studies with status “Release”. Finally, If the user is a administrator or project leader, then an add clinical study button is displayed for the user.

7.3.2 User Management



User Management

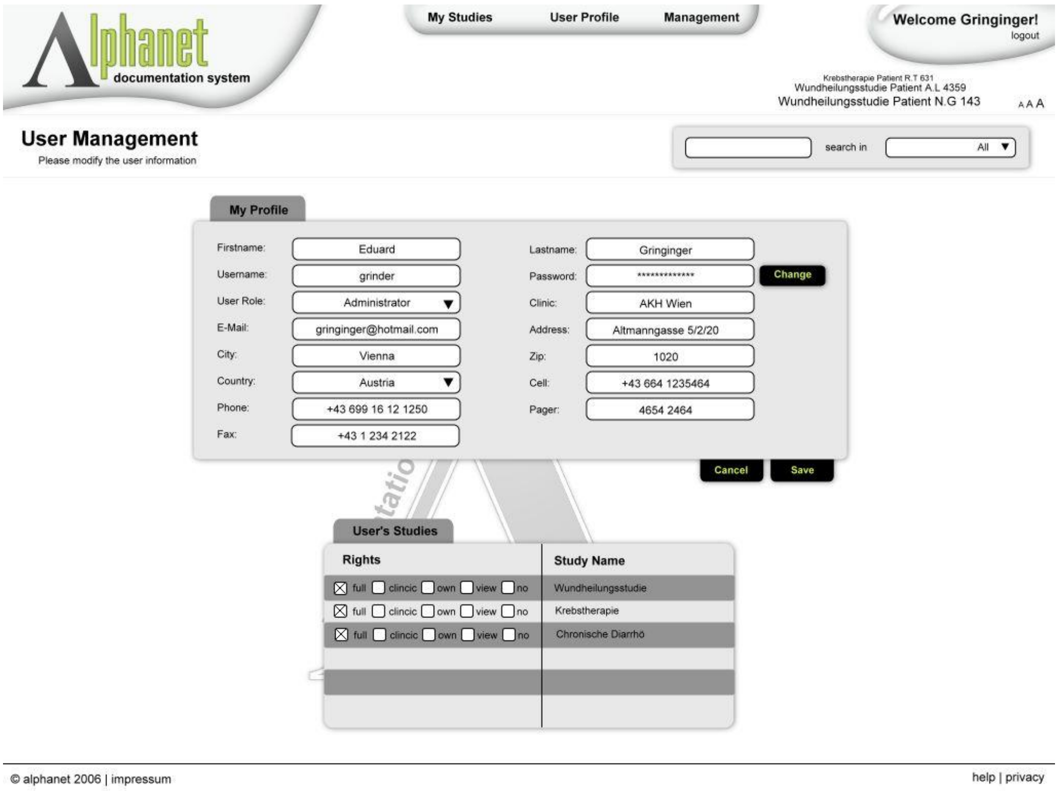
Please select a user

Lastname	Firstname	Username	E-Mail	Clinic	Address	City	Zip	Country	Phone	Cell	Enabled
Gringinger	Eduard	Grinder	grinder@gmail.com	AKH Wien	Altgasse 27	Wien	1130	Austria	+43 5465 35353	+43 664 2134654	true
Nicholas	Trieb	Jamironico	n.trieb1@gmail.com	AKH Wien	Altgasse 27	Wien	1130	Austria	+43 5465 21346	+43 664 5346792	true
Mair	Helmut	Hmair	hmair1@gmail.com	AKH Wien	Altgasse 27	Wien	1130	Austria	+43 5465 23525	+43 664 6579845	true
Birgit	Helm	Bhelm1	bhelm1@gmail.com	AKH Wien	Altgasse 27	Wien	1130	Austria	+43 3443 67454	+43 664 2516654	true

Diagram 24: User Management: User Interface Design

The goal of user management is to search, modify, delete and create users for the AlphaNet application. As previously mentioned, a user can pertain one out of five different user roles. These roles can be specified through this use case. Above is the user interface design for the general use case. This page is only visible for project leaders and administrators. First of all, the user is able to select one or more users and press delete in order to delete the selected users. Secondly, the user is able to select only one user to modify the user. And finally, the project leader or administrator is able to create a new user (see section 7.3.3).

7.3.3 Create/Modify User



User Management

Please modify the user information

My Profile

Firstname:	Eduard	Lastname:	Gringinger
Username:	grinder	Password:	*************
User Role:	Administrator ▼	Clinic:	AKH Wien
E-Mail:	gringinger@hotmail.com	Address:	Altmanngasse 5/2/20
City:	Vienna	Zip:	1020
Country:	Austria ▼	Cell:	+43 664 1235464
Phone:	+43 699 16 12 1250	Pager:	4654 2464
Fax:	+43 1 234 2122		

User's Studies

Rights	Study Name
☒ full ☐ clincic ☐ own ☐ view ☐ no	Wundheilungsstudie
☒ full ☐ clincic ☐ own ☐ view ☐ no	Krebstherapie
☒ full ☐ clincic ☐ own ☐ view ☐ no	Chronische Diarrhö

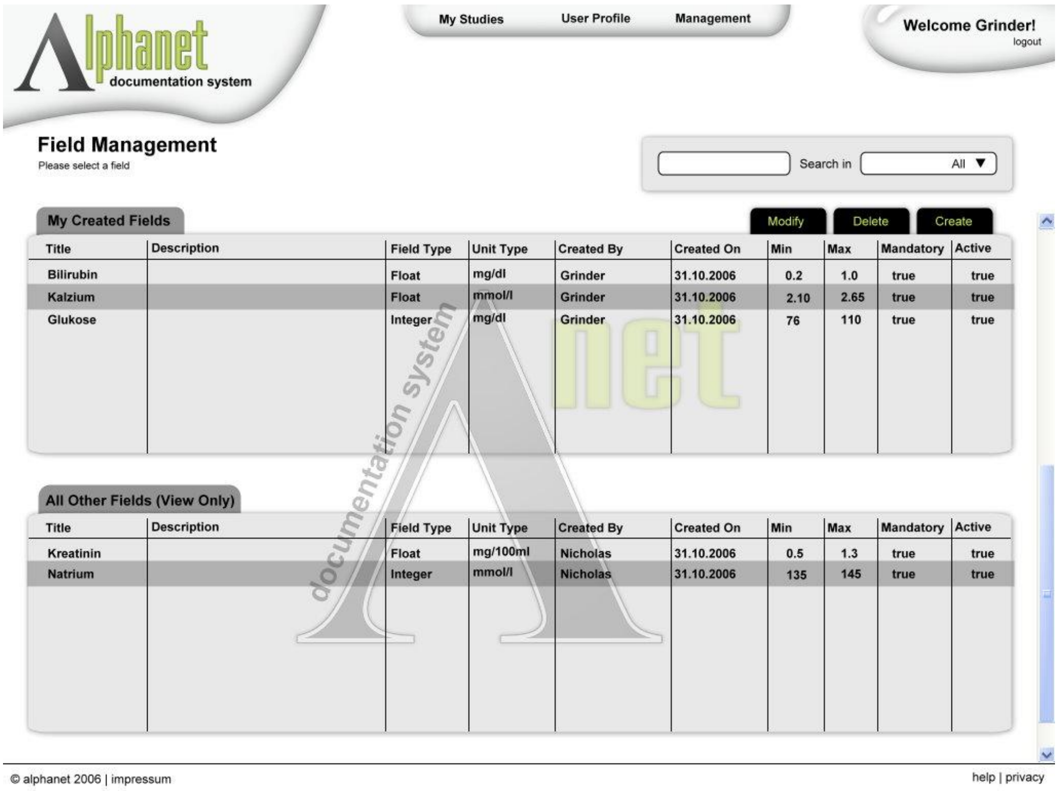
Diagram 25: Create/Modify User: User Interface Design

The above screen is used in order to create or modify a user's profile (see Diagram 25). This page displays the typical user information such as the email address, username, first and last name, etc. as well as the clinic where the user is located. The modify page is visible for all users, while the create page is only possible for a project leader or an administrator. Furthermore, only the project leaders or administrators are able to add the user to a clinical study, set the role of the user, as well as set the rights the user has for specific clinical studies. There are 5 different user rights (for more details see chapter 7.6.2.3 User Roles):

1. Full Access
2. Clinic Only Access
3. Only Own Patient Access
4. Read Only Access
5. No Access

On save, the system stores the information and on cancel the user is brought back to the user management page.

7.3.4 Field Management



Field Management

Please select a field

My Created Fields

Title	Description	Field Type	Unit Type	Created By	Created On	Min	Max	Mandatory	Active
Bilirubin		Float	mg/dl	Grinder	31.10.2006	0.2	1.0	true	true
Kalzium		Float	mmol/l	Grinder	31.10.2006	2.10	2.65	true	true
Glukose		Integer	mg/dl	Grinder	31.10.2006	76	110	true	true

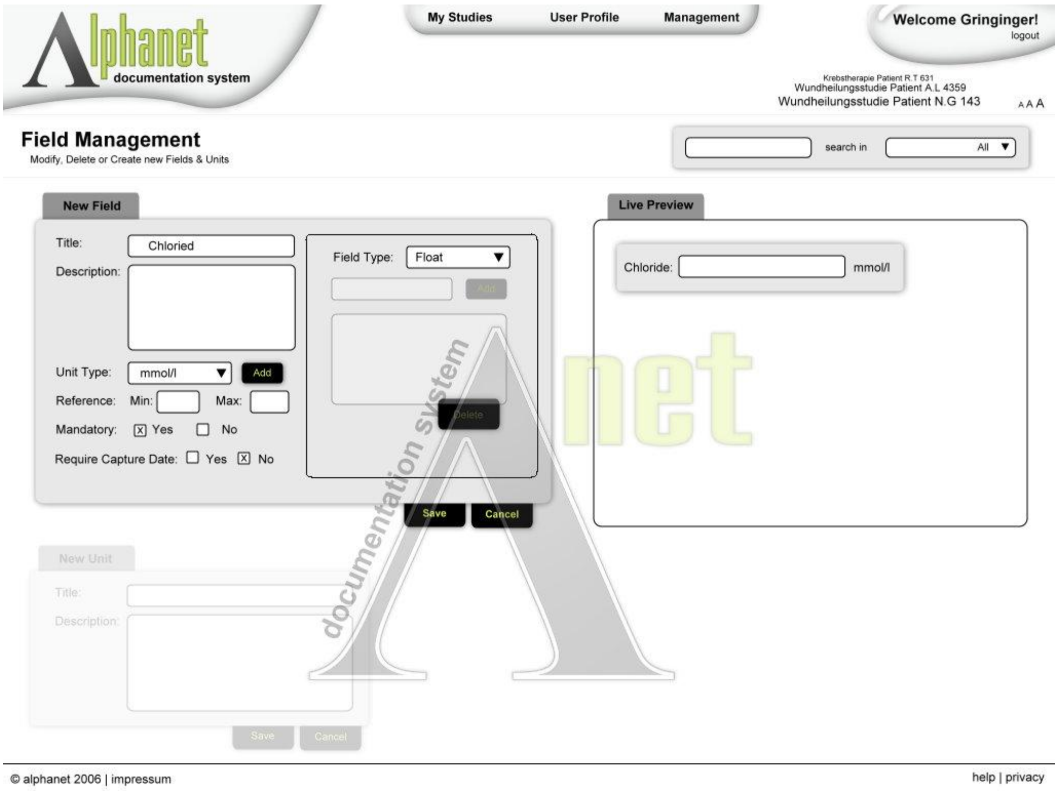
All Other Fields (View Only)

Title	Description	Field Type	Unit Type	Created By	Created On	Min	Max	Mandatory	Active
Kreatinin		Float	mg/100ml	Nicholas	31.10.2006	0.5	1.3	true	true
Natrium		Integer	mmol/l	Nicholas	31.10.2006	135	145	true	true

Diagram 26: Field Management: User Interface Design

Each clinical study can have any number of fields for the data input of a clinical study. The goal of this use case is to search, modify, delete and create these fields. An important aspect of this use case is that only the administrator and the project leader have the ability to create, modify and delete these fields. On this page, all the fields that a user has created, as well as fields that other users have created, are displayed. Only the fields which have not yet been used in a clinical study are able to be modified or deleted.

7.3.5 Create/Modify Field



Field Management
Modify, Delete or Create new Fields & Units

Title: Chloried
Description:
Field Type: Float
Unit Type: mmol/l
Reference: Min: Max:
Mandatory: ☒ Yes □ No
Require Capture Date: □ Yes ☒ No

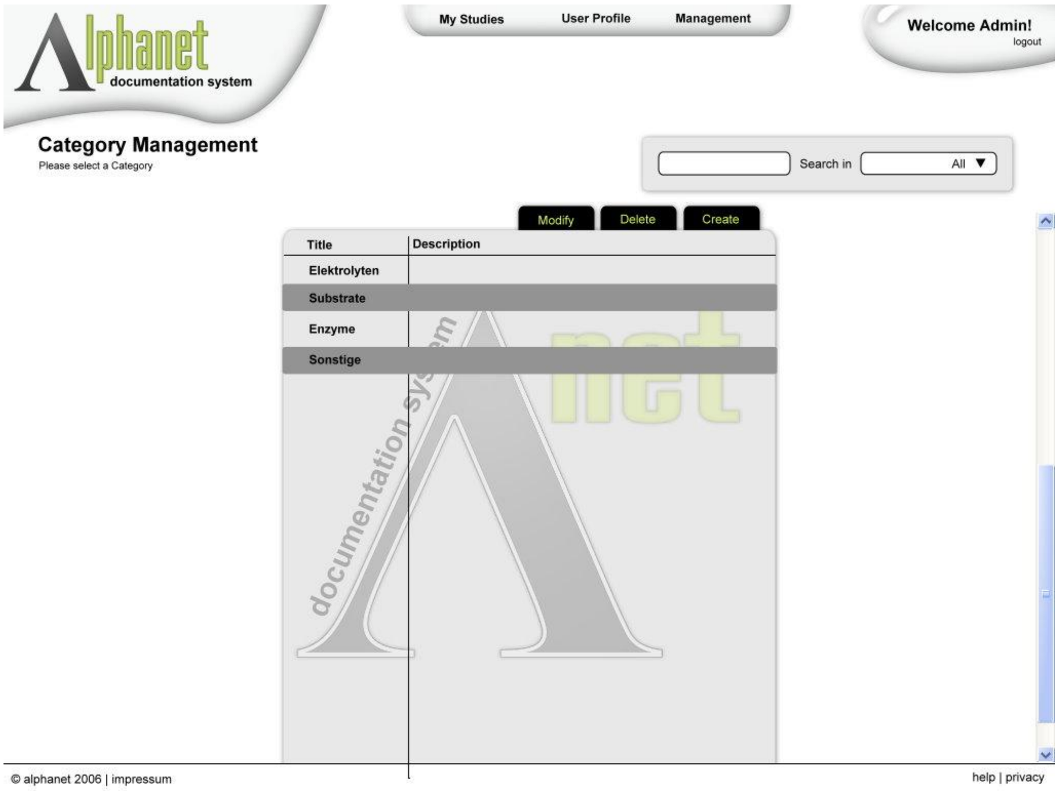
Chloride: mmol/l

Diagram 27: Create/Modify Field: User Interface Design

Once the user selects create, or modify field from the field management page, the above page is displayed. This page allows the user to enter the different field information such as the title, description, reference minimum, reference maximum, field type, unit type, if the field is mandatory or requires a capture date input. The field type is a predefined list (integer, drop down list, check box, date, etc), where each value requires different additional input. For example, for the drop down list, the user needs to enter all the values which belong into the drop down list. Furthermore, the user is able to add different unit types, which is then added to the drop down list of the unit types.

If the user selects the mandatory box, a red star is placed by the title of the field and the field becomes mandatory to be filled out during the clinical trials, meaning the trial input is not able to be saved unless the field has a value. If the "require capture date" field is selected, then an additional date field is placed next to the field which requires the user to enter the date of when this data was captured from the patient, during the data capture of the clinical study. All these field changes are visible while the user changes the settings in the live preview section of the page.

7.3.6 Category Management



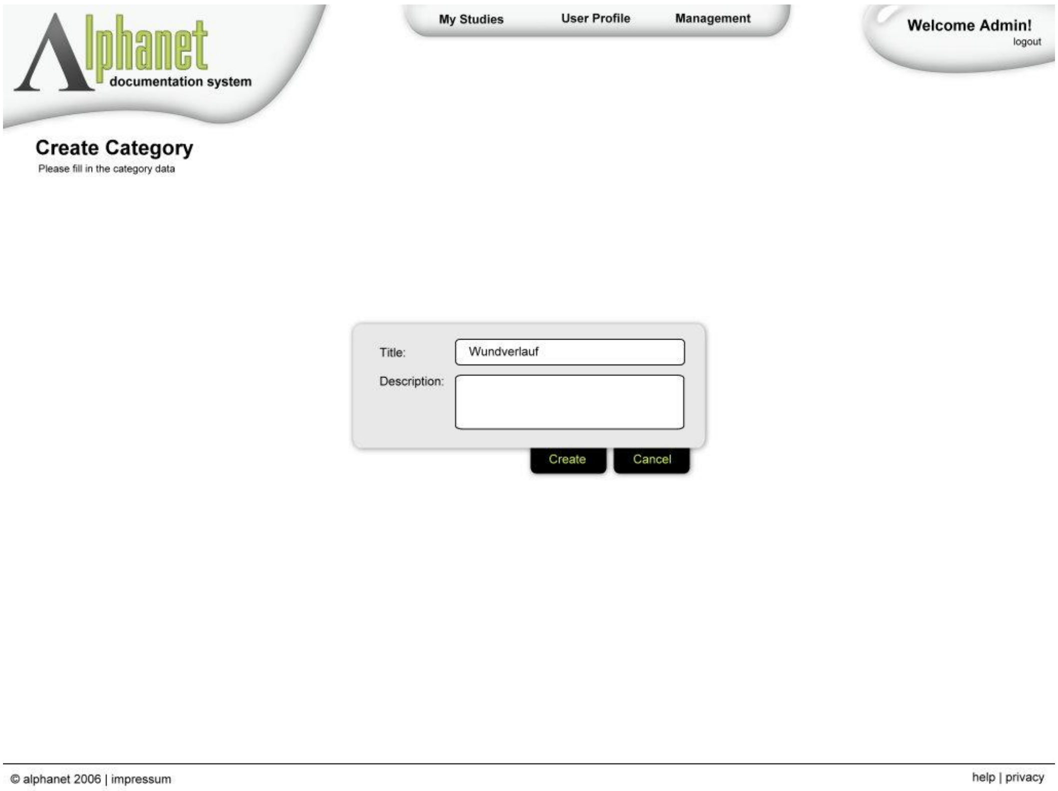
Category Management
Please select a Category

Title	Description
Elektrolyten	
Substrate	
Enzyme	
Sonstige	

Diagram 28: Category Management: User Interface Design

The main goal of categories is to help organize the clinical study. Each category can entail any number of fields. Similar to the users and fields, only administrators and project leaders can create, modify and delete categories. The goal of this page is to search, modify, delete and create these categories for the AlphaNet application. The user can select one category and press modify, which leads the user to the create/modify page, or select one or more categories and press delete, which removes the categories and refreshes the page without the deleted content. Only categories which have not been used in a clinical study are able to be deleted.

7.3.7 Create/Modify Category



Create Category

Please fill in the category data

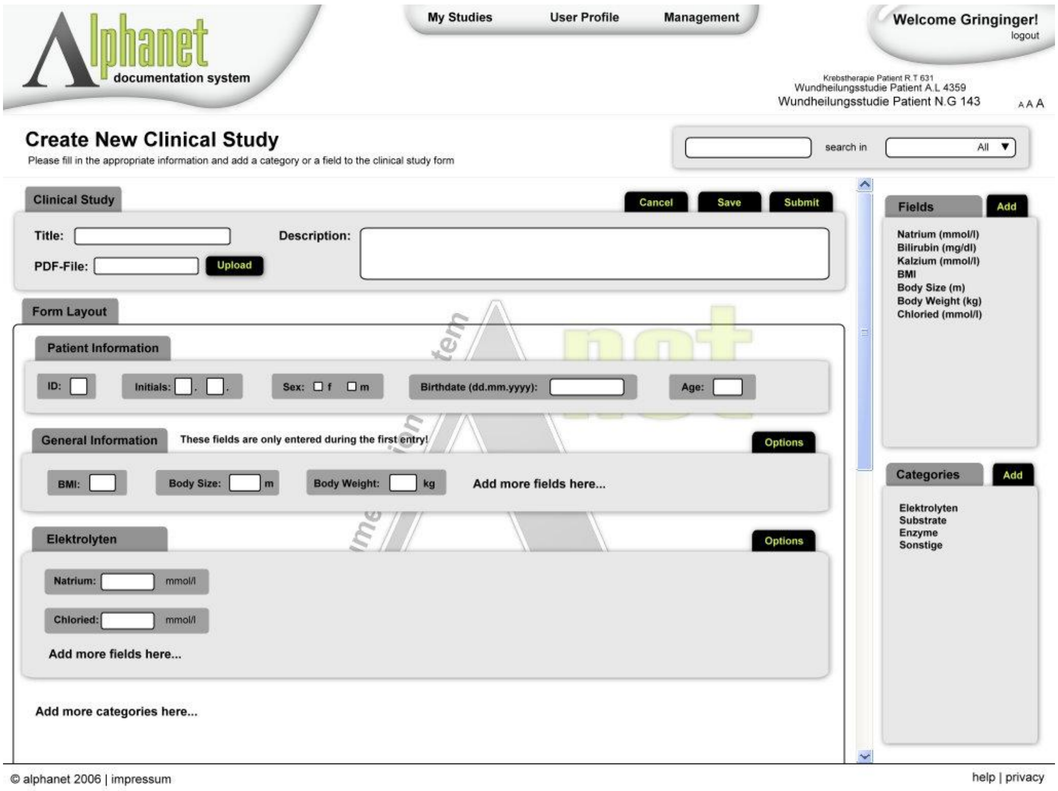
Title: Wundverlauf

Description:

Diagram 29: Create/Modify Category: User Interface Design

Once the user selects create, or modify from the category management page, the above page is displayed (see Diagram 29). This page allows the user to enter the category title and description and save the category to the database. In the clinical study creation page, the user will be able to add the different fields to the categories. On save the category is saved into the database and displayed on the category management page, and on cancel the user is forwarded to the category management page.

7.3.8 Create/Modify Clinical Study



Create New Clinical Study

Please fill in the appropriate information and add a category or a field to the clinical study form

Title:

PDF-File:

Description:

Patient Information

ID: □ Initials: □. □. Sex: □ f □ m Birthdate (dd.mm.yyyy): □ Age: □

General Information These fields are only entered during the first entry!

BMI: □ Body Size: □ m Body Weight: □ kg Add more fields here...

Elektrolyten

Natrium: □ mmol/l

Chloried: □ mmol/l

Add more fields here...

Add more categories here...

Fields:
Natrium (mmol/l)
Bilirubin (mg/dl)
Kalzium (mmol/l)
BMI
Body Size (m)
Body Weight (kg)
Chloried (mmol/l)

Categories:
Elektrolyten
Substrate
Enzyme
Sonstige

Diagram 30: Create/Modify Clinical Study: User Interface Design

The main advantage of AlphaNet is that the users have the ability to create their own clinical studies. Once the fields and the categories have been created, the user has the ability to implement these fields and categories into the clinical study. The goal of this use case is to create or modify a clinical study. Again, only the administrators and the project leaders have the ability to create clinical studies.

In this screen, the user has the previously created fields and categories listed on the right side. The user has the ability to drag and drop the fields and categories into the form layout of the clinical study, as well as rearrange the order of the fields and categories as desired. There exists one category which is called “Patient Information” which is present in every clinical study and holds the patient relevant information, such as the age, sex, birth date and initial’s. Secondly, there is a category for general information which only needs to be entered for the patient the first time a patient is added to the clinical study. Lastly, the user can add new categories below the above mentioned categories.

Upon dropping a category into the form layout, a large area is created where different fields can then be dropped. Once the fields are dropped into a category, the relevant information, such as the text box, title and unit type, are displayed within the category. In case the user wants to create new fields or categories, the user can press the add button next to the respective lists, which leads them to the previously mentioned screens. Upon saving, the user returns to this page, with the newly added category or field within the list on the right side.

Once the user has finished entering the necessary details of the clinical study, the user can press save, which allows the user to modify the clinical study at a later time, or submit, which opens the clinical study for entering patient data. On cancel, the clinical study is not saved and the user is brought back to the homepage.

7.4 Functional Specifications

The following section provides the detailed description of the user interface design which is necessary for the implement and testing of the AlphaNet system. The purpose of this section is to describe the features of AlphaNet and the behavior as seen by an external observer. The information is then used for the implementation of the application. This section defines the design and functionality of the application, but not how that functionality will be implemented. After a brief summary of all the use cases, the individual use cases will be discussed in greater detail.

7.4.1 Summary of all Use Cases

The below Table 2 contains a general overview of all the use cases in the AlphaNet application. At present, there are seven different use cases, but each use case has a number of sub use cases.

Use- Case Number	Use Case Description
1	Login
2	User Management
3	Field Management
4	Category Management
5	Create Clinical Study
6	Modify Clinical Study
7	Add User to Clinical Study

Table 2: Summary of all Use Cases

The next sections will discuss each individual use case in greater detail. Each use case is divided into user interface design and a detailed description of the use case and the required data elements.

The detailed description provides information on the preconditions, successful and failed post conditions, primary actors, secondary actors (if any), related use cases (if any), and the different scenarios of the use case. The required data elements section entails the fields that are required for the use case, including the format and the business rules for the page. Furthermore, the data elements section describes if the field is editable or only viewable and if the field is required (“R”), optional (“O”) or conditional (“C”).

7.4.2 Use Case 01: Login

The goal of this use case is for the users to log onto the AlphaNet Application. This use case is designed for all user roles.

7.4.2.1 Process Flow

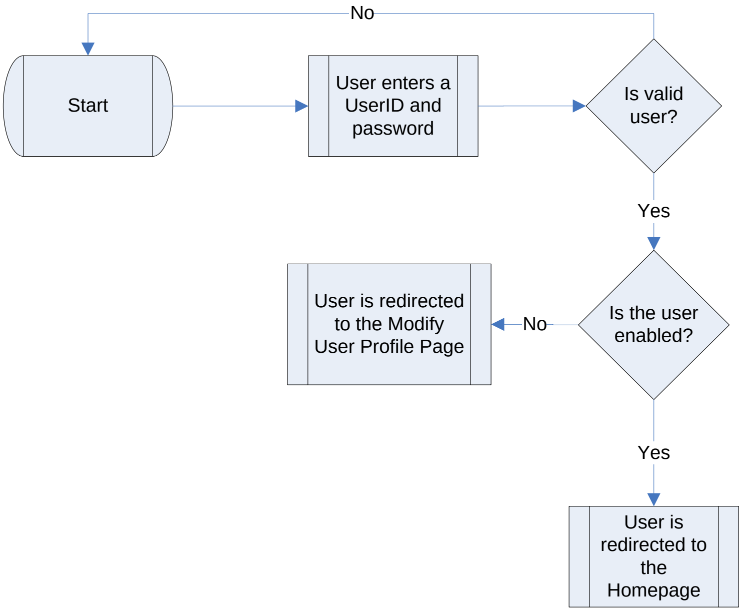

No
Start
User enters a UserID and password
Is valid user?
Yes
User is redirected to the Modify User Profile Page
No
Is the user enabled?
Yes
User is redirected to the Homepage

Diagram 31: Login: Process Flow

7.4.2.2 Use Case Diagram

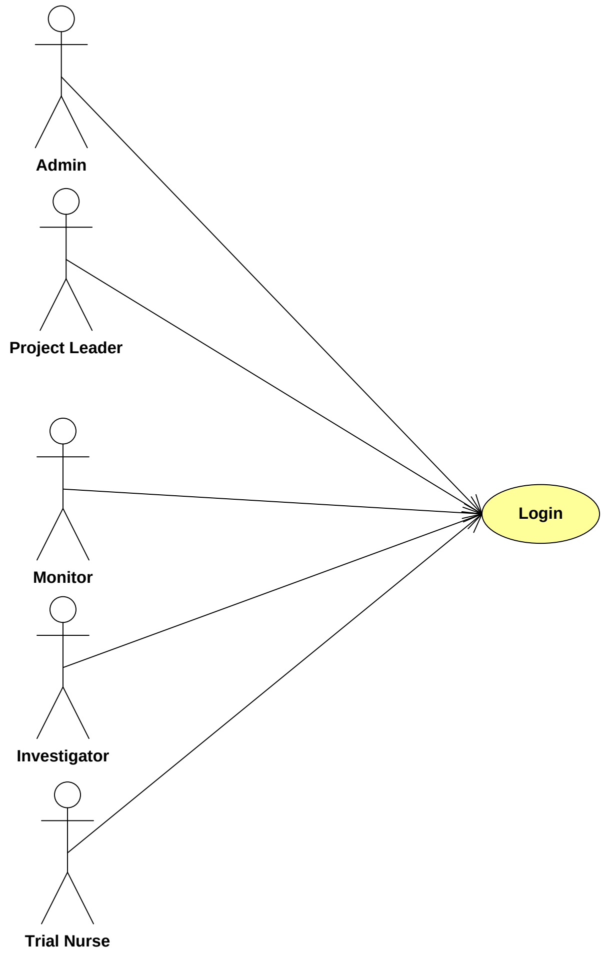


Diagram 32: Login: Use Case Diagram

7.4.2.3 Use Case Details

Characteristic Information	
Preconditions	• N/A
Successful Post Condition	• User has successfully logged in
Failed Post Conditions	• Login page with a red message stating “Username or password is incorrect!”
Primary Actors	• Admin, Project Leader, Investigator, Monitor, Trial Nurse

<table>
<tr><td><b>Secondary Actors</b></td><td colspan="2">• None</td></tr>
<tr><td><b>Related Use Cases</b></td><td colspan="2">• None</td></tr>
<tr><th colspan="3">Primary Scenario</th></tr>
<tr><th><i>Step</i></th><th><i>Scenario Action</i></th><th><i>Comments</i></th></tr>
<tr><td>1.</td><td>This use case starts when the user clicks on the AlphaNet URL.</td><td></td></tr>
<tr><td>2.</td><td>System displays the AlphaNet Login page.
• The Login page should entail two text fields, one for the Username and one for the Password and a Login button.</td><td></td></tr>
<tr><td>3.</td><td>User enters user name and password</td><td>System validates the user credentials. (System checks if the user entered the correct password and if the user has been deleted)</td></tr>
<tr><td>4.</td><td>If username or password is invalid or if the user has been deleted, the page is refreshed, stating:
• “Username or password is incorrect. Please contact your administrator for further details.”</td><td>The alert message is displayed in red on the login page itself.</td></tr>
<tr><td>5.</td><td>If username is valid, then the system checks if the user has been enabled.</td><td></td></tr>
<tr><td>6.</td><td>If user has been enabled:
• User is forwarded to the AlphaNet Homepage</td><td></td></tr>
<tr><td>7.</td><td>If user is still disabled:
• User is forwarded to the Modify User Profile page</td><td></td></tr>
<tr><td>8.</td><td>End use case</td><td></td></tr>
</table>

Table 3: Login: Use Case Details

7.4.2.4 Data Elements

Field Label & Description	**Format**	**Edit/ View**	**R/O/C**	**Business Rules for Page**
Username	Text	Edit	R	Minimum length of 8 and maximum length of 16
Password	Password	Edit	R	Password should be encrypted

Table 4: Login: Data Elements

7.4.3 Use Case 02: User Management

The goal of this use case is to search, modify, delete and create users for the AlphaNet application. As previously discussed, a user can pertain one out of 5 different user roles. These roles can be specified through this use case. Below is the user interface design for the general use case as well as for the sub use cases delete user, create user and modify user.

7.4.3.1 Process Flow

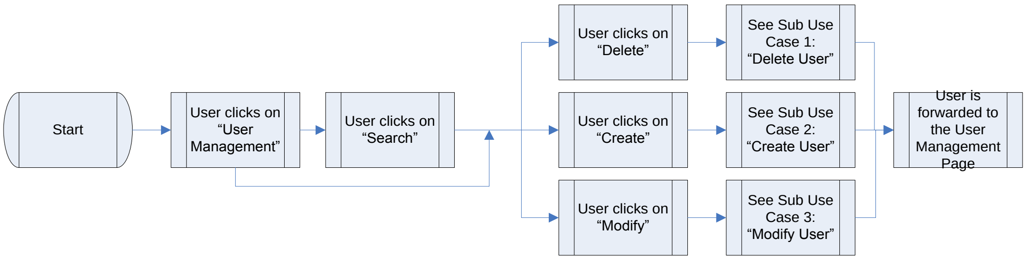

Start
User clicks on "User Management"
User clicks on "Search"
User clicks on "Delete"
User clicks on "Create"
User clicks on "Modify"
See Sub Use Case 1: "Delete User"
See Sub Use Case 2: "Create User"
See Sub Use Case 3: "Modify User"
User is forwarded to the User Management Page

Diagram 33: User Management: Process Flow

7.4.3.2 Use Case Diagram

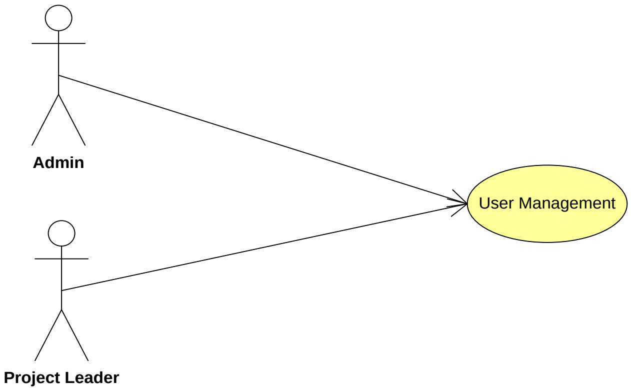


Diagram 34: User Management: Use Case Diagram

7.4.3.3 Use Case Details: Primary Scenario

Characteristic Information	
Preconditions	• User is logged in
Successful Post Condition	• User is successfully created/deleted/modified
Failed Post Conditions	• Error Page stating the reason of the failed user management.
Primary Actors	• All users
Secondary Actors	• None
Related Use Cases	• None

Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	The use case starts from the main menu. The user has two options, either, My Profile, or All Users. If the user clicks on "My Profile" under the "Üser Profile" menu item.	The All Users option is only shown for the Admin and Project Leader roles.
2.	User is forwarded to the Modify User Profile Page (see Sub-Use Case Modify User)	
3.	If the user selects "All User's" under the "User Profile" menu item, the user is forwarded to the User Management Page. The User Management Page displays: • Search Options: ○ A Text Box for entering the keyword. ○ A List Box which lists all the column names for the users as well as the option "All" ○ Search Button • A Table listing all the users and the user details • A Modify button • A Delete button • A Create New button	This option is only available for the Project Leader and Administrator. If the user is a Project Leader, then only the user's that were created by the Project Leader should be displayed. Deleted users should not be displayed. If the user is an Admin, then all existing users should be displayed, including the deleted users. By default sort the user table by Last Name
4.	User enters a keyword into the text field, selects a Column Name and clicks Search	

5.	Page is refreshed with a new table with only the result from the search displayed. If no results were found, then the message "No results were found. Please try another search." should be displayed in place of the user table.	
6.	User selects only one user and clicks the Modify button. (see Sub-Use Case Modify User)	If no user was selected or multiple users were selected, an alert message should be displayed stating: "Please select exactly one user!"
7.	User selects one or more users and clicks the Delete button. (see Sub-Use Case Delete User)	If no user was selected, an alert message should be displayed stating: "Please select one or more users!"
8.	User clicks on the Create New button. (see Sub-Use Case Create User)	
9.	End use case	

Table 5: User Management: Use Case Detail

7.4.3.4 Sub-Use Case: Modify User

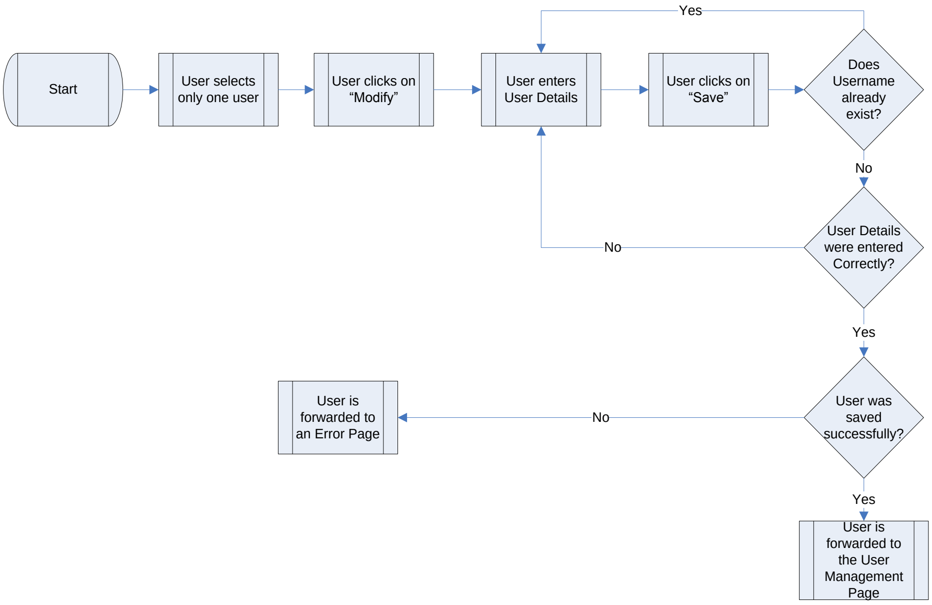

Start
User selects only one user
User clicks on "Modify"
User enters User Details
User clicks on "Save"
Does Username already exist?
Yes
No
User Details were entered Correctly?
No
Yes
User was saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the User Management Page

Diagram 35: User Management: Modify User

7.4.3.4.1 Sub-Use Case Details: Modify User

Sub-Use Case: Modify User		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Modify User Page, which lists all the user information in the corresponding text boxes and two buttons, Save and Cancel.	
2.	User can modify the following data: 1. First Name 2. Last Name 3. Username 4. Password 5. E-mail 6. Address 7. City 8. Zip 9. Country 10. Phone 11. Mobile Number 12. Pager A button, "Change", should be placed next to the password and the fields, Clinic and Institute, should be displayed as labels. Furthermore, a list of the clinical studies that the user is associated with should be displayed with the different rights as radio buttons next to the study. The rights include: 1. Full Access 2. Clinic Only Access 3. Only Own Patient Access 4. Read Only Access 5. No Access The study rights can only be modified by the project leader or admin.	If the user is entering into AlphaNet for the first time, then the user must change the password.
3.	User changes the data and clicks Save.	System stores the information.
4.	An alert message is displayed stating: "Are you sure you want to save the changes?" • On "Ok" the details are saved and the user is forwarded to the User Management Page • On "Cancel" no action is taken place.	
5.	End Use Case	

Table 6: Modify User: Use Case Details

7.4.3.5 Sub-Use Case: Delete User

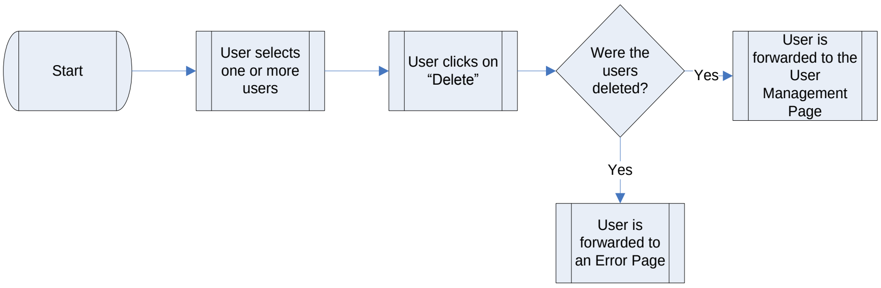

Start
User selects one or more users
User clicks on "Delete"
Were the users deleted?
Yes
User is forwarded to the User Management Page
Yes
User is forwarded to an Error Page

Diagram 36: User Management: Delete User

7.4.3.5.1 Sub-Use Case Details: Delete User

Sub-Use Case: Delete User		
Step	***Scenario Action***	***Comments***
1.	On the User Management Page, the user selects one or more users and clicks Delete.	
2.	An alert message is displayed stating: "Are you sure you want to delete the selected user(s)?" • On "Ok" the user is deleted and the page is refreshed displaying the changes. • On "Cancel" no action is taken.	On delete, the user is not removed from the database, but only the flag should be set to false.
3.	End Use Case	

Table 7: Delete User: Use Case Details

7.4.3.6 Sub-Use Case: Create User

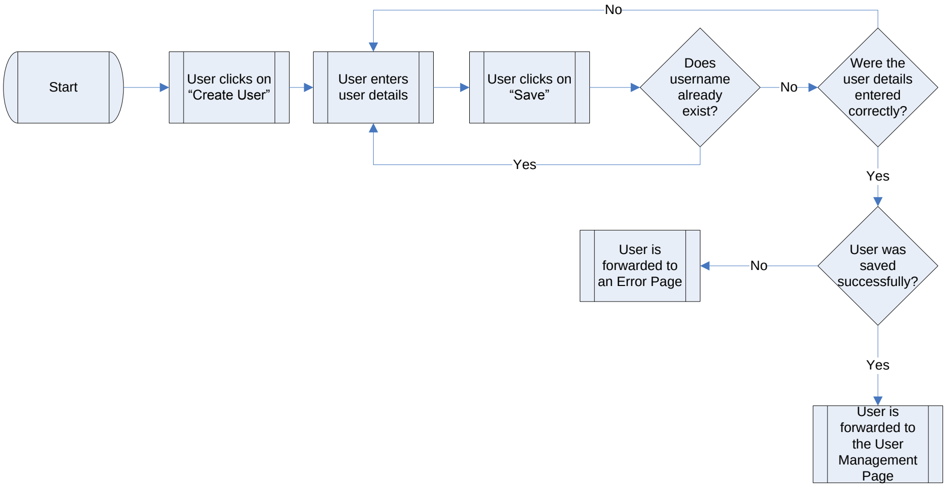

Start
User clicks on "Create User"
User enters user details
User clicks on "Save"
Does username already exist?
No
Were the user details entered correctly?
No
Yes
Yes
User was saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the User Management Page

Diagram 37: User Management: Create User

7.4.3.6.1 Sub-Use Case Details: Create User

Sub-Use Case: Create User		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Create User Screen.	
2.	The following information is displayed: 1. Username 2. E-mail 3. User Role 4. Clinic In addition, two buttons are displayed, Submit and Cancel.	Admin can create all types of users, while Project Leader can only create Monitor and below.
3	The user clicks Submit.	
4	System validates the fields and an alert message is displayed: "Are you sure you want to create this user?"	
5.	On Cancel, no action takes place. On Ok, an email is sent to the user being created saying: "The user <username> has been created in AlphaNet. Please click the below link to Login and finalize the user profile.	

	<AlphaNet Link>"	
6.	The user is forwarded to the User Management Page	
7.	End Use Case	

Table 8: Create User: User Details

7.4.3.7 Data Elements

Field Label & Description	Format	Edit? View?	R/O/C	Business Rules for Page
Search Text	Text	Edit	O	
Search List Box	List Box	Edit	O	Lists all of the user Column Names and the value "All" (Default: All)
First Name	Text	Edit	O	
Last Name	Text	Edit	O	
Username	Text	Edit	R	
Old Password	Text	Edit	R	
New Password	Text	Edit	R	
Confirm Password	Text	Edit	R	
Email	Text	Edit	R	
Clinic	Text	Edit	O	
Institute	Text	Edit	O	
Address	Text	Edit	O	
City	Text	Edit	O	
Zip	Text	Edit	O	
Country	Text	Edit	O	
Workgroup	Text	Edit	O	
Phone	Text	Edit	O	
Fax	Text	Edit	O	
Mobile	Text	Edit	O	
Pager	Text	Edit	O	
User Role	List Box	Edit	R	Lists all of the User Roles.

Table 9: User Management: Data Elements

7.4.4 Use Case 03: Field Management

Each clinical study can have any number of fields for the data input. The goal of this use case is to search, modify, delete and create these fields. An important aspect of this use case, is that only the administrator and the project leader has the ability to create, modify and delete these fields. Below user interface design for the general use case as well as for the sub use cases delete field, create field and modify field.

7.4.4.1 Process Flow

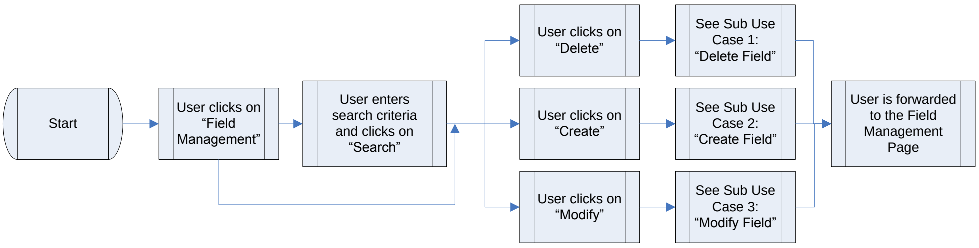

Start
User clicks on "Field Management"
User enters search criteria and clicks on "Search"
User clicks on "Delete"
User clicks on "Create"
User clicks on "Modify"
See Sub Use Case 1: "Delete Field"
See Sub Use Case 2: "Create Field"
See Sub Use Case 3: "Modify Field"
User is forwarded to the Field Management Page

Diagram 38: Field Management: Process Flow

7.4.4.2 Use Case Diagram

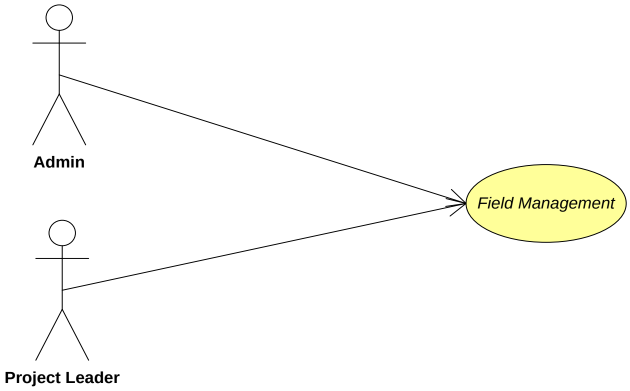


Diagram 39: Field Management: Use Case Diagram

7.4.4.3 Use Case Details

Characteristic Information	
Preconditions	• User is logged in as either an Admin or Project Leader
Successful Post Condition	• Field is successfully created/deleted/modified
Failed Post Conditions	• Error Page stating the reason of the failed field

	management.
Primary Actors	• Admin and Project Leader
Secondary Actors	• None
Related Use Cases	• None

Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	This use case starts when the user selects "Fields" under the "Management" menu item.	This option is only available for the Project Leader and Administrator.
2.	The user is forwarded to the Field Management Page. The Field Management Page displays: • Search Options: ○ A Text Box for entering the keyword. ○ A List Box which lists all the column names for the users as well as the option "All" ○ Search Button • A Table listing all the fields that were created by the user and the field details • A Table listing all the fields that were created by the rest of the users. • A Modify button • A Delete button • A Create New button	If the user is a Project Leader, then the deleted fields should not be displayed. If the user is an Admin, the column for State and Delete should also be displayed. By default the fields table should be sorted by the field name.
4.	User enters a keyword into the text field, selects a Column Name and clicks Search	
5.	Page is refreshed with the two tables, both of which display only the result from the search. If no results were found, then the message "No results were found. Please try another search." should be displayed in place of the table.	
6.	User selects only one field and clicks the Modify button. (see Sub-Use Case Modify Field)	If the user is a Project Leader, then only fields that were created by the user are able to be modified. If the user is an Admin, then all fields are modifiable. If the field is in "Active" state, then

		the field cannot be deleted. If no field was selected or multiple fields were selected, an alert message should be displayed stating: "Please select exactly one field!"
7.	User selects one or more fields and clicks the Delete button. (see Sub-Use Case Delete Field)	If no field was selected, an alert message should be displayed stating: "Please select one or more fields!"
8.	User clicks on the Create New button. (see Sub-Use Case Create Field)	
9.	End use case	

Table 10: Field Management: Use Case Details

7.4.4.4 Sub-Use Case: Modify Field

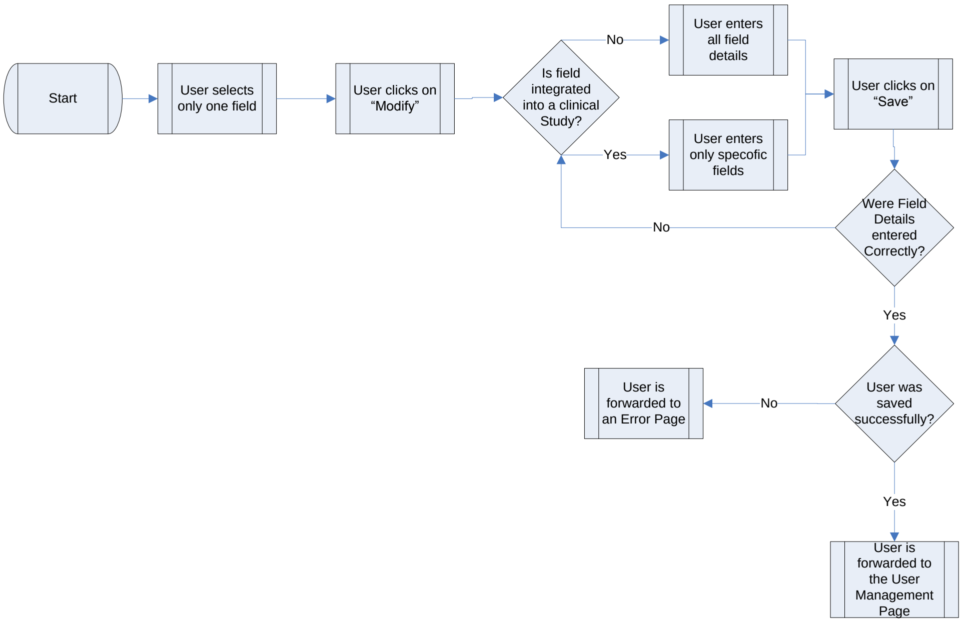

Start
User selects only one field
User clicks on "Modify"
Is field integrated into a clinical Study?
No
Yes
User enters all field details
User enters only specofic fields
User clicks on "Save"
Were Field Details entered Correctly?
No
Yes
User was saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the User Management Page

Diagram 40: Field Management: Modify Field

7.4.4.4.1 Sub-Use Case Details: Modify Field

Sub-Use Case: Modify Field		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Modify Field Page, which lists all the field information in the corresponding text boxes and two buttons, Save and Cancel.	
2.	User can modify the following fields: 1. Title (Text Box) 2. Description (Text Box) 3. Reference Min (Text Box) 4. Reference Max (Text Box) 5. Field Type (Drop Down) 6. Unit Type (Drop Down with an "Add" button) 7. Mandatory (Radio Buttons "Yes" and "No") 8. Require Capture Date(Radio Button "Yes" and "No")	The drop downs, Field Type and Unit Type, should be auto populated.
3.	User changes the data and clicks Save.	
4.	An alert message is displayed stating: "Are you sure you want to save the changes?" • On "Ok" the details are saved and the user is forwarded to the Field Management Page • On "Cancel" no action is taken place.	
5.	End Use Case	

Table 11: Modify Field: Use Case Details

7.4.4.5 Sub-Use Case: Delete Field

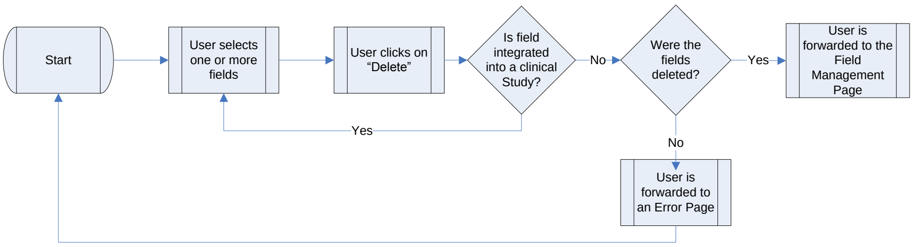

Start
User selects one or more fields
User clicks on "Delete"
Is field integrated into a clinical Study?
No
Yes
Were the fields deleted?
Yes
User is forwarded to the Field Management Page
No
User is forwarded to an Error Page

Diagram 41: Field Management: Delete Field

7.4.4.5.1 Sub-Use Case Details: Delete Field

Sub-Use Case: Delete Field		
Step	***Scenario Action***	***Comments***
1.	On the Field Management Page, the user selects one or more fields and clicks Delete.	If no field was selected, the alert message, "Please select a field." should be displayed. If the field is in "Active" state, then the field cannot be deleted.
2.	An alert message is displayed stating: "Are you sure you want to delete the selected field(s)?" • On "Ok" the page is refreshed with the selected fields deleted. • On "Cancel" no action is taken.	
3.	End Use Case	

Table 12: Delete Field: Use Case Details

7.4.4.6 Sub-Use Case: Create Field

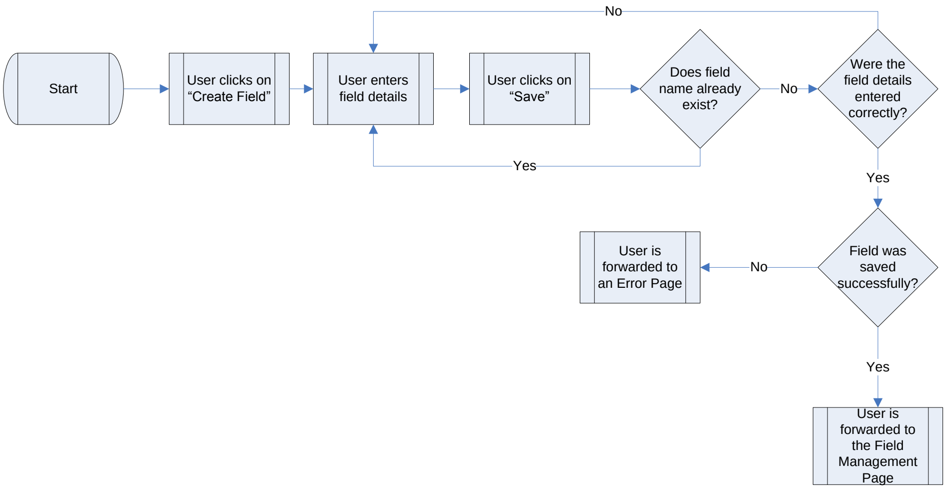

Start
User clicks on "Create Field"
User enters field details
User clicks on "Save"
Does field name already exist?
No
Were the field details entered correctly?
No
Yes
Yes
Field was saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the Field Management Page

Diagram 42: Field Management: Create Field

7.4.4.6.1 Sub-Use Case Details: Create Field

Sub-Use Case: Create Field		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Create Field Screen.	
2.	The following information is displayed: 1. Title (Text Box) 2. Description (Text Box) 3. Reference Min (Text Box) 4. Reference Max (Text Box) 5. Field Type (Drop Down) 6. Unit Type (Drop Down with an “Add” button) 7. Mandatory (Radio Buttons “Yes” and “No”) 8. Require Capture Date(Radio Button “Yes” and “No”) In addition, two buttons are displayed, Create and Cancel.	The unit type drop down should be automatically populated with the stored names from the database.
3.	The following field types should be displayed: 1. Integer 2. Float 3. Roman Numeral 4. Boolean 5. Small Text 6. Large Text 7. Drop Down List 8. Check Box List 9. Date 10. Time 11. File Upload For the field types “Drop Down List” and “Check Box List” a text field and an “Add” button should be placed next to the option in order to add a check box or drop down list entry.	
4a.	User clicks on the “Add” button next to the Unit Type	Unit Type is only available for the types Integer and Float.
4b.	User is forwarded to the Add Unit Type page. The page displays the Title text box and the Description text box in addition to the buttons Save and Cancel.	
4c.	User enters Unit Type details.	
4d.	On Save, the details are saved and the user is brought back to the Create Field page. On Cancel, the details are not saved and the user is taken to the Create Field page.	
5a.	The user selects either the field type “Drop Down List” or “Check Box List”	

5b.	The user enters a value into the text field and then clicks the "Add Button"	
5c	The value is added to the Check Box list on the same page, with a "Remove" button underneath the list	
5d.	User selects a value from the Check Box list and presses delete.	
5e.	The value is removed from the Check Box List	
6.	User selects "Yes" from the mandatory field	The field becomes mandatory to be filled out by the respective investigators and trial nurses. A red star is placed next to the title of the field
7.	User selects "Yes" from the require capture date field	A text box with type date is displayed next to the field.
8.	The user enters the rest of the fields and clicks "Create"	
9.	System validates the fields and an alert message is displayed: "Are you sure you want to create this field?"	
10.	On Cancel, no action takes place. On Ok, the details are stored and the user is forwarded to the Field Management Page	
11.	End Use Case	

Table 13: Create Field: Use Case Details

7.4.4.7 Data Elements

Field Label & Description	Format	Edit? View?	R/O/C	Business Rules for Page
Title	Text	Edit	R	
Description	Text	Edit	O	
Reference Min	Text	Edit	O	
Reference Max	Text	Edit	O	
Field Type	Drop Down	Edit	R	List of all the field types stored in the database
Unit Type	Drop Down	Edit	O	List of all the unit types stored in the database
Mandatory	Radio Button	Edit	R	
Require Capture Date	Radio Button	Edit	R	

Table 14: Field Management: Data Elements

7.4.5 Use Case 04: Category Management

The main goal of categories is to help organize the clinical study. Each category can entail any number of fields. Similar to the users and fields, only administrators and project leaders can create, modify and delete categories. The goal of this use case is to search, modify, delete and create these categories for the AlphaNet Application

7.4.5.1 Process Flow

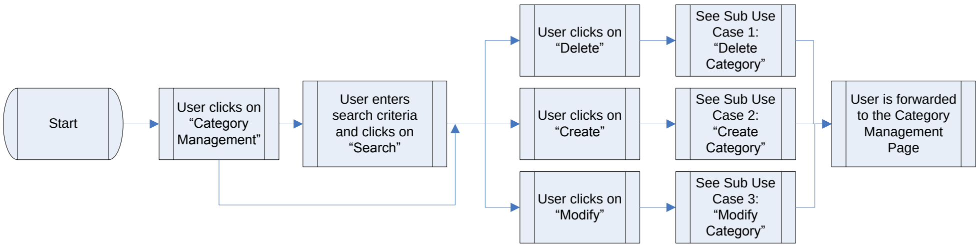

Start
User clicks on "Category Management"
User enters search criteria and clicks on "Search"
User clicks on "Delete"
User clicks on "Create"
User clicks on "Modify"
See Sub Use Case 1: "Delete Category"
See Sub Use Case 2: "Create Category"
See Sub Use Case 3: "Modify Category"
User is forwarded to the Category Management Page

Diagram 43: Category Management: Process Flow

7.4.5.2 Use Case Diagram

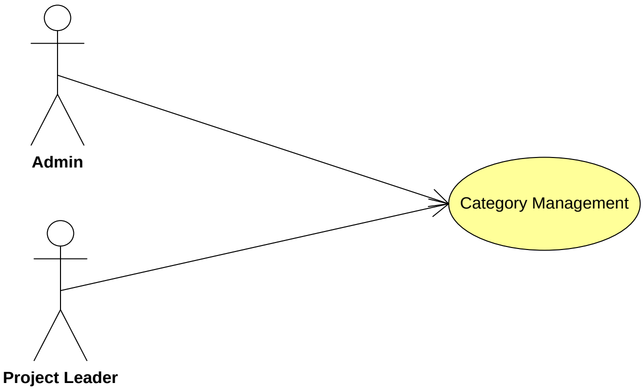


Diagram 44: Category Management: Use Case Diagram

7.4.5.3 Use Case Details

Characteristic Information	
Preconditions	• User is logged in as either an Admin or Project Leader
Successful Post Condition	• Category is successfully created/deleted/modified
Failed Post Conditions	• Error Page stating the reason of the failed category management.
Primary Actors	• Admin and Project Leader
Secondary Actors	• None
Related Use Cases	• None

Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	This use case starts when the user selects “Category” under the “Management” menu item.	This option is only available for the Project Leader and Administrator.
2.	The user is forwarded to the Category Management Page. The Category Management Page displays: • Search Options: ○ A Text Box for entering the keyword. ○ A List Box which lists all the column names for the users as well as the option “All” ○ Search Button • A Table listing all the categories that were created by the user and the category details • A Modify button • A Delete button • A Create New button	By default the categories should be sorted by the title.
4.	User enters a keyword into the text field, selects a Column Name and clicks Search	
5.	Page is refreshed with the table displaying only the result from the search. If no results were found, then the message “No results were found. Please try another search.” should be displayed in place of the table.	
6.	User selects only one category and clicks the Modify button. (see Sub-Use Case Modify Category)	

		If no category was selected or multiple fields were selected, an alert message should be displayed stating: “Please select exactly one field!” If the category is already used in a clinical study, then the category cannot be modified and an alert message should be displayed saying, “the Selected category is already being used in a clinical study. Please select another category to modify.”
7.	User selects one or more categories and clicks the Delete button. (see Sub-Use Case Delete Category)	If no category was selected, an alert message should be displayed stating: “Please select one or more fields!”
8.	User clicks on the Create New button. (see Sub-Use Case Create Category)	
9.	End use case	

Table 15: Category Management: Use Case Details

7.4.5.4 Sub-Use Case: Modify Category

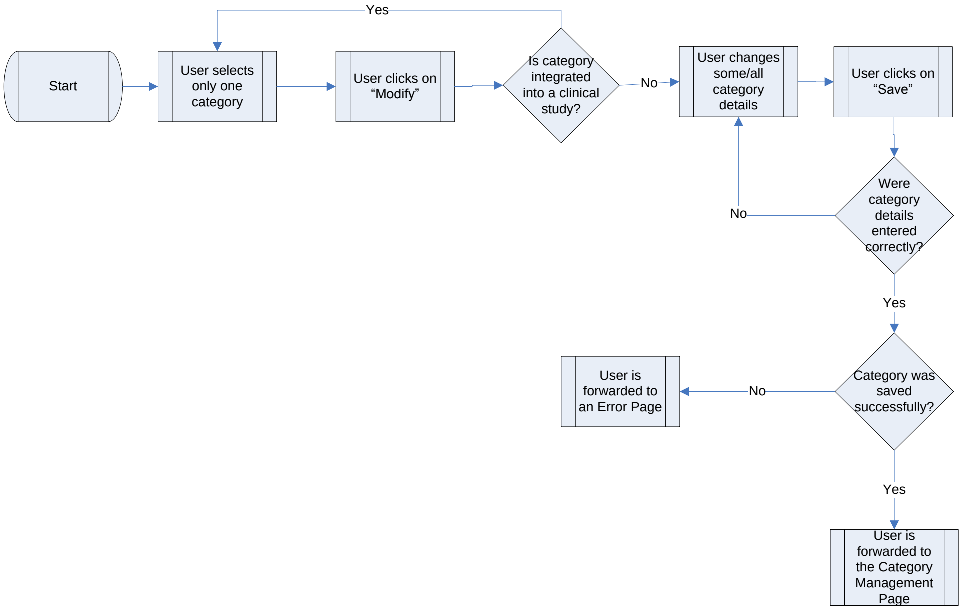

Yes
Start
User selects only one category
User clicks on “Modify”
Is category integrated into a clinical study?
No
User changes some/all category details
User clicks on “Save”
Were category details entered correctly?
No
Yes
Category was saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the Category Management Page

Diagram 45: Category Management: Modify Category

7.4.5.4.1 Sub-Use Case Details: Modify Category

Sub-Use Case: Modify Category		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Modify Category Page, which lists all the category information in the corresponding text boxes and two buttons, Save and Cancel.	
2.	User can modify the following fields: 1. Title (Text Box) 2. Description (Text Box)	The text boxes need to be auto populated with the corresponding information of the selected category.
3.	User changes the data and clicks Save.	
4.	An alert message is displayed stating: “Are you sure you want to save the changes?” • On “Ok” the details are saved and the user is forwarded to the Category Management Page • On “Cancel” no action is taken place.	
5.	End Use Case	

Table 16: Modify Category: Use Case Details

7.4.5.5 Sub-Use Case: Delete Category

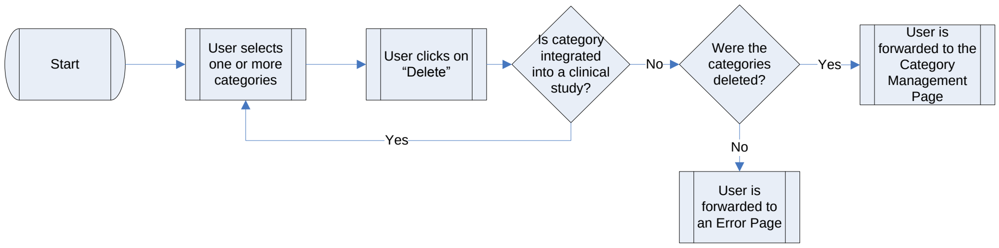

Start
User selects one or more categories
User clicks on “Delete”
Is category integrated into a clinical study?
No
Yes
Were the categories deleted?
Yes
User is forwarded to the Category Management Page
No
User is forwarded to an Error Page

Diagram 46: Category Management: Delete Category

7.4.5.5.1 User Interface Design

See 7.3.

7.4.5.5.2 Sub-Use Case Details: Delete Category

Sub-Use Case: Delete Category		
Step	**Scenario Action**	**Comments**
1.	On the Category Management Page, the user selects one or more categories and clicks Delete.	If no category was selected, the alert message, "Please select a category." should be displayed.
2.	If the selected category was used in a clinical study, then an alert message is displayed saying: • "The category is in use in a clinical study and can therefore not be deleted."	
3.	An alert message is displayed stating: "Are you sure you want to delete the selected category(s)?" • On "Ok" the page is refreshed with the selected categories deleted. • On "Cancel" no action is taken.	
4.	End Use Case	

Table 17: Delete Category: Use Case Details

7.4.5.6 Sub-Use Case: Create Category

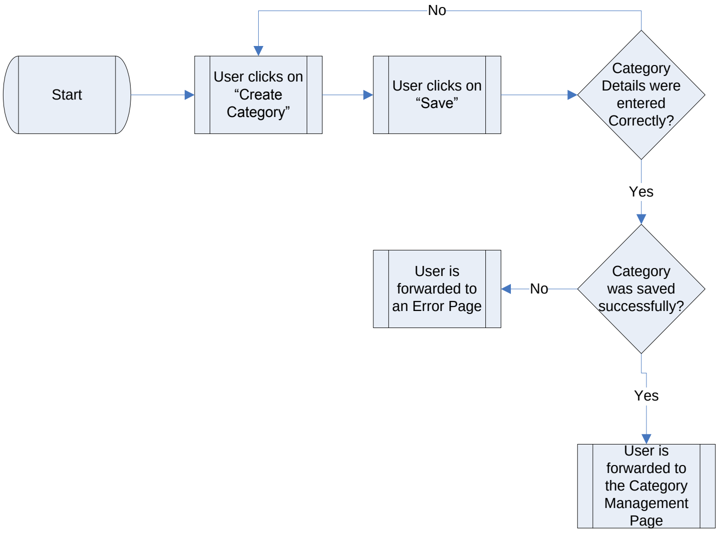

No
Start
User clicks on "Create Category"
User clicks on "Save"
Category Details were entered Correctly?
Yes
User is forwarded to an Error Page
No
Category was saved successfully?
Yes
User is forwarded to the Category Management Page

Diagram 47: Category Management: Create Category

7.4.5.6.1 Sub-Use Case Details: Create Category

Sub-Use Case: Create Category		
Step	***Scenario Action***	***Comments***
1.	User is forwarded to the Create Category Screen.	
2.	The following information is displayed: 1. Title (Text Box) 2. Description (Text Box) In addition, two buttons are displayed, Create and Cancel.	
3.	The user enters the details and clicks Create.	
4.	System validates the fields and an alert message is displayed: “Are you sure you want to create this category?”	
5.	On Cancel, no action takes place. On Ok, the details are stored and the user is forwarded to the Category Management Page	
6.	End Use Case	

7.4.5.7 Data Elements

Field Label & Description	**Format**	**Edit? View?**	**R/O/C**	**Business Rules for Page**
Title	Text	Edit	R	
Description	Text	Edit	O	

Table 18: Category Management: Data Elements

7.4.6 Use Case 05: Create Clinical Study

The main advantage of AlphaNet is that the users have the ability to create their own clinical studies. Once the fields and the categories have been created, the user is able to implement these fields and categories into the clinical study. The goal of this use case is to create a new clinical study. Again, only the administrators and the project leaders have the ability to create clinical studies.

7.4.6.1 Process Flow

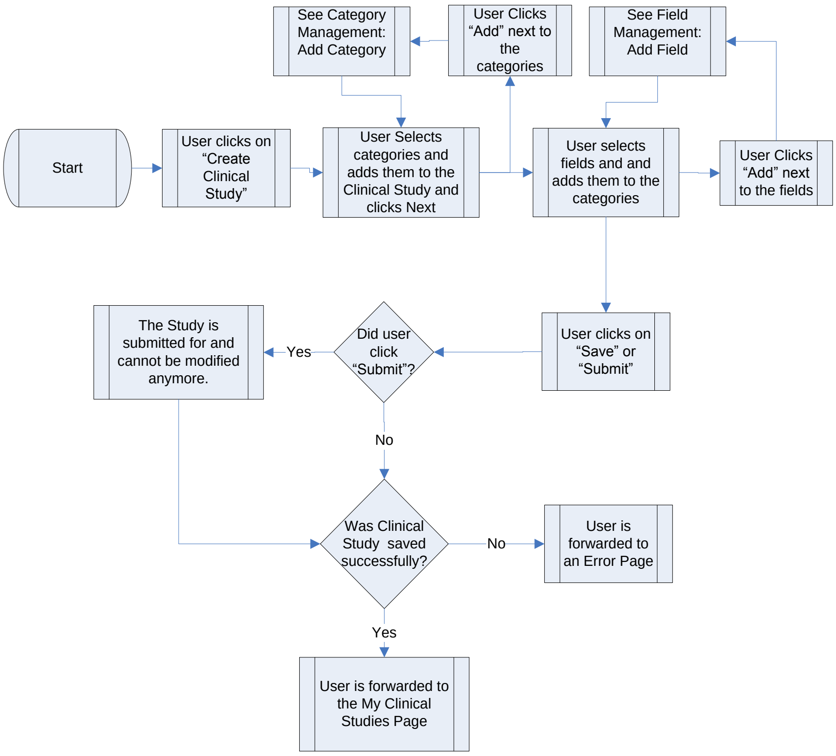

See Category Management: Add Category
User Clicks "Add" next to the categories
See Field Management: Add Field
Start
User clicks on "Create Clinical Study"
User Selects categories and adds them to the Clinical Study and clicks Next
User selects fields and and adds them to the categories
User Clicks "Add" next to the fields
The Study is submitted for and cannot be modified anymore.
Yes
Did user click "Submit"?
User clicks on "Save" or "Submit"
No
Was Clinical Study saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the My Clinical Studies Page

Diagram 48: Create Clinical Study: Process Flow

7.4.6.2 Use Case Diagram

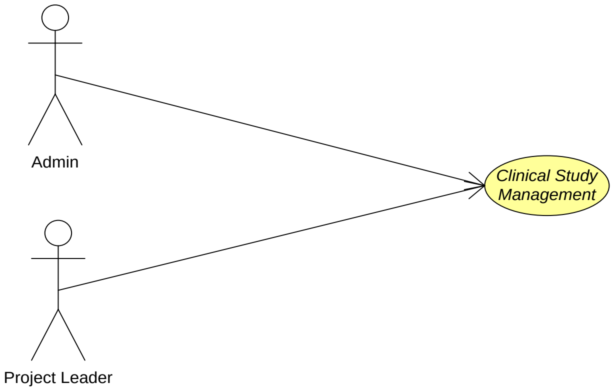


Diagram 49: Create Clinical Study: Use Case Diagram

7.4.6.3 Use Case Details

Characteristic Information	
Preconditions	• User is logged in as either an Admin or Project Leader
Successful Post Condition	• The Clinical Study was successfully created and saved
Failed Post Conditions	• Error Page stating the reason of the failed clinical study management.
Primary Actors	• Admin, Project Leader
Secondary Actors	• None
Related Use Cases	• My Clinical Studies, Add Category, Add Fields, Add Users

Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	This use case starts when the user selects “Create Clinical Study” from the home page.	
2.	The following fields are displayed under the category “Clinical Study” 1. Title (Text Box) 2. Description (Text Box) 3. PDF File (with “Upload” button) The following fields should be displayed under the category “Patient Information” 1. Age 2. Sex (Male and Female) 3. Birth date 4. Initials In addition there should be a section for “General Information” which is used for fields that are only entered once and a section for “Entry Information” with the fields: 1. Title (Text Box) 2. Description (Text Box) In addition, there should be two lists with all of the fields and categories populated from the database. Above each list should be an “Add” button. Finally, a “Save”, “Submit” and “Cancel” button should be displayed as well.	The “General Information” category should display a message “Add Field Here” inside of the category. Below the “Entry Information” category, a message, “Add Category Here” should be displayed.
3.	User selects a category from the list, and drags it under the “Entry Information” box.	The category should display a message “Add Field Here”

		inside of the category.
4.	The category is displayed and allows fields to be added to it.	
5.	The user selects a field from the list and drags it into the "General Information" category or the previously added category.	If the user drags a category or field into a non specified area, then an alert message should be displayed stating: "The field or category cannot be moved to that location."
6.	The field is displayed with its Title, field type and unit type.	The description can be displayed with a tool tip. If the field is mandatory, then a " * " should be displayed next to the field. Both categories and fields can be added any number of times and moved around in the form in any order at any time.
7.	The user clicks and drags a field or category from the form and places it back into the list.	The field is removed from the form.
8.	On "Cancel" an alert message should be displayed stating: "Are you sure you want to cancel the clinical study?" • On "Ok" the details are not saved and the user is forwarded to the homepage • On "Cancel" no action is taken place.	
9.	On "Save" an alert message is displayed stating: "Are you sure you want to save the clinical study?" • On "Ok" the details are saved and the user is forwarded to the homepage • On "Cancel" no action is taken place.	
10.	On "Submit" an alert message is displayed stating: "After submitting the clinical study you will not be able to make any more changes. Are you sure you want to submit the clinical study?" • On "Ok" the details are saved and submitted and the user is forwarded to the homepage • On "Cancel" no action is taken place.	
11.	End Use Case	

Table 19: Create Clinical Study: Use Case Details

7.4.6.4 Data Elements

Field Label & Description	Format	Edit/View	R/O/C	Rules for Page
Title (Clinical Study)	Text	Edit	R	
Description (Clinical Study)	Text	Edit	O	
PDF (Clinical Study)	Text	Edit	O	
Age	Text	View	O	
Initials	Text	View	O	
Birth date	Text	View	O	
Sex (Male and Female)	Text	View	O	
Title (Entry Information)	Text	View	O	
Description (Entry Information)	Text	View	O	

Table 20: Create Clinical Study: Data Elements

7.4.7 Use Case 06: Modify Clinical Study

Once a clinical study has been successfully created and saved, the administrator or project leader that created the study has the ability to modify the study. The goal is the modification of the clinical studies.

7.4.7.1 Process Flow

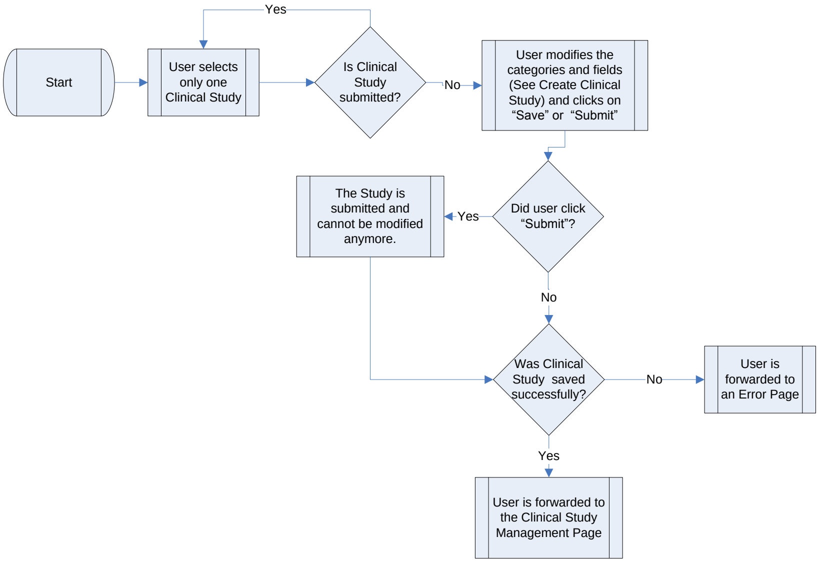

Start
User selects only one Clinical Study
Yes
Is Clinical Study submitted?
No
User modifies the categories and fields (See Create Clinical Study) and clicks on "Save" or "Submit"
Did user click "Submit"?
Yes
The Study is submitted and cannot be modified anymore.
No
Was Clinical Study saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the Clinical Study Management Page

Diagram 50: Modify Clinical Study: Process Flow

7.4.7.2 Use Case Diagram

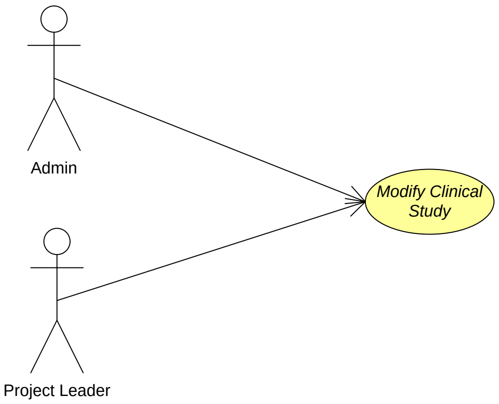


Diagram 51: Modify Clinical Study: Use Case Diagram

7.4.7.3 Use Case Details

Characteristic Information	
Preconditions	- User is logged in as either an Admin or Project Leader and a clinical study was saved previously without being submitted.
Successful Post Condition	- The Clinical Study was successfully created and saved
Failed Post Conditions	- Error Page stating the reason of the failed clinical study management.
Primary Actors	- Admin, Project Leader
Secondary Actors	- None
Related Use Cases	- My Clinical Studies, Add Category, Add Fields, Add Users

Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	This use case starts when the user selects “Edit” from a clinical study on the home page.	The clinical study has been saved but not submitted
2.	See use case 6, Create Clinical Study, step 2 for the display information. In addition, the “Title”, “Description” and “PDF” should be populated and all the saved fields and categories are displayed according to the previously saved clinical study.	
3.	See use case 6, Create Clinical Study, step 3 to 7 for adding and removing information	

4.	On “Cancel” an alert message should be displayed stating: “Are you sure you want to cancel the clinical study?” • On “Ok” the details are not saved and the user is forwarded to the homepage • On “Cancel” no action is taken place.	
5.	On “Save” an alert message is displayed stating: “Are you sure you want to save the clinical study?” • On “Ok” the details are saved and the user is forwarded to the homepage • On “Cancel” no action is taken place.	
6.	On “Submit” an alert message is displayed stating: “After submitting the clinical study you will not be able to make any more changes. Are you sure you want to submit the clinical study?“ • On “Ok” the details are saved and submitted and the user is forwarded to the homepage • On “Cancel” no action is taken place.	
6.	End Use Case	

Table 21: Modify Clinical Study: Use Case Details

7.4.7.4 Data Elements

See Use Case 6: Create Clinical Study.

7.4.8 Use Case 07: Add User to Clinical Study

Once the clinical study has been saved and submitted, the project leader or administrator has the ability to add users (Project leaders, investigators, monitors or trial nurses) to the clinical study. Furthermore, access rights are handed out to the users. The goal of this use case is adding users and their respective access rights to the clinical studies.

7.4.8.1 Process Flow

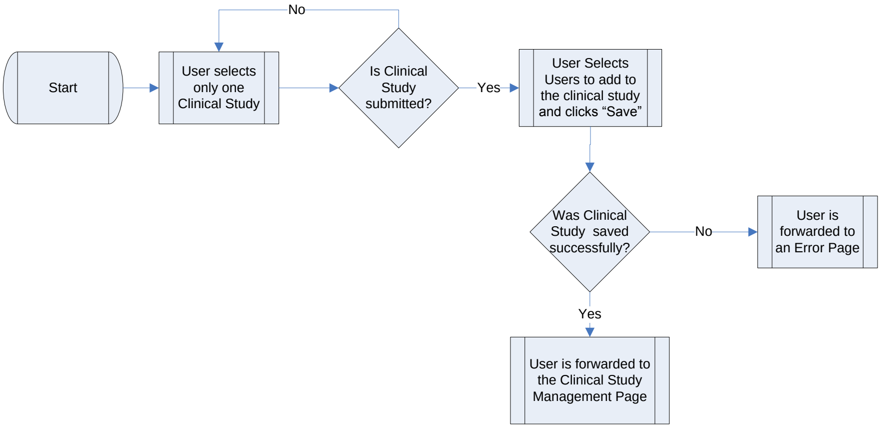

Start
User selects only one Clinical Study
Is Clinical Study submitted?
No
Yes
User Selects Users to add to the clinical study and clicks “Save”
Was Clinical Study saved successfully?
No
User is forwarded to an Error Page
Yes
User is forwarded to the Clinical Study Management Page

Diagram 52: Add user to Clinical Study: Process Flow

7.4.8.2 Use Case Diagram

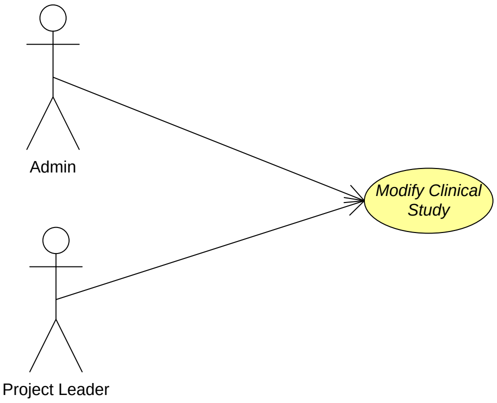


Diagram 53: Add user to Clinical Study: Use Case Diagram

7.4.8.3 Use Case Details

Characteristic Information	
Preconditions	• User is logged in as either an Admin or Project Leader and a clinical study was saved and submitted.
Successful Post Condition	• The user was successfully added to the clinical study

Failed Post Conditions	• Error Page stating the reason.	
Primary Actors	• Admin, Project Leader	
Secondary Actors	• None	
Related Use Cases	• My Clinical Studies, Add Category, Add Fields, Add Users	
Primary Scenario		
Step	***Scenario Action***	***Comments***
1.	This use case starts when the user selects “Add User” from a clinical study on the home page.	The clinical study has been saved and submitted
2.	A page is displayed with the following information: 1. A list of all the users that are in the same clinic as the signed in user 2. Radio Buttons with the following rights next to each user: a. Full Access b. All Patient Access c. Only Own Patient Access d. View Only Access e. No Access 3. And a “Update” Button.	
3.	The user chooses a right for all of the users and clicks “Update”	
4.	An alert message is displayed stating: “Are you sure you want to continue?”	
5.	On “Ok” the rights are stored for the users and the user is brought back to the homepage	
6.	On “Cancel” no action takes place	
7.	End use case.	

Table 22: Add user to Clinical Study: Use Case Detail

7.4.8.4 Data Elements

See Table 9: User Management: Data Elements.

7.5 Technical Design

The following section describes the technical design of our AlphaNet application. After our architectural overview of our hardware components, the different server types that we used in our implementation will be discussed. Finally, our software architecture will be described.

7.5.1 Infrastructure Architecture

The following diagram gives an overview over the hardware architecture of AlphaNet. Each user has the ability to login through his keycard on the client-side.

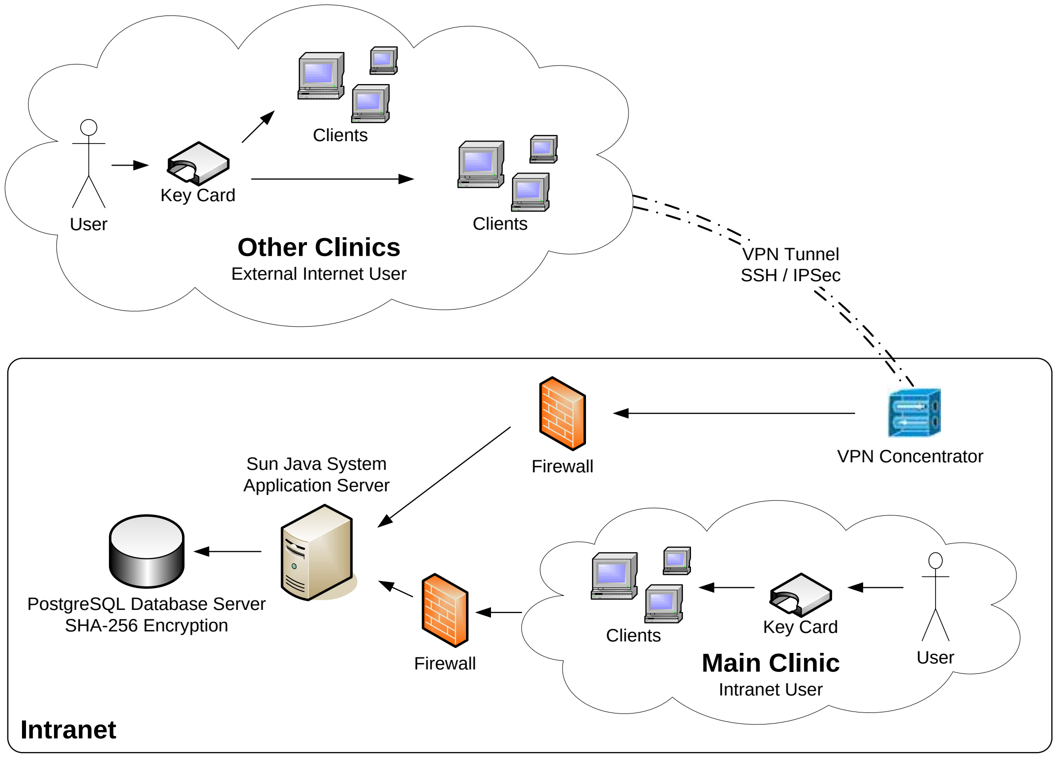


Diagram 54: Architecture Overview

Each user, regardless whether they are internal or external, will be required to login with a keycard on the client-side. External internet users are connected through a secure virtual private network (VPN) protocol including IPsec (IP security), so each VPN-client is securely connected to the concentrator (VPN-server). This route is only necessary for external clinics, for main user's, which are connected inside the intranet, only a simple login with their keycard is required. They do not need a VPN-tunnel. All connections pass through a firewall in order to get to the application server. The application server, a Sun Java System Application Server, has access to a PostgreSQL database server through SHA-256 encryption. The PostgreSQL will be used for its features and the open-source character. Among others, PostgreSQL has very good support for high precision numeric and large binary / character data types. PostgreSQL also supports storage of pictures, sounds, or video and is designed for very large databases, which clinical studies require.

7.5.2 Database Server

"[..] *A database can be defined as a structured collection of records or data that is stored in a computer so that a program can consult it to answer queries.* [..] *The term database refers to the collection of related records, and the software should be referred to as the database management system or DBMS."* (Wikipedia.org, Database, 2007)

There are some commercial database engines such as DB2[27] (IBM), Oracle DB[28] (Oracle Corporation), or open source database engines, such as PostgreSQL[29], MySQL[30], Firebird[31], Ingres[32] and MaxDB[33]. A good feature matrix of all these open source databases you can find in the research paper of Fallmann and others, 2005, on page 53-56.

Through the use of the platform independent standard Java Database Connectivity (JDBC), which is a standard library for accessing relational databases, every available relational database can be used for the system. During the AlphaNet implementation, PostgreSQL is used for its features and the open-source character. Among others, PostgreSQL has very good support for high precision numeric and large binary / character data types. It

[27] www.ibm.com/db2, Retrieved on 02.04.2007

[28] http://www.oracle.com/database/index.html, Retrieved on 02.04.2007

[29] http://www.postgresql.org/, Retrieved on 02.04.2007

[30] http://www.mysql.com/, Retrieved on 02.04.2007

[31] http://www.firebirdsql.org/, Retrieved on 10.04.2007

[32] http://www.ingres.com/, Retrieved on 10.04.2007

[33] http://www.mysql.com/products/maxdb/, Retrieved on 10.04.2007

includes most SQL92 and SQL99 data types, including INTEGER, NUMERIC, BOOLEAN, CHAR, VARCHAR, DATE, INTERVAL, and TIMESTAMP. It also supports storage of pictures, sounds, or video. It has native programming interfaces for C/C++, Java, .Net, Perl, Python, Ruby, and ODBC (Fallmann and others, 2005, p.61f). PostgreSQL is specialized for very large databases, which a study documentation system requires. It also offers features like replication, load balancing, multi-processor and cluster support (Fallmann and others, 2005, p.62). PostgreSQL supports Encryption methods like SSL[34] or MD5[35] and Kerberos[36] for authentication as well as database links. Its full-text search facility requires the use of a special data type and also the option of an online backup is available. PostgreSQL is released under the BSD[37] license (more details at PostgreSQL Global Development Group, Advantages, 2007). Since PostgreSQL is similar to Oracle DB, in case of increased requirements the Oracle database can be used with minimal costs of migration.

7.5.3 Application and Web Server

An application server delivers applications to clients. In addition, the server handles the business logic and data access of the application. The main benefit of application server technology is the ease of application development and the centralization of the system. A Comparison of available application servers can be found on Wikipedia (Wikipedia.org, Matrix of Application Servers, 2007).

Through the success of the Java platform the term application server is often referred to a J2EE application server and is slowly gaining more acceptance. There are many different use cases, such as platforms for e-commerce, content management systems, affiliate management systems and occasionally, even applied to simplistic web-site page builders and now also clinical trial systems.

7.5.3.1 JBoss Application Server

[34] http://en.wikipedia.org/wiki/Secure_Sockets_Layer, Retrieved on 10.04.2007

[35] http://en.wikipedia.org/wiki/MD5, Retrieved on 10.04.2007

[36] http://web.mit.edu/Kerberos/, Retrieved on 10.04.2007

[37] http://en.wikipedia.org/wiki/BSD_license, Retrieved on 10.04.2007

JBoss is one of the most widely used and accepted application servers for the EJBS architecture. It is open-source software with large community and support (Red Hat Middleware, JBoss Application server page, 2007). Because it is based on Java, JBoss can run on any operating system that supports Java. JBoss was the first professional open source business model where the interior developers of the project made a living off of their services.

7.5.3.2 Oracle Application Server

As a commercial alternative to JBoss often the Oracle Application Server is used. The server entails a HTTP Server and OracleAS Containers for J2EE (OC4J). The Oracle Application Server is unique because of its design of grid computing (Oracle Corporation, Oracle application server EJB 3.0, 2007).

7.5.3.3 Tomcat Web Server

Tomcat (Apache) is a web server that supports servlets and JSPs (Apache Software Foundation, Apache Tomcat, 2007). Through the open-source characteristic and all the available features, this application server has become widely used. Tomcat is more and more used as a standalone web server in high-traffic, high-availability environments (Wikipedia.org, Apache Tomcat, 2007).

7.5.3.4 Sun Java System Application Server

Sun Java System Application Server (SJSAS) is a platform for delivering server side Java applications and web services. The technology is based on Java EE and is a core part of the Java Enterprise System. SJSAS is a good solution for deploying next generation Web 2.0-based interactive applications since it includes Java Server Faces which supports Ajax. Also, SJSAS is integrated in development technologies such as Sun Java Studio Enterprise, Sun Java Studio Creator, and NetBeans (Sun Microsystems, Sun Java System Application Server, 2007). Through the integration with Sun's Java Studio Creator and the ability to integrate the PostgreSQL database (through the JDBC 4 driver), we decided to use SJAS as our application server for our implementation. Some other commercial application servers are: WebSphere (IBM) and Oracle OC4J (Oracle Corporation).

7.5.4 Software Architecture

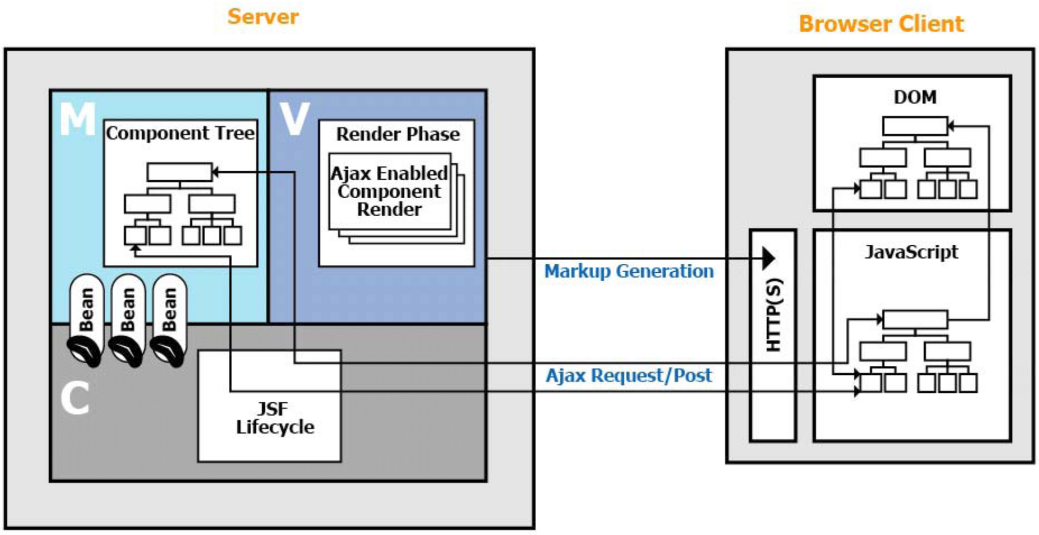


Diagram 55: JSF Architecture with Ajax (Maryka Stephen, 2006, p.6)

Through our research of Struts and JSF, we decided upon a Model View Control (MVC) architecture for our clinical study documentation system. The MVC architecture divides the presentation layer (Views) from the servlet (Controller) and the business logic (Model). The business logic consists of the different beans and services, as well as the data access layer (Buschmann, Meunier, Rohnert, Sommerland, 1996, p. 132f).

Maryka Stephen specifies the MVC architecture as a *"preserve back-end server-resident infrastructure, which eliminates the need for extensive JavaScript programming. Preserve developer core competencies, development practices, and tools and eliminates application fragmentation."*

(Maryka Stephen, 2006, p.6)

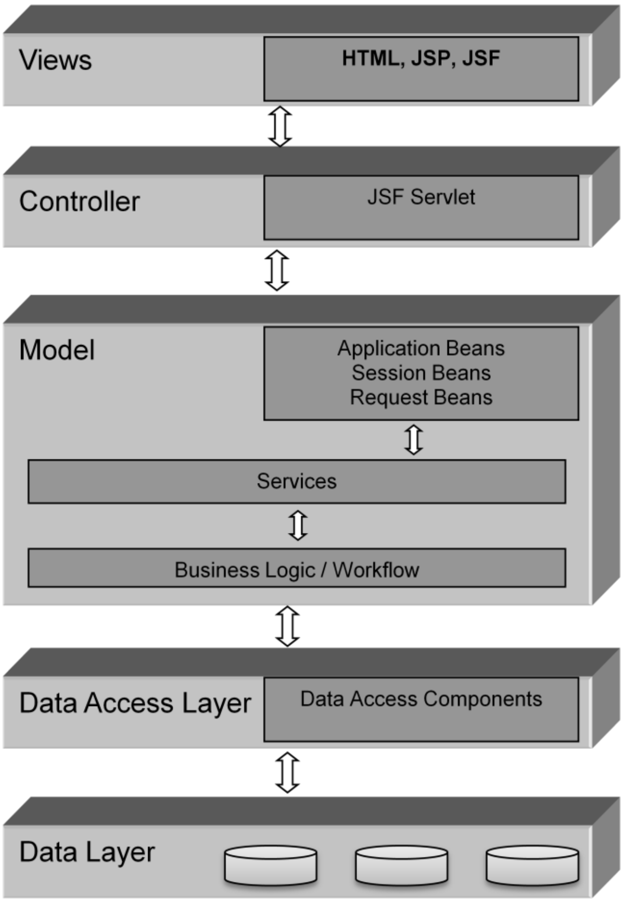


Diagram 56: Model-View-Control - Architecture

The MVC is a powerful architecture commonly used for graphical user interfaces. The MVC divides the application, or just a part of it, into the model, the view and the controller, allowing for an easier division of work for the presentation layer and business layer. These three parts must communicate with each other if the application should be able to handle a logical interaction with the user (Buschmann, Meunier, Rohnert, Sommerland, 1996, p. 130ff).

The model is based on the business rules or logic, which is comprised of the enterprise data beans and the services (Singh, Stearns, Johnson, 2002, p. 348). The content of a model is then displayed through the view (see Diagram 56). The view specifies how the received data from the model should be displayed. In case the model is changed, the view should still keep a consistent presentation of the data. There are two types of model interactions. First of all, the push model, where the model "pushes" an interaction to the view. The second type is the pull model, where the view "pulles" the data from the model when it needs to retrieve the most recent data (Singh, Stearns, Johnson, 2002, p. 348).

The controller (see Diagram 56) defines the behavior of the application and interprets the user's interactions in the view into activities for the model. In our web application AlphaNet a user interaction is determined through the GET and POST HTTP requests. The actions which are performed by the model include notifying the view of changes, responding to state changes or running different business processes. Depending on the user's interaction, and the models response, the controller reacts by selecting the corresponding view. (Singh, Stearns, Johnson, 2002, p. 349).

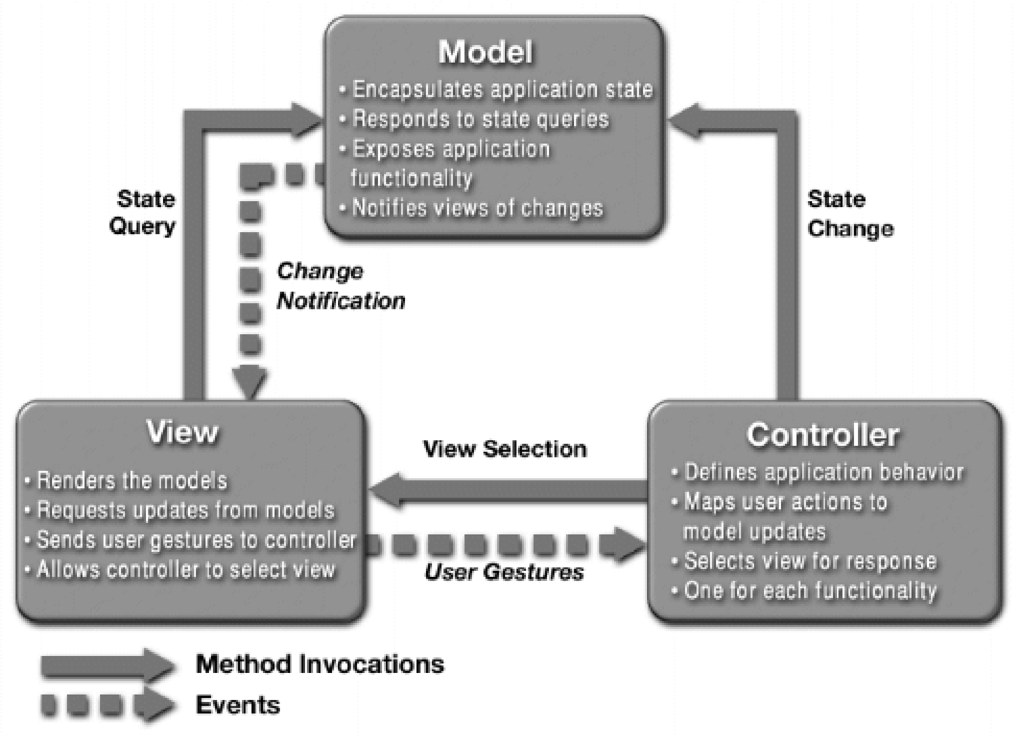

Model
• Encapsulates application state
• Responds to state queries
• Exposes application functionality
• Notifies views of changes
State Query
Change Notification
State Change
View
• Renders the models
• Requests updates from models
• Sends user gestures to controller
• Allows controller to select view
View Selection
User Gestures
Controller
• Defines application behavior
• Maps user actions to model updates
• Selects view for response
• One for each functionality
Method Invocations
Events

Diagram 57: MVC Structure (Singh, Stearns, Johnson, 2002, p. 349)

Our strategy is designed for web-applications. Therefore, we need the Enterprise Java Beans components for our model, Java Server Pages, as well as Java Server Faces, to create the view and the Java Servlets as the controller. The data access layer offers the basic access to the data layer which corresponds to the database as well as the file store.

7.6 Database Model

This section describes the database model used in our clinical study documentation system, AlphaNet. The chapter “Database Type” describes the open source database PostgreSQL, while the chapter “Table Descriptions” describes each table, value and its corresponding field type.

AlphaNet uses PostgreSQL as the database type. In contrast to MySQL, PostgreSQL has wider functionality, is more powerful and offers higher access rates. Compared to Oracle, PostgreSQL is an open source application which will allow easy maintenance in the future on the database itself.

PostgreSQL also has a plug-in for an SSL-connection for the client/server-communication. This feature is necessary for better security for the transfer of information. Encryptions, such as Md5, Sha1 and other algorithms, are integrated in PostgreSQL. The encryption on the database-layer will allow better security and the access-process will lose less performance. The required computing time is negligible in ratio to the hard disk access.

7.6.1 Database Model

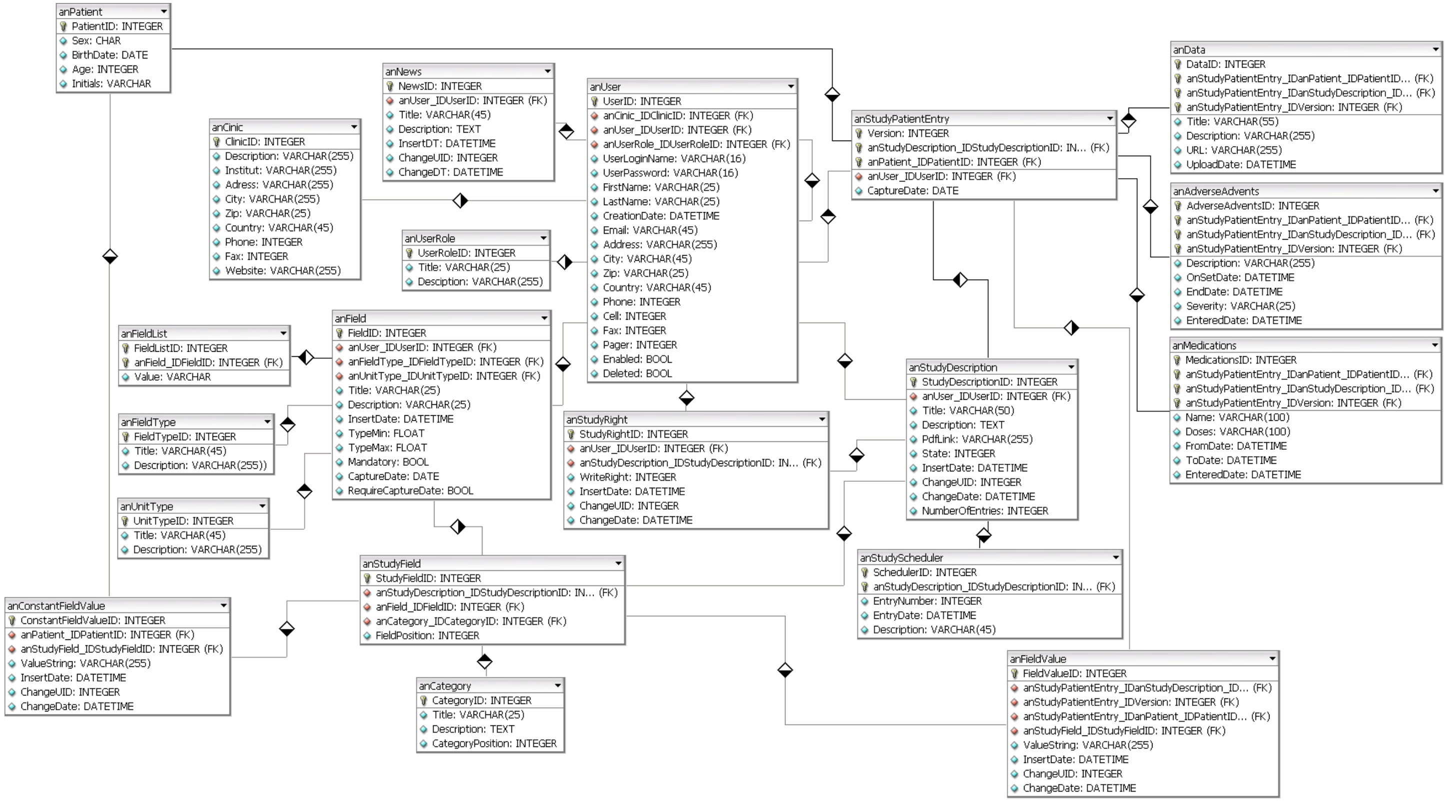


Diagram 58: Database Model

7.6.2 Table Descriptions

The following section describes all the tables in the database model. Each table is comprised of the name, the data type and the description of the field. Additional tables are located in some sections in case more details are required for the description of certain fields.

7.6.2.1 Users

The table "anUser" contains all the necessary information of user accounts. Along with the login name and password, personal information such as first, last name and address are stored as well. Furthermore, the user information includes a reference to the user role as well as to the clinic and institute where the user is employed. The "ClinicID" column is also used as a reference for the user's rights towards a clinical study.

Column Name	Data type	Description
UserID	Integer	Primary key
anUser_IDUserID	Integer	Foreign key for the person who created this person
anUserRole_IDUserRoleID	Integer	Foreign key, User rights for more details see Table 4
UserLoginName	Varchar (16)	Login name of the user (min. 8, max. 16)
UserPassword	Varchar (16)	Password (min. 6 – max. 16 Characters)
FirstName	Varchar (45)	First name of the person
LastName	Varchar (45)	Last name of the person
CreationDate	Datetime	Date and time of when the user was created
ClinicID	Varchar (255)	Foreign key of the clinic
Institute	Varchar (255)	Name of the institute where the user is employed
Address	Varchar (255)	Address
City	Varchar (45)	City
Zip	Varchar (25)	Zip Code
Country	Varchar (45)	Country
Phone	Integer	Landline Telephone Number
Cell	Integer	Cellular Phone Number
Fax	Integer	Fax Number
Pager	Integer	Pager
Enabled	Boolean	If the user was enabled by a project leader -> true (default: false)
Deleted	Boolean	Is User deleted? (default: false)

Table 23: anUser – Value Description

7.6.2.2 Clinics

The table "anClinic" contains all the information about the clinic itself. The clinic specifies the location where the user is employed and is the location where the trial information is gathered. The information includes description and address of the clinic.

Column Name	Datatype	Description
ClinicID	Integer	Primary key
Description	Varchar (255)	Foreign key for the person who created this person
Institute	Varchar (255)	Name of the institute where the user is employed
Address	Varchar (255)	Address
City	Varchar (45)	City
Zip	Varchar (25)	Zip Code
Country	Varchar (45)	Country
Phone	Integer	Landline Telephone Number
Fax	Integer	Fax Number
Website	Varchar (255)	URL of the Clinic-Website

Table 24: anUser – Value Description

7.6.2.3 User Roles

The table "anUserRole," holds each role that a user can have. Each user role entails the key, title and description. There are five different roles a user can have. These include administrator, project leader, investigator, and trial nurse. Further details are found in the table "Role Types."

Column Name	Datatype	Description
UserRoleID	Integer	Primary key
Title	Varchar(25)	Description of role
Description	Varchar(255)	Descibes the user role

Table 25: anUserRole – Value Description

Role - ID	Role Title	Description
1	Administrator	Access to all areas and technical services
2	Project leader	Create clinical studies, user management (Including the ability to add users with certain rights) and locking and unlocking of clinical studies
3	Monitor	View data and unlocking of clinical studies. As well as being able to set flags for certain fields for other users
4	Investigator	Data entries, uploading and submitting data, locking patient information, ability to see all of the patients, or only his own patients, depending on rights given by the project leader.
5	Trial Nurse	Only data entry.

Table 26: Role Types

7.6.2.4 Patient

The table “anPatient” contains all static patient-information. Each patient is stored anonymously in the database and is identified through the patient ID. Important is to remember, for the investigators and trial nurses, that the patients main frame of reference will be the “Initials” combined with the “Age”.

Column Name	Datatype	Description
PatientID	Integer	Primary key
Sex	Char	Sex
BirthDate	Datetime	Date of Birth (DD.MM.YYYY)
Age	Integer	Age of the time of admittance of the Patient
Initials	Varchar	Initials of the patient

Table 27: anPatient – Value Description

7.6.2.5 Study Description

The following table, “anStudyDescription,” depicts the general clinical study description. This includes a link for a pdf file which holds a more detailed description of the clinical study. Each clinical study has a lifeline of four states, which are described in the “Clinical Study States” table.

Column Name	Datatype	Description
StudyDescriptionID	Integer	Primary key
anUserID	Integer	Foreign key of a user which created the clinical study
Title	Varchar(50)	Title of the clinical study
Description	Text	Brief description of the clinical study
PdfLink	Varchar(255)	Link for the PDF File
State	Integer	Status of the clinical study.
InsertDate	Datetime	Date of creation
ChangeUID	Integer	User ID who modified the clinical study last.
ChangeDate	Datetime	Date of last modification
NumberOfEntries	Integer	Number of entries for each patient

Table 28: anStudyDescription – Value Description

ID	State
1	*Locked*: The study is being created and is not ready for data input. In this state, only the Admin, Project leader who created the study are able to modify the clinical study
2	*Released*: The study has been approved and released. This allows the employees now to input information for the patients. The clinical study itself is not modifiable
3	*Monitor*: The study has been sent to be approved by the monitor, who in change can release the project again for further changes, or sign it off for closing

4	*Closed*: The study has been completed and no more information can be entered for the patients. Only the Admin and Project leader can close a project

Table 29: Clinical Study States

7.6.2.6 Study Scheduler

Each clinical study can schedule the days for which the trial information should be captured and entered. The table „anStudyScheduler" entails the schedule information for the clinical study. For each entry that a clinical study has, the number of days of when the entry should be entered, counting from the previous entry date can be stored.

Column Name	Datatype	Description
StudySchedulerID	Integer	Primary key
anStudyDescriptionID	Integer	Foreign key of anStudyDescritpion
EntryNumber	Integer	The number of the entry for the clinical study
EntryDate	Integer	The number of days from the previous entry when the entry should be filled
Description	Varchar(45)	The description of the Schedule

Table 30: anStudyScheduler – Value Description

7.6.2.7 Study Rights

Table 7, "anStudyRight," describes the relationship between the clinical studies and the user. Since not every user has access to a clinical study, this table states which users has access to view or modify the clinical studies. The study project leader and the administrator are able to modify the user rights for each clinical study. The project leader is only allowed to set the user rights for the clinical studies that were created by him/her.

Column Name	Datatype	Description
StudyRightID	Integer	Primary key
anStudyDescriptionID	Integer	Foreign key of anStudyDescription
anUserID	Integer	Foreign key of anUser
InsertDate	Datetime	Date of creation
ChangeUID	Integer	UID which did the last change
ChangeDate	Datetime	Date of Change
AccessRights	Integer	Access rights, can the user modify the clinical study itself, modify the clinical study information for the patient, or only view the patients information(default: 4)

Table 31: anStudyRight – Value Description

ID	Description
1	*Full Access*: Once the study has been released, entering data, modifying and viewing of all the patients included in the clinical studies is possible
2	*Clinic Access*: Once the study has been released, entering, viewing and modifying of patient info is only possible for the patients which user from one clinic have created
3	*Only Own Patient Access:* Once the study has been released, entering, viewing and modifying of patient info is only possible for the patients which the user has created
4	*View Only Access*: The user can only view the information of the study and statistical analysis but not the specific patient information
5	*No Access:* The user is not able to view a selected clinical study. That option should be used if a user doesn't work any longer on a clinical study.

Table 32: Access Rights

7.6.2.8 Study Patient Entry

The following table, "anStudyPatientEntry", entails the values between the patient and the different studies. Since a patient can be integrated into numerous clinical studies, and vice versa, this table is required. All the primary keys of the tables "anPatient" and "anStudy" are stored in this table. In addition, a version is stored which allows the user to have numerous entries for a single clinical study.

Column Name	Datatype	Description
VersionID	Integer	Primary key
anUserID	Integer	Foreign key of anUser
anPatientID	Integer	Primary/Foreign key of anPatient
anStudyDescription	Text	Primary/Foreign key of anStudyDescription
CaptureDate	Date	Date of when the information was captured. Needs to be inputed by user, not the system.

Table 33: anStudyPatientEntry – Value Description

7.6.2.9 Data (Images, Videos, etc.)

Each entry, or version, for a patient can have multiple images or other files types which can be uploaded for further viewing. The table "anData" lists all of the images, videos and other files that were uploaded for a each entry.

Column Name	Datatype	Description
DataID	Integer	Primary key
anPatientID	Integer	Foreign key for the patients ID
anStudyDescriptionID	Integer	Foreign key of anStudyDescritpion
anVersion	Integer	Foreign key, version of uploaded files
Title	Varchar(55)	Title of the file
Description	Varchar(255)	Description of the file

URL	Varchar(255)	The url of the file
UploadDate	Date	The date when the file was uploaded

Table 34: anData – Value Description

7.6.2.10 Adverse Advents

Adverse advents are all the irregular occurrences during the capture of the patients data. The table „anAdverseAdvents“ entails all of the adverse advents which occur at a given entry. Each entry, or version, can have multiple adverse advents.

Column Name	Datatype	Description
AdverseAdventsID	Integer	Primary key
anPatientID	Integer	Foreign key for the patients ID
anStudyDescriptionID	Integer	Foreign key of anStudyDescritpion
anVersion	Integer	The version of where the adverse advents occured
Description	Varchar(255)	The description of the adverse advent
OnSetDate	Date	The date when the adverse advent first occured
EndDate	Date	The date when the adverse advent stopped
Severity	Varchar(25)	The severity of the adverse advent
EnteredDate	Date	The date when the adverse advent was entered. Should be specified by the system.

Table 35: anAdverseAdvents – Value Description

7.6.2.11 Medications

Each patient can take a number of different medications during the clinical trial. The table “anMedications“ entails all of the medications which are consumed by the patient during the clinical trial. Each patient can have multiple medications which can be entered.

Column Name	Datatype	Description
MedicationsID	Integer	Primary key
anPatientID	Integer	Foreign key for the patients ID
anStudyDescriptionID	Integer	Foreign key of anStudyDescritpion
anVersion	Integer	The version of where the adverse advents occured
Name	Varchar(100)	The name of the medication
Doses	Varchar(100)	The doses of the medication
FromDate	Date	The date when the medication was first taken

ToDate	Date	The date until when the medication needs to be taken
EnteredDate	Date	The date when the medication was entered. Should be specified by the system.

Table 36: anMedications – Value Description

7.6.2.12 Fields

The main part of every clinical trial, are the fields which need to be entered during the capture of the patients information. The table “anField“ entails the information of a specific field which is used for the clinical studies.

Column Name	Datatype	Description
FieldID	Integer	Primary key
anUnitTypeID	Integer	Foreign key of anUnitTypes
anFieldTypeID	Integer	Foreign key of anFieldTypes
anUserID	Integer	Foreign key of the user who created the field
Description	Varchar(255)	Description of the field
Title	Varchar(25)	Title of the field
InsertDate	Datetime	Date of when the field was created
TypeMin	Integer	The minimal value that an average patient should have for this field
TypeMax	Integer	The maximum value that an average patient should have for this field
Mandatory	Boolean	Is this field mandatory? (default: false)
CaptureDate	Date	The date of when the field was captured.
RequireCapture	Bool	Does the CaptureDate need to be shown for that specific field? (Default: false)

Table 37: anField – Value Description

7.6.2.13 Field Types

Each field of a clinical study can be of a certain type. These types are stored in the static table “anFieldType“. There are 11 different types of fields which can be stored in the database, which are listed in the table, “Field Types”.

Column Name	Datatype	Description
FieldTypeID	Integer	Primary key
Title	Varchar(45)	Title of the field type
Description	Varchar(255)	Description of the field type

Table 38: anField – Value Description

ID	Title	Description
1	Integer	A text field where only integers are allowed. Values with a decimal will not be accepted. (i.e. 4, 5, 123, 9034)
2	Float	A text field where only values with decimals will be accepted. (i.e. 4.32, 5.321, 56.3492)
3	Roman Numeral	A text field where only capitalized roman numerals are accepted (i.e. VII, XVII)
4	Boolean	Radio buttons with the options Yes or No (True or False)
5	Small Text	A small text field of 45 characters
6	Large Text	A large text field of 255 characters
7	Drop Down List	Drop Down list with multiple entries (See also anFieldDropDownList table)
8	Check Box List	A single check box with a description.
9	Date	Allows only date with "dd/mm/yyyy" format
10	Time	Allows only time field with "hh:mm:ss " format and a 24 hour clock
11	File Upload	Uploads the given file to the server and stores the URL in the database. Requires a "Browse" button next to the field

Table 39: Field Types

7.6.2.14 Unit Types

If the file is of a type integer or float, the field may require a measuring unit (i.e. year, min, day, hour, ml, cm, mm, pH, percent, mg/l). The table "anUnitType" depicts this information.

Column Name	Datatype	Description
UnitTypeID	Integer	Primary key
Title	Varchar	Title
Description	Text	Description of the unit type

Table 40: anUnitType – Value Description

7.6.2.15 Field List

In case a field is a drop down list or a checkbox, the user needs to enter the values of the drop down list or checkbox. The table "anFieldList" stores all of the values for these drop down list and checkboxes.

Column Name	Data Type	Description
anFieldDropDownList	Integer	Primary key
anFieldID	Integer	Foreign key from anField
Value	Varchar	The value of the list box

Table 41: anUnitType – Value Description

7.6.2.16 Study Field

Table “anStudyField” depicts the database table anStudyField. This table connects the fields with the clinical studies, as well as to the categories. A clinical study can have any number of fields, and a field can be used in any clinical study. For each specified clinical study, a field can be grouped into a category.

Column Name	Datatype	Description
StudyFieldID	Integer	Primary key
anFieldID	Integer	Foreign key of anField
anStudyDescriptionID	Integer	Foreign key of anStudyDescription
anCategoryID	Integer	Foreign key of anCategory
FieldPosition	Integer	Position of the field in a category

Table 42: anStudyField – Value Description

7.6.2.17 Category

In order to organize the clinical study, each field is entered into a certain category. The table „anCategory“ holds the category information that a field can be specified under.

Column Name	Datatype	Description
CategoryID	Integer	Primary key
Title	Varchar	Title of the category
Description	Text	Description of the category
CategoryPosition	Integer	Position of the Category

Table 43: anCategory – Value Description

7.6.2.18 Field Value

Once a field is added to the clinical study, the investigators and trial nurses can input the captured information. The table “anFieldValue” represents the values of the selected field of a clinical study for a specific patient which needs to be entered for every version. The table “ValueString for Boolean Fields“describes the value of the string if the field type is a Boolean.

Column Name	Datatype	Description
FieldValueID	Integer	Primary key
anStudyFieldID	Integer	Foreign key of anField
anStudyPatientID	Integer	Foreign key of anStudyPatient
anStudyDescriptionID	Integer	Foreign key of anStudyPatient
anStudyPatientVersion	Integer	Foreign key of anStudyPatient
ValueString	Varchar(255)	The value of the field
InsertDate	Datetime	Date of creation
ChangeUID	Integer	The user ID of the user who changed the value last.
ChangeDate	Datetime	The date the value was changed

Table 44: anFieldValue – Value Description

ID	Boolean Value
1	True
2	False
3	Not selected

Table 45: ValueString for Boolean Fields

7.6.2.19 Constant Field Value

Certain patient information only needs to be entered into the system one time. The database table “anConstantFieldValue” represents the values of the selected field of a clinical study for a specified patient which only needs to be entered the first time the clinical study was created for that patient.

Column Name	Datatype	Description
ConstantFieldValueID	Integer	Primary key
anStudyFieldID	Integer	Foreign key of anField
anStudyPatientID	Integer	Foreign key of anStudyPatient
ValueString	Varchar(255)	The value for the field
InsertDate	Datetime	Date of creation
ChangeUID	Integer	UID der die Nachricht geändert hat
ChangeDate	Datetime	The date when the field was changed.

Table 46: anFieldValue – Value Description

8 Conclusions and Future Work

Clinical Studies are one of the most important techniques to evaluate medical treatments. The most common clinical studies evaluate either drugs, medical devices, psychological therapies or other interventions in a strictly regulated environment. In each clinical trial, the individual patients are observed and the outcomes of the treatments are captured and measured by the investigators. The observation and capture of the patient's information is associated with high degree of organizational effort.

Through the new technologies Ajax and JSF it is possible to create a clinical study documentation system which achieves the requirements necessary to improve the efficiency of clinical studies. The technologies enable the construction of a dynamical environment which allows the creation of any type of clinical study, let it be wound analysis, bacteriological reports, nutritional data or even laboratory reports.

The clinical study documentation system, AlphaNet, is designed to improve the management and reduce the effort and time required for clinical studies. Furthermore, since the system is a web application, the clinical study is not only carried out at one location, but can be carried out at numerous locations at the same time, which in return allows more results to be compared, which improves the end result of the clinical study. The simplified user interface design allows for easy creation of clinical studies through the web browser, while keeping an application like look and feel. Through the field management and category management systems, the documentation system allows the user to create a clinical trial with a clear overview of the different sub sections. In general, AlphaNet will allow the user to set up a clinical study, manage the clinical study with all of the respective patients while upholding the users and patients privacy rights, without requiring any database or programming knowledge.

In conclusion, the further development, and new development, of information technology solutions for the assistance of documenting clinical studies can only be an advantage. Internet based concepts, like the clinical study documentation systems, hold a high rational potential. A basic study documentation system should entail the following features:

- A central database
- No duplicate documentation or transfer of data
- Permanent access to the information
- Input control (Monitor, Study Leader)
- Automated assistance for the monitors

Clinical study documentation systems hold the following advantages:

- Less time and effort required for the participants
- Lower costs for the documentation and testing forms
- Higher quality of the documentation
- Better recruitment and number of participants (easier access)
- Improved information flow
- Less time needed to finish the clinical study
- Easier monitoring

An important aspect is to define the standards and guidelines. There is no way around a well thought through plan in order to achieve a successful product. Another important aspect is that the user interface of a clinical study documentation system should be easy to understand for the different users (doctors, investigators, monitors, trial nurse's, etc.). This is an important aspect during the planning and development phases of the application. Another factor is the cost of the development of such an application. Sponsors can be very helpful, but certain dependencies are always connected to that. Finally, the problem of security and privacy need to be solved in an adequately and efficient manner.

All these problems are possible to solve, but exactly for those reasons, the systems in the past were hindered from being distributed to a larger realm. Only the future will show the development of such clinical study documentation systems, and if it is possible, even connect the systems with the electronic health cards. In general, one can say that the potential in this field is far from being reached.

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