

CLINICALTRIALS

MED solutions | the clinical studies web based platform



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1 CLINICALTRIALS

ClinicalTrials is the web-based Sinaptica IT platform aimed at capturing clinical trials data. Thanks to ClinicalTrials, clinical research can benefit from a dedicated, highly performing IT tool, which is efficient and cost-effective, and guarantees a secure data transfer fulfilling the needs of any kind of clinical study.

A web-based access enables you to get online available data in real time, streamlining workflow, data control, and analysis. ClinicalTrials can be used with any web browser (Internet Explorer, FireFox, Safari, Chrome, Opera), without having to install any further software and without any constraint relating to hardware or operative system.

The characteristics of ClinicalTrials make it a perfect tool within an international clinical trial environment:

- A Bilingual version (English - Italian) is available.
- There is a web-based platform for worldwide access, as long as an Internet connection is available.
- It does not need to be installed: it is possible to activate centers and users anywhere in the world by using the remote mode.

ClinicalTrials is a tool, which offers full control and thorough flexibility in managing clinical trials data. Thanks to its parametric structure, it can be adapted to the needs of any clinical trial protocol. Indeed, you can generate and modify, completely on your own, eCRFs (electronic Case Report Forms) and their related workflow, just as access profiles can be personalized according to the needs of any one of the different actors playing a role in the study (data

manager, biostatistician, investigator, system administrator and patient).

In order to efficiently implement most complex therapy protocols, ClinicalTrials uses advanced solutions to manage the logical and temporal study flow, for example, the Time plan, the different data checks applicable to single fields, sections and entire forms, and the sophisticated randomization tools.

The ClinicalTrials platform includes all the functions enabling an effective and efficient management of a clinical trial, which are designed to simplify professional users' daily activities, thereby ensuring that the system itself carries out all repetitive and routine activities.

The following are among such functions:

- Clinical trial Planner.
- Integrated management of Queries.
- Automated alerts and messages.
- XML format data export (SAS-compatible).
- Easy and user-friendly user interface.

ClinicalTrials utilizes the HTTPS web data transfer protocol through the SSL code system at 128 bits, as it guarantees maximum data security as well as a security logic that is fully compliant with Italian Data Privacy Legislative Decree (196/2003). Furthermore, it has been designed so as to adhere to GCP (Good Clinical Practice) and to the Italian Data Protection Supervisor "Guidelines for Data Processing within the Framework of Clinical Drug Trials" (nr. 52, 24 July 2008).

1.1 WORKING CYCLE

ClinicalTrials' working cycle has been carefully designed and field-tested so as to streamline the steps, which characterize the capturing of data relating to clinical studies. It provides Users with an efficient tool enabling them to fulfill their own role responsibilities in a more efficient manner:

- Participation by centers and pre-screening of patients: creation and management of Users and Groups.
- Design and implementation of case report forms: eCRFs Templates design and creation (by which the logical time flow of the study is managed).
- Data capture: eCRFs creation and following workflow validation.
- Export: data export.

Centers participation and pre-screening of patients

The evaluation of operators participation and the determination of which patients to enroll are represented in ClinicalTrials by Users creation. These are divided into Operators and Patients. The system's Administrator is in charge of the Operators' profile creation, while Investigators are in control of profile creation relating to Patients.

Design and implementation of case report forms and clinical study flow

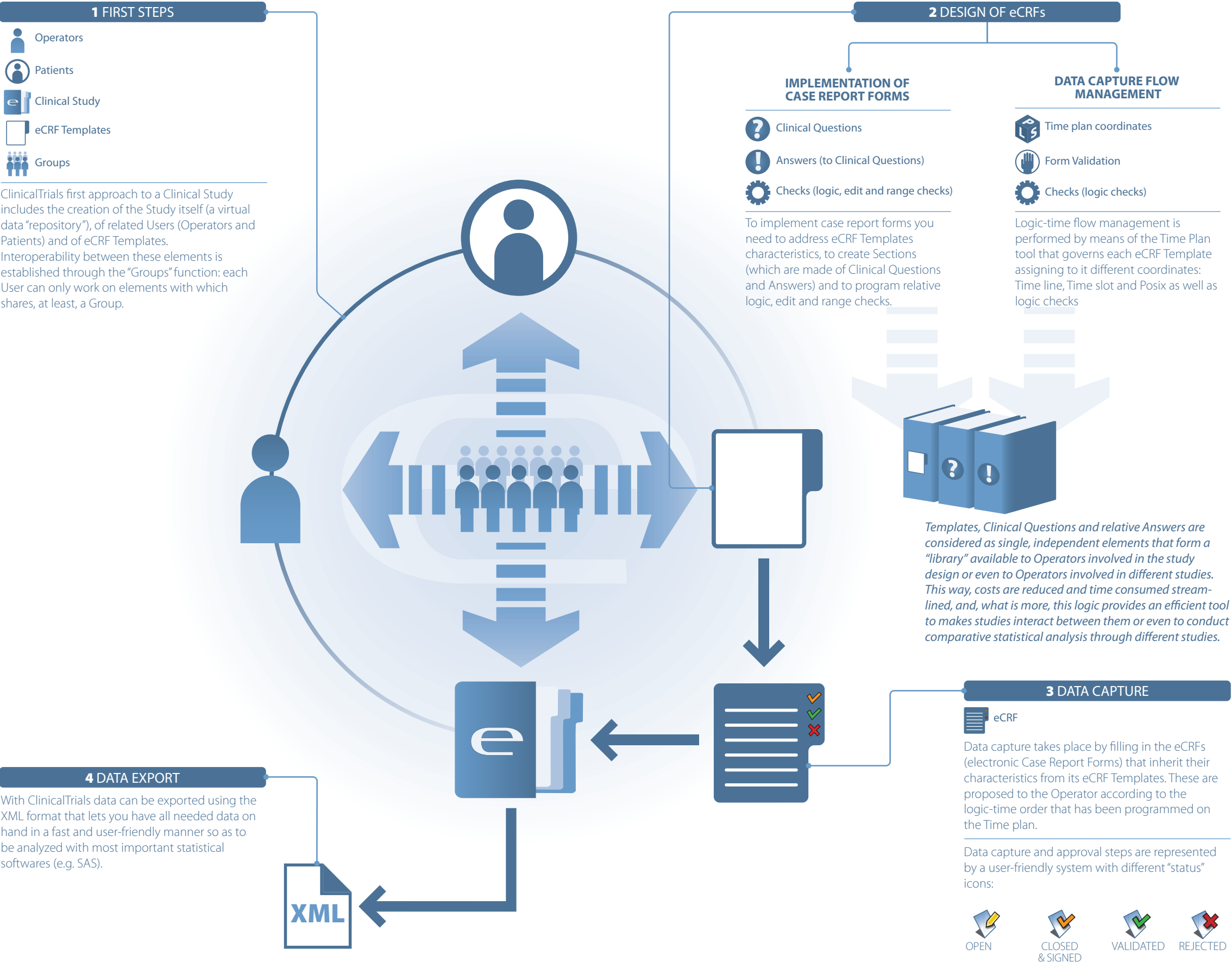
With ClinicalTrials, the design and implementation of case report forms and their logic-time flow is done by creating the so-called eCRF Templates, along with its related checks, via a parametric and modular pattern which enables you to build a "library" of case report form templates and single Clinical Data Items that can be reused at any time, either during the study design itself or in connection with different studies.

The Time plan tool is a vital element within the design and implementation phase. It allows a full control of the study flow owing to a user-friendly coordinates system (Time line/Time slot/Posix), which is applied to each case report form.

The study flow can be further refined by performing mandatory logic checks on single study forms according to mandatory study flow (Validation Needed) and/or by the mutual exclusion of forms or even by cross-field checks, cross-form checks or cross-study checks, provided that all studies are managed through ClinicalTrials.

Data Capturing

Data capturing takes place by filling in the eCRFs (electronic Case Report Forms) which are shown to the Operator according to the logic-time order that has been programmed on the Time plan. ClinicalTrials offers an efficient and user-friendly procedure in order to compile and



approve eCRFs. This is enhanced by an icon system, which is based on the different “statuses” of forms:

- Not yet closed: the eCRF has been created and is ready to be filled in.
- Closed & signed: the eCRF has been filled in and is waiting for either Data Manager validation or rejection.
- Validated: the eCRF has been validated by the Data Manager.
- Rejected: the eCRF has been rejected by the Data Manager.

ClinicalTrials also provides further features aimed at addressing complex situations, which have the effect of rendering Operators’ tasks much easier:

- Clone function: whenever a form has been rejected by the Data Manager, it cannot be further modified or deleted. In this case, the Data Manager is able to “clone” the rejected form by obtaining a new one, which is available to the Investigator so as to let him modify those fields (the so-called Sections), which have not yet been validated by the Data Manager. This feature guarantees that all activities are logged by keeping a track of them (audit trail), and, at the same time, it makes Investigator’s tasks easier and faster.
- Query function: ClinicalTrials allows you to manage Queries, that is, a question submitted by the Data Manager to the Investigator. It does so through the medium of three different logic statuses: the Data Manager can make inquiries to the Investigator, who answers them and gives effect to the final decision regarding Query outcome by the Data Manager. The system foresees the possibility of monitoring Queries directly through the welcoming page and through the Homepage, by distributing information according to logical steps. It is possible to make Queries, which relate to an entire CRF or merely to single Sections within a given form. Furthermore, according to the Query object, it is possible to assign a level of priority to the different Queries that have been issued.

ClinicalTrials also introduces the concept of a “Section” within an eCRF: a Section is a part of the eCRF and it is formed by a Clinical Data Item and the appropriate Answer fields; a Section might be signed or validated/rejected by means of the same procedures which are used in respect of entire eCRFs.

This solution makes of ClinicalTrials a perfect tool for complex situations, one in terms of which doing work on the single Sections of an eCRF makes things much more user-friendly and efficient for both subjects, i.e. the Investigator and the Data Manager.

Exporting data

With ClinicalTrials, you can export data in the XML format. That allows Operators to obtain, in a fast and user-friendly way, all the necessary data. This feature is extremely useful, as it lets you migrate clinical datasets to most commonly used statistics software, such as SAS.

1.2 STRUCTURES PERTAINING TO USERS AND GROUPS

ClinicalTrials offers a most flexible method of managing the access and operation profiles of users, due to a logical structure, which is divided into Users and Groups.

This structure has been widely developed by Sinaptica IT and field-tested on the clinical case history ClinicOnline®, where it has shown to be the only really efficient solution capable of guaranteeing the following:

- Maximum flexibility.
- Genuine control of usage access levels.
- Accurate interoperability management.

The ClinicalTrials system encompasses all the actors who are required for carrying out a clinical trial: Data manager, Investigator, Biostatistician, Administrative manager and Patient.

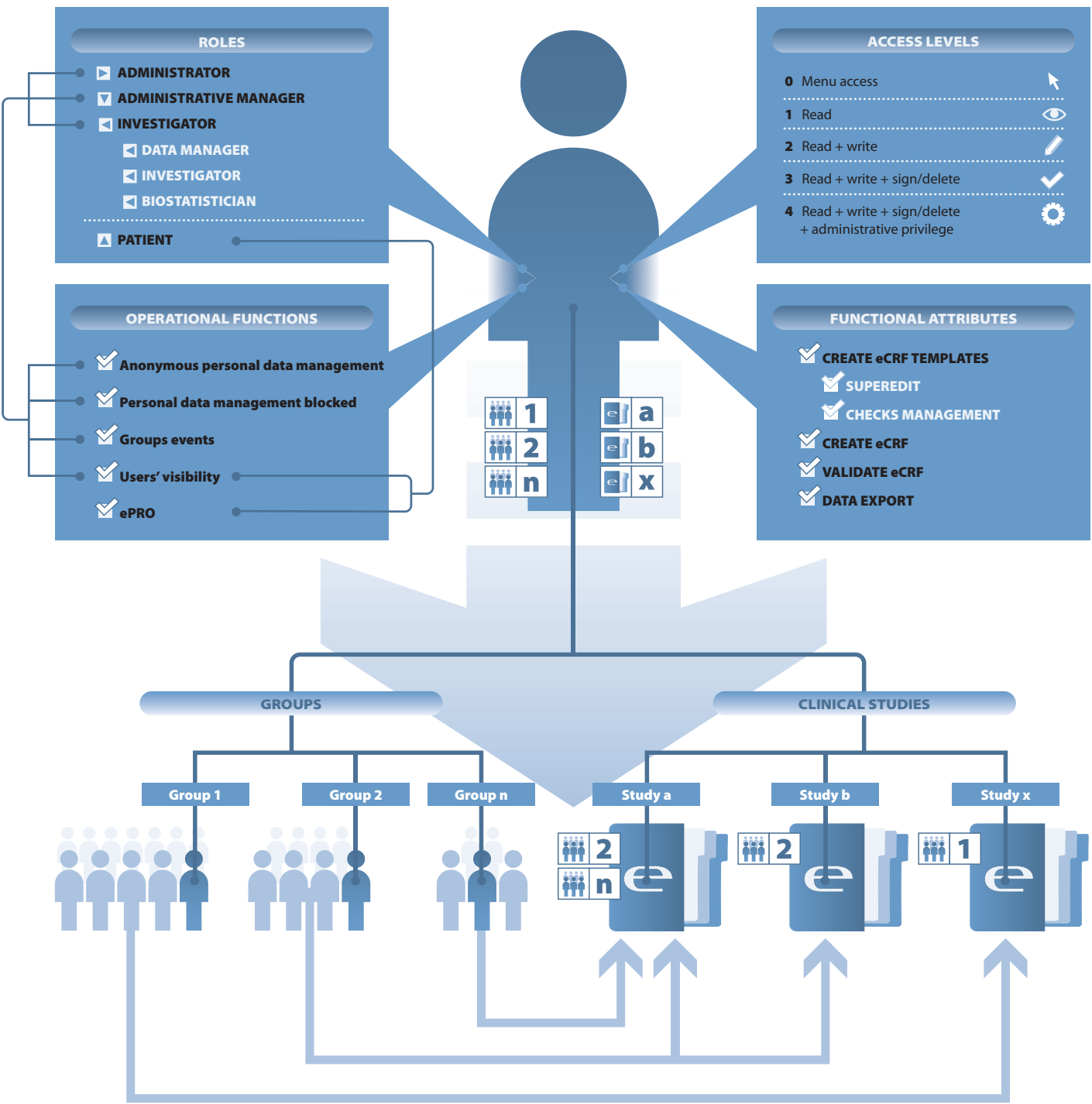
Each of these roles can be further customized so as to meet the needs of different clinical studies and structures in respect of which extremely specialized subjects are needed or, on the contrary, in respect of which a few people only perform a wide range of different roles.

In order to customize each User, you will have to go through the following steps:

- Selection of the different Access levels.
- Role definition (System administrator, Administrative manager, Investigator, Patient).
- Specification of functional Attributes (eCRF Templates creation, Superedit, Checks management, eCRF creation, eCRF validation, Data export), which characterize and distinguish each relevant role.
- Definition of operational options: Management of users’ personal information, Management of anonymous personal information, Events per Group, ePROs (electronic Patient Reported Outcomes), User visibility.
- Allocation to one or more Groups.
- Allocation to one or more Clinical Studies.

The Groups structure is the cornerstone of ClinicalTrials, and it is one of the characteristics of the system making it extremely flexible and precise.

The goal of the Groups feature consists in assigning to the



Each user can work on Clinical Studies to which he/she has been associated (in the example, studies a, b and x) only if he/she has a Group in common. In the example, both, User and Study x are linked to Group 1, and thus, the User will be able to work on Study x, as well as all other Users from Group 1 that may have been linked to Clinical Study x.

elements making up the system the appropriate interoperability (Users, Clinical studies, eCRF Templates and eCRFs) as between them, so that each User can only work in those areas in respect of which he/she shares at least one Group.

It is therefore extremely important to assign a Group to a given User so as to activate him on a given Clinical study. For example, it is not enough to assign a Clinical study to a given User: in order to render the User fully operational, we also need to assign to him a Group shared by the Clinical Study in which he/she intends to work.

In that manner, ClinicalTrials makes repetitive activities faster and automatic, without having to deploy manpower or economic resources.

The Groups management tool provides you with a completely flexible measure for the purpose of defining study settings: indeed, they may coincide with single centers participating in the study, though they do not necessarily need to do so. Furthermore, the fact that each element of the system can be associated with one or more groups makes ClinicalTrials really useful when dealing with complex organizational and logistical realities. On the other hand, as regards to those centers which work with a few small studies only, it is sufficient to create a single Group in which all Operators and Patients are active members.

An attractive highlight of this feature is the Patient's "transitive characteristic". Indeed, whenever a Patient is a member of more than one Group, the Operators from those Groups can have access to each other's Patient-related data. Nevertheless, in order to guarantee privacy and security standards, this function can be disabled on a single User's basis (by using the Groups Events option).

1.3 TIME PLAN: MANAGEMENT OF THE CLINICAL STUDY LOGIC-TIME FLOW

ClinicalTrials enables you to mold and accurately manage the clinical study eCRF compilation flow in a flexible manner. This is made possible by the Time plan tool, developed and implemented by Sinaptica IT, which allows you to control the logic-time therapy flow through some simple eCRF Templates parameters.

The position of a single CRF Form within the logic-time flow is controlled by means of three coordinates, which are related to the eCRF Template:

- Time line: it shows the temporal line in which we want to position the form.
- Time slot: it shows the moment in time when we want the form to be created and filled in.

- Posix: it shows the position in which the form is situated compared to other forms within the same Time line and Time slot.

In that way, operators can easily implement the time flow whereby forms are offered to Users according to Time plan rules. That is done as follows:

- Once a Time line has been selected, you need to retain it until no other form with the following Time slot is shown to you.
- You can only go forward in time (i.e., towards the following Time slot).
- In order to proceed to the following Time slot, it is mandatory that all previous forms have been opened (except for mutual exclusive forms or for limits relating to control functions, which prevent you from opening a given form, or where validation is needed).
- The system automatically checks whether there is any form in the next Time line within the same Time slot; in the event that none exists, the system offers to the Operator all the forms available at the next Time slot, albeit on a different Time line (e.g., randomization arms).
- eCRF Template forms which have the very same coordinates (Time line/Time slot/Posix) are mutually exclusive, which means that, once you have chosen to create and fill in one of them, all the others are automatically excluded.
- eCRF Template forms which have a null Time line and Time slot (equal to 0) are "timeless", which means that they can be created and filled in at any moment in time.

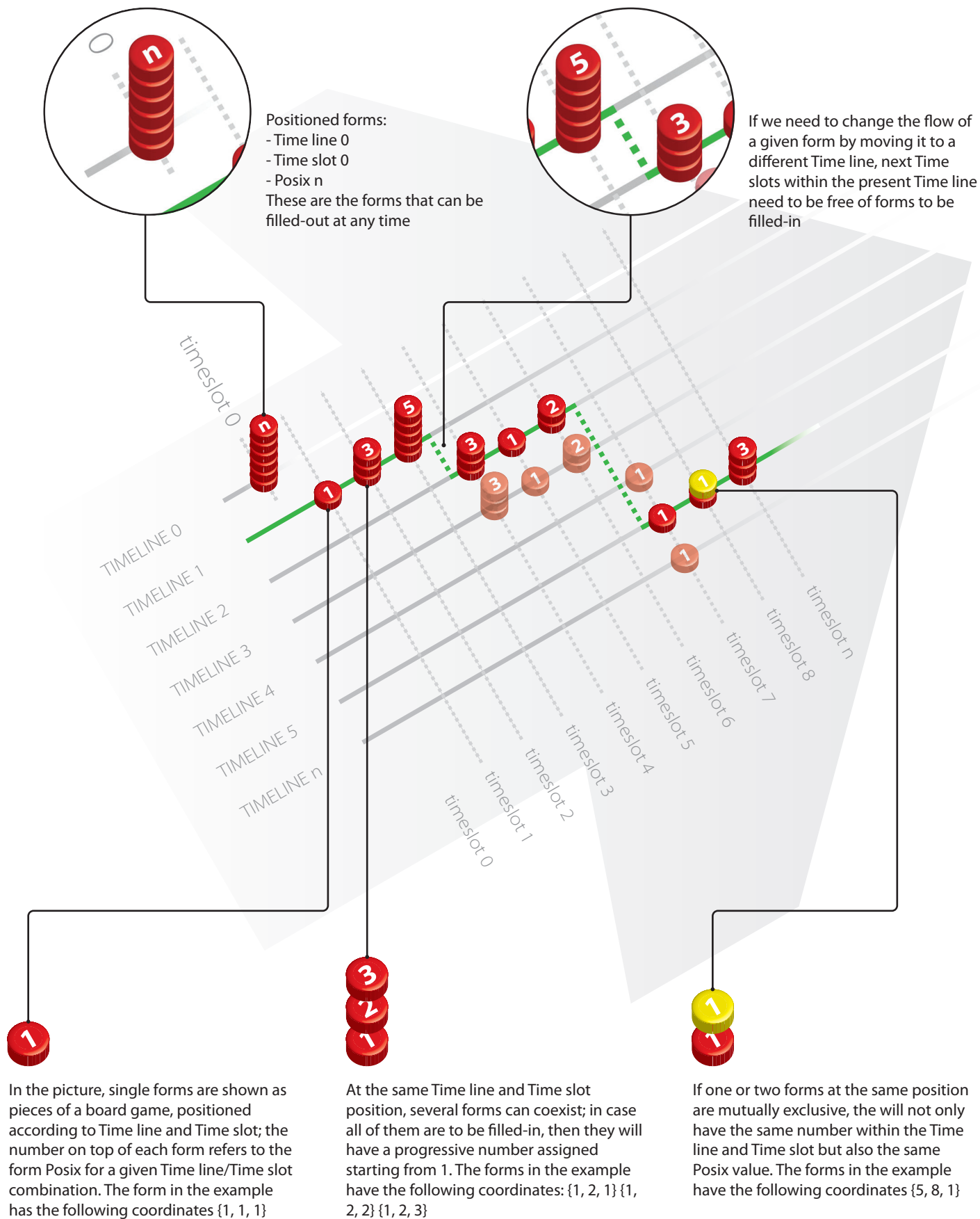
ClinicalTrials is thus able to provides you with a tool to design a model which is capable of foreseeing different paths through time, such as randomization arms, by easily displaying the appropriate forms on a different Time line than the source one.

Time plan further empowers you to program the logic-time flow of the study by means of two additional tools:

- Validation Needed (related to the Form).
- Checks on whether a form can be open or not.

By applying a logic check on an entire form (through the eCRF Template "Form Validation Needed" tool) it is possible to stop the workflow at a given Time slot, until all the requested data are present, that is, until the corresponding eCRF has been closed and signed.




On the other hand, by running these logic Checks on an entire form, it is possible to establish when a form can be created and filled in according to values deriving from a previous form or from a different study (logic cross-form



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PARAMETERS




eCRF Templates parameters are based on identification (through a unique code which is combined with a freely chosen name), and on the affiliation to one or more Groups as well as a Study within ClinicalTrials.

-  Arbitrary code
-  Groups
-  Clinical Trial

Within these eCRF Template parameters, it is also possible to let patients use a given case report form (ePRO – function).




TIMEPLAN

The logic-time flow of the study is managed by means of the Time Plan tool through the following coordinates which are assigned to each eCRF Template: Time line, Time slot and Posix, and through appropriate checks (Validation Needed) and cross-form edit checks, in accordance with values that are already present within the study or values derived from a different study.

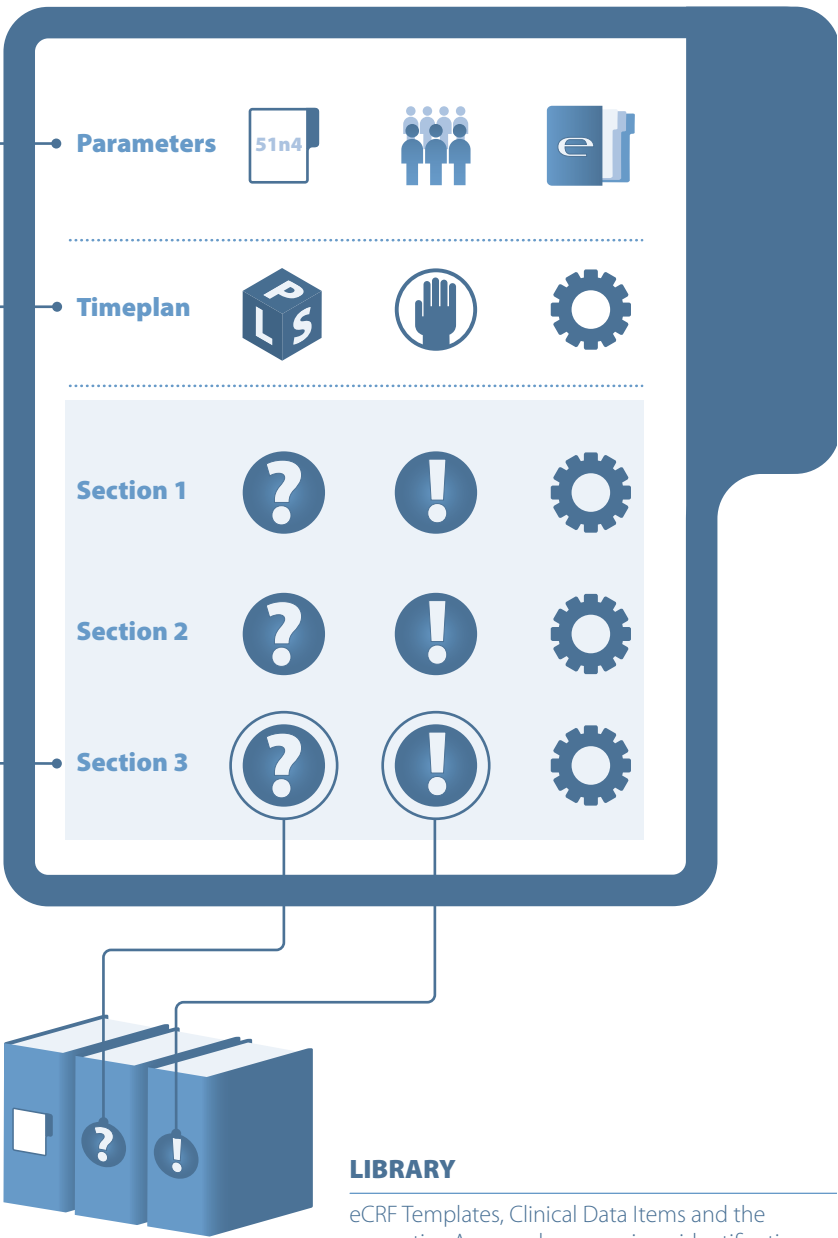
-  Time plan coordinates
-  Validation Needed
-  Edit and logic status Checks

SECTIONS

Data capturing fields are implemented in the so-called Sections, which are organized as follows:




-  Clinical Data Items
-  Answers (to Clinical Data Items)
-  Checks (edit and range checks)

Each eCRF Template can have more than one Section. Each Section can have multiple Answers to the same Clinical Data Item. Checks enable you to limit data entry on a given Section according to other study values or to values related to different studies (logic cross-forms and cross-studies checks), as well as to define the parameters of a given Answer range (range checks).



LIBRARY

eCRF Templates, Clinical Data Items and the respective Answers have a unique identification code and are part of a data repository, a “library”, which is available, at any given moment, to operators working on the study they originate from or on other studies, so as to carry out a comparative statistical analysis which streamlines the time needed and the costs associated with design.

-  eCRF Templates
-  Clinical Data Items
-  Answers (to Clinical Data Items)

checks and logic cross-study checks).

Furthermore, the system foresees the randomization management through an appropriate module wherein you can provide desired fields and stratification variables, in addition to the possibility of imposing a limited number of patients with regard to a given form (this tool may also be implemented so as to control cohorts in phase I studies). In this way, ClinicalTrials enables you, to efficiently implement complex protocols, in so doing offering a wide spectrum of possibilities for randomization (pure random, deterministic randomization, patients’ balancing), according to stratification variables.

1.4 A MODULAR TOOL: eCRF TEMPLATES, CLINICAL DATA ITEMS AND CHECKS FUNCTIONS

ClinicalTrials is an extremely efficient platform for designing clinical studies, owing to its parametric and modular structure. As a matter of fact, this comes to light at the stage of implementing form collection data, in particular in the case where the so-called eCRF Templates are created.

Each eCRF Template is made of:

- Its own parameters and Time plan check parameters.
- Sections with Clinical Data Items and Answers.
- Edit and logic status Checks (impacting on the eCRF Form), edit and range Checks (impacting on single fields).

The logic behind this structure is to view every eCRF Template, Clinical Data Items or Answer, as a single, independent element which is a part of a “library”, one that turns into a repository Operators can consult at any given time while working on the design of a particular study or even on the design of future ones. These elements or bits of data retain their own parameters, such as their own range Checks or units of measurement.

This implies a turning point as to what the terms efficiency, efficacy and costs mean:

- Elimination of repetitive operations.
- Optimization of human resources and economic burden.
- Reduction in the risk of data entry errors.
- The possibility of conducting comparative analyses between different studies within the same ClinicalTrials platform.
- The possibility of carrying out clinical trials with double data entry.

1.5 ACCESSIBILITY, SECURITY AND DATA-LOGGING

ClinicalTrials is an innovative tool inspired by the idea of creating a light infrastructure along with maximum operational security. It has been designed according to the following paradigms:

- Accessibility.
- Security.
- Operations data logging.

Accessibility

ClinicalTrials is a web-based platform, which works through any web browser adhering to W3C international standards (Internet Explorer, FireFox, Safari, Chrome, Opera). Therefore, ClinicalTrials can be used with any device connected to the Internet (PCs or handheld devices such as ultra mobile PCs, etc.) without any physical constraint, and it is a “worldwide system”, which means that it can vehicle data wherever you might be in the world, through Internet, Intranet or Extranet equipped with wired (ISDN and XDSL) or wireless connections (Wi-Fi , WiMax, Gsm-Gprs-Umts, satellite).

This technological solution offers several highlights, many of them being particularly relevant within the international clinical research field, where, most of the time, participating centers are far away from each other:

- It is compatible with any operating system (Windows, Apple OSX, Linux).
- No particular software needs to be installed.
- There is no need to buy any particular hardware.
- Operators can be activated in a remote way.
- Platform updates take place in real time, in the process becoming available to any user without any technical support on site or any program update being sent.

Security

ClinicalTrials handles and resolves problems relating to data security, both as regards web data transfer and Italian framework regulations, which apply to data privacy within the clinical research field (Personal Data Treatment Information in compliance with Legislative Decree 196/2003 under Italian Law and the Guidelines issued by the Italian Data Protection Supervisor on 24 July 2008).

In order to guarantee an utmost degree of data security, ClinicalTrials does not only adopt all state of the arts technological solutions relating to IT security, but it has also been designed so as to integrate some particular innovative features as developed by Sinaptica IT:

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- HTTPS data transfer protocol.
- Secure Socket Layer 128-bit encryption.
- VeriSign Secured EV digital encryption certificate.
- IES - Integrated Encryption System: ClinicalTrials encrypts any data going through the platform, whereupon only authorized users are able to access and read encrypted data.
- 3A - Authentication, Authorization and Access in Real Time. At each click by a user, the ClinicalTrials system enhances a three-phase control as follows:
 - 1) Authentication: it checks who is the User online;
 - 2) Authorization: it checks what the User intends to do and whether it is compatible with the Role's usage rights (according to Groups membership and Clinical studies, Access level and operational privileges);
 - 3) Access: if he is an authorized user, it allows the User to go ahead with the requested operation. The 3A control system is performed in Real Time, which means that it immediately reacts to any change in the User's access rights, without needing to wait for the next login in order to apply it.
- Managing access according to Users and Groups.
- Ensuring Patients' full anonymity, which is managed by means of a unique 8 numbers code that is automatically generated by the system (number combination is completely random).
- Regulated access to Patient's personal details according to each User.

Data-logging (audit trail)

In addition to using the best technological solutions, ClinicalTrials also guarantees maximum security on the

strength of an accurate system of data logging for all Users operations and registration of data.

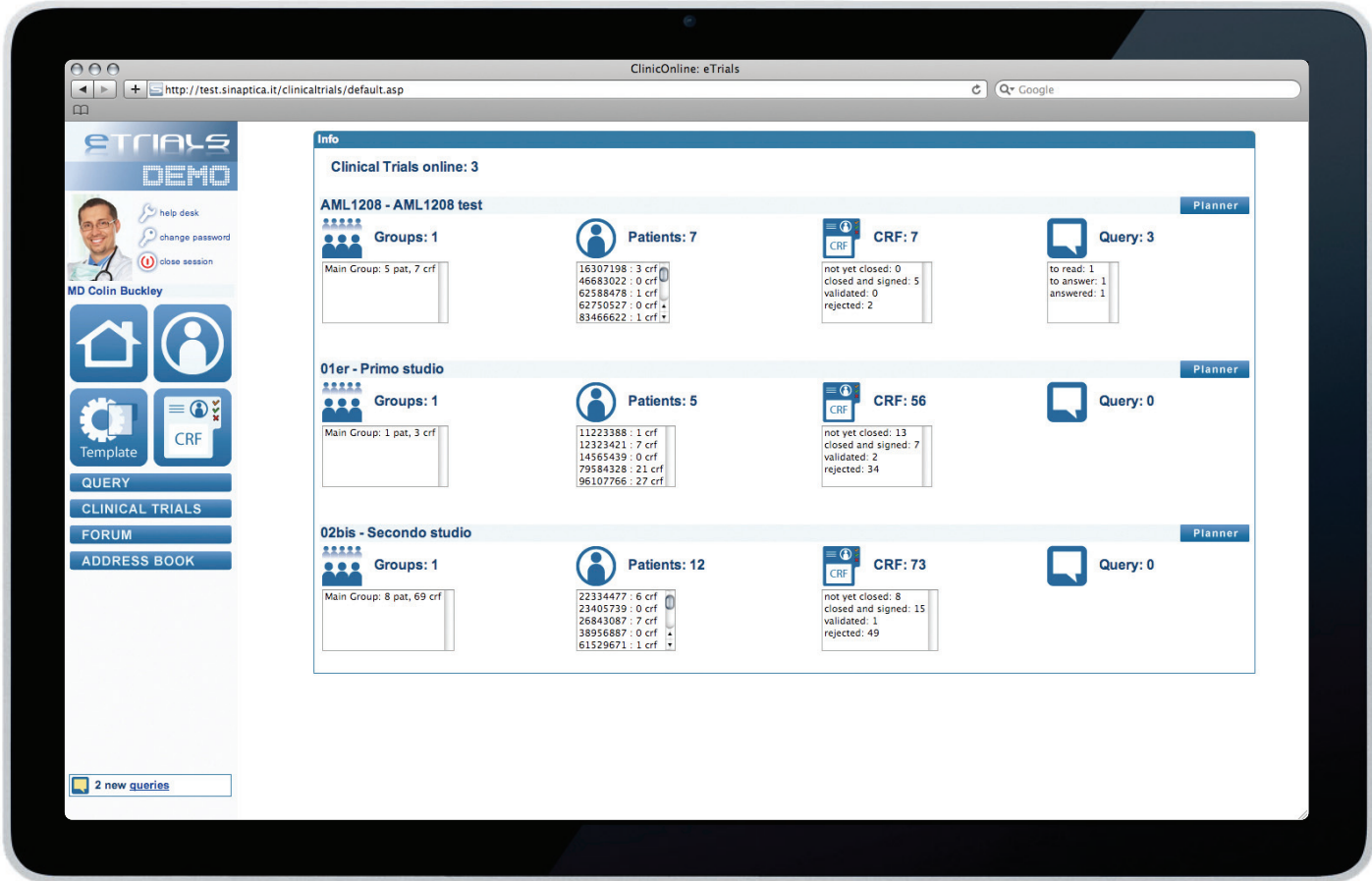
In the first place, the system includes some specific features, which keep track of all operations performed:

- Access log: the system automatically generates an un-modifiable file containing all access operations performed by any User, even if he/she is not a registered.
- SMS log: the system automatically generates an un-modifiable file containing all SMSs sent.
- Audit log: any operation performed on ClinicalTrials is tracked in an un-modifiable way, thereby guaranteeing Operators' activities and Patient's data security.
- Reminders log: the system traces the flow of Reminders sent to Investigators. It is not possible to alter this log.

The paradigm of data-logging strongly characterizes the case report form approval procedure as well, by means of the sequence of closing and signing, validating and rejecting and, whenever necessary, cloning the form. In the last-mentioned event, the Clone feature is the cornerstone of the system for the purpose of guaranteeing a real data log of the data capturing process.

Thanks to this feature, ClinicalTrials enables you to secure a dual objective:

- To track case report forms which have not been approved by the data manager as yet.
- To make a "new" case report form available to the operator so as to change or modify those data which have not been approved by the data manager.



Homepage

2 CLINICALTRIALS HIGHLIGHTS

ClinicalTrials is a clinical studies data capturing tool designed in conformity with the paradigm of Efficiency, Efficacy and Cost-effective services within the world of clinical research.

ClinicalTrials, designed and developed "in the field" owing to the many years of experience of Sinaptica IT in providing consultancy and technical support to organizations dealing with international clinical studies, combines a pragmatic approach with a long-lasting experience on state of the art technology.

An example of this is represented in the system homepage, where a control view is displayed, showing Users information per Groups, Patients, eCRFs and Queries, without needing to look for data elsewhere.

ClinicalTrials' several highlights are attributed to its base architecture (web-based, parametric and modular, cost-effective), as well as to its particular solutions, as they are expressly designed and developed in order to reduce repetitive operations. That is the case for instance of the "clone" feature, which allows you to track any event and eliminate activities dealing with data entry relating to already existing data, since they are, very often, a source of error. In that manner, ClinicalTrials makes it possible to free professional resources and economic funds while preserving the quality of work and scientific results intact.

Some important ClinicalTrials highlights come to light only when one is using the platform for a long time and in a continuous way.

Web based platform	
Access via internet	Accessible all over the world Operators can be activated from anywhere in the world Compatible with any operating system
Does not need any particular hardware	No hardware investment
Does not need to be installed	No license and installation costs
Automatic update	No upgrade and installation costs

Security and privacy	
HTTPS protocol of data transmission	Safety standard used in bank transfers
Secure Socket Layer at 128 bits coding	Safety standard used in bank transfers
Digital certificate VeriSign Secured EV	Safety standard used in bank transfers
IES - Integrated Encryption System	Any data is encrypted in transfer
3A - Authentication, Authorization and Access in Real Time	Real time control on User credentials
Access management by Users and Groups	Maximum data security on Users management
All operations are logged (audit trail)	Maximum data security and audit trail
Access log	Maximum data security and audit trail
SMSs log	Maximum data security and audit trail
Reminders log	Maximum data security and audit trail
Anonymous Patients management	Maximum data security and audit trail
Patients personal data access controlled	Maximum privacy
8 numbers unique code to identify patients	Anonymity guaranteed/maximum privacy

Efficiency, efficacy and cost-effective	
Bilingual (English/Italian)	Already available for international studies
eCRF Templates, Clinical Data Items and Answers library	Avoids repetitive operations Reduces the risk of compilation error Conducts a comparative statistical analysis between different studies
Parametric and modular structure	Maximum customization Maximum flexibility
Clone feature	Avoids repetitive operations
Defines roles by Functional Attributes and Access Levels	Maximum customization of Users
XML export	Compatible with data analysis software (e.g. SAS)
Time plan tool	Sharp control of logic-time flow parameters
Logic checks and checks that prevent you from opening a given form	Possibility of interacting with other studies Maximum data quality control
Appropriateness, range and edit Checks	Possibility of interacting with other studies Maximum data quality control
Automatic e-mail when a form is closed and signed	Maximum productivity
Optional automatic e-mail when a form gets rejected	Maximum productivity
Automatic programmable e-mail Reminders	Maximum productivity
Query integrated management	Maximum productivity
Patient Time plan function	Maximum productivity
Clinical Study Planner function	Maximum productivity
Stratified randomization	Proper protocol implementation
Randomization arms balancing	Proper protocol implementation

3 MAIN CLINICALTRIALS FUNCTIONS

3.1 CREATION AND MANAGEMENT OF USERS AND GROUPS

3.1.1 Users

3.1.1.1 Users - Features

ClinicalTrials envisages two main categories of users: Operators and Patients. The following features define each User:

- Qualification.
- Attributes.
- Role (potential).
- Access Levels.
- Management of personal data.
- Other features.

3.1.1.1.1 Qualifications, attributes and roles

The Operators category integrates three Qualifications: Administrator, Investigator and Administrative Manager. The Administrator is a single figure, and only one Administrator is found in the system. His role consists in administering the system as a whole (except for the creation and management of eCRFs). According to the Attributes he is endowed with, the Investigator can perform different Roles:

- The Investigator: he is a User having the capacity of an Investigator and endowed with an active eCRF Creation functional Attribute, but without any other Attributes.
- The Biostatistician: he is a User having the capacity of an Investigator and endowed with an active Data Export functional Attribute, but without any other Attributes.
- The Data Manager: he is a User having the capacity of an Investigator and endowed with any combination of Attributes which are not already contemplated as falling within the roles of Investigator and Biostatistician.
- The Administrative manager is a User in charge of subsidiary clinical trial data capturing and management operations.

The Patients category only envisages the Attribute of Patient. By default, Patients do not have access to the system, unless the ePRO function is enabled to fill in their own eCRFs (e.g. relating to quality of life). Qualifications, Attributes and Roles are assigned during the creation of the User or when it is modified. The functional Attributes which can be allocated to Operators are the following:

- eCRF Creation: it allows eCRF creation/filling in.
- eCRF Validation: it allows the validation of each single eCRF or its Sections.
- Data export: it allows XML format data exporting.
- eCRF Templates Creation: it allows the construction of eCRF Templates; two further Attributes can be allocated to Operators to whom this Attribute has been entrusted:
 - Superedit: it enables maximum Time line management as well the maximum number of patients in eCRF Templates.
 - Data Checks Management: it allows the implementation of Data Checks in the eCRF Templates and in their Sections.

3.1.1.1.2 Access Levels

ClinicalTrials envisages 5 different System Access Levels:

- Level 0: no operation (only menu access).
- Level 1: read mode.
- Level 2: read mode + write mode.
- Level 3: read mode + write mode + sign/delete.
- Level 4: read mode + write mode + sign/delete + Administrator’s privilege.

3.1.1.1.3 Personal Data Management

ClinicalTrials allows Operators to determine the procedure whereby Patients' Personal Data can be accessed. It is possible, in respect of each Operator, to set two particular options:

- Blocked Personal Data Management: in the event that it is set up, the Operator cannot create new Patients nor manage their personal data.
- Anonymous Personal Data Management: in the event that it is set up, the Operator cannot see nor change the Patient's date of birth and/or sex in his personal data form.
- The options allocated to a given Operator as regards Patients' personal data management are applicable to the entire ClinicalTrials system.

3.1.1.1.4 Other features

ClinicalTrials envisages further options as far as Users are concerned:

- Group events: in the event that it is set up, the User cannot take advantage of the “transitive characteristics” of a patient, which means that he will only be able to see/manage data created by Operators of his own Group/s.
- ePro (electronic Patient Reported Outcomes) function: in the event that it is set up, Patients have the possibility of creating/filling in eCRFs meant for patients; this option is only active for Patients equipped with an active eCRF Creation functional Attribute.
- User's Visibility: in the event that it is set up on “yes”, the User is visible within the system, except in relation to authoritative privileges; in the event that it is set on “no”, the User is no longer visible: this option specifically addresses the need to “virtually” delete a Patient (e.g. in the event of errors in personal data entries) without violating the rules governing the obligation to keep a trail of all the data which are registered.
- End of authorization date: in the event that it is set up, it determines the Operators' time limit within the system.

3.1.1.2 Users - Creation and Management

The creation and modification of Users is done through the Users function.

The Operators who are authorized to see to the creation and management of Users are the following:

- Administrator: he can create and manage any user.
- Data Manager and Investigator: they can create and manage Patients belonging to their own Groups, on condition that they have an Access Level of 2 (read mode + write mode) or higher. The Users function is marked with a Patients label in respect of Data Managers and Investigators.

3.1.1.2.1 Allocation of Users to one or more Groups

The allocation of Users to Groups is done through the Users function. The Operators authorized to allocate one or more Groups to Users are:

- Administrator: he can allocate any User.
- Data manager and Investigator: they can allocate Patients from their own Groups, on condition that they have an Access Level of 2 (read mode + write mode) or higher. The Users function is marked with a Patients label in respect of Data Managers and Investigators.

3.1.1.2.2 Allocation of Users to one or more Clinical Trials

The allocation of Users to Clinical trials is done through the Users function. The Operators who are authorized to allocate Users to one or more Studies are the following:

- Administrator: he can allocate any User.
- Data manager and Investigator: they can allocate Patients (from their own Groups) but only to their own Clinical Trials, on condition that they have an Access Level of 2 (read mode + write mode) or higher. The Users function is marked with a Patients label in respect of Data Managers and Investigators.

3.1.2 Groups

The Groups are the ClinicalTrials system's access mechanism. Indeed, only through the correct management of the Groups can Users utilize the system in full compliance with demarcated authoritative rules. Groups empower a logic interconnection between Users, Clinical Trials, eCRF Templates and the relevant eCRFs.

3.1.2.1 Groups - Creation and management

The creation and modification of Groups is done through the Groups function.

The creation and management of Groups are exclusive prerogatives of the Administrator.

Each group is defined by what follows:

- Code.
- ID.

Both the Code and ID of every group must be a unique one within the whole system.

3.1.2.2 Groups - Allocation

With ClinicalTrials all Users can fulfill a given operation only on elements (Users, Clinical Trials, eCRF Templates and Forms) that belong to the same Group/s.

In order to be able to consider as complete and correct the Group management, we need the same Group to be allocated to:

- All Users that belong to the Group.
- Clinical Trials to which the Group belongs.
- Clinical Trial eCRF Templates to which the Group belongs.

3.1.2.2.1 Allocation of Groups to Users

The allocation of Users to the different Groups is done through the Authorization function.

The Operators who are authorized to allocate Users to Groups to are the following:

- Administrator: he can allocate any User.
- Data Manager and Investigator: they can allocate Patients to their own Groups, on condition that they have an Access Level of at least 2 (read mode + write mode) or higher. The Users function is marked with a Patients label in respect of Data Managers and Investigators.

3.1.2.2.2 Allocation of Groups to Clinical Trials

The allocation of a Group to a Clinical Trial is done through the Clinical Trial function. This function is an exclusive prerogative of the Administrator.

3.1.2.2.3 Allocation of a Group to eCRF Templates

The allocation of a Group to an eCRF Template is done through the eCRF Template function.

The allocation of a Group to an eCRF Template can be done by the Administrator or by an Investigator endowed with an enabled Edit eCRF Template Attribute; the allocation is done individually in each eCRF Template, or directly from the Clinical Trial through the apposite checkbox.

3.2 CREATION AND MANAGEMENT OF A CLINICAL TRIAL

In ClinicalTrials, the creation and management of a Study is done through five integrated procedures:

- Creation of the Clinical Trial itself.
- Creation and management of eCRF Templates.
- Creation and management of Sections: Clinical Data Items and related Answer fields.
- Creation and management of the logic-time flow of the eCRF: Time plan, position and compulsoriness of eCRF Templates, eCRF edit checks that prevent you from opening a given form, and Section or Fields edit checks.

3.2.1 Clinical Trial

3.2.1.1 Clinical Trial - Creation

The creation of a given Clinical Trial is done by Sinaptica IT. During the creation phase, the following features are assigned to a given Clinical Trial:

- Code.
- Name of the Clinical Trial.
- Clinical Trial start date.
- Clinical Trial end date.
- Date on which the Clinical Trial has been enabled within the system by Sinaptica IT.
- Date on which the Clinical Trial has been disabled within the system by Sinaptica IT (after this latter date, it is still possible to see clinical data and export data using the XML format).
- Maximum number of Study Patients.
- Maximum number of Study Operators.

3.2.1.2 Allocation of one or more Groups to a Clinical Trial

The allocation of one or more Groups to a Clinical Trial is done through the Clinical Trial function. This function is an exclusive prerogative of the Administrator.

3.2.1.3 Automatic allocation of Groups to eCRF Templates of a Clinical Trial

ClinicalTrials envisages a set of functions through which a Group that is assigned to a given Clinical Trial is automatically added to all eCRF Templates relating to the study itself. This option can only be enabled by the Administrator.

3.2.1.4 Clinical Trial - Users Monitoring

ClinicalTrials enables one to monitor in real time the number of Patients and Operators who have actually been linked and screened/registered in a given Clinical Trial. This information is available, through the Clinical Trial function, only to the Administrator and to Operators endowed with Access Level 4 (Administrator's privileges).

3.2.1.5 Clinical Trial - Allocation of the maximum number of Time lines

ClinicalTrials allows one to specify the maximum number of Time lines that can be used in the demarcation of the Clinical Trial Time plan (see paragraph 3.2.4.1). This function is available, through the Clinical Trial function, only to the Administrator and to Operators endowed with an Access Level of 2 (read mode + write mode) or higher, and in possession of a Superedit functional Attribute.

3.2.2 eCRF Templates

3.2.2.1 Creation of eCRF Templates

The creation and modification of eCRF Templates is done through the eCRF Templates function.

The Operators who are enabled to create and manage eCRF Templates are the following:

- Administrator.
- Operators to whom the Edit eCRF Template function has been allocated, and who are equipped with an Access Level of 2 (read mode + write mode).

In this phase, the creation of eCRF Templates is defined by the selection of the following values:

- Clinical Trial to which the eCRF Template belongs.
- Form code.
- Name.
- Position coordinates within the logic-time Clinical Trial flow.
- Groups to which the eCRF Template belongs.

- Information regarding Patient's access: this option is programmed in respect of those cases in which one wishes to obtain data directly from the patients themselves, as in the case of questionnaires (ePRO).

3.2.2.1.1 Creation and management of eCRF Templates classification

The creation and management of the eCRF Templates Classification is done through the eCRF Templates function.

The Operators who are enabled to create and manage this Classification are the following:

- Administrator.
- Operators endowed with an eCRF Validation functional Attribute.

During the creation phase, each Classification is defined by means of allocating the following:

- Clinical Trial.
- ID.
- Description.

3.2.2.2 Management of eCRF Templates

During the following phase of managing eCRF Templates, the following features can be controlled:

- Classification: it enables the allocation of the eCRF Template to one of the available Classifications for the Clinical Trial (the Classification is relevant both at the time of looking for an eCRF Template and for the sake of visualization in the Clinical Trial Planner).
- Planner: it enables the allocation of a # value (number of progressive order) and the description of the eCRF Template, which things determine the visualization of the eCRF Template in the Clinical Trial Planner.
- Validation Needed: it imposes the duty to fill in (close and sign) the relevant eCRF so as to pursue the compilation of the following eCRFs in a logic-time scheme.
- Compulsoriness of the registration of the date on which the Operator fills in a given eCRF (or the date when that is done automatically by the system).
- Automatic communication to the appropriate Data Manager when an eCRF has been closed and signed; the system can be programmed to additionally send the same automatic communication to specific e-mail addressees, and/or to the Investigator signing the form, and to the clinical trial coordinator.
- Registration of the maximum number of Patients for which a given eCRF can be created (this feature can be really useful, particularly when dealing with Phase I Trials).
- Repeatability of a given form without any limit on the number of times it is repeated.
- Publication of the eCRF Template (enabled status online/offline).
- Implementation of eCRF Edit Checks; in the event that the value "in configuration" is selected, the Operator will not be able to fill in the relevant form, and an attention icon will be displayed along with a potential informative text.
- Implementation of logic status Checks (true or false) in the relevant eCRFs.
- Possibility of programming the automatic mode of sending by e-mail a predetermined message to suitable e-mail addresses, in conformity with the logic status of the eCRF when this is closed and signed.
- Possibility of programming the sending of automatic planned Reminders to Investigators (by e-mail) according to the logic Status of the eCRF, likewise escorted by subsequent reminders in accordance with what has been planned.
- Possibility of registering potential versions and dates of the eCRF Template that will be visible in PDF print.

3.2.2.3 Cloning of eCRF Templates

ClinicalTrials makes the "clone" function available. This function enables one to obtain a copy of an already existing eCRF Template. The clone function is activated through the relevant icon in the eCRF Template function. Administrators and Operators endowed with Creation of eCRF Attribute and Access Level 2 (read mode + write mode) are authorized to clone eCRF Templates.

When cloning a form, the Operator can choose whether to perform a simple cloning, which has the effect of enabling a duplicate of an eCRF Template that preserves all inner elements except for Checks, or utilizing the Clone All function, which also includes in the new Template all the Checks that were present in the original form.

3.2.2.4 eCRF Templates PDF Print

ClinicalTrials allows one to print eCRF Templates using PDF (Portable Document Format), an international ISO 32000-1 standard since 2008.

The PDF Print function is available through the relevant icon in the eCRF Template function.

For an efficient management of a potential paper print, the PDF format file will show on the footer the page number, the progressive number, the applicable version, and the date relating to the eCRF.

3.2.3 eCRF Template Sections

The fields making up the eCRF Sections are the following:

- Clinical Data Items.
- Answers to these Clinical Data Items.

ClinicalTrials manages the following types of fields:

- Text.
- Date.
- Numeric field; a numeric field can be represented by a field where one fills in the requested value, alternatively by mutually exclusive radio buttons.

From a mere operative point of view, the phases of work are as follows:

- Creation of Answers to Clinical Data Items.
- Creation of Clinical Data Items.
- Creation of Sections.

3.2.3.1 Creation of Answers

The creation and modification of Sections is done through the Clinical Data Items function.

The Administrator and the Operators endowed with the Edit eCRF Template functional Attribute who boast Access Level 4 are allowed to create Answers to Clinical Data Items.

Each answer is made up of the following information:

- Code.
- Numeric value.
- Text value.

3.2.3.2 Creation of Clinical Data Items

The creation and modification of Sections is done through the Clinical Data Items function. The creation and management of Clinical Data Items is a prerogative reserved for the Administrator and for Investigators endowed with the Edit eCRF Template functional Attribute who boast Access Level 4. Each Clinical Data Item is made of the following information:

- Code.
- Description.
- Unit of measurement unit.
- Minimum and maximum reference values per female patient.
- Minimum and maximum reference values per male patient.
- Minimum and maximum limit value that may be entered.
- Potential Answer/s to the Clinical Data Item.

3.2.3.3 Creation of Sections

The creation and modification of Sections is done through the eCRF Template function.

Creation and management of Sections is a prerogative reserved for the Administrator and for Investigators endowed with an Edit eCRF Template functional Attribute and boasting an Access Level equal to 2 or higher.

Sections are made up of Clinical Data Items and one or more answer fields which can be of different kinds. Furthermore, a text field is envisaged to be used as “title” of the Section.

Sections can have the following characteristics:

- Unknown (that applies to the management of data in respect of which it is not possible to know the value).
- Mandatory Section.
- Closing and signing of the single Section.
- Edit and range Checks.
- Section date.

3.2.3.4 Deletion of Clinical Data Items and Answers to Clinical Data Items

ClinicalTrials forbids the deletion of Clinical Data Items and related Answers from an eCRF Template if they have already been used in the system by at least another eCRF.

3.2.3.5 Sections Checks

The creation and management of eCRF Template Checks is done through the eCRF Template function during the modification phase, in that part which is linked to Programmable Checks Logic.

The Operators who are authorized to attend to creation and management of Checks are the following:

- Administrator.
- Operators endowed with Edit eCRF Template and Checks Management functional Attributes and boasting an Access Level of 2 (read mode + write mode) or higher.

The checks applicable to eCRF Section Templates are as follows:

- Edit checks.
- Conditioned and programmable Range Checks.
- Range Checks on fields with absolute numeric values.

3.2.3.5.1 Edit Checks

Edit Checks enable one to regulate the possibility of filling in an answer field in a given eCRF in accordance with the values of pre-existing fields:

- In the same eCRF.
- In another eCRF from the same Clinical Trial.
- In another eCRF from different Clinical Trials which may be present within the same ClinicalTrials platform.

Edit Checks are applicable to both numerical fields and date fields.

3.2.3.5.2 Limit Checks

ClinicalTrials enables one to implement range Checks on values that have been filled in the different fields. The system envisages two integrated methods of using range Checks:

- Static Range Checks, which are registered within the Clinical Data Item (these are preserved for a possible repeated use in other eCRF Templates in the future, even if related to different Clinical Trials).
- Dynamic Range Checks, which are applied to single data and/or to numerical fields, and have the effect of verifying whether the data are correct on the basis of predetermined conditions.

3.2.4 Logic-time flow of a Clinical Trial: Time plan

ClinicalTrials enables the shaping up and the accurate and flexible management of the logic-time flow of a Clinical Trial. This is done thanks to the Time plan tool, which enables the pursuit of desired logic-time routes. The Time plan tool is controlled through the use of values and options, which are suited to each eCRF Template:

- Position (Time line, Time slot, Posix).
- Mandatory compilation (Validation Needed).
- Form editing and logic status Checks.
- Maximum limit of Patients.
- Randomization.

3.2.4.1 Positioning of the eCRF Template

An eCRF Template position within the Time plan is selected by resorting to the eCRF Template function, both at the creation stage and at the stage of modifying it. Each eCRF Template position is defined by three coordinates:

- Time line: it shows the time line where we want to position the given eCRF.
- Time slot: it shows the moment at which we want this eCRF to be created and filled in.
- Posix: it shows the position where the eCRF is related to a given combination of Time line/Time slot.

3.2.4.1.1 Creation of an eCRF Template without time editing constraints

The allocation of a 0 (zero) value to a Time line and Time slot allows one to obtain timeless eCRF Templates, i.e. forms that can be filled in at any moment, irrespective of the logic-time flow of the Clinical Trial.

3.2.4.1.2 Creation of mutually exclusive eCRF Templates

The allocation of the same Posix value to two or more eCRF Templates sharing the same Time line/Time slot combination renders the relevant eCRF's mutually exclusive, that is, the Operator will need to choose which one to fill in to the exclusion of all other forms sharing the same Time line/Time slot coordinates.

3.2.4.2 Compilation compulsoriness (Validation Needed option)

The Check on the mandatory compilation of the eCRF Template is done through the eCRF Template function during the modification phase. By selecting the option Validation Needed, it is in fact possible to interrupt the flow at any given moment (Time slot), until the relevant eCRF has been closed and signed.

3.2.4.3 Checks that prevent you from opening a given eCRF

The creation and management of eCRF Template Checks that prevent you from opening a given Template is done through the eCRF Template function during the phase of modification in the part, which is linked to the programmable Check logic.

Operators who are authorized to create and manage Checks are the following:

- Administrator.
- Operators endowed with the Edit eCRF Template and Checks Management functional Attributes and boasting an Access Level of 2 or higher.

The forms' Edit Checks function enables one to influence the opening of a given eCRF in conformity with pre-existing values:

- In other eCRFs within the same Clinical Trial.
- In other eCRFs belonging to different Clinical Trials but within the same ClinicalTrials platform.

3.2.4.4 Logic Status Checks

The creation and management of logic status Checks of the eCRF Template is done through the eCRF Template function during the modification phase in that part which is linked to the Programmable Checks Logic.

The Operators who are authorized to create and manage logic status Checks are the following:

- Administrator.
- Operators endowed with the Edit eCRF Template and Edit Checks functional Attributes and boasting an Access Level of 2 or higher.

Logic Status Checks enable one to assign a true or false value to a particular case report form, in conformity with current conditions:

- In other eCRFs within the same Clinical Trial.
- In other eCRFs pertaining to different Clinical Trials but within the same ClinicalTrials platform.

3.2.4.5 Maximum number of Patients

The check on the maximum number of patients in respect of whom a given case report form can be filled in, is performed through the eCRF Template function, during the modification phase, by allocating to the form an appropriate value in the Patients MAX field.

3.2.4.6 Randomization

ClinicalTrials enables you to manage randomization directly from the system, through an appropriate module where the following items can be selected:

- eCRF randomization Template.
- Number of randomization arms.
- Number of patients per randomization arm.

The system allows you to conduct randomization via a purely random function, or a deterministic one, or even by allocating the exact number of patients per randomization arm so as to balance them. Stratification variables used in randomization are shown in the appropriate randomization Template, where all the above-mentioned checks can be implemented.

Randomization management is set within the Clinical Trial function, during the modification step. The Administrator and Operators endowed with eCRF Template and Superedit functional Attributes are authorized to perform this operation.

3.3 DATA CAPTURE, MANAGEMENT AND EXPORT

With ClinicalTrials clinical data capturing and data management are done through the following operational steps:

- eCRFs Creation and compilation.
- eCRFs status monitoring and management.
- Data export.

3.3.1 eCRF Creation and Compilation

Creation and compilation of eCRFs is done through the eCRF function.

It is also possible to create a given eCRF through the user control panel, which is displayed in the homepage, either when accessing the system or through the patients search results.

Data Managers endowed with Edit eCRF functional Attribute, as well as Investigators boasting an Access Level equal to 2 (read mode + write mode) or higher, are eligible to use this function.

As for those Operators who, besides the creation and compilation of the forms, must additionally be able to carry out the irreversible operation of "closing and signing", they need to have an Access Level equal to or higher than 3 (read mode, write mode and "signature/delete").

The aforesaid enables a possible distribution of tasks between Operators in charge of the data entry and Operators in charge of data validation.

Forms which are created through the "new" button become "open", and display the set-up and characteristics of the corresponding eCRF Template. An eCRF which has already been created can be opened by using the "open" button.

Each eCRF is uniquely linked to a Patient, to a Clinical Trial, and to a specific Group.

3.3.2 eCRF Management

In ClinicalTrials the eCRFs can be set in different statuses:

- Not yet closed: the eCRF has been "created" and is ready to be filled in; Operators authorized to create eCRFs are Data Managers endowed with a Edit eCRF functional Attribute, as well as Investigators boasting Access Level which is equal to 2 or higher.
- Closed and signed: the eCRF has been "closed and signed"; Operators who are authorized to close and sign a form are Data Managers and Investigators boasting an Access Level equal to or higher than 3; after this operation, the form can no longer be modified.
- Validated: the eCRF has been validated by a Data Manager equipped with a Validate eCRF functional Attribute; from this status onwards, the eCRF can only be rejected or corrected.
- Rejected: the eCRF has been rejected by a Data Manager equipped with a Validate eCRF functional Attribute; from this status onwards, the eCRF can only be cloned or corrected.

3.3.2.1 Cloning eCRFs

ClinicalTrials makes the “clone” function available. This function enables one to obtain a copy of rejected eCRFs (hence no longer modifiable), thereby obtaining a new eCRF which is completely identical to the previous one, and which is made available to the Investigator in order for him to effect all the necessary modifications.

Sections which have already been validated within the eCRF before the cloning process cannot be modified once in the cloned form. This solution guarantees the audit trail of all clinical trial steps and, at the same time, makes the Investigator’s activities easier and faster.

The clone function can be accessed through the relative icon in the eCRF function.

Operators who are authorized to use the clone function are Investigators (regardless of their role) or Administrative Managers endowed with a Validate eCRF functional Attribute, and whose Access Level corresponds to 2 (read mode + write mode) or higher.

3.3.2.2 Management of sections

ClinicalTrials enables one to manage the status of single Sections of the eCRF, by resorting to a procedure which is similar to the one applicable to an entire eCRF, and which is accompanied by the same authorization privileges for Operators. Accordingly, Sections can be in one of the following statuses:

- Open.
- Closed and signed.
- Validated.
- Rejected.

Sections status management is regulated by the following conditions:

- If the eCRF status is not yet closed, it is possible to close and sign every single Section.
- If a Sections is Validated, it cannot be further modified, even if the eCRF is cloned.
- If the eCRF is closed and signed, all Sections are automatically considered as closed and signed.
- If the eCRF is closed and signed, the Data Manager equipped with a Validate eCRF functional Attribute can validate or reject single Sections.

An eCRF with a rejected Section cannot be validated.

3.3.3 Communications relating to the eCRF management

ClinicalTrials integrates different communication functions, including programmable and automatic messages, so as to make the eCRF compilation and approval management cycle easier:

- Automatic notification of closing and signing.
- Automatic notification of a rejection.
- Automatic notification of planned Reminders.
- Queries.

3.3.3.1 Automatic notification of closing and signing

ClinicalTrials can be programmed in such a manner as to send to the appropriate Data Manager an automatic alert message stating that a given eCRF has been closed and signed. This function can be programmed by using the eCRF Template function during the modification phase.

This message can be sent either by e-mail or both by e-mail and SMS. Furthermore, the same message can also be sent to:

- The Investigator who signs the form.
- The Investigator who is the study coordinator.
- Other e-mail addresses.

The alert message can also be completed through an appropriate predetermined free text.

3.3.3.2 Automatic notification of a rejection

When a Data Manager rejects a given eCRF, ClinicalTrials can automatically send the appropriate alert message by

e-mail to the Investigator who has signed the form.

The choice concerning whether to send the appropriate communication or not is done through the eCRF rejection, through the use of the eCRF function at the time of modifying the form.

When rejection of the eCRF is confirmed, the Data Manager can choose whether to send or not the alert message through the appropriate mandatory choice menu; by default, the menu is set on the option not to send it.

3.3.3.3 Automatic notification of planned reminders

ClinicalTrials envisages the possibility of programming an eCRF Template so that the system might be empowered to automatically send planned Reminders (by e-mail) to the Investigator in conformity with the logic status of the eCRF (true, false, indifferent or undetermined).

This function is programmed within the eCRF Template function during the modification phase.

Operators who are authorized to plan Reminders are the following:

- Administrator.
- Operators endowed with the Edit eCRF Template and the Edit Checks functional Attributes, and whose Access Level corresponds to 2 or higher.

Reminders may include subsequent requests in accordance with the planned flow.

Each Reminder is characterized by:

- E-mail text to be sent.
- Date and time when the planned Reminder e-mail has to be sent (the date is always linked to a date within the eCRF).
- Conditions relating to the creation and suspension of the planned Reminder notification.

The cancellation of the Reminder notification is an exclusive prerogative of the Administrator.

The activities of dispatch (or cancellation) of the Reminder notifications are trailed in the system and are available to the Administrator in the System Log function, wherein, the transmission status of each notification is displayed (to be sent, not sent, sent, deleted by the Administrator).

3.3.3.4 Queries

ClinicalTrials enables its Users to manage the question and answer activities between Data Managers and Investigators from the platform itself. That is done via the Query function.

Each Query cycle envisages the following phases:

- Creation and sending.
- Reading and answering.
- Report.

A status light icon, the color of which is related to the Query status pursuant to the following convention, identifies each phase:

- Yellow: the Query has been sent to the addressee and an answer is awaited.
- White: an answer has been registered and the final result is awaited.
- Green: Query result is positive.
- Red: Query result is negative. The number of status icons depends on the priority level (ranging from 1 to 3) as specified during the creation phase.

The main characteristics of the Query function are the following:

- Creation of a Query is done through the eCRF function and can be related to an eCRF or to a Section in it.
- Creation of a Query is an exclusive prerogative of Operators who perform the role of Data Managers.
- The Query is addressed to the Investigator who has signed the eCRF (that is, to the Investigator who has signed the eCRF Form Section).
- An answer to a Query might be given by any of the Operators performing the role of Investigator or Data Manager and belonging to the same Group of the eCRF to which the Query refers.
- The Query result is a prerogative of the Operators performing the role of Data Managers and belonging to the same Group of the eCRF to which the Query refers.
- It is possible to create a new Query directly from an already existing Query: in such case, the reference to the

addressee and to the eCRF is preserved (as well as the one to the potential Section within the eCRF).

- The Queries visualization can be customized in conformity with the Operator’s role: for example, Operators exercising the role of Investigators are only able to see Query and Answer fields, whereas Operators exercising the role of Data Managers are capable of seeing the Result field as well.

3.3.4 eCRF PDF Print

ClinicalTrials enables eCRFs to be printed in PDF (Portable Document Format), an international ISO 32000-1 standard since 2008. The PDF Print function is utilized through the relative icon in the eCRF Function.

For an efficient management of a potential paper print, the PDF format file will show on the footer the page number, the form progressive number, its version, and the date. It is possible to print in PDF an eCRF when its status is closed and signed, and that will accordingly include the ones that have been validated or rejected.

3.3.5 Data export

ClinicalTrials enables the exporting of data, which are already present within the system, and which relate to every study using the XML format (eXtensible Markup Language). The XML format is a standard formatting of data in structured documents, which has the advantage of being extremely compatible with other analysis systems, such as SAS.

The exporting can be done in either a relational or a tabular way. Data exporting is carried out through the eCRF function. Operators who are authorized to export data are the following:

- A Biostatistician whose Access Level amounts to 1 (read mode) or higher.
- A Data Manager equipped with the Data Export functional Attribute and whose Access Level amounts to 1 (read mode) or higher.
- An Administrator who is endowed with the Data Export functional Attribute.

During the exporting phase, it is possible to implement research filters by making use of the following parameters:

- Clinical trial.
- eCRF Form.
- Group.
- Date and time interval between dates.
- eCRF Status: not yet closed, closed and signed, validated, rejected.

3.4 PRODUCTIVITY, COMMUNICATION AND CONTROL FUNCTIONS

ClinicalTrials integrates within its fold productivity, communication and control functions, which are part of the system itself. On the strength of such functions, it is possible to work in a more efficient manner, and, at the same time, all communications relating to a given clinical trial are trailed.

Productivity functions consist in what follows:

- Homepage.
- Clinical Trial Planner.
- Patient’s Time plan.

Communication functions are the under-mentioned ones:

- Forum.
- Address book.
- Alerts.
- Requests to the technical Help Desk.

Control functions are those set out here under:

- Access Log.
- SMS Log.
- Reminders Log.
- Resources used.

3.4.1 Homepage

ClinicalTrials Homepage shows a control panel of the Users’ activities which provides a summary at once, without needing to perform customized searches, and which targets the relevant activities, which are sub-divided into Group, Patients, eCRFs and Queries.

The Homepage tool is accessed by selecting the namesake function button in the Navigation Area.

3.4.2 Clinical Trial Planner

The Clinical Trial Planner tool provides a global and immediate view of the activities within the Clinical Trial, as well as a rapid access to further information through an efficient system of tool-tip and links to related eCRFs. The visualization of the eCRFs within the Planner can be customized according to logistical needs, and enables one to establish an absolute order or a possible grouping under homogeneous Classifications (such as follow-up).

The Clinical Trial Planner tool is accessed by selecting the namesake function button in the Homepage, and from the Clinical Trials function.

3.4.3 Patient’s Time plan

The Patient’s Time plan tool allows the visualization of the state of progress of a given Patient within a clinical protocol. The Patient Time plan provides a global and immediate view of the activities, which are conducted in respect of every patient, and, furthermore, it empowers the direct accessing of appropriate eCRFs, thereby making work more efficient and effective.

The Patient Time plan tool is displayed within the Patient’s function.

3.4.4 Forum

The Forum is a tool through which the Investigator and Data Manager can talk to each other about pre-established topics. Creation and modification of a topic within the Forum is done through the Forum function.

Operators who are authorized to create and manage topics within the Forum are the following:

- Data Managers endowed with the Edit eCRF Template functional Attribute and boasting an Access Level of 2 (read mode + write mode) or higher.
- Administrator: he can only search and reopen a topic previously closed by the Data Manager. Only the author of the topic can close it.

Each topic refers to a specific Clinical Trial. The notification to the Operator about a topic, which has been opened, can be done by e-mail or SMS.

3.4.5 Address Book

The Address Book function displays Users contact details with relative hypertext links. This information is gathered from the corresponding fields about Users’ personal data.

The Address Book data can be accessed from the Address Book function.

All Users can access the Address Book.

It is possible to control a User visibility within the Address Book through the Visible field found in the User’s appropriate personal data form (User’s function). If the field is set on “yes”, the information is shown to all Users except for visitors. If the field is set on “no”, the information is shown only to the Administrator.

3.4.5.1 Address Book information

In the event that it is found within a User’s personal data, the following information is shown in the Address Book:

- Family name.
- First name.
- Title.

- Information.
- Upload image.
- Telephone.
- Cellular phone.
- E-mail.
- Skype contact.

The presence within the Address Book of a mobile phone number, an e-mail address or a Skype contact, enables one to set-up an automatic communication:

- SMS's are generated by the ClinicalTrials system that trails them in the SMS Log.
- E-mails are set-up through the predefined program in computer which the User is busy with at that time.
- In the event of a Skype contact, a phone call/chat is set-up through the Skype software (provided it is present in the computer which the User is utilizing at that time).

The Info field is a free text field wherein User's information may be registered, such as the specific organizational role within the research activity that is part of the clinical trial.

3.4.6 Alerts

Alerts are communication tools of the ClinicalTrials system within a Group.

It is possible to send an Alert within the system itself or to send it through e-mail and SMS to suitable Users, who are selected according to their Qualification.

All Alerts are trailed, thereby guaranteeing reliability and security.

The creation and management of Alerts is accessed through the Alerts function.

Creation and management of Alerts is an exclusive prerogative of the Administrator:

3.4.6.1 Creating and sending Alerts

Each Alert is created by defining the following parameters:

- The Group to which it refers.
- The User who has created it.
- The Alert text.
- Forward option: it defines the way of forwarding the Alert (availability within the system/forwarding it by e-mail/ forwarding it by e-mail + SMS).
- User qualification: it enables the selection of an addressee within the selected Group:
 - All.
 - Investigator.
 - Administrative Manager.
 - Technical Assistance.
 - Administrator.

3.4.7 Technical Assistance requests

ClinicalTrials integrates the functionality of requesting technical assistance. Each Operator of the system can create a technical assistance Ticket specifying a Clinical Trial, a Group and a message.

The request is then sent to all Operators with a Technical Assistance Qualification who belong to the specified Group, as well as to the Administrator.

The operation is processed by assigning a priority level and possible intermediate actions, until one reaches the closure of the Ticket, accompanied by the relevant e-mail communication to the Operator who generated the request itself.

3.4.8 Access Log

This function enables the visualization of all accesses to the system by any User, whether registered or not registered.

Through the Log function, it is possible to access the visualization of the active Log.

The visualization of the active Log is an exclusive prerogative of the Administrator.

The active Log is automatically generated by the system, and cannot be modified, as it is necessary to ensure that all performed operations are traceable.

3.4.9 SMS Log

This function enables one to visualize all sent and received SMSs to and from the system. Through the Log function, the visualization of the SMS Log can be accessed. The SMS Log is an exclusive prerogative of the Administrator.

The SMS Log is automatically generated by the system, and cannot be modified, as one needs to ensure the traceability of all performed operations traceability.

3.4.10 Reminders Log

This function allows the visualization of all Reminders that are generated by the system and the relative statuses (to be sent, sent, or deleted). Through the Log function, the visualization of the Reminders Log can be accessed. The visualization of the Reminders Log is an exclusive prerogative of the Administrator.

The Reminders Log is automatically generated by the system and cannot be modified given the need to guarantee that all performed operations should be traceable. The Administrator has the possibility of marking as deleted a Reminder that still needs to be sent, so that, in actual fact, it is not going to be sent.

3.4.11 Resources used

This function enables the visualization of the status of the system's resources. By resorting to the Resources Used function, the visualization of the resources can be accessed. The visualization of the Resources Used is an exclusive prerogative of the Administrator.

ClinicalTrials Presentation – Version 2.4

The most updated version is always available for download on the website www.sinaptica.it



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