niAnalytics EDC/CTMS – niServices

niAnalytics enables our customers to focus on what they do best: efficiently, effectively and successfully run their clinical trials.

electronic data capture – clinical trial management system – clinical data management – statistical services

- **assistance with trial set-up**
- **advanced eCRF**
- **almost unlimited EDC capabilities**
- **electronic Trial Master File**
- **collaborative document management tolls**
- **back-end statistical services**

niAnalytics GmbH offers a unique and comprehensive set of software and services solutions for pharmaceutical and medical device companies, sponsors, contract research organizations, as well as academic institutions and hospitals.

Our comprehensive data management approach supports all types of clinical trials and post-marketing studies. Whether you are a pharmaceutical or medical device company, academic or clinical institution, the niAnalyitcs ecosystem will help you succeed.

The niAnalytics ecosystem is comprised of two parts, our custom niAnalytics EDC/CTMS and our niServices. Collectively they enable us to provide our customers with a full data management solution that is truly Beyond Electronic Data Capture.

The niAnalytics EDC/CTMS system was created to facilitate minimum lead time for eCRF and database creation and validation. At niAnalytics we can create your eCRF and database in a matter of days, not weeks or months, resulting in dramatic savings. We can perform your in-trial changes in a manner of minutes to hours instead of days or weeks.

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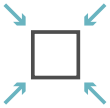
niAnalytics EDC/CTMS Overview

Our niAnalytics EDC/CTMS system modules include:

Document Management

Data Capture (eCRF, forms, eTMF, Reports, WebPRO)

Double Data Entry



Centralized Query Manager

Patient Dashboard

Patient Calendar

Study Metrics

The niAnalytics EDC/CTMS is a robust system which provides intuitive easy to use resources and facilitates the performance of any clinical trial no matter how small or large.

We make the entire process easy, smooth and cost effective. The niAnalytics EDC/CTMS is simple to use, flexible and can be fully customized to the customer's business processes. Any type of EDC document can be created, not only eCRFs. Your imagination is our limit!

- Every device, every browser
- Multiple trials on a single system
- Simultaneous multiple language support (user level adjustability)
- eTMF for simultaneous multiple studies
- Rapid eCRF creation and in-trial eCRF changes (minutes to hours)
- Automatic eCRF export (single page or entire eCRF)
- Unlimited data capture forms including cloud-based visit reporting
- Double Data Entry
- Remote monitoring
- Automatic (S)AE reporting and categorization
- Automatic query generation and assignment
- Query metrics
- WebPRO
- Granular control of SDTM tabulation
- Custom granular user security and permission control
- Detailed user activity metrics
- Full audit trails and histories, including queries

niAnalytics EDC/CTMS adds value and help our customers save money

TRIAL SETUP	CRF DESIGN & SETUP	DATA COLLECTION	DATA VERIFICATION	STATISTICAL ANALYSIS
Randomization & allocation	Fast eCRF setup (3-5 days)	User friendly	Better overall data quality	Interim analysis and prediction ●
Data management and statistical analysis plan	Language management	Document management (all related documents in one place) ●	Queries for any document type	Continuous sample size and power calculator ●
Remote collaboration ●	Document and object library	Real-time adverse event alerts	Study metrics ●	Biostatistical consulting and analysis
Custom granular user permissions for docs, actions, sites, trials, ect ●	In-trial changes ●	Automatic patient timelines, ePRO, ePIC ●	All data and metadata accessible for analysis at any time	

● Normally requires other system incurring additional costs

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Compliance

niAnalytics™ was built for conducting clinical studies and it therefore complies with all relevant regulatory requirements such as:

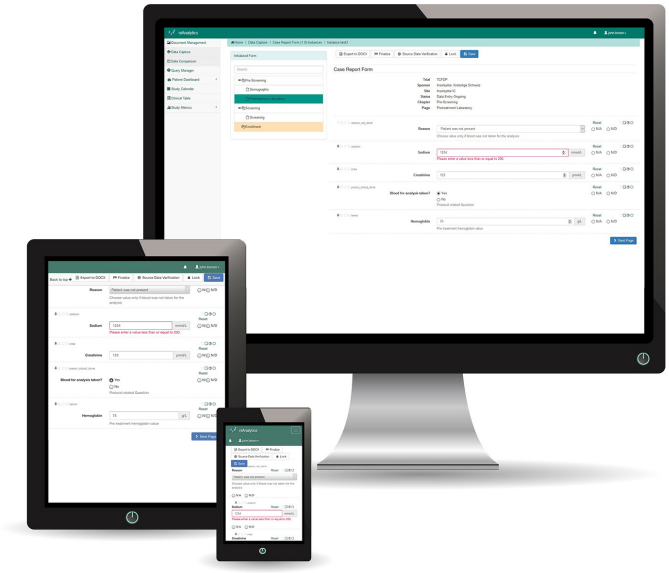
- CDISC - clinical data interchange standards consortium
- 21 CRF Part 11 - an FDA guideline on electronic records and electronic signatures
- HIPAA - the Health Insurance Portability and Accountability Act by the US Congress
- GAMP 5 - guidance for the validation of automated systems in the pharmaceutical industry
- GCDMP - Good Clinical Data Management Practice

niAnalytics™ fulfills all necessary requirements for use in clinical trials. Additionally, it can easily be validated as a productive system in a clinical setting.

We will gladly assist you in carrying out a vendor audit. Our preferred third-party auditors are also readily available to accompany the process if required.

cdisc · ISPE GAMP 5 · GCDMP Good Clinical Data Management Practices · FDA 21 CFR Part 11 · HIPAA COMPLIANCE

niAnalytics EDC/CTMS



The niAnalytics EDC/CTMS is a unique integrated SaaS solution that, due to its built-in flexibility, is designed for all clinical trial types and organizations regardless of their size.

The niAnalytics EDC/CTMS integrates EDC, double data entry, eTMF, WebPRO, Source Data Verification, integrated advanced Query Module and metrics, automatic trigger and query generation as well as assignment, automatic AE reporting and categorization and much more. The niAnalytics EDC/CTMS has been built for the ground up with the latest clinical data standards in mind including CDISC and Good Clinical Data Management Practice.

The niAnalytics EDC/CTMS is accessible from any browser, supports any language including right-to-left languages. It is built to support multiple trials in a single instance of the system, meaning that all your studies and associated documents will be on a single system with one simple log-in. A user can have different roles with different permissions and only have access to system modules, documents and reports across multiple trials simultaneously, all with one log-in.

Key features:

- Every device, every browser
- Multiple simultaneous trials on a single system
- Simultaneous multiple language support (user level adjustability)
- eTMF for simultaneous multiple studies
- Unlimited EDC form creation
- Custom granular user security and permission control
- WebPRO
- Per variable for
- Detailed usage metrics and comparison by:
  - User
  - Site
  - Organization
  - Document
  - Query
  - Time on system
  - Number of log-ins

niAnalytics System Features Overview

eCRF – Turnkey Solutions

eCRFs are the core EDC functionality of any clinical trial data management system. The niAnalytics system has been built on CDISC standards with SDTM tabulations, making end-of-trial data analytics compatible with all applicable regulations.

We know that you are busy performing your core business activities, those activities that you are best at. Therefore, why would you have to be bothered with being trained to create eCRFs in a foreign system?

We take eCRF creation out of your hands and offer a turnkey solution. Our data management experts work with you personally to create your eCRF, validate it, and stand behind our work with our industry leading support.

Key features:

- User specific multi-language support
- Granular custom user permission settings
- Multiple simultaneous trial-specific user permission settings
- Rapid eCRF creation
- In-trial eCRF changes (minutes to hours)
- Insertion of running record chapters for AEs, SAEs, CMs
- Automatic eCRF Form export (single page or entire form)
- Rule and formula editor
- Custom calculate fields
- Automatic triggers, query generation and assignment
- Automatic (S)AE reporting and categorization
- Documentation of concomitant medications
- Double data entry (DDE)
- Upload of any type of data file
- Notes, comments, queries on any document field (with history)
- Detailed granular access control for each document type
- Full audit trail and history of changes
- SDTM Tabulation

The entire niAnalytics EDC/CTMS system has been constructed so that any and all EDC forms created have the same functionalities as eCRFs by default.

niAnalytics Clinical Trial Management and eTMF

The niAnalytics EDC/CTMS enables complete collaborative study management by having the electronic Trial Master File as well as administrative forms such as visit reports and study logs in a single cloud based system. The niAnalytics team can create any type of EDC form including visit report forms, logs, or any other form that your trial may require.

The flexibility of the niAnalytics EDC/CTMS means that you do not use predefined forms, rather our expert staff works with you to create exactly the tools that you need for your organization-specific workflows. Data in any form created in the niAnalytics system is handled in the same manner as eCRFs, thus providing the same level of security, accountability, data review, communication and analysis as an actual eCRF.

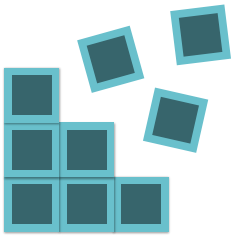
Key features:

- User, site, organization, and trial administration
- Granular document, site, and trial-specific user permissions
- Staff management
- Reports - site initiation, visit, close-out, audit
- Logs - temperature, transport, etc.
- Upload of any read-only document
  - .pdf, .doc, .xls, etc.
  - Contracts, letters, regulatory filings, insurance

The ability to upload and control the access permissions for any read-only document, enables the niAnalytics EDC/CTMS to be the place for all your clinical study data, not just eCRFs. Why use and learn multiple systems when with the niAnalytics EDC/CTMS your team has the access to all the documents they will ever need in one convenient location.

SDTM Tabulation

The niAnalytics EDC/CTMS is built with SDTM tabulation at its heart, allowing for each variable and field to be individually designated for SDTM tabulation upon creation of any EDC form. Thus, enabling us to create CDISC-SDTM-compliant datasets which are ready for reporting, analysis and submission directly inside of our database. Mapping instructions include rules for data derivations and data conversions.



Key features:

- Per variable SDTM mapping
- Creation of define.xml
- Mapping of EDC datasets and SDTM datasets
- Setup of SUPPQUAL domains
- Creation and export of SDTM-annotated eCRFs
- Our data team and statisticians review and if necessary clean any data (if required)
- Ready to export into any statistical software

niAnalytics Double Data Entry

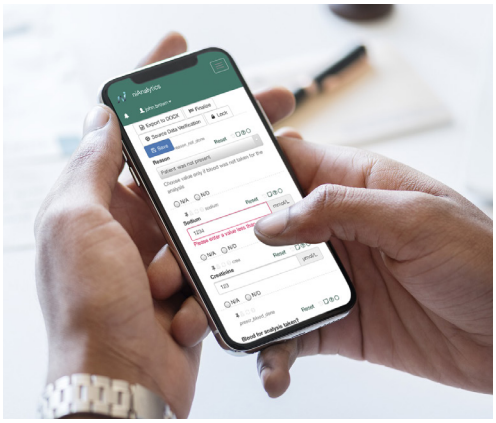
In the niAnalytics EDC/CTMS system any EDC document can be designated for double data entry, not only eCRFs. Upon the creation of a document instance (or patient in the case of an eCRF) the system automatically creates two independent versions of the document. EDC documents are filled out as any standard EDC document with all automatic data checks, triggers, queries etc. Upon the completion of data entry into both versions of the document, the user enters the Data Comparison module where the double data check is performed. In one form only data discrepancies are presented, and the user is prompted to choose from only the data discrepant data in either of the tow entered forms. Once the data is selected, the system combines the two forms into one finalized dataset and enters it into the database. The two previous forms are still available for review.

Key features:

- Double data entry for any EDC document type, not only eCRF
- Blind double data entry into two independent, but connected forms
- Automatic discrepancy detection
- Presentation only of discrepant data during the data comparison process
- Full audit trail and data export of one, both or merged document data

WebPRO

Patient Reported Outcomes (PRO) are increasingly important for all types of studies. Whether they are questionnaires, patient diaries, or data from wearable devices, the niAnalytics system can handle it all. For the niAnalytics EDC/CTMS, WebPRO is not a special system module rather a natural inherent extension of the EDC system. As such, it runs on any web browser, on any device and in any language. All that is required is an internet connection, and no special software. Our system can be adapted to integrate data from most any wearable device.



Key features:

- Use on any device including computer, tablet, or smartphone
- Simple user interface
- Subject account management
- Reminders and notification emails
- Reports
- Role-based permissions for the visibility of patient data
- Simple question
- Integration of data from wearables

Query Manager

The niAnalytics EDC/CTMS has a dedicated Query Manager Module which gives a detailed overview of all queries that a user has the right and permissions to either view, ask, respond to or close. The Query Manager lists all queries and their details including query type, trial, investigational center, instance (patient) ID, query location and creator as well as the date of the last change and full query history. Clicking on the query location directly opens the exact eCRF and document field (query location). Additionally, the niAnalytics system automatically tracks time to answer, resolve and close a query.

Key features:

- Automatic query generation based on predefined field rules and triggers
- Automatic query addressing
- Full query history
- Addition of notes to a query
- The ability to comment on a query and address the comment to a user
- Conversational comment thread
- Detailed query management
- Query metrics

The advanced query system built into the system has features that makes it one of the most comprehensive query systems available.

niServices

At niAnalytics we pride ourselves on helping our customers succeed. What better way to do so than by taking care of them from study inception all the way to the final Clinical Study Report (CSR). To this end, niAnalytics provides full data management and statistical services which free you to concentrate on what you do best, running an efficient and successful clinical trial. As data management is what we do best, our niServices are designed to leverage our expertise.

Our niServices include:

- **Data Management and EDC Deployment Services**
- **Statistical Services**
- **Custom Solutions**
- **Training Services**
- **Customer Support**

Data Management and EDC Deployment Services

Our niAnalytics Data Management services follow you from trial and site set-up, through to the creation of the finished trial database. They include:

- In-system trial setup
- eCRF creation and validation
- Validation Report writing
- Clinical Data Management Report writing
- EDC document creation, including:
  - Site Initiation Visit Reports
  - Monitoring Visit Reports
  - Close-Out Reports
  - Study Logs
  - WebPRO
  - and much more...
- Creation of in-system organization structure
- Creation of granular roles and permissions for:
  - Trials
  - Organizations
  - Documents
  - Document types
  - Document versions
  - Queries
  - System Modules
- Creation of custom trial and role dependent user manuals
- Custom reports and data exports
- SDTM Tabulation
- Database export
- Data preparation and cleaning

When performing trials with us, you will have access to a niAnalytics service specialist dedicated to your organization. We say dedicated to your organization, not trial, as the niAnalytics CTMS allows your organization and trial sites to run multiple trials on a single instance of our system. This makes our service specialists truly your specialists.

Custom Solutions

At niAnalytics we understand that try as we may, it is impossible to create a one size fits all solution, and that you will still need custom solutions. Our team is ready to help develop custom solutions for your specific trial, organization, or institution.

Some custom solution requests include:

- Clinical or hospital information system integration
- Wearable integration
- Laboratory data integration
- Stock and inventory management
- Logistics and shipping management
- Shipping based on on-site stock
- Custom reports
- ... and much more

Please do not hesitate to contact us, and we will work with you to fullfil your custom requirements.

Biostatistics

Along with data management and EDC deployment, niAnalytics provides our clients with a full complement of biostatistical services. niAnalytics can fulfill any biostatistical service and/or analysis request. Our team of expert biostatisticians is comprised of PhD level researchers specialized in medical statistics, pharmacokinetics and pharmacodynamics, as well as population pharmacokinetics. In association with our biostatisticians, niAnalytics professional medical writers can write your clinical trial statistical analysis plan and statistical analysis report according to IHC E3, IHC E9, and industry best practice guidelines.

- **Sample size and power calculations**
- **Randomization**
- **Statistical analysis plan writing**
- **Statistical analysis report writing**
- **Pharmacokinetics and pharmacodynamics**
- **Population pharmacokinetics**

We recommend to our clients to leverage the benefits of a vertically integrated data management strategy. It is incredible how easy and efficient the entire process becomes when the niAnalytics team follows your clinical trial from the protocol, to the creation and deployment of the eCRF and EDC documents, to data management, statistical analysis plan writing, statistical analysis, and all the way to the writing of the final statistical analysis report.

Randomization

Our niAnalytics EDC/CTMS system is preprogrammed with the most common randomization schedules including:

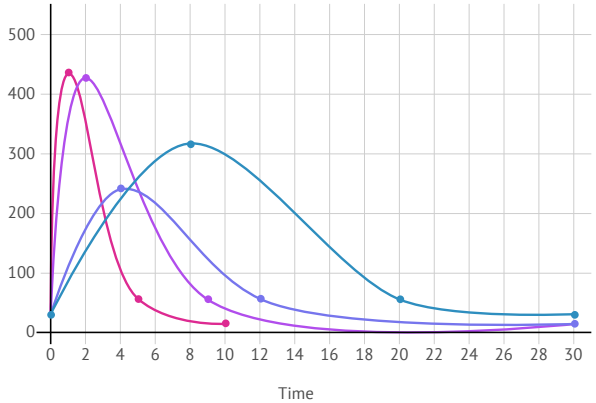
- **Simple randomization** is the simplest and most frequently used algorithm. It can result in an imbalance between the groups, however with the large number of iterations our niAnalytics system can perform, it can usually provide the desired allocation ratio.
- **Random Sorting** is applicable for any allocation type and any number of trial arms. This type of randomization can result in a significant imbalance in subject allocation over the course of the randomization process, but in the end it results in assignments which match the target groups.
- **Random Sorting Using Maximal Allowable Percent Deviation** is similar to the random sorting algorithm however, the percentage of deviation at any point during the allocation process is limited by users' specification.
- **Efron's Biased Coin** is only applicable for studies with two arms. It achieves longitudinal balance (dynamic changes of allocation probabilities) with a user specified probability parameter.
- **Smiths's randomization** is only applicable in studies with two arms. It achieves a longitudinal balance (dynamical changes of allocation probabilities) with a user specified exponent parameter.
- **Wei Urn randomization** can be used in studies with two or more arms. It achieves longitudinal balance (dynamical changes of allocation probabilities) with a user specified A and B parameters.

If the above methods do not meet your needs, we will work with you to meet your randomization requirements, including randomization blocks and stratification.

Pharmacokinetics, Pharmacodynamics, and Population Pharmacokinetics

Pharmacokinetic, pharmacodynamic as well as population pharmacokinetic analyses are performed by PhD level experts in these fields. niAnalytics thus ensures that these complex analyses and their reporting are performed with the care and expertise that they require.

If you require consultation regarding these analyses for your trial, please feel to contact us and we can even provide assistance with the set-up of the pharmacokinetic and pharmacodynamic analyses for your trial protocol.



Medical Writing

At niAnalytics we employ expert medical writers who only work with data generated by the niAnalytics EDC/CTMS and which has been statistically analyzed by our team of biostatisticians. This level of integration results in seamless information flow between our team members and an unprecedented level of efficiency.

Using data captured via our niAnalytics EDC/CTMS, managed by our staff, and analyzed by our biostatisticians our medical writers efficiently and professionally write essential trial documents, including:

- The statistical analysis plan is prepared in accordance with industry best practice guidelines.
- Interim statistical reports.
- The final statistical analysis report is written in accordance with ICH E3 guidelines and includes full patient listings and the annotated eCRF(s). Therefore, it is ready to be inserted into the final clinical study report.

Our medical writers have constant access to all eCRF and EDC documents, as well as statistical analyses and biostatisticians. In this manner we ensure that the resulting statistical analysis plan and statistical analysis report are written efficiently and with maximal precision.

Next Level Customer Support

We at niAnalytics are responsible for our database back-ups and security and guarantee 99.99% server uptime. Using our fully encrypted internet connection you will have access to a secure your niAnalytics domain dedicated to your organization.

Our niAnalytics support structure provides a specialist or if necessary, specialists dedicated to your organization. We firmly believe that niAnalytics will become an integral part of your organization. As such, we will work with you to define a communications and escalation plan to ensure all your organization's needs are met at all times.

Of course, you do not need to use all the functionalities or services we provide. Please do not hesitate to contact us and we will work with you to provide a package customized to the needs of your organization and clinical trial.

Contact Information

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Please do not hesitate to contact us, we are looking forward to exceeding your expectations and helping your clinical trials not only succeed but excel.

niAnalytics

BEYOND ELECTRONIC DATA CAPTURE