XClinical Software & Services

XClinical was founded in Munich (Germany) in 2002 with a vision to build a new EDC system leveraging CDISC standards to accelerate the database build and reduce data management programming efforts.

The company has successfully grown its client base to more than 80 customers, including more than 40 CROs performing study builds independently of XClinical and conducting clinical trials using Marvin. Over the past 5 years we have opened offices in New Jersey (USA), Basel (Switzerland) and Nantes (France). In addition, we have business partnerships in Chennai (India) and Tokyo (Japan).

We are an active member of the CDISC organization because we are convinced that the widespread use of this standard for data interchange, data submission and archiving facilitates the efficient use of e-Trial technology and processes.

We focus on your specific requirements and provide you with the flexibility to adapt to ever-changing needs.

Corporate Experience and Expertise

<table>
<thead>
<tr>
<th>Year of Foundation</th>
<th>2002</th>
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<tbody>
<tr>
<td>Number of trials to date</td>
<td>Over 850 trials in more than 67 countries and 130 studies started in 2018</td>
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</table>
| Types of trials | • Phase I–IV pharmaceutical trials  
                    • Medical device trials  
                    • Non-interventional studies and registry studies |
| Therapeutic areas | Cardiovascular, Oncology, Ophthalmology, Dermatology, Respiratory, CNS, Endocrinology, Gastrointestinal, Reproductive Health, etc. |
| Number of subjects in all studies | Over 300,000 |
| Regulatory compliance | Compliance with all relevant regulatory requirements of the FDA and EMA, in particular 21 CFR Part 11 and ICH-GCP |
| Technology transfer | We enable our customers to set up and manage their own clinical trials independently of XClinical |
| ODM certified by CDISC | Since 2007 |
Marvin

XClinical offers an integrated suite of software products for CROs, (bio)pharmaceutical and medical device corporations, sponsors and non-profit organizations, all unified under the product name "Marvin".

Marvin supports the complete data management process for all types of clinical trials and post-marketing studies. Thanks to the use of CDISC standards from CRF design to data collection, data cleaning and data export to tabulation and archiving, Marvin provides maximum benefits in form of cost and time savings and improved data quality.

Our solution combines various integrated modules, optimally supporting clinical trial processes such as study build (Composer), EDC data collection, IWRS & drug management (randomization), WebPRO (Marvin for patients), SDTM mapping/define XML, MedDRA and WhoDrug Coding (Coder), Double Data Entry (Marvin for Paper), reporting (Reporter) and CTMS (Trial Manager).

In addition, we offer risk-based monitoring, esource/lab data upload, safety notifications, clickable images, eLearning etc.

The suite is offered as Software as a Service (SaaS) model running on any browser and in any language.

Figure 1: Portfolio
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**Marvin your Study!**
Software

01 Marvin

Marvin EDC runs on any browser in any language and leverages CDISC standards to accelerate study build, conduct and manage all data processes. Marvin was one of the first EDC software products to be officially CDISC-certified for the ODM standard.

Marvin EDC offers the following key capabilities:

- Multi-language dynamic eCRFs e.g. Chinese, Japanese, Russian ...
- Source Data Verification (SDV) including Risk-based Monitoring
- Data review including central adjudication
- Advanced query management
- (S)AE Notifications/Alerts
- Electronic Signatures
- Documentation of concomitant medication
- Clickable images and scales
- Integration/upload of any type of binary data (Images, X-rays, etc.)
- Handling of central and local lab data
- Reports and Dashboards
- Electronic archiving in PDF and XML formats
- Fine-grained access control
- Complete Audit Trail
- Quick implementation of study amendments
- Out of the box standardized ODM database
- Inbound and outbound web services API for integration with external systems
- Extensive import capabilities for transferring studies from legacy systems into Marvin

Marvin can receive data from central laboratories, randomization systems, wearables, medical devices etc. It is also possible to deliver data to pharmacovigilance systems, CTMS and Data Warehousing systems.

Marvin integration with external systems can be implemented with little effort. It supports SOAP/XML, CSV data extraction and REST/JSON.

Considering the list of capabilities above, Marvin provides a new dimension of flexibility to conduct your clinical trials according to your requirements.
02 Composer

Never again struggle with the pain of turning to a mix of MS Word, Excel, and Powerpoint docs into a folder to try to customize your study startup. With XClinical's Composer, you can produce eCRF designs, document links, and more to live in a single intuitive interface for your team. Data managers can use Composer as the single tool to generate annotated CRFs, data validation plans, study metadata, visit matrix, database specs and all relevant documentation from a single, central XML-based set of metadata. Automatic, system-generated documents ensure accuracy and consistency, thereby eliminating the manual transcription effort required to maintain different documents.

Data managers can utilize Composer to build all elements of a study using an eCRF library. The library functionality enables the effective and consistent reuse of existing items, forms, etc., across different studies.

The tool automatically ensures compliance with the international CDISC ODM standard format, enabling the eCRF and database design to be exchanged within different systems and organizations (for example between sponsors and CROs).

Customers using an EDC system that can import CDISC ODM metadata as Composer supports the automatic setup of an EDC database. With an EDC system that does not have this capability, Composer still provides the best possible, unambiguous eCRF specifications, including an underlying database and data validation plan. This guarantees the most efficient communication between different teams and organizations.

Composer highlights

- Any edit checks, including cross-page and cross-visit edit checks, can be designed in a graphical point-and-click / drag-and-drop manner → no programming knowledge is required.

- Library functionality enables the user to copy and paste everything from single questions to entire case books for reuse in another study.

- Study amendments are easily implemented without any database programming. Composer automatically implements the CDISC version control mechanism.
Key features are:

- Intuitive graphical user interface for quick and easy study setup
- Smart search & copy functionality to create and use a library
- Rule and formula editor enables the easy and unambiguous definition of a comprehensive data validation plan without the necessity of programming knowledge
- Automatic output of the annotated CRF, visit matrix and data validation plan
- Easy setup and management of amendments
- Validated CDISC ODM-compliant storage and export of the CRF design
- Can be used in combination with any EDC system
- Operates offline (MS Window, Linux, MacOS) and online (any browser)
03 SDTM Tabulation

The Composer supports end-to-end tabulation and allows the consistent and seamless use of a unique set of XML-based metadata from CRF design to data submission.

It is an Extraction-Transformation-Loading (ETL) solution that leverages the CDISC define.xml standard and enables data managers to create CDISC SDTM-compliant datasets that are ready for reporting, analysis and submission inside the EDC database.

Moreover, the Composer also supports custom tabulations such as sponsor-specific data set formats. Mapping instructions include rules for data derivations and data conversions.

**Key features are:**

- Creation of define.xml
- Mapping of CRF datasets and SDTM datasets
- Intuitive graphical user interface
- Copy & paste of value-level metadata between CRF and SDTM datasets
- Easy setup of SUPPQUAL domains
- Creation of SDTM - annotated CRFs
- Independent from SAS or any other statistical software
04 SDTM Reviewer

The SDTM Reviewer is an interactive tool for a fast, efficient review of your SDTM datasets created by Composer Tabulation. It may be accessed via any modern browser and will not impact the performance of any of your studies. The result of utilizing the many preconfigured, fully integrated reports is a much faster, in-depth analysis of your data than from any other comparable product on the market.

Additionally the SDTM Reviewer can be used as a stand-alone solution.

**Key features are:**

- Provides a powerful graphical SDTM Data review tool
- Pre-defined, integrated reports
- Dramatically increases the value of doing SDTM mapping before study start
- Web-based, data visualization solution based on R Shiny, Apache and Linux
- Software-as-a-Service business model
- Interactive filtering on multiple parameters

![Figure 3: Study Characteristics Overview](image)
05 Randomization (IWRS & Drug Management)

The Randomization Module is an Interactive Web Response System (IWRS) built into Marvin and does not require any interface to an external system. The system supports open or double-blind randomization with an unlimited number of stratification factors and therapy groups, using a block list or a configurable minimization algorithm.

**Block-based Randomization**

The block-based randomization is configured by importing a randomization list into Marvin. Additionally, Marvin can import a list of investigational medical products and other materials as required. A randomization list can include blocks of any size, each linked to a set of stratification parameters. The standard block randomization process is illustrated in the figure below.

![Figure 4: Block-based randomization - process diagram](image-url)
Minimization Algorithm

The standard minimization algorithm in the Marvin IWRS is variance minimization. This is configured using the Composer. This process is illustrated below.

Additionally, Marvin supports the covariate-adjusted response-adaptive randomization algorithm. In this scenario, the probability of assigning a patient to a therapy group is gradually adapted to increase the number of patients in the superior therapy.

Adaptive Trials

Marvin provides comprehensive support for adaptive trials. Using multiple lists of investigational products, with different dosage, a wide variety of dose scenarios can be configured. Switching between different scenarios during the study is triggered by a flexible set of different criteria.
Drug Management

Marvin provides a module to manage the inventory and shipping logistics of investigational medical products (IMP) and other materials.

Shipments of materials from a central stock to different sites are managed manually via the web interface or automatically utilizing an algorithm that triggers shipments when stocks fall below pre-defined thresholds.

Marvin will assign IMPs to subjects based on the available stock while observing expiry dates. Optionally, site staff is required to enter a verification number printed on the IMP in order to avoid administering an incorrect treatment to the subject.
06 Marvin for Patients (WebPRO)

Patient Reported Outcomes (PRO) are increasingly important for all types of studies. Marvin includes a fully integrated WebPRO module, called “Marvin for patients”, that can capture patient diary information, quality of life questionnaire data or other patient recorded data.

Marvin WebPRO runs on any web browser in any language and supports all internet-connected devices. Moreover, Marvin has been integrated with various wearable devices.

Key features are:

- Simplified user interface
- Clickable images and scales
- Subject account management by site staff
- Reminder and notification emails
- Separate storage of patient identifying data in compliance with data privacy legislation
- Inline reports
- Role-based visibility of patient data
- Simplified question labels
- Integration of data from wearable devices

Figure 7: Pain scale
07 Marvin for Paper: Double Data Entry (DDE)

Marvin supports DDE both for paper and hybrid studies (combining paper and eCRFs).

Marvin for Paper implements two independent Data Entry steps and subsequent verification of discrepancies in a tabular overview. Every DDE field provides additional text and comment fields to capture all information from the paper form (e.g. data not matching the correct datatype). Data queries are triggered after the verification step.

Using blind DDE, two different users enter data from paper into electronic forms independent of each other. A dedicated reviewer (a third user) starts a verification process in which the system identifies the discrepancies between both versions and presents them to the reviewer to be resolved. Marvin’s DDE user interface provides an easy way to select the correct entries.

Key features are:

- Each item allows predefined formats as well as free text entries and a comment field for more information about the item value.
- Automated selection of matching forms, batch verification
- Attachable ‘memos’ for internal notes and workflow support
- Automated and manual query workflow including query printing
- Full DDE audit trail and data export
- Hybrid DDE/EDC mode by patient, by site or by page
XClinical’s Coder modules are web-based tools to classify safety-related data such as adverse events or concomitant medications. They include standard MedDRA and WHODrug dictionaries to automatically and manually encode verbatim terms by use of powerful search mechanisms.

The coder modules are fully integrated in Marvin via a Web Service API. Hence it is even possible to utilize them in other solutions (or EDC Systems). Its key advantage is eliminating any import/export processes for data managers.

The Coder modules include a review workflow with 21CFR11-compliant signatures. Coded information can be transferred back to the EDC system to allow reporting and queries.

**Key features are:**

- Web-based system, working on all modern standard browsers
- Powerful search engine on all MedDRA dictionary levels (LLT, PT, HLT, HLGT, SOC)
- Versatile search engine for all elements of WHODrug like indication, dosage, ATC
- UMC certified support for WHODrug B3 and C3 standards
- Automatic and manual coding including sponsor- or study specific set-ups
- Integration with EDC systems based on web services
- Automated transfer of coding related queries to an EDC system
- Stand-alone web application – can be used independently of any EDC system
- Online participation of sponsor staff for review of difficult cases and validation
- Full audit trail documentation
- Project-based coding (multiple studies can use the same coding instance)
09 Reporter

Marvin provides standard reports, custom reports, dashboards and interactive ad-hoc reports.

The intuitive self-service ad-hoc web reporting system enables authorized users to create and publish their own reports and listings without programming knowledge.

Study managers and monitors no longer depend on their IT department or external service providers to add custom reports to the EDC system.

**Key features are:**

- Real-time data
- Built-in security (users only see data for which they are authorized)
- Automatic linking of reports to the eCRF to accelerate your daily routine and decision making
- Patient profiles and other multi-page report formats
- Select data from any page and any visit with a simple mouse click
- Choose between bar charts, pie charts, scatter plots and any other type of reports
- Add filtering, sorting and grouping
- Publish your reports for colleagues in any format (excel, pdf., powerpoint or interactive html tables)
Marvin provides a CTMS module that includes a set of customizable administrative forms to collect study management data. Such data is collected and processed in the same way as in the Marvin eCRFs, providing the same mechanisms of data review, reporting and communication as in the EDC system.

For example, a manager can review the completeness and correctness of administrative data entered by monitors using reports as well as automated and manual queries (sent to the monitors instead of to investigators).

Data can be automatically extracted from different EDC systems into the XClinical CTMS via web service interface or via data import procedures avoiding double entry of administrative information.

Monitoring reports can be automatically generated after data has been reviewed, approved and signed by a manager.

The XClinical CTMS is not an out-of-the-box application but is always customized according to your individual requirements. This mechanism makes the system very agile because CTMS pages and reports may be changed at any time without losing data, just like a mid-study amendment in an eCRF.

**Key features are:**

- User and site administration
- General study information
- Study team management
- Site initiation and closure
- Site monitoring visits and monitoring reports
- Site contract management and financial information
- Site logistics (e.g. shipments of material and documents)
- Management of approval by ethics committees or institutional review boards
- Management of approval by regulatory authorities
- Subject insurance management
- Audits and quality management visits
Risk-Based Monitoring

The Marvin EDC system supports the source data verification (SDV) process by distinguishing different risk levels for each specific study center. Customized verification rules are defined in a detailed Monitoring Plan containing different risk levels. It makes the system adaptable to the site and data handling workflow.

The Monitoring Plan may also be changed and amended at any time to ensure maximum flexibility in a fast-changing clinical study environment.

The Monitoring Plan, combined with the Sponsor’s identification of critical data plus close control of entered data by automated plausibility checks is an effective and cost efficient way to guarantee the safety of subjects and the quality and integrity of clinical trial data.

Key features are:

- Flexible definition of risk levels
- Site risk levels may be adjusted at any time
- Rules to define which parts of the CRF need to be verified for which patients
- Additional flags to document customized data review
- SDV to do lists provide guidance for CRAs
- SDV reports
XClinical offers a new online interactive training system. With the end user in mind, eLearning incorporates the tell/show/do training methodology.

**Marvin for Sites**

Marvin for Sites is an eLearning module especially created for the site's personnel (e.g., study nurse), who need a basic understanding and knowledge of the operation and functionalities of Marvin EDC. At the end of the module, the learner should pass a quiz, to obtain a certificate of completion. This module gives detailed information on:

- Login & Authentication
- User Interface (UI)
- Data Entry
- Query
- Investigator Signature
- Quiz

**Marvin for Sites with WebPRO**

Marvin for Sites with WebPRO is based on the module Marvin for Sites. It has additional content about the Marvin WebPRO functionality. After finishing the theoretical part, the learner should complete an extended quiz to obtain a certificate of accomplishment. In addition to the information provided in the module Marvin for Sites, this course gives insight information on:

- WebPRO
- WebPRO workflow in Marvin
- Administration of the WebPRO account

**Marvin for Monitors**

Marvin for Monitors is an eLearning module especially created for monitors, who’s work will be supported by a basic understanding and knowledge of the validation functionalities of Marvin EDC. At the end of the module, the monitor should pass a quiz, to obtain a certificate of completion. This module gives detailed information on:

- Login & Authentication
- User Interface (UI)
- Subject Navigation
- Query Handling
- Source Data Verification (SDV)
- Monitor Signature
- Quiz
In addition to superior technology, XClinical offers fast, flexible and focused services. We can provide full service eCRF build and support or with technology transfer, we train you to create your own studies. You may do everything yourself or select the services you require from XClinical thus creating an ideal mix of professional study setup, consulting and training services to meet your specific needs.

The following professional services are available:

- eCRF build
- Configuration of Edit Checks/Queries
- Creation of user roles and access rights
- Creation of (customized) online reports and data exports
- Configuration of specific modules such as Randomization, Drug Management and Logistics
- Configuration of laboratory data import

A dedicated professional services specialist will always be assigned to your study.

Because we are solely a software vendor, XClinical does not provide typical CRO services such as monitoring, data management, biostatistics, protocol writing, etc.
02 Training Services

We offer a variety of trainings for the various system modules. Trainings can be held on-site or via web conference, depending on the complexity of the subject matter.

The initial on-site training for data managers will take 3 days including the setup of eCRFs and edit checks.

We provide "train-the-trainer" sessions to enable our customer to train investigators, study nurses and monitors. All training modules include training material and exercises as well as a certificate.

For more information about our training offers, please refer to our training concept brochure.

03 Overview Training Concept

In general, any customer-specific process can be trained as a workshop. The listed workshops above are ideas/suggestions on possible workshops.
Numerous XClinical customers have performed successful vendor qualification and system validation audits. Our QMS ensures compliance with all relevant regulations.

Compliance with:

- 21 CFR 11
- GCP System validation
- CDISC ODM certification
- GAMP
- HIPAA
- Data privacy regulations

Our advanced agile software development process includes:

- Automated system testing
- Traceability matrix
- SCRUM
XClinical is your international eClinical Software Vendor!

Our software solutions and technical services accelerate your global trials.

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