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Trial Services

The allround trial specialist in cardiology Leading since 1983

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Trial design

The key factor in achieving a successful clinical trial is to have a well-prepared, consistent trial design, protocol and Case Report Form (CRF).

Two main advantages of working with Cardialysis are its extensive experience in clinical cardiology trials and academic expert assistance. These give the sponsor maximum efficiency in the trial preparation phase and an excellent start to the clinical trial itself.
Cardialysis has established Standard Operating Procedures (SOPs) for the development of clinical trial protocols and CRFs. With these SOPs, Cardialysis is able to design tailor-made protocols and CRFs that are compliant with Good Clinical Practice guidelines and other clinical research guidelines.

Design or Review

The services requested from Cardialysis differ from trial to trial. Therefore, all Cardialysis project proposals are tailor-made. The same applies to trial design, the protocol and the CRF. Although Cardialysis is experienced in designing protocols and CRFs from scratch, projects are also run with pre-designed protocols and CRFs from the sponsor. In this case, documents are simply reviewed for consistency with the activities that will be performed by Cardialysis.

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Project management

Good project management is essential for running clinical trials efficiently. A few important project management activities are listed on this page.

Coordination

Conducting clinical trials requires experienced and committed human resources. Regardless of whether the trial involves 50 or 10,000 patients, as soon as a sponsor decides to work with Cardialysis, one of the experienced Project Managers is appointed. The appointed Project Manager leads a Cardialysis project team and coordinates all contact between the investigators, committee members, sponsor representatives and Clinical Research Associates (CRAs) in a smooth and client-friendly way. He or she is also primary contact for all agreements made with the sponsor on timelines, quality and costs of the trial.

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Site Selection

For site selection, two factors are really important: whether the sites can be selected quickly, and whether they meet the requirements (high quality, the requested patient volume, necessary equipment and expertise, motivated investigators and dedicated team). Cardialysis has close contact with over 1,200 cardiology sites world-wide ensuring quick site selection based on the highest quality possible.

Meetings

One of the tasks in project management is the organisation of meetings and conference calls, to ensure good communication with all parties. These can be Steering Committee meetings, sponsor meetings or investigator meetings. Since most sponsors and investigators are present at all major cardiology congresses, the investigator and steering committee meetings are often organised near the congress venue.

Manuals and Documents

Apart from the protocol and CRF, all kinds of documents need to be developed to comply with research guidelines, rules and regulations and to ensure smooth and fast progress of the trial. Experience and clockwork organisation are the keywords in this part of project management that both apply to Cardialysis. In close collaboration with the sponsor, the Project Manager takes a leading role in the development and maintenance of numerous manuals and critical documents.

Progress Reports

Cardialysis offers its customers different types of reports to keep all parties up-to-date on the status of the trial. These reports will ensure the sponsor stays informed, and will help to keep the commitment of the investigators at the highest possible level. Cardialysis considers these reports as an important instrument in guaranteeing the high quality for which Cardialysis is renowned, and for staying within the requested timelines. In addition to this, newsletters are drawn up together with the sponsor, and circulated at regular intervals to keep the site study team updated on the trial. Dependent on the size and scope of the trial a study website can be set up.

Clinical monitoring & site management

In all clinical trials, monitoring visits have to be conducted at the participating sites to ensure adherence to the protocol and all trial regulations and guidelines. The frequency and type of monitoring visits depends on the phase of the trial, its complexity, the duration of treatment, the rate of patient enrolment and the percentage of source document verification.

Cardialysis operates in virtually all Western and Eastern European countries, through its network of local monitors. With over 1.200 clinical sites in our site database, Cardialysis has access to a large part of the clinical trial population in the world. Cardialysis works with in-house (lead) Clinical Research Associates (CRAs) and local monitors in the field. We have a network of monitors in each individual European country. These local monitors have over 5 years of (cardiovascular) experience, work according to Cardialysis SOPs, exclusively work on Cardialysis studies and are trained on a regular basis by Cardialysis.

Regulatory submission

With representation and experience in Europe, Cardialysis offers submissions of clinical trials to national Competent Authorities and central and local IRBs for your clinical development program. Our experience will help the sponsor having a clear estimation of lead times, resulting in realistic planning for the sponsors clinical development objectives.

Site Management

General site management covers all site management activities outside the scope of the on-site monitoring visits, e.g. responding to questions from the sites, assisting with study-specific procedures, obtaining signatures, doing site performance counts, reminding sites about queries to be answered, follow-up visits to be planned and study deadlines and sending updated documents to sites for filing in the Investigator Site File.

Cardialysis offers four types of on-site monitoring visits.

Pre-Study Visit

Pre-study visits or telephone calls are made to ensure that the participating sites meet the trial-specific requirements and Good Clinical Practice (GCP) guidelines. This initial contact is also important for establishing good site collaboration and for detecting and solving any problems in advance.

Initiation Visit

A well-organised initiation visit to a qualified site results in greater compliance of the investigator and staff and helps to ensure a successful trial programme. Cardialysis offers the advantage of a long-term relationship with many investigators; a large number of sites are already familiar with Cardialysis procedures.

Monitoring Visit

Although the costs of monitoring are considerable in every clinical trial, good monitoring helps to reduce costs elsewhere. Good monitoring reduces the amount of edit queries, improves the total quality of the data and increases the percentage of patients completing the trial.

Close-Out Visit

In a close-out visit, the Cardialysis CRA visits the site to ensure the completeness of the Investigator Site File and all trial documents, including the regulatory documents. It is the responsibility of the CRA to solve all edit queries and to ensure that all data are complete before the close-out visit is performed.

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Data management

Cardialysis Data Management provides a variety of services. All services are targeted on the quality, consistency and completeness of the data.

eCRF Development

Cardialysis designs the electronic Case Report Form (eCRF) in close collaboration with the Steering Committee (comprising sponsor, investigator and Cardialysis representatives), using the standard Cardialysis format. The Cardialysis eCRF includes all the forms required to collect the clinical data of a trial. After approval of the CRF design, the eCRF structure is developed first (visits, forms and items as well as dynamic behavior of questions), followed by the specification of system generated edit checks.

eCRF review

The eCRF may have been designed by an external party, while Cardialysis provides data management and/or statistical services for the trial. The draft eCRF is then reviewed by Cardialysis with respect to:

- Consistency with the study protocol;
- Clarity, uniformity, layout, necessity and order of questions;

eCRF database

If database building is performed by Cardialysis, XClinical's Study Composer is used as database development tool. Within this system, both eCRF structure and edit checks are defined. Additionally, roles and permissions are defined and if required, a randomization module can be built in the eCRF.

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User Acceptance Test

When the eCRF database is developed, by Cardialysis or any other external party, a User Acceptance Test (UAT) must be performed, for which Cardialysis will define the plan upfront. The UAT plan consists of a general description on how the UAT is set up and the test scripts to be used during UAT.

Test scripts are written and reviewed for each UAT round, assuming that the complete UAT required for an average trial consists of three rounds. The complexity of the UAT Plan development depends on the number of variables, and edit checks in the eCRF.

Unless otherwise explicitly requested differently by the Sponsor, Cardialysis performs a full UAT on the electronic Case Report Form (eCRF). UAT findings will be reported to the database programmers according to Cardialysis procedures. After the database changes have been made, the UAT findings will be re-tested during a second UAT. Only after the last UAT results in zero findings, the eCRF can be finalised and used by the sites.

Central Tracking System (CTS)

The Central Tracking System is a sophisticated automated system for tracking all pre-defined activities within a trial. The tracking system is attached to the main trial database to monitor the day-to-day progress of the trial. It is also used to generate reports that are sent to the sponsor on a regular basis.

Query resolution and Data cleaning

Cardialysis will perform continuous data review of the eCRF data to ensure that it is accurate and clean throughout the course of the study. This review allows data analysis to be performed at pre-defined study timelines. This process may include:

- Review of answers of Electronic Data Capture (EDC) System generated standard queries e.g. ranges, completeness and consistency checks, if these are not closed by the system.
- Review of automated checks outside the system which are programmed based on the data download of the EDC system. Create and review manual queries based on visual review of the eCRF.
- Review of text fields, to prevent errors in important data that cannot be detected by automated check rules, e.g. on Protocol Deviation, AE pages and “other specify” fields.
- Handling of Freezing / Locking of Forms

Safety reporting

Due to close collaboration with local monitors, our Data Management department, the Data Safety Monitoring Board and the Safety Reporting team at Cardialysis, an efficient process has been established for adverse event reporting. Our team has in-depth experience in cardiology, resulting in cleaner data, less queries and high quality reporting to Competent Authorities and Medical Ethical Committees.

Serious Adverse Event (SAE) Reporting

Cardialysis reports all SAEs to Competent Authorities or Sponsor within agreed timelines enabling the Sponsor to notify the Competent Authorities within the stipulated time window. Cardialysis will collect all event-related documents, write event narratives and provide these to the Sponsor.

Data Safety Monitoring Board (DSMB)

Data safety monitoring is the assessment of general trial progress, the safety data, and the critical efficacy endpoints by an independent DSMB comprising 3 to 5 experts. In consultation with the Steering Committee and the Sponsor, Cardialysis appoints the DSMB members, assists with the development of the DSMB procedures, organises the DSMB meetings, and provides the DSMB with safety data during the recruitment phase of the trial.

Clinical Event Adjudication

Cardialysis is accustomed to setting up and running the entire event adjudication process: from preparing the event dossiers to organising the Clinical Event Committee (CEC) who will adjudicate the events. The web based adjudication system offers numerous advantages, one of the most important being the immediate availability of the results. Please refer to next page for more info.

Hotline Service

In complex trials, the investigators appreciate the opportunity of having a second opinion from a cardiologist. If requested, Cardialysis can offer a 24-hour telephone service staffed by medical experts to answer trial-specific (medical) questions from the research team at an investigational site.

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Web based Clinical Event Adjudication

Cardialysis has a 100% web based system for your clinical trial event/endpoint adjudication, the WebCEC application.
This system is very user friendly and quick and you can decide on the main configuration settings.
Whether during face to face Clinical Event Committee (CEC) meetings, or remote, an event adjudicator can log on to the WebCEC application any time he or she wishes.

Receipt and Scanning of Event-Related Documents

Event-related documents are digitised at Cardialysis, entered into a tracking system and attached to the relevant event that requires adjudication. These documents will become available for the event adjudicators for their review in an easy way. The user-friendliness of WebCEC is well recognized by CEC members.

Event Management

Potential trial endpoints are filtered from the central study database into the Cardialysis system. Potential trial endpoints can be derived from investigator reported events in the eCRF, from the Core Lab database (e.g. stent thrombosis triggers) and/or from data entered in the eCRF (e.g. unreported MI's triggered from lab results in the eCRF). Cardialysis links the electronic event-related documents to these potential events and assigns the resulting "e-dossiers" to the CEC members for adjudication.

Event Adjudication

Whether remote or during face to face meetings, a CEC member can log on to the WebCEC application at any time. And without any paperwork; the trial protocol, event definitions, event-related documents and adjudication questionnaire are all on-line. The web based application itself is protected (by username and password) and environment-secure.

Immediate results

The application checks the consistency among the adjudicators' individual answers instantly. Matching results are final and immediately available for statistical processing. Inconsistently adjudicated cases are discussed amongst CEC members and resolved during CEC consensus meetings (face-to-face or conference call). Consistency rules can be defined as deemed necessary.

Advantages of using Cardialysis web based event adjudication

Advantages for the CEC

- Electronic adjudication remotely, or during meetings – convenient, quick and easy
- No paperwork – User Manual, trial protocol, event definitions, event-related documents all online
- Daily overview of current workload and e-mail alerts in case of backlog
- A 24/7 help desk for technical assistance

Advantages for the sponsor

- 100% electronic: direct upload of eCRF data and electronic documents at Cardialysis
- Central preparation of electronic patient "event dossier" by Cardialysis
- CEC queries via e-mail
- Highly configurable – the client decides on user rights and roles, CEC workload
- The distribution process and the adjudication and consensus methodology can be defined
- Adaptable to trial-specific terminology
- Immediate adjudication results
- Automated e-mails with to adjudication progress reports
- FDA 21CFR part 11 compliant
- Protected (by username and password) and secure environment
- Centralized CEC training by Cardialysis
- Reduced CEC travel costs due to remote adjudication

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Statistics

The Statistics Department at Cardialysis has extensive experience in the analysis of data from clinical trials.

The statistical staff is involved in trial design, protocol and Case Report Form development, and the overall process ensuring high quality, consistency, and completeness of the data. During data collection, programs are prepared for statistical data analysis to ensure rapid reporting of the trial. The amount and level of statistical analysis varies from trial to trial, depending on the protocol, CRF or requests of the sponsor and the investigators. The staff at Cardialysis collaborates closely with the sponsors, Data and Safety Monitoring Board (DSMB) and Steering Committee to perform interim, safety and final analyses. Often the scientific interest continues beyond the initial presentation of the data.
Other statistical services include: statistical consulting and pooled analyses in which databases from different trials are combined to conduct additional analyses.

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About Cardialysis

Cardialysis is a leading specialist clinical research organization (CRO) with an exclusive focus on cardiovascular clinical trials. Cardialysis provides the full range of clinical research and cardiovascular core laboratory facilities necessary for the fast-track, high-quality development of medical devices, pharmaceutical products and combinations in phase II and phase III clinical studies, registries, post-marketing studies and investigator sponsored studies. All processes are in compliance with Good Clinical Practice (GCP), guidelines of the European Medicines Agency (EMA), Food and Drug Administration (FDA) and according to International Conference on Harmonization (ICH) and ISO standards.

Cardialysis is headquartered in Rotterdam, the Netherlands and operates in virtually all Western and Eastern European countries and the United States. Through its network of over 1,200 clinical sites monitored by specialized local CRAs, Cardialysis has access to a large part of the cardiological clinical trial population in the world.

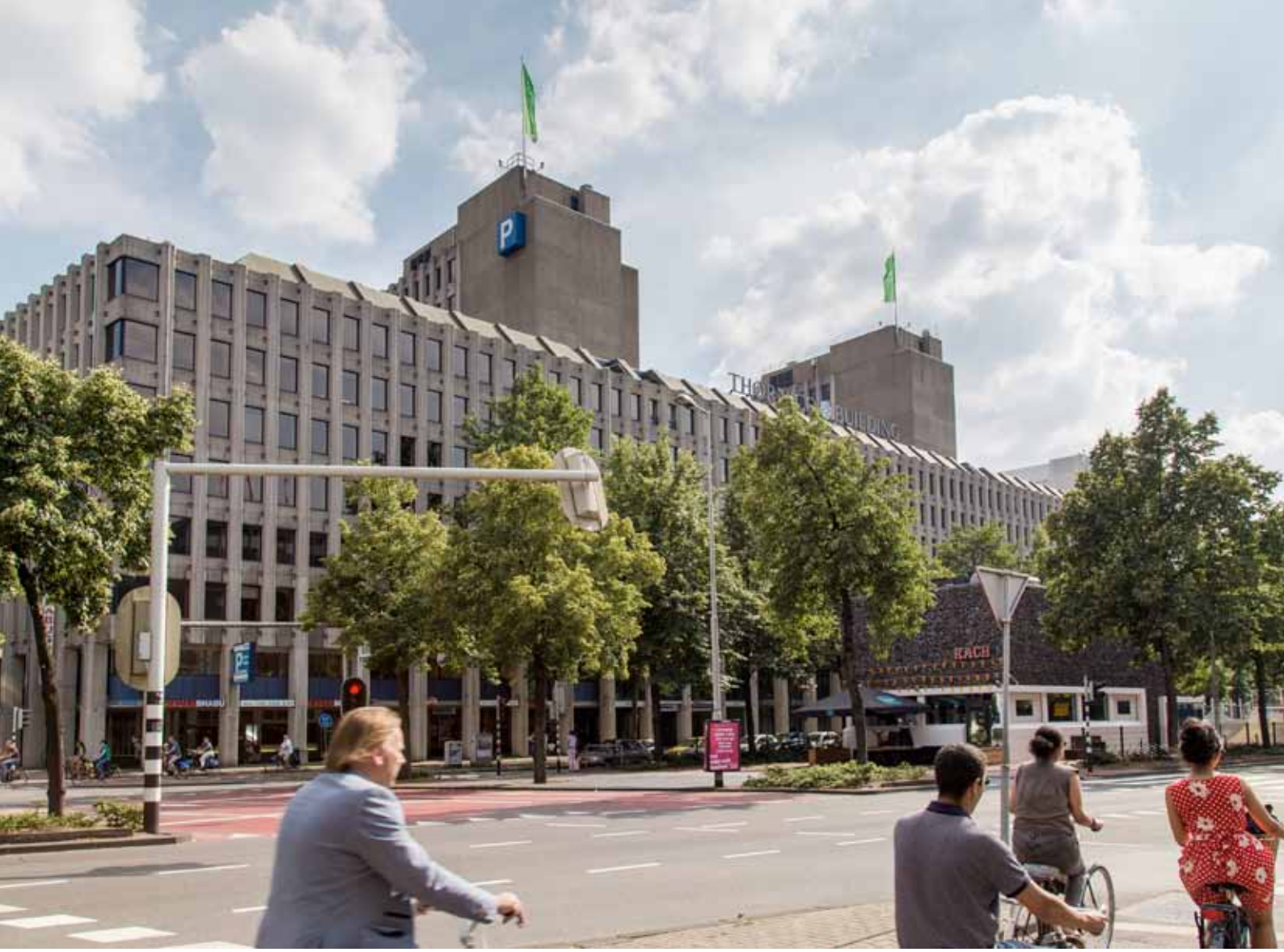
The company has a track record of over 250 clinical development studies including several landmark trials that have contributed to the major advances in the Cardiology field over the last 30 years and to the approval of drugs and devices currently used in every-day practice across the globe.

Mission and vision

To serve the interests of our clients, our global network of collaborating cardiology professionals and most importantly to pursue improvements in the care of patients by offering and continuously improving our unique state-of-the-art full service infrastructure for the design and conduct of the smartest studies with the world's most promising innovations.

History

Cardialysis was incepted in 1983 by cardiologists from the Thorax centre of Erasmus Medical Centre, the Netherlands, the centre that still plays a prominent role in the expanding international faculty that surrounds Cardialysis today. From a small Holter data analysis unit in the early eighties Cardialysis has developed into an internationally recognized independent clinical research organization, having collaborative activities with major scientific, medical device and pharmaceutical partners from around the globe. Nowadays, Cardialysis has a long diversified track record and is one of the leading specialized global organizations in the field of cardiology drug and medical device development.



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