CRO Charité Research Organisation

scientifically driven

Where would you like to run your Early Phase Trial in Germany?

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Early phase research is the fundament and guide in the decision making process forthe development of new drug candidates. “First-in-human” and “first-in-patient” studies prepare the necessary scientific basis and shape the subsequent clinical development program, and therefore must deliver the highest possible standards.

In addition, early phase trials create important data supporting a fast decision making by our customers using the “quick win – fast fail” approach. Quality of care, medical expertise, experience, volunteer/patient recruitment and regulatory compliance are key aspects.

If you want to embrace new concepts of agility and flexibility to reduce costs and accelerate the time to market for your new therapeutic and diagnostic products, you may choose to outsource your research activities to independent service providers especially in the early phases of drug development.

Charité Research Organisation GmbH

The Charité Research Organisation GmbH (CRO) is an affiliate of Germany’s top-ranked university hospital, the Charité Universitätsmedizin Berlin delivering high-quality services and tailored contract research activities for your early phase trials. It takes advantage of an extensive clinical network and a patient centric setting with the Charité being spread over four campuses and including more than 100 clinics and institutes bundled in 17 centers.

Centrally located in the heart of Berlin, CRO is perfectly suited to provide services in clinical research and offers ideal partnership for the pharmaceutical, biotech and medical device industry. Main areas of expertise are cardiovascular, CNS, dermatology, gastroenterology, immunology, oncology, and orthopedics as well as nutraceuticals and translational research. The CRO full service comprises customized and innovative solutions to sponsors of any size including investigator initiated and government-funded research worldwide.

Our consultative approach is scientifically driven and ensures that each drug-development program receives personal consideration and commitment. We provide exceptional clinical trials services to meet your unique needs. CRO stands for complete clinical trial management complying with a competent and transparent feasibility assessment as well as a professional recruitment service (healthy trial volunteers or patients in particular indications). We can inform you about study progress daily. We have complex knowledge and experience necessary to guide you through the clinical trial process, from planning and approval to the final study report.

We offer advice and consulting services in the field of clinical research, particularly in the conduct of clinical trials. Regulatory submissions, monitoring, data management, PK/statistics and medical writing complete our full service approach.

CRO profile - facts and numbers

CRO operates a state of the art Phase I unit dedicated to nurturing medical breakthroughs. Accessing Berlin's highly diverse population of 3.6 million and an extensive network of medical experts, CRO excels at recruiting both healthy volunteers and patients into highly complex studies including immunotherapy and large vaccine trials. This has resulted in over 454 trials in just 15 years for our worldwide customers.

Number and type of trials conducted in CRO

372 Interventional trials under German Drug Law including **332** Phase 1 (FIH, POC) and **40** Phase 2 trials)

5 Interventional trials with medical devices under Medicine Product Law

9 Non-interventional trials

12 Investigator Initiated trials (IIT)/Translational Research Projects

16 Nutritional and dietary intervention trials

40 Consultancy services and activities covering individual aspects of clinical trials and supporting Scientific Advice preparations

454

trials since 2006 (in total)

Research unit

Specializing in a full range of early-phase trials, the modern facility contains 72 beds including an 8-bed ambulatory cardiac telemetry monitoring, and conducts Phase I clinical trials from "first-in-human" to "proof-of-concept" as well as phase II projects with 250 highly qualified medical, scientific and regulatory employees.

Our medical team consists of 23 physicians, among them 4 internists, 1 cardiologist, 1 anesthesiologist, 1 ENT, 3 clinical pharmacologists, 1 pharmacologist & toxicologist, and 1 psychologist. The team is supported by 15 experts in natural sciences resulting in scientifically driven clinical research. For CNS/brain monitoring trials, electroencephalography (EEG) can be adopted for a wide range of assessments, especially to track safety, pharmacokinetic and pharmacodynamic endpoints as well as biomarker development. In addition, CRO features an outpatient day-care centre with an integrated CRO own laboratory for bioanalytical sample processing and analysis. A cGMP compounding area is about to start. CRO experts continuously train clinical researchers and study physicians to assure best clinical standards for clinical trial volunteers.

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Competence network

CRO has a large and flexible competence network at its disposal, which provides the expertise and competencies required to carry out successful early phase studies. The competence network can be applied to any research study, regardless of disease focus and type of research. Uniquely positioned within the Charité, we have longstanding and close interactions with scientific and medical key opinion leaders with proven leadership in medical associations for various disciplines. Among them are renowned scientists like Christian Drosten; his research group was instrumental in the development of the world's first diagnostic test for the coronavirus SARS-CoV-2.

Recruitment

With an active database of more than 200.000 participants, CRO teams conduct around 50 studies per year and perform innovative research for their local and international clients. The CRO marketing method for healthy volunteers and patients that has been established as very successful over the years is performance marketing: We build target groups with different technologies, reach these target groups especially on mobile devices and with compensation only in case of successful contact or a registration. Where necessary – e.g. to recruit in rare populations - this approach is extended Germany-wide. A highly professional in-house call center, consisting of 16 employees, handles the many incoming contacts.

In the exemplary phase I trial below, performance marketing delivered around 3.000 registrations resulting in 206 completions:

Recruitment of study with healthy volunteers

Study Population

Healthy Volunteers

Area
Clinical Pharmacology (Biosimilar)

Approach
n=210 subjects in a single-centre setting

Challenges
- ✓ Expedited timelines
- ✓ 5-day in-house period for 12 subjects per week
- ✓ Strict lab ranges at SCR

Enrolment Rates
12 per week

Recruitment Strategy
Direct-to-subject marketing and existing database

Duration of Participation
- ✓ 4 weeks screening
- ✓ 5 days in-house for dosing
- ✓ 8 weeks follow-up

Interviewed	Informed	Screened	Enrolled
2.453	1.273	799	210

Completion 206

Clinical Data Management

Clinical data management is a key process step in study conduct that must ensure that high quality, reliable, and statistically usable data are obtained from clinical trials. Clinical data managers provide the bridge between data acquisition and analysis, and are actively involved in all phases of clinical trials, from inception to completion. The interdisciplinary CRO data management team consists of highly qualified and experienced professionals able to cope with rapidly changing technology while always adhering to regulatory standards. Clinical trials are no longer conceivable without the collection of electronic data and require both Good Clinical Data Management Practices (GCDMP) and standards for electronic data collection defined by the Code of Federal Regulations (CFR), 21 CFR Part 11.

Increased regulations and trial complexities lead to high requirements when choosing electronic data management systems. If requested by our customers, the planned studies are set up by the CRO-Data Management using the electronic data capture (EDC) system Medrio eClinical, which is fully compliant with ICH/GCP, 21 CFR Part 11, GDPR, HIPAA and EU Safe Harbor. An important component of Medrio's data security plan is the contract with Google Cloud Platform to house and secure data servers in restricted access locations. In Europe, servers are located in Germany as primary, with back-up in Finland. This way, cybersecurity requirements, and rules for database security are adequately addressed.

Extensions of Medrio (ePRO, electronic patient reported outcome) have already been successfully used in epidemiological studies. In addition to CDISC compliant variable designations and ODM-XML (platform –independent format) export, Medrio enables upload of laboratory data and medical coding with CRO held licenses, MedDRA and WHO Drug Global. When CDISC data standards are implemented, high quality, interpretable data can be exchanged easily and efficiently between clinical research organizations and sponsors.

Key DM procedures, from EDC data capture, cleanup, reconciliation, coding, data mapping and transfer to database closure, are described and standardized through standard operating procedures (SOPs) to align with the world's leading electronic data capture and management solutions. The experienced use of advanced, robust and secure EDC systems for clinical trial site, patient, and lab data capture and management offers fast implementation and maximum control to support studies of any size, and/or complexity.

Publication of clinical trial results & transparency

Publishing clinical trial results helps building trust and fosters confidence into pharmaceutical research even beyond the scientific community. We consider it important that participants can see the type of our research happening and the outcomes from finished studies. Although, there is no regulatory requirement to publish the results of early phase trials, CRO takes an active part to foster trust and supports publication activities around the clinical trials conducted. In fact, many of the main findings were made accessible after study completion in a peer-reviewed journal. For example, the first-in-human study of doravirine to be used as monotherapy in NNRTI-naive HIV-infected men was conducted by our CRO in cooperation with Dirk Schürrmann (Principle Investigator) from the Department of Internal Medicine/Infectious Diseases and Pulmonary Medicine of the Charité. The results of the trial were published in a peer reviewed journal shortly after study completion (Schürrmann et al. AIDS 2016, 30:57–63). Doravirine was approved in August 2018 in the US and in November 2018 in EU. Likewise doravirine, several of the investigational products tested at our CRO did already reach the US and EU markets such as lixisenatide and semaglutide for the treatment of type 2 diabetes mellitus, or risankizumab for the treatment of moderate to severe plaque psoriasis.

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Regulatory /Submission & Consultancy

CRO features a Scientific Service team dedicated to regulatory and scientific consulting and business services. We provide our international clients customized support with European regulatory requirements. We offer expert guidance and technical knowledge to optimize the time to submissions to reach your milestones for "first patient in" and "last patient out". Our aim is to ensure that patients get access to innovative and good medicines without unnecessary delay.

Customer profile (distribution of trials per category)

Company Size

338	Big pharma
45	mid-sized companies
75	small companies

Location

70	Europe
34	US
4	Japan
1	China
1	Korea
1	India

We have successfully delivered on this promise for more than 15 years, for our worldwide clients in Europe, US, and Asia-Pacific. In total, we submitted 267 studies under German Drug Law or Medicine Product Law in 15 years. We have filed around 14 complete submissions per year to the responsible national competent authorities (BfArM: Bundesinstitut für Arzneimittel und Medizinprodukte or PEI: Paul-Ehrlich-Institut) and local ethics committee in the past 5 years. Our employees are experienced consultants who have previous involvement with pharma companies of any size and with academic research projects.

Our service also includes scientific advice and protocol assistance, and contractual supports. We are networking with specialist consultants with complementary expertise, so that we are able to provide you with cutting-edge knowledge in a broad range of indications and products. We also offer full-service including medical writing of regulatory documents. In the past 5 years, we delivered eight study protocols and four Investigator's Brochures for early phase trials including translational research, which were approved by the responsible national competent authorities (BfArM or PEI).

Privacy Regulations

In the last four years, new privacy regulations were implemented in many countries and states, such as the General Data Protection Regulation (GDPR, 2018) in Europe. The GDPR aims to protect the privacy of all EU citizens and applies to any public or private organization processing personal data. The GDPR requirements have been implemented in the CRO's data protection rules and are an integrative part of CRO. The data protection officer (DPO) of our CRO ensures, in an independent manner, that the GDPR, which protects individuals' personal data, keeps implemented.

Quality Assurance & Quality Management

Our comprehensive QA&QM system yields a proactive state of Inspection Readiness. It secures that areas of greatest focus such as study conduct or data integrity are subject to continuous internal audits in line with regulatory standards.

Our QA&QM teams comprise exceptional qualified and experienced staff with effective communication skills. The scope of QA is to assess compliance with accepted Quality Standards (e.g. GCP, current laws & regulations, requirements and documented procedures) for conducted clinical trials. Therefore, activities of our QA team comprise surveillance whether all aspects of studies under CRO responsibility are following those standards. At the same time, the QM team implements the specific procedures to assure smoothly study conduct, appropriate trial documentation, and a high quality of the collected data and surveys control of procedural documents as well as general associated trainings. Based on the established procedures, interdepartmental interfaces and clinical monitors are managed and their overlapping responsibilities clarified before a clinical trial can start. If requested by the sponsor, CRO clinical monitors can accomplish 100 % Source Data Verification (SDV) during on-site monitoring visits.

In the last five years, CRO underwent two inspections by the local authority (LAGESO, Landesamt für Gesundheit und Soziales). Both inspections delivered favorable outcomes without critical findings. Under normal (non-pandemic) conditions, CRO clients perform 5 to 6 audits per year. In general, the client audits are study-specific on-site audits or system or qualification audits.

At project close, CRO uses increasingly the tool of "lessons learned" meetings. Gaining "lessons learned" knowledge has proven very useful in preparation of audits or site qualifications. In addition, the CRO QA team performs internal study-specific and system audits and surveys subcontractors by qualification/re-qualification activities including audits. Technologies are in place, enabling remote site qualifications, if required by the sponsor or certain circumstances.

Areas of greatest focus during internal study audits

- **Trial documentation (TMF)**
- **Essential Investigator Activities:** Informed Consent, Eligibility, Randomization, Dosing, Safety
- **Overall Study Conduct**
- **Critical trial data and analysis (data integrity)**
- **Team knowledge and preparation**

The Charité Research Organisation GmbH is the perfect partner for your early phase project offering medical and scientific competence and personal engagement to deliver best quality yet keeping ambitious timelines.

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