Clinical trial regulations

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The Centre for Human Drug Research (CHDR) is an independent institute specialising in innovative, early-stage clinical drug research. All processes at CHDR comply strictly with the ICH Guideline for Good Clinical Practice (GCP), Clinical Trials Regulation 536/2014 and the Medical Research Involving Human Subjects Act (WMO). After reading this brochure, you will:

1. Understand the CTR process in the regulatory field.
2. Understand the legal background for conducting your clinical trial at CHDR.
3. Understand the timing of the regulatory process.
4. Understand the requirements for an EU legal representative and a GDPR representative for sponsors based outside the EU.
5. Understand the roles and responsibilities.
6. Find answers to frequently asked questions.

Highlights

- CHDR provides all the services needed to optimise development and streamline approval of a new protocol.
- CHDR is dedicated to keeping up with CTR key facts and translating them to CHDR business processes.
- CHDR has procedures in place to guide sponsors to prepare and follow the EMA requirements for trials according to CTR.
- CHDR can serve as a legal representative within the EU, if desired.

Conducting clinical trials in the European Union

All clinical trials conducted in the European Union (EU) must follow the ICH-GCP guidelines. If the trial includes an investigational medicinal product (IMP), it is also subject to the Clinical Trials Regulation 536/2014 (CTR), which came into application on 31 January 2022. The CTR aims to improve information-sharing and collective decision-making on clinical trials, while ensuring high standards of safety for all participants. Clinical trials without IMP are subject to national legislation. In the Netherlands, this is covered by the Medical Research Involving Human Subjects Act (WMO).

Every trial within the scope of CTR must be submitted through the Clinical Trials Information System (CTIS). This centralised EU portal is built and maintained by the European Medicines Agency (EMA). The CTR operates to strict timelines for all Clinical Trial Applications (CTAs) in the CTIS. These timelines are enforced within the CTIS portal and apply both to parties making the application (clinical trial sponsors) and the reviewing party (authorities).

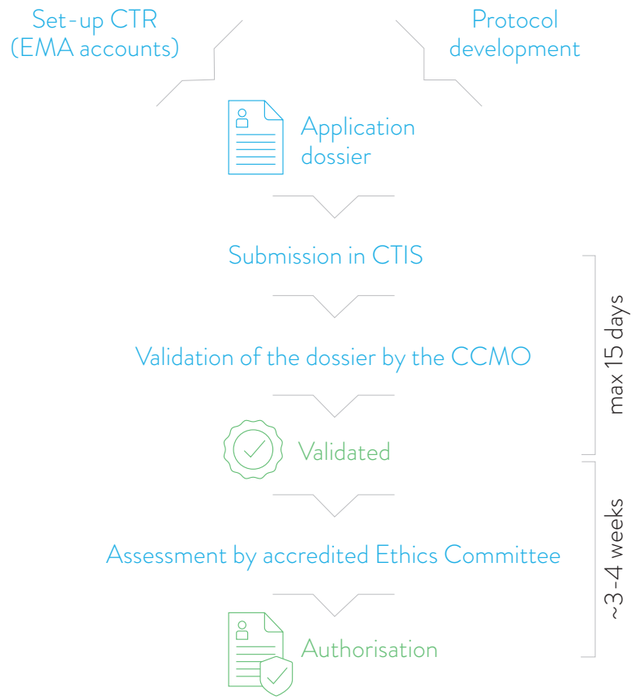
The application is divided into two parts. Part I contains documents about the study protocol, product and study design. This is the same for all member states involved. Part II contains documents about recruitment arrangements, information sheet and informed consent form and site suitability. This is specific to each member state.

The assessment of CTAs consists of two phases: the validation phase and the assessment phase. The competent authority in the Netherlands is the *Centrale Commissie Mensgebonden Onderzoek* (CCMO). It validates the CTA by assessing the scope and completeness. After validation by the CCMO, the assigned and accredited Ethics Committee (EC) will perform their review and authorise the trial. The EC assesses Part I and Part II of the CTA.

CHDR services

CHDR can conduct trials with and without IMP, and we have sound knowledge of the EU CTR 536/2014 and the WMO. We can support sponsors to prepare and submit the CTA for regulatory authorisation of both regulations, or we can lead the process. After submission, we continue to monitor studies submitted to the CTIS, and update notifications when necessary.

CHDR provides more competitive timelines than required by the CTR, thanks to our established agreements with the CCMO and our preferred ECs. In most cases, we can obtain approval within six weeks of submitting the application. A schematic overview of the CTA process is presented below.



Our services include:

- Protocol development and writing.
- Application submission (including document preparation) - initial, resubmission, amendments.
- Redacting of documents for publication (necessary for trials under CTR).
- Managing trials in the CTIS.
- Advice on regulatory issues.

Sponsor requirements

Sponsors not based in the EU will require a legal representative to ensure compliance with the obligations of the CTR. At the sponsor's request, CHDR can serve as the legal representative to meet this requirement.

Sponsors not based in the EU must also have an EU-based General Data Protection Regulation (GDPR) representative as per GDPR Art. 27. In addition, a responsible person based in the EU is required for pharmacovigilance (PV) requirements. CHDR cannot act as GDPR representative or a PV responsible person for the sponsor. We can however recommend parties to provide this service.

IMPs without market authorisation should be registered in the EMA central database for tracking pharmaceutical product data by the PV responsible person.

Roles and responsibilities

Sponsor	CHDR
Before submission	
Protocol development	Protocol development
Create trial in CTIS and grant CT High-level Administrator role to CHDR	Manage access for CHDR project team
Provide documents as per submission tracker	Prepare documents as per submission tracker
Redacting of final IB – if applicable	Redacting of documents except IB – if applicable
Review CHDR documents (including redacted versions)	Prepare application
Approve application (content and documents)	Submit application
After submission	
Prepare response to Requests for Information (RFIs)	Communication with EC and CCMO
	Check and relay RFIs to sponsor / prepare response
	Submit responses to RFIs
After authorisation	
Annual safety reporting of IMP	Notifications of study life cycle
SUSAR reporting in EudraVigilance	Create amendments (if applicable)
	Reporting of serious breaches, unexpected events, and safety measures in CTIS
	Submit summary of CSR

Depending on agreements between CHDR and the sponsor, roles and responsibilities can be shared.

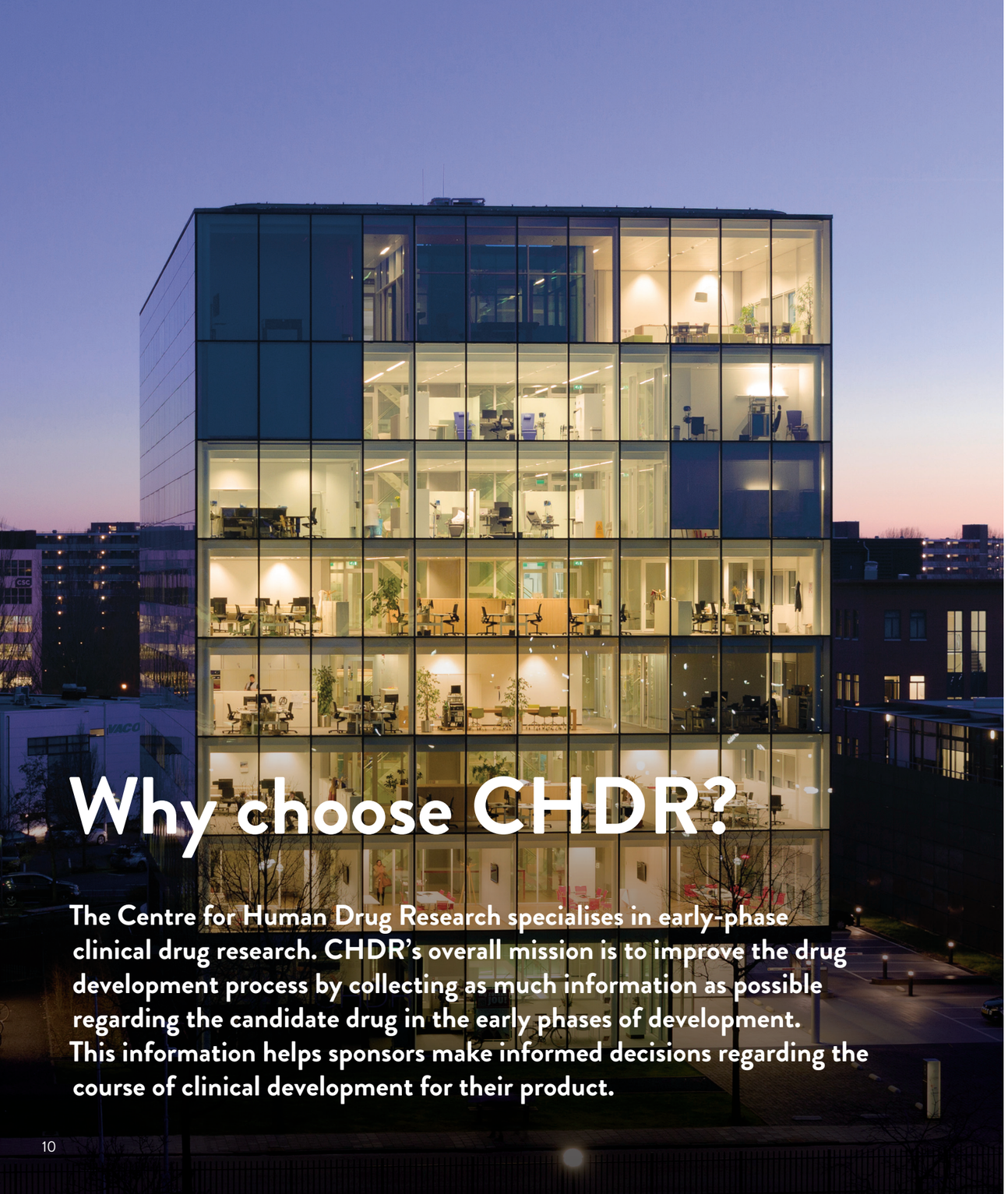
FAQ

1. **Does GDPR apply to individuals outside the EU?**
   It depends. It applies to all companies that process the personal data of EU citizens, regardless of whether a company is based in the EU.

2. **Can CHDR act as a GDPR representative within the EU?**
   No. This representative needs to be a sponsor-appointed party based within the EU. It cannot be CHDR. CHDR can however recommend parties that can take on this role.

3. **Can CHDR act as a legal representative within the EU?**
   Yes. CHDR can act as the legal representative for the sponsor if desired.

4. **Who is responsible for pharmacovigilance of the product?**
   The sponsor is responsible for finding an EU-based responsible person to perform the requirements for pharmacovigilance for their product. This includes registering the product in the dedicated EU database necessary for submission.



Why choose CHDR?

The Centre for Human Drug Research specialises in early-phase clinical drug research. CHDR's overall mission is to improve the drug development process by collecting as much information as possible regarding the candidate drug in the early phases of development. This information helps sponsors make informed decisions regarding the course of clinical development for their product.

Our research

Research at CHDR covers a wide range of fields, including the central nervous system (CNS) and pain, the cardiovascular system, haemostasis, immunology, and dermatology. In addition, CHDR is at the forefront in developing novel biomarkers and methods for measuring drug-related effects in all of these research areas.

Pharmacology matters

Whether studying a new cognitive-enhancing drug, a next-generation painkiller, or a new monoclonal antibody designed to treat rheumatoid arthritis, the goal is to determine how the compound's effects correlate with both the dose and blood concentration at any given moment. In addition, understanding which biological systems are activated is an essential first step towards quantifying this relationship. At CHDR, our focus on pharmacology is reflected clearly in what we call question-based drug development.

Question-based drug development

CHDR actively uses question-based drug development - or QBD - as a more rational approach to drug development compared to conventional approaches. QBD can be best described as a series of questions that are addressed throughout the process. These questions often seem simple enough, but failing to answer even one question - or even addressing the questions in the wrong order - can have dire consequences. Thus, using this approach can potentially save companies millions of dollars by helping predict a catastrophic issue early in the development process, before the more expensive latter stages (for example, large-scale clinical trials or the marketing phase).

From a general perspective, the most important questions are:

1. Does the biologically active compound and/or active metabolite(s) reach the intended site of action?
2. Does the compound cause its intended pharmacological and/or functional effect(s)?
3. Does the compound cause any unintended pharmacological and/or functional effect(s)?
4. Does the compound have a beneficial effect on the disease and/or clinical pathophysiology?
5. What is the compound's therapeutic window?
6. How does any variability with respect to the drug response in the target population affect the product's development?

Contact

To learn about CHDR's full range of services, contact us today.

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