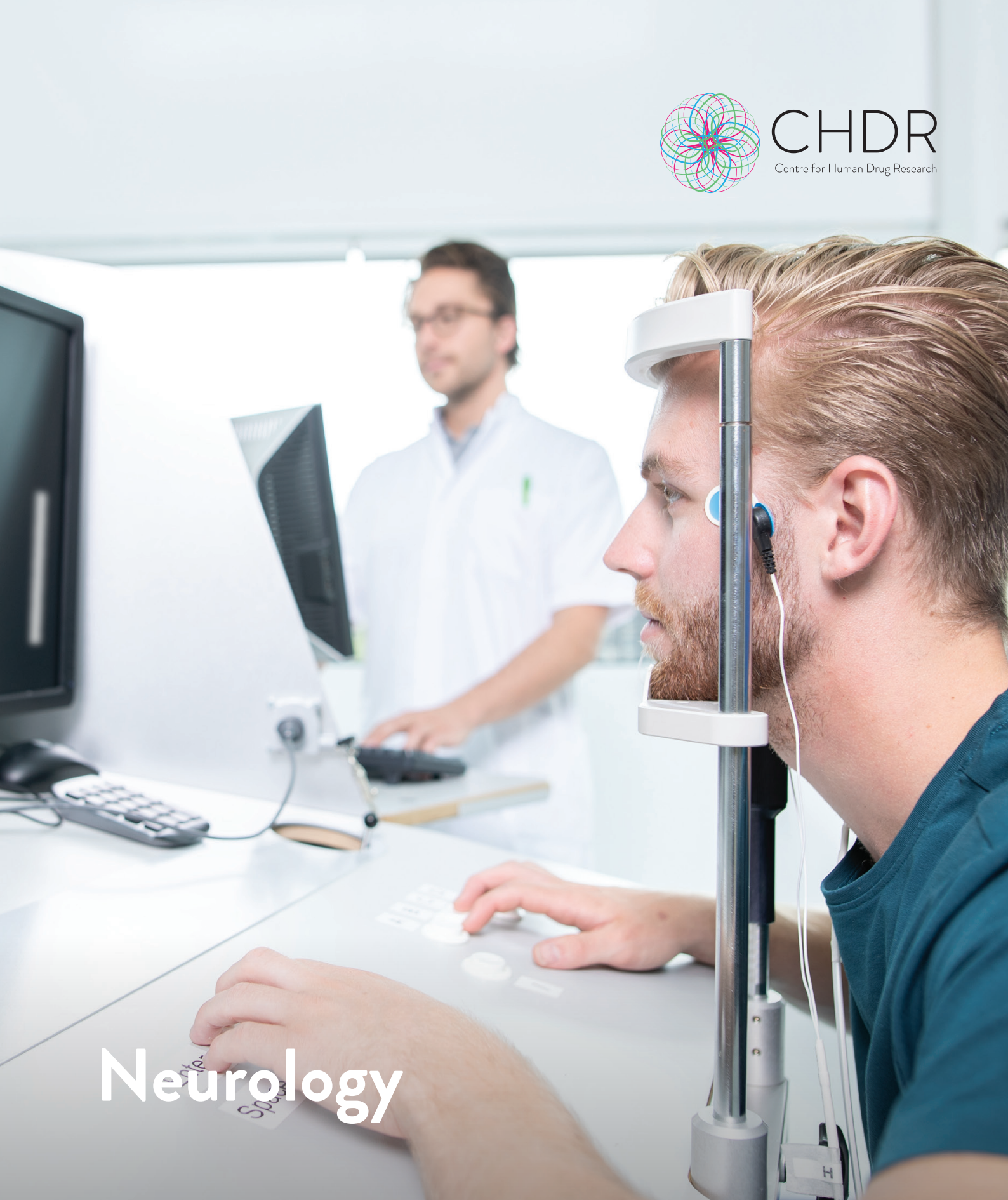
CHDR
Centre for Human Drug Research



Neurology

What CHDR offers:

- Extensive experience in testing novel CNS compounds in early-phase clinical trials, with both healthy volunteers and patients
- Combined expertise of two board-certified neurologists and post-doctorate clinical scientists with neuroscientific backgrounds
- A range of biomarkers for different mechanisms, with capacity to develop and tailor methods according to client needs
- In-house ‘wet’ biomarker processing in our state-of-the-art bioanalysis laboratory, including collection of PBMCs and other specific cell types
- Access to a range of specific patient populations, through our own database as well as in collaboration with partner hospitals across the Netherlands
- Comfortable, hotel-style accommodation, offering an optimal environment for long-duration and patient studies

Neurology

Neurology is one of the most challenging areas for early phase drug development. At CHDR, our mission is to overcome drug development challenges by gaining in-depth insight into the pharmacology of new compounds at the earliest stages of development. To do so, we offer a wide variety of methods that enable the study of a diverse range of neurological indications.

Extensive expertise

We have many years of experience in studying neurological indications, dating back to CHDR's foundation in 1986. Neurology remains a pillar of our research activities to this day, with recent studies covering Parkinson's disease, amyotrophic lateral sclerosis (ALS), Huntington's disease, multiple sclerosis, migraine, epilepsy, Alzheimer's disease, sleep disorders and various types of pain, as well as rare diseases such as facioscapulohumeral muscular dystrophy (FSHD) and Lambert-Eaton myasthenic syndrome (LEMS). An important focus of our research is the development of drugs to address areas of great unmet medical need. Next to numerous development programmes involving first-in-human studies in healthy volunteers, we also have unparalleled access to a wide range of specific patient populations.

Dedication to biomarker development

At CHDR, we recognise the importance of incorporating relevant biomarkers in development programmes right from the start. Biomarkers are of crucial importance in the early stages of drug development, enabling us to evaluate the pharmacological activity of a drug and determine the effective dose to be investigated in patients. Equipped with a state-of-the art biomarker research laboratory, we are passionate about developing and implementing biomarkers for specific mechanisms of action.
To support the study of a wide variety of mechanisms and effects, we offer a diverse range of methods and tools:

- NeuroCart®, a comprehensive neurophysiological and neurocognitive test battery[1]
- PainCart®, a multimodal evoked pain test battery[2]
- Measures of cortical, neuronal and muscle excitability, such as Transcranial Magnetic Stimulation (TMS) coupled with electromyography (EMG) and electroencephalography (EEG)[3], excitability threshold tracking of peripheral nerves, and muscle velocity recovery cycles (MVRCs)
- Electroencephalography (EEG), including resting-state EEG recordings as part of the NeuroCart® test battery, as well as task-related EEG tools offering markers of stimulus or information processing[4]
- Cerebrospinal fluid (CSF) sampling[5], through lumbar punctures and spinal catheters
- Blood sampling, to provide blood-based biomarkers for the measurement of effects on molecular pathways

[1] https://chdr.nl/library/neurocart/download
[2] https://chdr.nl/library/paincart/download
[3] https://chdr.nl/library/transcranial-magnetic-stimulation-tms/download
[4] https://chdr.nl/library/eeg/download
[5] https://chdr.nl/library/csf-sampling/download

Developing a drug for Parkinson's disease: from biomarker validation to healthy volunteer and patient studies

CHDR's team were recently tasked with performing a single and multiple ascending dose study in healthy volunteers and patients with Parkinson's disease. CHDR first drove a study for the genetic screening of over 3,600 PD patients throughout the Netherlands, laying the groundwork for a proof-of-concept study in this patient population who display a certain genetic mutation. In parallel, a phase 0 biomarker study was conducted in healthy volunteers and PD patients, to determine the within-day and day-to-day within-subject and between-subject variability of the biomarkers. The single and multiple ascending dose study in healthy volunteers was performed to first establish the most promising dose for the study in patients with the specific mutation. This patient study was then performed with subjects selected on the basis of results from the genetic screening study. This complex, multifaceted development programme was performed to competitive timelines, with the entire programme being concluded within 16 months of the start of the first trial.

RIP1 kinase inhibitors: from proof-of-mechanism to ALS patient study

In collaboration with a biotech company, CHDR was recently involved in a programme for an investigational RIP1 kinase inhibitor designed to be CNS penetrant, performing a first-in-human SAD/MAD study and a study in ALS patients. This mechanism of action designed for a centrally-acting drug was thoroughly investigated through a set of well-designed early phase clinical pharmacology studies. Besides measuring outcomes related to safety and pharmacokinetics, the collaborative team measured pharmacodynamic effects by jointly setting up a blood-based biomarker assay. This assay was successfully used in the first-in-human SAD and MAD study with healthy volunteers. In a patient study, recruitment of eligible ALS patients was undertaken in collaboration with the national centre of expertise for ALS at UMC Utrecht. In addition, all patients were subsequently enrolled in the open label extension study that followed.

Imaging techniques

Where imaging techniques would offer added value to your study, these can easily be included. We have a range of options available for imaging of disease and drug effects. In addition to (f)MRI facilities at our disposal, we are also able to perform PET studies, magnetic resonance (MR) spectroscopy and mitochondrial function measurements in both muscle and cortex.

Programme leaders

Our team is experienced in leading Neurology development programmes, offering the combined expertise of two board-certified neurologists and a number of post-doctorate clinical scientists with neuroscientific backgrounds. Our dedicated in-house bioanalysis lab is equipped to set up and/or implement a wide variety of assays for biomarkers, including cell-based assays. And if a biomarker that would be relevant for a specific compound is lacking in our portfolio, our Method Development group is on hand to develop an assay or method to meet your needs.

Collaborative networks

Thanks to our close ties with several university hospitals in the Netherlands, we can offer access to a variety of patient populations, including a database of several thousand patients with Parkinson's disease. Through our collaborative networks at a national level, we can also tap into leading expertise on a wide range of specific disease areas. Our recent studies on ALS, for example, have benefited from our partnership with the University Medical Center in Utrecht, which is home to the Dutch national centre of expertise for ALS. Meanwhile, studies involving (f)MRI are made possible in collaboration with our partner hospital, the Leiden University Medical Center, with its dedicated research scanner.

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.

Why choose CHDR?

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.

+31(0)71 524 64 00

info@chdr.nl

www.chdr.nl