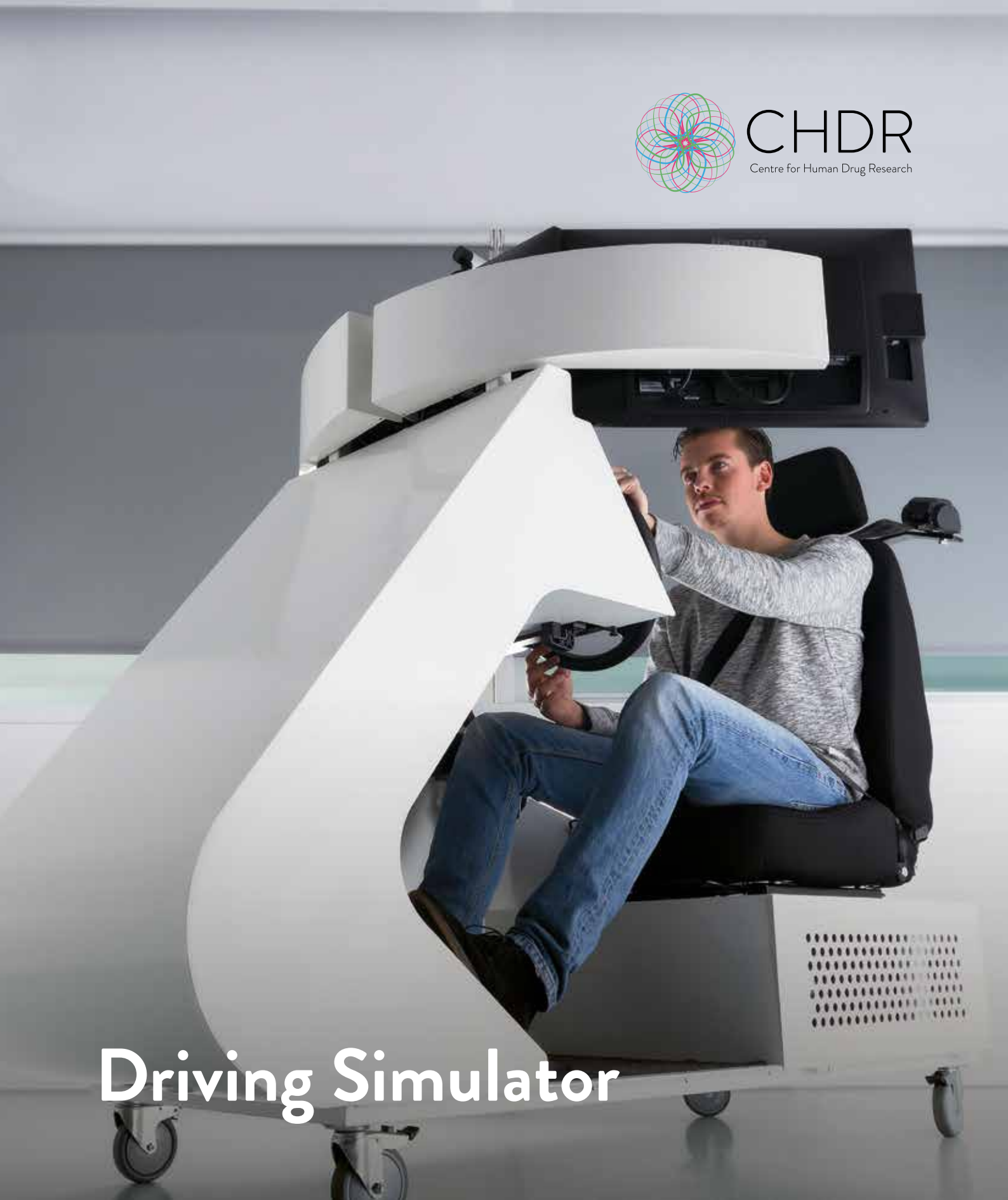
CHDR
Centre for Human Drug Research



Driving Simulator

A safer way to measure the effects of drugs and disease on driving performance

CHDR uses computer-based driving simulators made by Green Dino to safely measure the effects of pharmacological compounds and/or diseases on driving performance. These tests can be performed repeatedly, yielding highly reproducible data and allowing researchers to establish dose-effect curves for a number of CNS functions.

Practical answers to important research questions

Does our compound affect driving performance?

With many classes of drugs, one must eventually measure whether it is safe to operate a vehicle or other heavy equipment while under the influence of the compound. To address this important question, CHDR's driving simulator can be used early in the clinical phase of drug development, before subjects who take the compound get behind the wheel of their own vehicle. With this information, the sponsor can then decide how to deal with any potential issues that might arise in later phases of drug development.

How might specific CNS conditions affect driving performance?

CHDR, in collaboration with Leiden University Medical Centre, is conducting studies in a variety of patient groups with specific conditions that may affect driving ability. These studies will provide a frame of reference for measuring drug-induced effects using the driving simulator, and they will provide important information regarding the interaction between CNS conditions, pharmacology, and driving ability

'The driving simulator is a safer version of the standard driving test, providing a robust measure of a drug's effects on attention and motor control.'

Driving simulator highlights

- The driving simulator is a safer version of the standard driving test, providing a robust measure of a drug's effects on attention and motor control.
- The simulator can be programmed to measure specific effects, impairments, and other disabilities that may affect driving performance, for example decision-making, motor control, risk-taking behaviour, and spatial memory.
- The results are recorded automatically and can be correlated with blood values and other physiological parameters.
- The simulator is a standardised testing environment with sufficient variations to minimise learning effects in cross-over experiments.
- The tests can be repeated frequently, allowing the researcher to measure the time course of driving performance during dosing.
- The effects of a new compound can be compared to benchmark compounds such as alcohol intoxication or medications known to impair driving ability.

Validation and clinical relevance

The effects of alcohol on driving performance have been measured extensively at CHDR using our validated 'ethanol clamp' method. With this protocol, the subject receives an intravenous infusion of ethanol. The infusion rate is adjusted continuously based on breath alcohol samples in order to maintain ('clamp') the subject's blood alcohol concentration. The researcher then measures the effect of intoxication (in the Netherlands, the legal limit is defined as 0.5 g/L alcohol) on driving performance in the simulator. The effects of a new drug can then be compared to the effects of alcohol intoxication. In addition, the reaction profile has been established in subjects following a 1-mg dose of alprazolam, a widely prescribed anxiolytic drug often taken during the day, potentially before getting behind the wheel; the results revealed that taking a dose of alprazolam has a more severe effect on driving performance than alcohol intoxication (see Figure).

Driving simulators versus standard driving tests

Driving simulators offer clear advantages over standard, 'on-the-road' driving test. Because all settings are controlled by the investigator, a driving simulator presents the subject with extremely reproducible conditions. In addition, a driving simulator does not require the presence of a driving instructor or test operator. Driving simulators are also completely safe, as the test is performed in a closed, secure environment, and the simulation can be stopped immediately if necessary. Finally, performance on the driving simulator can be correlated easily with drug dose and with a variety of other measurements such as NeuroCart®, our battery of CNS tests.

The driving simulator and CHDR

At CHDR, the tests used in the driving simulator can be readily adapted to meet the study's objectives. For example, the core driving protocol is based on the standardised on-the-road driving test. After a 5-minute training period (in which the subject becomes familiar with the simulator), each session typically includes a 15-minute session with the participant 'driving' on a standard two-lane highway, during which standard deviation of the lateral position (SDLP) is measured. After this session, several additional road conditions can be added to test other aspects of driving skill. For example, customised conditions and situations can be included, thereby providing important information regarding alertness, arousal/wakefulness, attention, processing speed, reaction time, psychomotor function, sensory and perceptual functioning, and executive functions such as decision-making and risk-taking behaviour. Because a typical session lasts around half an hour, the tests can be repeated several times during the day, allowing the researcher to examine the correlation between the dose administered and driving ability. This system also works well with studies that use a cross-over design.

Using the driving simulator to measure CNS performance

CHDR's driving simulator can also be used to measure neurological performance in patients with neuromuscular disorders such as Huntington's disease. Patients with this progressive form of neurological degeneration can develop mental, psychiatric, and motor symptoms that can ultimately affect their ability to drive safely. In collaboration with the Neurology Department at Leiden University Medical Centre, CHDR is creating a protocol to objectively and quantitatively evaluate driving performance in patients with Huntington's disease and other neurological and/or psychiatric conditions. This protocol can also be adapted to yield key information regarding how clinically relevant drugs can affect driving performance.

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.

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