
CHDR
Centre for Human Drug Research
Ready-for-Research™

Pre-screened patients on standby for early-stage clinical trials

Sometimes the best idea is the opposite of established procedures. CHDR's Ready-for-Research programme is a perfect example of this philosophy in action. Rather than recruiting patients for a given clinical study on an as-needed basis, Ready-for-Research establishes a pool of well-defined patient groups who are ready and willing to participate in new trials, significantly reducing recruitment time and patient screening.

Prof Joop van Gerven, Research Director, explains this innovative approach

'With Ready-for-Research, we recruit patients who have specific medical conditions and are interested in participating in drug studies,' says van Gerven. 'We then screen these patients using specific protocols that have been approved by an ethics committee. With Ready-for-Research, patients are invited to our facility at CHDR. After providing written informed consent and a full medical history, patients receive a comprehensive physical examination, including bloodwork, and we test their performance on some of our test batteries (for example, NeuroCart®). The experience is like visiting an outpatient clinic, and we try to make the patients as comfortable as possible – after all, they are making the effort to come to us, with no tangible benefit to themselves aside from a modest payment for their time.'

Depending on their specific medical condition and disease stage, patients can return to CHDR on a regular basis (for example, annually or semi-annually) for re-screening in order to assess their condition, general health, and other possible factors that may affect their ability to participate in an upcoming study.

Once a sizable cohort of patients with the same diagnosis has been established, this cohort is now ready for research. Sponsors with an interest in studying this condition can approach CHDR to discuss a clinical trial. And of course, CHDR can approach potential sponsors who are developing drugs for this target patient group. 'We can offer sponsors a relatively large cohort of patients with a well-defined set of symptoms,' says van Gerven. 'All of the patients are available for participation at the same facility using the same procedures. In this respect, patients are recruited even before the trial exists. This method is an important addition to our Monocentre approach.'

Clear benefits, clear results

To develop the Ready-for-Research programme, van Gerven shifted away from his clinical duties at the Leiden University Medical Centre outpatient neurology clinic. ‘I believe this is an important advance in the process of drug development. Once we establish a pool of patients who are willing to participate in clinical studies, we know what we have to offer sponsors. Unlike the classic approach to patient recruitment – in which you try to find patients who match the inclusion and exclusion criteria for a finalised protocol – we can now write a study protocol that is designed to match a group of patients who are already screened. We already know that this approach is feasible, and we can reliably determine recruitment rates and establish clear time lines for the study. And if we need more patients, we have an idea of how long it might take to recruit them.’

Even in the early phases of drug research, relatively large numbers of patients may be needed. Indeed, van Gerven estimates that up to a hundred patients might be needed for studying most disorders. ‘Patients are generally a more heterogeneous group than healthy volunteers, so you need larger numbers. And when you have access to a large group of patients, you can also define patient subgroups. For example, because inflammation is an important pathogenic pathway in many psychiatric disorders, we can include patients with biomarkers that indicate active inflammation. So if a sponsor in our network is interested in a specific biomarker, we can easily add this to the Ready-for-Research protocol.’

Why patients?

At CHDR, we believe that patients should be included as early as possible in clinical drug research. Prof van Gerven explains the underlying philosophy. ‘You can never be absolutely certain that patients will have the same pharmacodynamics and pharmacokinetics profiles that you measure in healthy volunteers. Indeed, the very system that the drug is designed to target is often altered by the disease.’ He adds with an emphasis that CHDR focuses on what he calls proof-of-pharmacology, showing that the drug affects the pharmacological mechanism, not necessarily the disease itself. ‘A drug is designed to have a specific pharmacological activity,’ adds van Gerven. ‘This is a clear prerequisite for a therapeutic effect. Unfortunately, many drugs fail in clinical trials because their pharmacological activity cannot be ensured. When you interpret the outcome of a failed trial, it makes a large difference if you can demonstrate whether the drug had – or did not have – the expected pharmacological effect in patients. So we need to develop better ways to measure these effects in patients.’

In many ways, conducting research with patients is more challenging than using healthy volunteers. For example, patient cohorts often have more variability and can be more difficult to recruit. ‘Once you have the approved protocol,’ says van Gerven, ‘you –and your sponsor – want to proceed with the study as soon as possible. So you usually don’t have much time to recruit the required number of patients. That is why even in the early phases of development, most studies are multicentre trials, which increases patient numbers and the likelihood of achieving sufficient recruitment. On the other hand, the selection criteria often require a compromise, resulting in patient characteristics that do not necessarily reflect clinical reality. In addition, it’s often impractical – or even impossible – to provide all participating centres with the more complicated tests needed for proof-of-pharmacology. For example, even though our NeuroCart test battery is designed to be fully portable, we may not be able to provide all participating centres with the necessary training. Thanks to our Ready-for-Research programme combined with our Monocentre approach, NeuroCart can be used on all patients in a single study, as they will all be at the same location.’

‘Thanks to our Ready-for-Research programme combined with our Monocentre approach, sophisticated tests can be used on all patients in a single study, as they will all be at the same location.’

Recruiting Ready-for-Research patients

In 2016, the first Ready-for-Research patients were invited to CHDR for screening. For these patients, we focus on disorders with which we already have considerable experience, including Alzheimer's disease, depression, and anxiety disorders, as well as diabetes and rheumatoid arthritis. Patients are recruited through advertisements placed in newspapers and online, through patient organisations, and through physician referrals. In the case of physician referrals, CHDR keeps the referring physician informed of the patient's screening results. 'On one hand,' says van Gerven, 'patients are generally better informed than in the past, and I think our approach empowers patients to make their own choices. On the other hand, it's extremely important that CHDR maintain a solid relationship with the patients' physicians. We ensure that our screening process and studies do not interfere with the patient's care or therapy, and we keep the physicians updated on our findings, both at the level of the individual patient and with respect to the entire clinical study.'

One of the first Ready-for-Research cohorts is patients with Huntington's disease. Neurologists and geneticists at Leiden University Medical Centre have studied this devastating hereditary neurological disorder for decades. Prof van Gerven elaborates: 'Huntington's disease is a highly complex progressive condition with many neurological and psychiatric symptoms. At CHDR, the challenge is to assess our patients' symptoms using NeuroCart and other tests. But for physicians, sponsors, and patients, overcoming this challenge may help pave the way to finding and testing new treatments. And of course, as specific candidate drugs for treating Huntington's disease are developed, we'll be in an excellent position to test them in patients.'

The future of Ready-for-Research
In the coming years, it is our hope that sponsors will appreciate the clear value provided by our Ready-for-Research approach, and van Gerven is confident that sponsors will seize this opportunity. 'It may take some time to get accustomed to the idea,' says van Gerven, 'but I'm sure our sponsors will see the value. After all, we're doing more research in patients already, so this is the logical next step. For patients, even the screening process will be informative. For example, patients will receive a thorough check-up, and we can evaluate their symptoms using state-of-the-art equipment. More importantly, we can also validate our tests in a well-defined patient population.'

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Ready-for-Research: a brief overview

- CHDR's biomarkers and test batteries provide proof-of-pharmacology results in the early stages of drug development.
- Because pharmacodynamics and pharmacokinetics profiles can differ between patients and healthy subjects, early testing in patients is essential.
- To resolve the bottleneck created by patient recruitment, CHDR establishes pre-screened groups of patients who are ready and willing to participate in a study.
- As soon as a sponsor is ready to test a product in this patient population, CHDR is ready with pre-selected patients.
- By combining Ready-for-Research with our novel Monocentre approach, all patients participate at one central location, thereby minimising variability by using validated test batteries and biomarkers.
- CHDR collaborates closely with patient advocacy groups and physicians, ensuring that everyone benefits from this innovative approach.

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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