Best Practices For Evaluating Immunologically Active Compounds

An Interview With Matthijs Moerland, Research Director R&D lab and Immunology

Because the immune system is highly complex, all new immune-based treatments must be evaluated thoroughly. Moreover, early clinical development of new immunologically active drugs requires both scientific and clinical expertise in order to ensure the subjects' safety and to maximise the resulting clinical and economic benefits.

CHDR is committed to overcoming the scientific and practical challenges associated with the early clinical development of these new treatments. Specifically, several new methods for evaluating immunologically active compounds have been developed and validated at CHDR. With access to in vivo, in vitro, and ex vivo systems, we can systematically evaluate the efficacy and safety of new test compounds in the earliest stages of development.

We spoke with Matthijs Moerland, Research Director R&D lab and Immunology at CHDR, about the challenges of immune-based treatments and what best practices a CRO should employ to overcome them.

Q: How can we be sure that an immunomodulatory compound reaches its molecular target and produces the intended effect?

A: Demonstrating the pharmacological activity of a novel immunomodulatory compound in early clinical development can be challenging. Often, the physiological pathway the compound is designed to target may not be sufficiently active in healthy volunteers. At CHDR, we've developed the expertise and infrastructure to address this challenge. By using both in vivo and ex vivo systems, we can actively induce and monitor the relevant pathway. This enables us to quantify the compound's effect, even in healthy volunteers, and provide early confirmation that the drug is engaging its intended target.

Q: How do you determine the optimal dose for use in patients?

A: Determining the right dose early on is critical for successful clinical development. At CHDR, we have created, and continue to refine, innovative challenge models that simulate relevant immune responses. These models, applied in healthy volunteers, allow us to investigate the relationship between drug concentration and pharmacological effect. This data is invaluable for predicting the optimal dosing strategy in patient populations, helping to de-risk later clinical phases and accelerate development.

Q: What about unintended immune-related side effects, how are those assessed?

A: Safety is always a top priority, especially when working with biotherapeutics that may interact with the immune system. To identify any unintended immunostimulatory effects, whether due to the compound's mechanism of action, potential impurities or cross-reactivity, we use sensitive ex vivo incubation assays with human immune cells. Thanks to our strong clinical network, we have consistent access to fresh biological samples from both healthy volunteers and patients, enabling rapid and reliable safety assessments.

Q: How does CHDR bridge the gap between preclinical and clinical drug development?

A: At CHDR, we're especially focused on making the critical transition from preclinical research to clinical development as smooth and informed as possible. We carefully select, validate, and apply a broad range of biomarkers, challenge models, and clinical strategies, always tailored to the specific research question. A well-designed translational strategy not only maximizes data quality but also enhances safety for both current

study subjects and future trial participants. This knowledge-driven approach is particularly valuable in the complex and evolving field of immunology.

Q: What makes CHDR uniquely equipped for translational research?

A: CHDR was founded in an academic environment, and that scientific mindset is still deeply embedded in how we work. Our researchers are closely involved in ongoing scientific studies and maintain strong ties with academic groups and clinical experts across disciplines. This gives us access to specialised knowledge and laboratory resources far beyond what's available in most CROs. Combined with our in-house (wet lab) research facilities, this collaborative ecosystem allows us to offer tailor-made translational strategies for every sponsor.

Q: How do you measure the effects of a drug using immunological biomarkers?

A: We use a combination of in vitro, ex vivo, and in vivo methods to evaluate the effects of investigational compounds. One of our most powerful tools is our extensive library of immunological biomarkers, which we continue to expand. These biomarkers allow us to detect and quantify pharmacological activity with high sensitivity, even in the earliest phases of development.

Whenever possible, we build upon the work of the preclinical teams who first developed the compound, incorporating familiar tests and procedures into the clinical phase. While the biomarkers we use in early-stage studies may differ from those typically used in clinical settings, the key objective is always the same: to demonstrate target engagement and early efficacy. Of course, if clinically relevant biomarkers are preferred, we can include those as well.

Q: What role do in vitro models using human cells play in this process?

A: Thanks to our close ties with Leiden University Medical Center (LUMC) and other hospitals, we have direct access to fresh human biological samples from both specific patient populations and healthy volunteers. These samples can be used in vitro to assess a compound's pharmacological activity. For instance, we can measure immunological effects in whole blood, isolated peripheral blood cells, or skin samples by observing changes in cellular physiology.

However, these effects aren't always detectable under baseline conditions. If a compound is designed to act on a specific inflammatory pathway, non-activated cells may not show any measurable response. In such cases, we apply a 'challenge' model to first activate the relevant pathway, allowing us to assess the compound's effects on pre-stimulated immune cells. This targeted approach enables us to evaluate efficacy even in subtle or highly specific mechanisms of action.

Q: Finally, how would you summarise CHDR's approach to early-phase immunological drug development?

A: Our focus is on translating complex immunological mechanisms into practical, data-driven strategies that support early clinical decision-making. By integrating clinical biomarkers, immune challenge models, and close collaboration with clinical partners, we're able to design studies that provide meaningful insights, even in the most challenging therapeutic areas.

At CHDR, we aim to provide a clear and scientifically grounded bridge between preclinical research and early clinical development. By combining in-depth immunological expertise with access to advanced models and human biological samples, we help researchers gather meaningful data on pharmacological activity, safety,

and dosing, even in the earliest phases of development. This approach supports well-informed decision-making throughout the clinical development process.