Cerba Research

Transforming research, advancing health together.

# Translating Scientific Questions into Pre-Clinical Experiments

Despite extensive international efforts, infectious diseases continue to pose a large threat to global human health. The evolutionary game of cat and mouse between pathogens and their hosts is central to this ongoing battle, and understanding these interactions relies on suitable pre-clinical models.[1] Fundamental in understanding the mechanisms behind disease, pre-clinical models are (in most cases) required for the development of new and effective intervention strategies.

Knowledge of host-pathogen interactions is central to developing biomarkers and testing vaccines, drugs, antivirals, antibodies, etc. However, the translation of pre-clinical results into the clinical setting is still very challenging. Challenges often emerge during the selection of an appropriate pre-clinical model due to factors such as pathogen genetic variability, variations in immune responses, the need for specialized/customized protocols, and access to relevant strains, equipment, and expertise, especially when studying highly virulent or dangerous strains.

This article aims to explore the challenges faced by infectious disease pre-clinical research and highlight how Cerba Research's pre-clinical techniques and expertise are helping researchers face these challenges. It will also demonstrate how Cerba Research can effectively translate a research question into a pre-clinical experiment that can best answer this research question.

## Understanding Pre-Clinical Models

The importance of pre-clinical research models is reflected in the need to test the safety and efficacy of an intervention strategy before it can be presented in a clinical setting. Pre-clinical models are vital in ensuring treatments reach their full treatment potential with little to no side effects.[2] Pre-clinical models must reflect the clinical scenario as closely as possible while still accounting for the 3Rs – replacement, reduction, refinement.

## Challenges in Infectious Disease Research

### Model Selection

Ethical concerns with pre-clinical model selection pose a major challenge in infectious disease research. Animal models are fundamental in characterizing host immune responses to infectious diseases. However, before selecting an animal model for an infectious disease study, adequate ex vivo and in vitro data are required to justify the animal model selected, and ethical considerations must be addressed. Numerous factors, including welfare, regulatory guidelines, and the 3Rs, must, therefore, be thoroughly examined during pre-clinical model selection.[3]

Selecting the appropriate pre-clinical model can be daunting, often prone to misinterpretation and incorrect execution. A wide array of in vivo, ex vivo, and in vitro models exist, demanding careful consideration during the design of your pre-clinical research. Additionally, there is the challenge of locating and accessing these models, along with mastering the correct techniques essential for conducting your pre-clinical study.

Ideally, pre-clinical models should precisely replicate the relevant characteristics of the infection in its host, including pathogen-host susceptibility, disease onset, and immune responses. Researchers must ensure the availability of substantial in vitro and ex vivo evidence to underpin pre-clinical trials involving animals. Selecting an unsuitable model not only leads to inaccurate results but also results in wasted time and resources on unnecessary experiments.[4]

### Pathogen Variability, Access to Relevant Strains, and Customizing Pre-Clinical Testing

Access to relevant strains for studying pathogen resistance can also be challenging. Certain strains can be hard to source and require unique expertise and containment. Along with this, assessing pathogen variability is challenging due to limited information on trait susceptibility and pathogen variability, which reduces reproducibility.

The design of the experiment is extremely important to ensure that it produces relevant and reliable data. Understanding what the research question is and how to customize your experiment to best answer this requires a high level of knowledge and expertise in pre-clinical testing.

### BSL-2/BSL-3 Pre-Clinical Studies

Performing research involving infectious diseases demands specially designed and constructed containment facilities operated by highly trained staff. This is vital for safeguarding staff members and averting potential environmental contamination from biohazards. Maintaining and operating these specialized containment laboratories requires substantial investment, which, as a consequence, may result in restrictions on required testing of treatments during development.

## Cerba Research NL's Expertise in Pre-Clinical Research

Cerba Research NL's location, Schaijk, is a leader in pre-clinical research, offering a diverse range of services to test the efficacy and safety of treatments for infectious diseases, along with biomarker discovery. Our vast team of in-house experts have extensive experience in studying many viral targets, from SARS-CoV-2 to Poliovirus, and are committed to developing innovative models to determine efficacy (and, if needed, antiviral resistance developments) for a wide variety of therapeutic targets.

**Cerba Research NL's Schaijk location can help you overcome pre-clinical challenges for more insightful results and can assist you from the very beginning of your pre-clinical process up until the clinical testing phase 3, which can also be conducted in Cerba Research NL.**

### In vivo Models

We have numerous animal models available, including mice, hamsters, rabbits, guinea pigs, cotton rats, ferrets, and others. Our services encompass diverse in vivo assays for evaluating vaccine and antiviral pre-clinical efficacy, treatment pharmacokinetics, and comprehensive pathology assessments. Our commitment to ethical research is reflected in our constant efforts toward model development, and we are always ready to create customized models that adhere to the principles of the 3Rs.

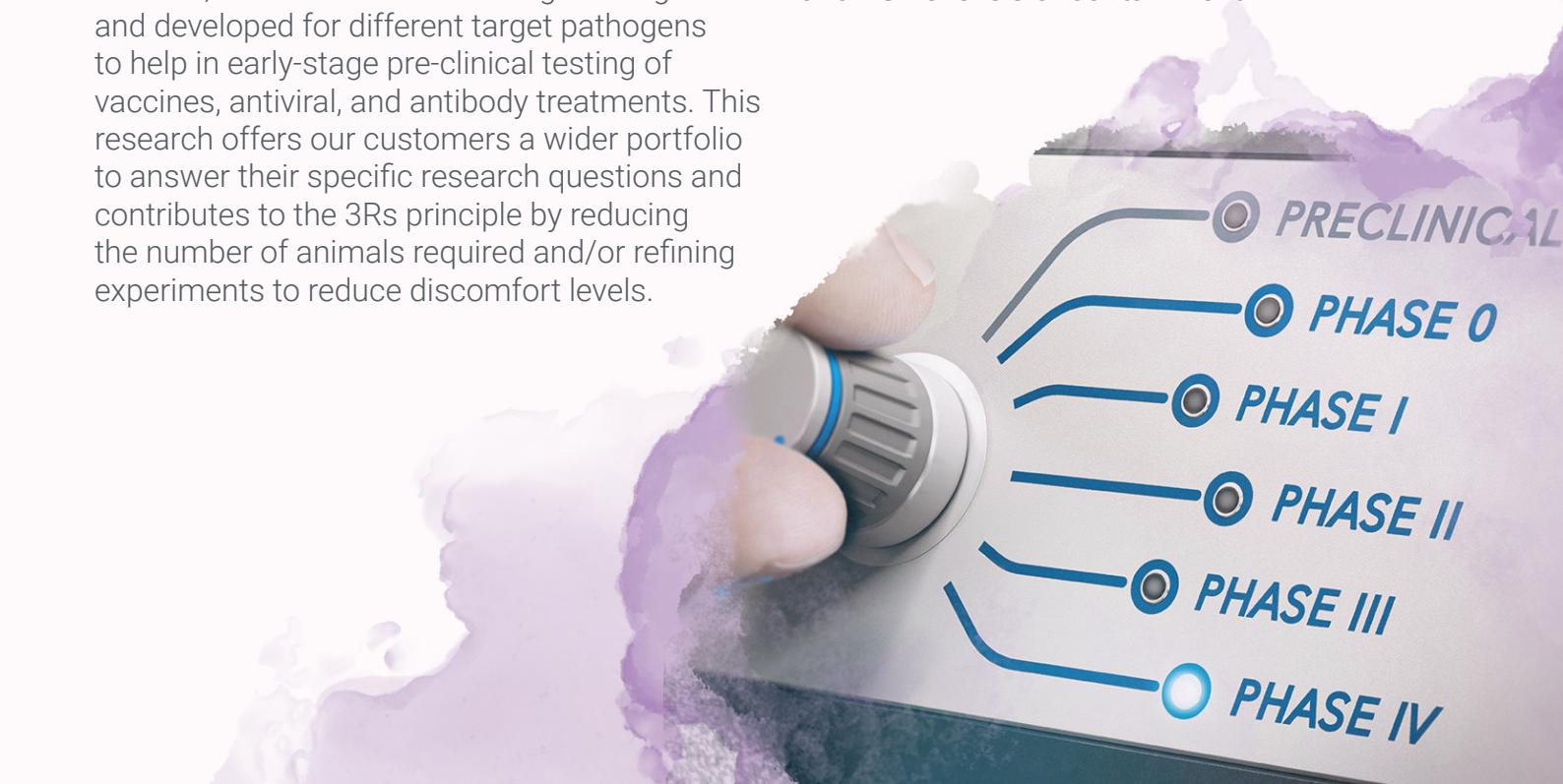
### Ex vivo Models

Ex vivo pre-clinical models may offer a reasonable intermediate solution to the challenges that arise with in vivo and in vitro models. At our Schaijk Cerba Research NL location, ex vivo models are being investigated and developed for different target pathogens to help in early-stage pre-clinical testing of vaccines, antiviral, and antibody treatments. This research offers our customers a wider portfolio to answer their specific research questions and contributes to the 3Rs principle by reducing the number of animals required and/or refining experiments to reduce discomfort levels.

Cerba Research offers a variety of in vitro/ ex vivo models for early-stage efficacy testing (including the 3Rs). We continue to work on developing models that are applicable to various viral and bacterial targets and offer a diverse range of read-outs: virus titers, antibodies, pathology, virus copies, and so on.

### BSL-2 and BSL-3 facilities

Thanks to our BSL-2 and BSL-3 facilities, operated by highly qualified technical and biotechnical staff, we can offer complex experiments with infectious diseases to test effective intervention strategies. Cerba Research NL's Schaijk location continues to develop research techniques using a wide variety of models for numerous pathogens at both BSL-2 and BSL-3 levels of containment.



## Conclusion

Cerba Research's state-of-the-art techniques and vast expertise can help you overcome pre-clinical challenges and provide models that best suit your study's unique requirements.

Dedicated to advancing the field of infectious disease research, our models and/or assays can be tailored to your study's requirements, and with high flexibility, we can assist both small biotech companies and large pharmaceutical firms. Cerba Research NL's Schaijk location is your trusted partner for designing appropriate pre-clinical models.

From pre-clinical to phase 3 trials, we can assist you in all stages of vaccine or antiviral treatment development. To kick-start your pre-clinical research, whatever the stage, contact Cerba Research NL today, and our experts will be in touch to help you with any challenges you can face throughout your study.

## References and Further Reading

1. Sarkar, S. and Heise, M.T. 2019. Mouse models as resources for studying infectious diseases. Clinical therapeutics. 41(10), pp.1912-1922.

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