# Title of Challenge: Virtual Infectious Disease Research

## Background

Control of infectious diseases remains a key priority in human and veterinary medicine. The World Health Organisation (WHO) estimates that respiratory and diarrhoeal infections, HIV, tuberculosis, malaria and measles are responsible for 90% of human deaths (1) and a plethora of animal pathogens threaten food security at a time of fast accelerating demand.

Many different species, from non-vertebrates to rodents and non-human primates, are used to study infection, host response and efficacy of drugs and vaccines. Typically, animals are infected with an infectious agent to test therapeutic efficacy, resulting in symptoms of differing severity. A reliable *in silico* model of infection and the host response would result in the reduced use of animals. Ideally such a model would provide the foundation for future models which would help predict the efficacy of drugs, vaccines and other treatments.

There is a focus across the biosciences on using the availability of large datasets to exploit computational tools to generate results that are not obvious from single experiments. 'Virtual' data for infectious diseases includes diverse information relating to i) the repertoire, sequence, transcription, translation, regulation and function of pathogen and host genes, ii) the host immune response, iii) the impact of modulation of pathogen and host functions by genetic modification, drugs or vaccines on the outcome of infection, and iv) the temporal and spatial migration, interactions and activities of pathogen and host cells or their products. The challenge is how to use this data to develop testable predictions, particularly when such data often reflect an average within a tissue at a specific time interval and may therefore not fully reflect events at a finer spatial and temporal level.

While complex mathematical models are being used to model spread of infection and immune response throughout human populations, it is less common for models to be used to study within-host dynamics of infection and response. The focus of this Challenge is on using *in silico* methods to model infection and the host response in an individual animal. The aims are to employ *in silico* methods to i) reduce the use of animals, ii) model *in vivo* pathogenesis and protection, and iii) model the potential impact of drugs or vaccines to accelerate the development of treatments to infectious diseases.

## 3Rs benefits

Animal use in a typical rodent efficacy study for new antibiotics or vaccines can involve approximately 100 animals per candidate. The animals are infected with the pathogen after vaccination or treated with the drug of interest. Untreated controls are always used. The resulting disease in control animals and those in whom the vaccine or drug are ineffective can cause severe suffering. The use of *in silico* approaches to study disease biology and predict efficacy would reduce the number of animals used.

## Need for collaboration

Expertise in immunology, microbiology, mathematics, modelling and software design is required to deliver a platform that can model events leading to pathology and protection. Collaboration across academia and industry would be welcome.

## Overall aim

To develop a virtual platform that models infection and the host response to pathogen assault for basic research and enhances new target development in infectious diseases.

## Key deliverables

### Phase 1

- Identify chosen host and pathogen on an evidence basis with justification and scientific merit along with projected 3Rs impact
- Propose infrastructure for the platform outlining the integration of animal based evidence and literature with a mathematical and computational approach
- Demonstrate the level of predictivity of the system, including the limitations
- Develop a simple prototype of how the information will be assimilated and presented to the user
- Provide a strategy for validation of the model in Phase 2 including key criteria that will define success
- Provide evidence of collaborative expertise, including wet scientists, to progress into Phase 2
- Consideration of a suitable business model to disseminate the platform including potential market

### Phase 2

The successful Phase 2 candidate will have delivered a proof-of-concept model for their chosen pathogen and host during Phase 1. Certain deliverables will be influenced by the Phase 1 outcome, but the common requirements will be:

- The delivery of a virtual platform, including predictive tools, quantitative techniques and mathematical models that will describe and predict the spread of infection and the host response for a single, or combination of, pathogens

And/or

- A model to determine how vaccines or adjuvants influence the host response

**The model should be able to:**

- Predict/ biology of the pathogen in the host
- Detail the internal microbial processes of the pathogen
- Track the dissemination of the pathogen within the host
- Describe the interaction of the pathogen with the host immune system
- Identify new and improved diagnostic and therapeutic targets. There should also be the capability to detect and test novel responses associated with resistance
- Demonstrate how the model would be used in practice to accelerate the transition into the clinic of new diagnostic and therapeutic modalities

**The project management team should provide evidence of:**

- Consultation with industry and academic experts in this area to access the data sets needed to deliver the brief
- The needs and market of the end user

**The consortia should deliver:**

- A system that will be taken up across all areas in the bioscience sector
- Strategy for commercialisation and uptake

**What we don't want**

- Models for measuring the spread of pathogens through populations

## Sponsor contributions

### Phase 1 & 2

The NC3Rs will provide funding for the Challenge and also access to experts and networks in both the academic and industrial sectors.

## Duration

Phase 1: six months. Phase 2: up to three years

## Budget

Phase 1: up to £100K. Phase 2: up to £1 million

## Sponsor

The NC3Rs