HUMAN CHALLENGE TESTING
CLINICAL RESEARCH SOLUTIONS
DE-RISKING
Faced with increasing pressures on timelines and budgets, clinical research practices need to continuously evolve in order to ensure pipeline development remains effective and efficient. To meet this demand, SGS has set up a unique, European-based, Human Challenge testing facility enhancing the existing services offering for its clients in the fields of infectious disease and vaccine development.

The challenge model has been proven to:

- enable accelerated development of pipeline compounds
- provide robust efficacy data for candidate selection
- effectively translate animal data to human endpoints and to relate healthy volunteer data to field outcomes

# PROGRAMS

## CHOOSING A RELIABLE CLINICAL PARTNER

SGS is a leading life sciences CRO providing clinical research and bioanalytical testing with a specific focus on early stage development and biometrics. Delivering solutions in Europe and in the Americas, SGS offers clinical trial services (Phase I to IV) encompassing full early phase drug development, consultancy, clinical project management and monitoring, biometrics, PK/PD modeling & simulation and regulatory & medical affairs services.

## BENCHMARK CLINICAL PHARMACOLOGY FACILITITES

SGS’s clinical pharmacology unit is located in Antwerp, Belgium with a total of 88 hospitalization bed. The Clinical Pharmacology Unit (CPU) has successfully passed several US FDA inspections during recent years. For optimized early phase clinical trials, SGS features:

- biosafety Level 2 quarantine facility
- GMP pharmacy for on-site formulation
- full eSource clinic automation (EDC) including sample tracking for safety lab data

## EARLY CLINICAL TRIALS EXPERTISE

For over 40 years, SGS has built up a unique expertise in early phase clinical trials including First-In-Human studies, QT/QTc prolongation, radio-labeled 14C ADME & PET scan trials, human challenge testing, biosimilars and complex PK/PD studies.

For a faster, targeted patient recruitment across the Americas and Europe, clients can rely on SGS’s:

- extensive database of investigators and key opinion leaders with therapeutic expertise in Infectious Disease
- specific skill-sets to successfully execute studies in HIV, HBV / HCV, vaccines, vaccine delivery (devices) and respiratory diseases
- a favorable regulatory environment in Belgium with very short Phase I trial approval timelines (14 working days)
DEVELOPMENT BENEFITS

- Smaller sample size required to obtain meaningful results. The challenge model requires substantially lower numbers for PoE than for community-based studies and naturally acquired infection.
- Predictions of effectiveness in later field studies (de-risking).
- Collection of data in controlled environment.
- Reduced need for extensive Phase II trials, reducing timelines and associated costs and negating the reliance on high incidence or prevalence of infective agents in seasonal diseases e.g. influenza, RSV, hRV, other.
- Facilitates the development of prophylactic and therapeutic small/large molecule drugs and vaccines, as well as providing early safety assessments in healthy volunteers.

The challenge model is not only helpful as a proof-of-concept for effectiveness, but also as proof-of-mechanism for new targets e.g. in asthma, and is increasingly being employed outside of academia to de-risk programs and pipelines.
SGS’s hospital-embedded, Human Challenge Unit (HCU) offers a 20-bed, en-suite or ward-style, quarantine facility that is Biosafety Level 2 compliant. The quarantine unit is equipped according to international, benchmark standards with the latest technologies for remote monitoring as well as HEPA-filtered, negative pressure HVAC systems. Volunteers are provided with either individual, en-suite or ward-style cubicles. The challenge facility is served by a dedicated clinical trial laboratory equipped with a flow cabinet, acid cabinet, dedicated work space and workflows to handle specific (viral) cultures, using also HEPA-filtering and an airlock system.

SGS has developed a newly emergent, wild-type strain of influenza A for use as a challenge agent in healthy volunteers studies. A/Belgium/4217/2015 [H3N2] agent has been manufactured to (c)GMP and is approved for use as a challenge agent in studies with the capacity to demonstrate early efficacy for novel influenza drugs and vaccines. Challenge agent manufacture was undertaken by SGS in conjunction with an international CMO and a world leading academic institute to ensure regulatory guidelines compliance with:

- GMP / GLP
- ICH-GCP
- US IND (FDA) and EU IMP (EMA)

Phylogenetic Lineage (NJ analysis)

- Phylogenetic analysis of the SGS A/Belgium [H3N2] challenge virus shows it to retain 100% homology to the original wild-type isolate
- A/Belgium/4217/2015/(H3N2) = 3C.3b - no adaptive changes were evidenced following a single production round in embryonated eggs relative to original virus HA sequences

SGS conducts human challenge studies in order to efficiently and effectively develop and evaluate new-generation vaccines and treatments, including influenza and RSV. New approaches outside of large-scale field trials must be considered to provide early evidence of proof-of-principle in humans. Our viral challenge testing facility provides the means for clients explore these new options.
**THE HUMAN CHALLENGE MODEL DESIGN (VACCINE)**

**A LARGE SCOPE OF INVESTIGATION**

Human Challenge Tests provide for a carefully controlled, systematic, and efficient method in which a number of outside variables can be controlled or even eliminated, with the subjects continuously monitored in a sequestered environment.

SGS offers the unique advantage of extensive experience over several decades with a wide range of pharmacological techniques and interventions.

SGS and CPU / HCU specialist provisions include:

1. different challenge techniques (e.g. virus, histamine, LPS) in both healthy volunteers and patient populations
2. prolonged periods of quarantine and intense sampling regimens
3. screening large volunteer populations for difficult IC/EC or other protocol criteria
4. laboratory assays with complex sampling and/or preparation requirements for biomarker analysis (virus, protective antibodies, cellular immunity (PBMC), other)

The challenge model also enables detailed assessment of immune parameters that may help in identifying immunological correlations of infection and disease.
A randomized, placebo-controlled, double-blind Phase 2a trial was designed to assess the efficacy and safety of a novel mAb in healthy human volunteers challenged with a 2009 pandemic strain of H1N1 influenza virus.

**KEY CHALLENGES**
- Identifying a susceptible cohort (60-80 HVs - HAI <10)
- 10d isolation of subjects within a specialised HCU
- Intense NP swab SoA / intense pre-screen PCR schedule

**OUTCOMES**
- A total of 332 subjects were screened; 31 were enrolled - 20 subjects met the definition of laboratory-confirmed infection (mAb, n=13; and placebo, n=7) (AR = 62%)
- vAUC for mAb treated subjects was reduced by 92% (p=0.019); peak viral load was reduced by 2.2 logs (p=0.009) (interim result data @ 6 months)
- mAb was generally safe and well tolerated. There were no drug-related discontinuations or serious adverse events (SAEs) reported in the study
- Based on the interim results - the comparative portion of the trial was ended.

Read about SGS’s Infectious Diseases Clinical Trial Solutions
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**CONTACT INFORMATION**

**EUROPE**
+ 32 15 27 32 45
clinicalresearch@sgs.com

**NORTH AMERICA**
+ 1 877 677 2667
clinicalresearch@sgs.com

WWW.SGS.COM/CRO

FOLLOW US ON LINKEDIN
www.sgs.com/linkedin-life

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