PHARMACODYNAMIC CLINICAL TRIAL MODELS

DRUG DEVELOPMENT SOLUTIONS

SGS

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SGS Life Science Services has 35 years of experience as a contract service organization providing integrated solutions from preclinical activities to phase I-IV clinical trials, bioanalytical, quality control testing, biosafety, and biologics characterization.

Serving the pharmaceutical, biotechnology and medical device industries across Europe and North America, SGS operates two state-of-the-art clinical pharmacology units and the world's largest network of GMP/GLP compliant laboratories. We have more than 1,500 employees and provide a complete range of services along the pharmaceutical development process.

With innovative study designs, optimal clinical and bioanalytical facilities, tailored biometrics services and strong regulatory intelligence, SGS can significantly improve your drug development timelines and decision-making processes.

MAKING THE RIGHT DECISION

Pharmacodynamic models within the early phase clinical trial development process, along with safety assessments, are the key parameters to evaluate the potential activity and efficacy of a compound. SGS has the expertise and experience to select, develop and implement the appropriate PD model that will enable the sponsor to safely bridge Phase I trials with later phase studies encompassing proof of concept, proof of mechanism, and proof of principle data. Most of these PD models can be performed during the First in Human trials in healthy volunteers or patients.

SGS clinical pharmacology experts have been working on numerous PD models across therapeutic areas with specific expertise in CNS, Cardiovascular and Respiratory. SGS is highly flexible and capable of implementing various complex techniques in a minimum amount of time, the list below are examples of the techniques SGS can deliver:

PD MODELS

ANESTHESIA
- Acceleromyography
- End-tidal CO_2 clamping
- Opioid challenge

CARDIOVASCULAR
- Platelet aggregation
- Thromboelastography
- Tilt table
- Impedance cardiography
- Echocardiography (TT & TE)
- Exercise test
- Vascular plethysmography

CNS
- Cerebral spinal fluid sampling
- *In vivo* CSF Aβ and sAPP turnover using C-13 Leucine
- Qualitative and quantitative EEG
- Holter-EEG
- Psychometric tests : various testing batteries, questionnaires and scales available
- Scopolamine challenge testing
- Ocular blood flow (migraine)
- Body sway
- PET
- MRI
- Nasal biopsies for PD markers olfactory epithelium
- Car driving model (real life and simulator)

DERMATOLOGY
- Photosensitisation
- Skin bioavailability (biopsies-blisters)
- Vasoconstriction assay for corticosteroids
- Small plaque assay (POC)
- Skin blister
- Photographic captures
- Chromametry
- Echography

GASTROINTESTINAL
- Dual electrode gastric pH
- Gastroscopy

HEMATOLOGY
- Bone Marrow Extraction
- ROI intensity readings
- Cr-51 labelling red blood cells

IMMUNOLOGY
- Vaccines : serum conversion
- Wheal and flare planography
- Antihistaminic effect markers
- PBMC harvesting

METABOLIC
- EnteroTest for hepatobiliary metabolite testing
- Oral glucose tolerance test
- Blood and serum markers requiring special sample preparation
- Hyperinsulinemic Euglycemic glucose clamping
- Graded Glucose Infusion
- Glucagon Induced Glycemic excursion
- Matabolic Rate testing (O_2 and CO_2 consumption under hood)
- Muscle biopsies (fractional synthesis rate)

NEPHROLOGY
- Glomerular filtration using Cr-51 EDTA
- Renal Blood flow
- PK under hemodialysis

OPHTHALMOLOGY
- Intraocular blood pressure & flow
- Ocular pressure
- Saccadic eye movements
- Standard tests
  - Slit lamp
  - Tonometry
  - Autorefractometer
  - Visiotest
  - Pupillometry

PAIN
- Cold pressor test
- UVB skin burn model
- Nociceptive and Hoffmann reflex measurements
- Quantitative Sensory Testing
- Intradermal capsaicine testing
- Migraine:
  - Ambulatory / Hospitalization
  - Crisis triggering

RESPIRATORY

- Spirometry
- Asthma : Methacholine challenge, exercise challenge
- COPD: whole body plethysmography
- Sputum induction : slides, cytospins and mRNA
- Bronchoalveolar lavage

UROLOGY

- Erectile dysfunction (Rigiscan)
- Bladscan

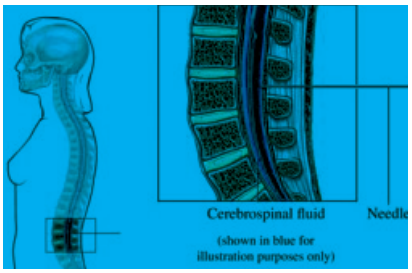
OTHER

- *In vivo* LPS challenge for sepsis and related biomarkers
- Interferon challenge test
- Stress oxidative tests
  - UV skin exposure
  - Hyperoxia
  - Ischemia / reperfusion test
- Fibroscan in hepatic disease
- Viral Challenge/Innoculation Trials

PD MODEL EXAMPLES

HYPEROXIA

- Principle
  - To create an oxidative stress in lungs
  - Challenge test for anti oxydative compound
  - Inhalation of 100 % Oxygen for 1 hour
- Coupled to cardiac impedancemetry (measurement of cardiac index) and vascular plethysmography (measurement of vascular resistance)
- Exhaled breath condensation collection
- +/- Induction of sputum collection



CSF SAMPLING

- Suspected Poor Correlation between blood and CSF (PK/PD)
- Direct PK/PD assessment in CNS compartment necessary for substances extensively metabolised in peripheral blood compartment
- Speed up clinical development by immediate detection of BBB penetration or PD effect on CNS specific biomarkers (e.g. Histamine/telehistamine, Amyloid and associated proteins...)
- Spinal Catheter for serial CSF sampling to assess PK/PD profile correlations in the effector compartment

VASCULAR PLETHYSMOGRAPHY

- Principle
  - Measurement of vascular resistance
  - Used in academic hospitals
  - Evaluate the efficacy by measurement of peripheral resistance in patients with HTA and treated by α blockers or Calcic inhibitors or angiotensin II antagonist or ACE inhibitors

CONTACT INFORMATION

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WHEN YOU NEED TO BE SURE

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