



TRIAL FORM SUPPORT

# TFS and Karolinska

Your trusted partners in early  
clinical development



### Knowledge and experience

Aside from the technical resources of Karolinska, TFS also provides clients with the hospital's most valuable resource — its collective knowledge and experience. This way the trial design can be evaluated and refined by experts in the therapeutic area before the trial starts.

# A unique resource for early clinical development

## About the TFS Research Unit

The TFS Research Unit is located at Karolinska University Hospital in Stockholm, Sweden. The unit is backed by the combined industrial and academic expertise of both TFS and Karolinska. Together, our aim is to ensure the success of early clinical development in Phase 0/1 trials. That means ensuring the safety of participants, accuracy of results and compliance with regulations — all delivered on time and on budget.

Northern Europe has a tradition of close partnerships between academia and the healthcare industry. The TFS Research Unit at Karolinska University Hospital is a prime example of that cooperation. Combining the expertise of Europe's top medical university with Europe's top clinical CRO provides an unequalled resource throughout the early clinical development investigation.

The facility itself offers the highest degree of professionalism and care. Our clinical trials are supported by the technical resources of Karolinska including its acclaimed PET (Positron Emission Tomography) centre. TFS can also provide access to Karolinska's top experts in all major therapeutic areas. They can be enrolled in a scientific review board to guide and advise on the clinical development outline and study design.

Our goal at TFS has always been to provide the best service, technical resources and knowledge for our clients. Our Research Unit at Karolinska is one more way in which we are delivering on that promise.

Take a few minutes to discover the added benefits TFS can offer clinical trials in its early development stage.

## About Karolinska University Hospital

The world-renowned Karolinska University Hospital is one of Europe's largest medical university hospitals. The hospital has 1,600 beds and is visited by 1.4 million patients each year. It is also Sweden's largest centre for medical training and research, employing 2,100 researchers assisted by 200 post-graduate students annually. Virtually all clinical research at Karolinska University Hospital is carried out in close collaboration with the Karolinska Institute. Research is conducted within all clinical disciplines — from basic to applied research.

Since 1901, the Karolinska Institute has been honoured with awarding the Nobel Prize in Physiology or Medicine. This has given the Karolinska Institute an invaluable contact network throughout the medical scientific community.



# From first-in-man through proof of concept trials

## Facility

The TFS Research Unit is located in the Karolinska Trial Alliance (KTA) at Karolinska University Hospital in Stockholm, Sweden. The unit is a unique resource for early clinical development trials in Phase 0/1 as it combines the strengths of both partners. TFS maintains a staff presence in the unit at all times. To further ensure that our quality standards are maintained, all operational work is conducted in strict accordance with our Standard Operating Procedures (SOPs). This includes continuous training of the investigational staff.

The Research Unit is fully equipped with:

- 24 beds for 24-hour studies and 30 beds for over-day studies
- On-site food preparation and dietary consultation
- Security and surveillance equipment to ensure study volunteers' safety
- Dedicated area for sponsor/monitoring visits
- Modern examination rooms and lab facilities
- Hospital lab next door
- -80° C freezer with continuous monitoring and refrigerated centrifuges
- Access to Hospital Pharmacy with capacity to prepare study medication

- State-of-the-art electrocardiogram (ECG) equipment
- Holter and telemetry equipment
- Secured facilities for trial medication storage and accountability
- Computerized network for retrieving rapid lab results
- Computerized database of compliant, healthy volunteers
- Proven record for quality data and surpassing sponsor enrolment goals
- Trained, experienced research staff
- Consistent history of excellence in sponsor audits
- Successfully inspected by Swedish Medical Products Agency in March 2008

## Services

We offer early clinical development services from first-in-man through proof of concept trials in compliance with national and international regulations, valid SOPs, and ICH guidelines. The Research Unit assists and supports clients with different services including preparation of study outline, protocol development, project planning, administration, CRF development, clinical performance, monitoring, data management, biostatistics and medical writing. The Research Unit can also provide scientific input by drawing on the extensive network of specialists associated with Karolinska University Hospital.



The focus of the Research Unit is to conduct trials for:

- First-in-man administration (single and multiple dose)
- Imaging studies with PET, PET/CT and MRI/Micro-dosing studies
- Food and drug interaction studies
- Special patient population studies

Please contact us to discuss other type of studies.

### **Scientific Advisory Board**

Aside from the technical resources of Karolinska, TFS also provides clients with the hospital's most valuable resource – its collective knowledge and experience. We can offer your team access to Karolinska's top experts by arranging a review of your study's objectives and outline by the hospital's Scientific Advisory Board. This way the trial design can be evaluated and refined by experts in the therapeutic area before the trial starts.

# Shorten the time to proof of concept

## Positron Emission Tomography studies

The TFS Research Unit offers the possibility to perform PET studies. PET can provide patient data early in the clinical drug development stage and therefore shorten the time to proof of concept. PET contribution to early drug development studies includes:

- Monitoring drug effect, including dose-response evaluations where the occupancy on a receptor system is monitored at increased doses and at different times after dosing
- Labelling a potential candidate drug to obtain organ PK, including studies of drug entry over blood–brain barrier
- Micro-dosing, providing an early opportunity to test the candidate drug in man

TFS can assist with the development of labelling and validation for new PET tracers. Development time for labelling procedures, including Good Manufacturing Practice documentation, depends on the molecule. That's why planning and coordination should start as early as possible.

Between 80% and 90% of suggested organic molecules can be labelled with  $^{11}\text{C}$ . This offers the possibility to involve the PET team in later stages if required.

## Imaging centre capabilities for clinical research

The TFS Research Unit collaborates closely with the PET centre at Karolinska University Hospital in Stockholm, Sweden and with

the Biomedical Research Park in Barcelona, Spain. These two PET centres offer functional and molecular imaging services applied to clinical research within the major therapeutic areas such as CNS, oncology, cardiology and inflammatory diseases. The latest state-of-the-art equipment for imaging is available for clinical research at the centres, for example PET Siemens ECAT EXACT HR + scanner, Siemens/CPS High Resolution Research Tomograph (HRRT), Siemens Biograph TrueV (4 Ring HighRez PET, 64 slice CT), PET-CT GE Discovery ST hybrid scanner, Signa 1.5T MR GE scanner, Online Arterial Blood Sample System and Near implantation of 3T MR.

Some common uses of imaging technology include:

**Oncology:** diagnosis, monitoring treatment response and radiotherapy planning

**Neurosciences:** cerebral flow and activation studies, characterization of dementias and psychiatric disorders, early diagnosis of Alzheimer's disease and neurotransmitter–neuroreceptor studies

**Cardiology:** myocardial viability identification

Together with our partners, we have the sophisticated image processing and mathematical tools required to extract all the possible information from PET and MRI scans. They enable, for instance, the combination of scans conveying complementary information (multimodal image fusion), the determination of several physiological parameters (neuroreceptor concentration,



## Positron Emission Tomography

The TFS Research Unit offers the possibility to perform PET studies at Karolinska University Hospital or at the Biomedical Research Park of Barcelona. PET can provide patient data early in the clinical drug development stage and therefore shorten the time to proof of concept.

metabolic rates, etc.) or the performance of statistical analysis directly on functional neuroimages (Statistical Parametric Mapping).

## Radiopharmaceutical Laboratory

The radiopharmaceutical laboratory is equipped with a cyclotron (able to produce Fluorine-18, Carbon-11, Nitrogen-15 and Oxygen-15), shielded Hot Cells, automated modules especially designed for the synthesis of PET radiotracers and state-of-the-art quality control equipment. This allows the manufacturing of radiopharmaceuticals in a GMP-controlled and validated environment.

A wide range of radiotracers are already available, for example [18F]FDG, [18F]FMISO, [11C]Methionine, [11C]Acetate, [11C]PK11195, [11C]Raclopride, [11C]Flumazenil, [11C]Choline, [15O]H<sub>2</sub>O, [13C]NH<sub>3</sub>. It's also possible to adapt procedures for the manufacture of already known radiotracers or to design and automatically produce new procedures of synthesis and formulation.

## Preclinical Image Department

We can provide the facilities and equipment to conduct preclinical PET studies in rodents. The equipment can be used for both longitudinal and transversal studies, as well as to study the pharmacokinetics of the radiotracers used. The preclinical image

department features:

- MicroPET scan
- Level II biosafety cabinets
- An area for microsurgery and dissection
- A cell culture laboratory allowing *in vitro* uptake assays
- A system allowing autoradiography images after *in vivo* or *ex vivo* administration of a radiotracer
- Anaesthesia by isoflurane inhalation
- An animal facility equipped with cage-individualized ventilation

This department also has access to an optical imaging device for bioluminescence that allows the monitoring of cellular populations *in vitro*, as well as grafted *in vivo*.



### Extended Academic Collaboration

TFS Trial Form Support and Karolinska University Laboratory have a strategic partnership agreement with regard to laboratory services for early clinical development.

# The Karolinska advantage

## World-class resources

The Karolinska University Laboratory is closely associated with the Karolinska Institute. Most services at Karolinska University Laboratory focus on analysis, interpretation and advice to serve clinicians who are in direct contact with patients. The Laboratory is divided into eight departments:

- Local Healthcare and Pre-analysis
- Clinical Chemistry
- Clinical Microbiology
- Clinical Immunology/Transfusion Medicine
- Clinical Pathology/Cytology
- Clinical Pharmacology
- Clinical Genetics
- Centre for Inherited Metabolic Diseases

This breadth of clinical capability makes the Karolinska University Laboratory one of the largest and most complete clinical laboratories in the world. Each year the lab's 1,700 employees perform 20 million analyses for some 40,000 clients.

## Cutting-edge technology

The demand for quality data communicated rapidly and accurately is growing. At TFS we meet this challenge head-on with fully automated management of referrals and test results. Not least, this

applies to advancements in clinical chemistry where we use laboratory robotics in analytical systems.

The Karolinska University Laboratory's Department of Pharmacology is dedicated to the analysis of therapeutic and abused drugs. The department is recognized globally for its unique expertise in pharmacokinetics and pharmacogenetics. The laboratory specializes in the selective and sensitive methods and has invested in the latest technology for LCMS analysis. We are able to set up new methods in approximately four weeks. Today, over 100 methods are in routine use. All work is performed meeting GLP requirements. Karolinska University Laboratory is accredited according to international and European standards.

The Karolinska University Laboratory has established a Centre for Clinical Trials with the objective to offer an optimal service in clinical trials and research with focus on GCP. The centre is interacting on a daily basis with the TFS Research Unit and can provide a complete solution with specific requisition forms, sampling material, logistics, instruction manuals and electronic report of results.

# With you all the way

## **Operational Services**

Operational services are fully integrated with the TFS Research Unit and include support from regulatory submission to the final clinical study report. These operational services are an essential complement to the practical clinical performance by the research staff at the unit.

## **Regulatory Affairs**

Regulatory Affairs has extensive experience in managing all aspects of regulatory services. The services include regulatory advice, preparation of documentation, submission and liaison with competent authorities. Regulatory Affairs has a long and productive track record in liaison with many of the most respected competent authorities throughout Europe, USA and Asia.

## **Clinical Operations**

Clinical Operations has extensive experience in managing all aspects of early clinical development in Phase 0/1. The services include all the necessary stages from the study outline to the final clinical study report and its publication including the outline, planning, coordination, management, performance, termination and reporting of the trials.

## **Clinical Data Management (CDM)**

CDM efficiently manages all aspects of data management ensuring accurate data and timely completion of the clinical database. CDM has experience in working with all stages of data management, electronic data capture, DataFax and web-based trials. Databases and software are validated in compliance with European, ICH and FDA standards.

## **Biostatistics**

Biostatistics manages all the statistical issues related to clinical trials. Our validated software and computer systems are approved by regulatory authorities and are compliant with the appropriate ICH guidelines, particularly E9 (Statistical Principles for Clinical Trials) and E3 (Structure and Content of Clinical Study Reports), thereby enabling safe and accurate analyses. All analyses are performed using the latest applicable versions of SAS® programs.

## **Drug Safety**

Drug Safety has extensive experience in managing all aspects of national and international drug safety procedures in early clinical development. The services include all the different stages, from serious adverse event handling to Periodic Safety Update Reports (PSURs) and Annual Safety Reports for health authorities and ethical committees.

### **Cost effective**

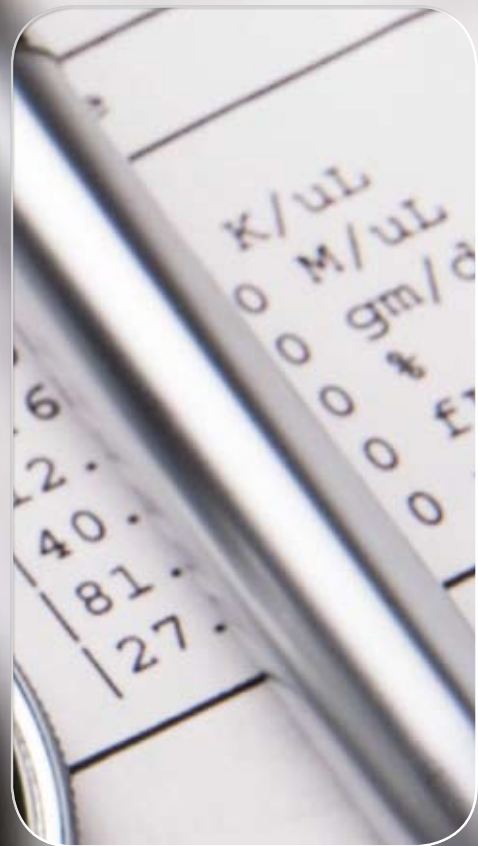
The combination of scientific competence, well-designed studies and a stable financial platform is a prerequisite for drug development today. These are areas in which both TFS and Karolinska contribute for the benefit of Phase 0/1 studies. Moreover, the Research Unit can offer these combined strengths at a price that is significantly lower than that offered by less prestigious institutions.

### **Medical Writing**

Medical Writing has extensive experience in clinical research and in writing medical documents for large pharmaceutical firms as well as biotech and medical device companies. Medical writers are qualified and experienced. They compile, organize, write, edit and produce a wide range of medical or scientific documentation required to support product development efforts.

### **Quality Assurance**

Quality Assurance is an independent unit within the company. It assures that clinical trials are planned, conducted and reported in compliance with regulatory requirements, Standard Operating Procedures (SOPs) and ICH guidelines. The unit assists, guides and controls all quality aspects of the clinical trials from the early study outline to the final reporting of the trial results.



## About TFS Trial Form Support

TFS Trial Form Support International is a full-service clinical CRO with headquarters in Lund, Sweden. Since 1996, TFS has provided the life science industry with a wide range of clinical contract services. TFS is currently conducting pan-European clinical trials in 20 countries. Over 470 highly competent employees are working in 16 countries across Europe, India, Japan and the USA.



**TRIAL FORM SUPPORT**

## Contact TFS Research Unit

Karolinska University Hospital  
TFS Research Unit A2:01  
Karolinska Trial Alliance  
SE-171 76 Solna, Stockholm  
SWEDEN

Tel: +46 8-440 76 00

Fax: +46 8-440 76 01

E-mail: [pharmacology.unit@trialformsupport.com](mailto:pharmacology.unit@trialformsupport.com)

[www.trialformsupport.com](http://www.trialformsupport.com)