profil
ANSWERS FOR DIABETES

Profil

The leading CRO in metabolic research

Your partner for clinical trials in diabetes and obesity

As a full-service CRO for early phase clinical trials focused on diabetes and obesity, Profil provides our clients with the scientific and regulatory expertise and services for successful drug and device development.

Profil shares your goals: developing successful treatments for diabetes, prediabetes and obesity and improving the quality of life of people with these conditions. As a full-service CRO, we will help you find critical answers for the development of compounds, devices and treatment methods. Our scientific experts use a wide spectrum of sophisticated experimental methods and will assess and optimize your study designs. If desired, we can also present your study results to regulatory authorities or the medical community.

Over 15 years of clinical trial experience

Founded in 1999, Profil has grown to become a unique entity: a partner for clinical trials with an excellent record for professional conduct and scientific expertise in research on diabetes and other metabolic diseases. The results of trials conducted with us have been pivotal in the development of diagnostic technologies and therapies for diabetes and obesity. We have been involved in the development of many of the major currently available anti-diabetic compounds. The dedication of our team of scientists and clinical workers is unquestionable. With several hundred papers in peer-reviewed journals, Profil's experts have gained international acclaim for contributions to the understanding of diabetes, obesity and nutrition, and for advances in medical technology.

Full-service support for clinical trials

What do we mean by "full-service CRO"? Profil is certified according to ISO 9001:2008. We have a vast volunteer database of over 30,000 people, a dedicated regulatory department, a fully GMP-certified pharmacy, two in-house clinics, a clinical development consulting team and a statistics and data management team. Between our two clinics we have 80+ beds – an ideal capacity to reliably perform clinical studies within agreed timelines.

Focused on diabetes, obesity and metabolic disorders

Profil's expertise with diabetes and related conditions is unrivalled. Our key competence is the performance of glucose clamp studies, often in combination with isotope dilution techniques and muscle or fat biopsies. In our medical technology department, we have scientists experienced with all types of devices from straightforward needle studies to implantable glucose sensors or artificial pancreas devices. Thanks to our vast experience with diabetes trials and treatments as well as obesity, prediabetes, NAFLD and cardiometabolic research, Profil is your ideal partner for developing treatments for these conditions.

Watch our scientific webinars at www.profil.com/webinars

Profil in the words of founder, Dr. Tim Heise

Over the 15 past years Dr. Tim Heise and his co-founders have gathered a team of medical and scientific experts to build a full-service CRO with considerable achievements.

What does Profil mean to you personally?

Dr. Heise: Profil is a dream come true. Until 1999, the other founders and I were part of an academic group at the Clinic for Metabolic Diseases and Nutrition, led by Professor Michael Berger, at the University of Düsseldorf, a WHO Collaborating Centre for Diabetes. We realized that if we wanted to take things further and become deeply involved in the development of treatments, we would have to go private. We've been able to gather and retain scientific experts with the same drive to discover and become part of work that improves people's lives.

> "Profil is the leading site for glucose clamp studies in the world."

What has been the most exciting challenge?

Dr. Heise: Profil is the leading site for glucose clamp studies in the world. When it became clear that the Biostator – the first device we used for glucose clamp studies – was becoming obsolete and no longer supported by its manufacturer, we set out to develop our own device. That was the birth of ClampArt®, our CE-marked glucose clamp device. Developing it was a fascinating and rewarding process.

What's next for Profil?

Dr. Heise: Naturally, we will continue to grow! With our two clinics, we can comfortably recruit patients from two of the largest metropolitan areas in Germany and continue to expand our already large patient database; a prerequisite for further growth. More importantly, we will work to keep the scientific drive that has always motivated us. We want to stand as a partner, doing more than just run studies. We intend to continue to work together with our clients and drive forward the development of new treatments for diabetes and obesity.

Dr. Tim Heise – Founder and lead scientist

Benefit from working with Profil

- → Profil is a clinical contract research organization focused on early phase trials in diabetes and obesity. Working with us means working with true experts.
- → We offer a vast array of sophisticated methods for optimized study design.
- → We are the largest and most experienced glucose clamp center in the world, with 28 automated glucose clamp devices.
- → Our two clinics have an 80+ bed capacity.
- → We offer consulting services to optimize study design and regulatory submissions: we are your partners from before the first patient enters the clinic until the very end of your project.
- → Our scientists have published several hundred peer-reviewed original articles and reviews and over 500 abstracts at scientific conferences. Working with us means your study will have the scientific credentials it needs.

The world's leading glucose clamp site

Profil has over 15 years' experience in glucose clamp trials, and has even developed its own CE-marked glucose clamp device: ClampArt®.

Profil is the largest glucose clamp center in the world. Our setup allows us to run glucose clamp trials 24 hours a day and 7 days a week, all the while gaining more experience with various glucose clamp designs.

Profil's own ClampArt® – a modern automated glucose clamp device

Glucose clamps involve the maintenance or clamping of blood glucose concentrations at a predefined target level. They measure the action of a test compound by antagonizing its effect with a varying glucose infusion rate (GIR).

Profil is renowned for expertise in assessing the glucodynamic activity of all kinds of insulin formulations, including ultra-long acting, ultra-rapid acting and premixed insulin. We carefully adapt the clamp design to the study objectives and the compound studied to ensure the most meaningful results.

Whatever glucose clamp design you need, Profil can support you: hyperinsulinemic euglycemic clamps for the assessment of insulin sensitivity, hyperglycemic clamps for the determination of beta-cell function, hypoglycemic clamps for the quantification of counter-regulation, and pancreatic clamps to determine the metabolic role of hormones such as those from alpha- and beta-cells.

ClampArt® – next-generation glucose clamps

ClampArt® is Profil's own CE-marked modern automated glucose clamp device. It meets all EU regulatory standards and can be used to generate data for the EMA, FDA and other regulatory authorities. This state-of-the-art technology uses modern sensor technology and infusion pumps to give improved quality and utility. Confounding factors such as disturbances in blood flow are taken into account and automatically corrected for through the continuous determination of blood glucose and blood dilution factor.

Thanks to the very high clamp quality provided by ClampArt®, the pharmacodynamic effect of glucose-lowering agents can be determined with the high precision and accuracy demanded by regulatory authorities. This makes it particularly effective in trials of biosimilar insulins for which pharmacodynamic equivalence has yet to be proven.

Profil and glucose clamp studies at a glance

- → We can run up to 28 glucose clamps in parallel.
- → We can run glucose clamps of up to 48 h duration.
- → We offer all the required types of glucose clamp: hyperinsulinemic euglycemic, hyperglycemic, hypoglycemic and pancreatic.
- → Our ClampArt® is CE marked for glucose clamp studies.
- → Using ClampArt®, glucose clamp studies at Profil reach otherwise unattainable clamp quality.

See a list of our recent publications at www.profil.com/publications

Unrivalled portfolio of methods at Profil

Whatever your diabetes and obesity study needs, Profil stands ready to provide our scientific and regulatory expertise.

Profil uses a wide spectrum of sophisticated methods. With a focus on early phase studies, we have vast experience in all these methods, having been involved in the development of many of the major currently available anti-diabetic drugs. Profil does more than just carry out studies: we pride ourselves on aiding our clients to design the very best clinical trials: optimum participant groups and test environments, best-fit methods, and support for analyses and dissemination of results.

We have considerable experience in working with large pharmaceutical companies that are looking to in-source new technologies. That collaboration lets us to get a head start on designing studies to test new technologies according to potential licensor's needs.

Profil's methodological expertise

Pharmacodynamics and pharmacokinetics

We have experience with testing all classes of new and modified anti-diabetic drugs with regard to their pharmacodynamic and pharmacokinetic effects using methods such as glucose clamp, isotope dilution techniques, and muscle or fat biopsies.

Safety and tolerability studies

Safety and tolerability studies for novel compounds are a core expertise for Profil, making us an ideal partner for first-in-man studies and single or multiple ascending dose studies focused on diabetes or obesity treatment.

Bioequivalence trials

We've performed numerous bioequivalence trials with different insulin formulations and can advise on optimization of study design to ensure regulatory requirements of the FDA and EMA are met.

Bridging studies

Data from clinical trials performed at Profil are used and accepted by the authorities for NDAs in Japan. Accelerate your approval process in Japan considerably (from an average of 56 to 32 months) by doing your bridging study with us. We have Japanese staff members to run these studies and our database has 300 Japanese volunteers and can easily be extended.

Technology studies

We're experienced in all aspects of medical technology in the area of diabetes and obesity. We played a leading role in the development of the artificial pancreas and we have a dedicated team for medical device projects. Profil is ISO 13485 certified and has substantial regulatory experience in medical technology trials.

Follow our scientific blog at blog.profil.com/blog

World-class services from first draft to final paper

Profil goes beyond running trials to ensure that you get the most out of our support, from trial preparation through performance and even to publication.

When you plan a clinical trial or research project with Profil, you choose the services you want from our portfolio, which covers every aspect of clinical investigations, from initial concept to publication. We are here to be your scientific partner to the extent that you need, not just a mere "workbench" to run experiments – and our high number of returning clients is testament to the value we provide.

As a full-service CRO, we will help prepare your trials, perform as many experiments and studies as needed, analyze the results and even support publication. We have expertise in protocol development and writing, regulatory filing, ISO-certified quality assurance and high-quality data management and statistics. We also offer a GMP-standard licensed pharmacy that manufactures sterile medication and oral solutions.

Experts in clinical trial conduct

- For smooth trial conduct, Profil's clinical development consulting team supports the design of clinical trials and their submission to the authorities.
- Our GMP-certified pharmacy has a full GMP manufacturing license for investigational medicinal products.
- Our data management team works on very competitive timelines and utilizes our in-house EDC solution specifically developed for phase I trials.
- After trial completion, our statistics and medical writing teams help with the analysis and write-up of trial data and prepare publications.
- If requested, our scientists present the clinical trial data at international meetings and publish them in scientific journals.

- **This is just a selection of the services on offer. Contact us to discover how else we can support you in the design and running of your clinical trial.**

Recruitment at Profil

Successful clinical research depends on rapid recruitment. Profil has a vast database with a range of patients and healthy volunteers.

Rapid enrollment is key to the successful and timely completion of clinical trials in every field. To ensure that you experience no delays, Profil has spent years assembling an extensive database of patients and healthy or obese subjects that meet the criteria for every type of diabetes and obesity study.

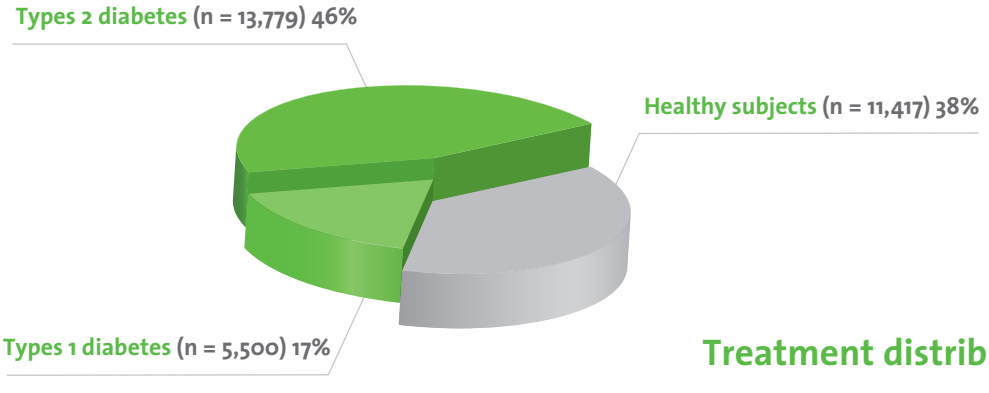
A highly searchable database for accurate estimates of recruitment times

To meet specific study requirements, this patient database can be searched for individual subject characteristics, including medical history, laboratory values and concomitant medication. This allows us to give a very accurate estimate of whether we can recruit a study and how long it will take. Profil prides itself on the high accuracy of these estimates and our timely inclusion of study participants. As timely recruitment is one of the most important metrics in clinical trial conduct, our success in doing so is one of the reasons for our extremely high repeat business rate.

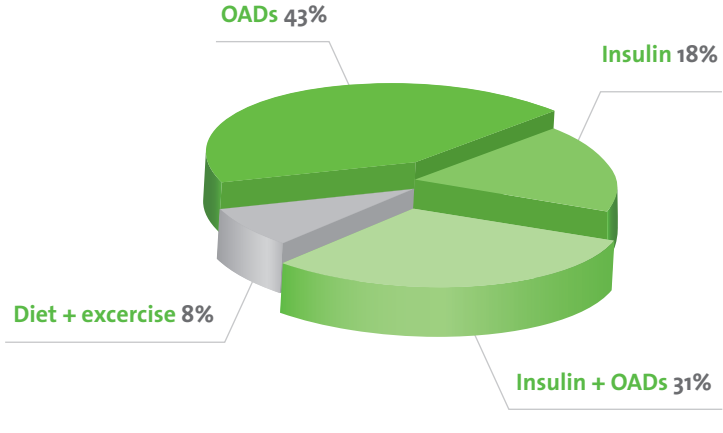
Diabetes complication studies, bridging studies and more

We recognize the need for very specific study populations for different types of clinical trial. We have patients in our database with comorbidities such as cardiovascular disease, neuropathy, retinopathy and different stages of diabetic kidney disease and we cooperate with local specialists to ensure we can keep finding new subjects. We also have diabetic and healthy subjects ready to take part in Japanese bridging studies – a unique resource for accelerating regulatory approvals in Japan.

Patient database



Treatment distribution



Profil – Your Partner

→ **Contact Profil to learn more about how we can best support your investigations of diabetes and obesity. We share your desire to provide a better life for patients worldwide.**

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