

Sweden for Clinical Research

Report on Sweden's competitive advantages for clinical development

The Delegation for Cooperation in Clinical Research was appointed by the Ministry of Enterprise, Energy and Communication in collaboration with the Ministry of Social Affairs and the Ministry of Education and Research with the objective to create better conditions for the cooperation between stakeholders involved in clinical research in Sweden, namely the health care sector, academia/universities and relevant industry. The Delegation, which consists of delegates representing top executives in the three sectors, will finish its work by the 31st December 2009.

The Delegation identified a need for a collective vision and information aimed at foreign stakeholders regarding the opportunities to conduct world class clinical research in Sweden and how these opportunities stand in an international comparison. In collaboration with Invest in Sweden Agency and Swecare, the Delegation therefore initiated this report and an information material based on interviews with Swedish and foreign representatives for stakeholders in clinical research.

The report was finalized in December 2009 by author Björn Bergstrand, BBD Corporate Communications.

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INTRODUCTION

Quality and reliability in clinical trials and drug assessment

Current progress within basic biomedical science creates new potential to understand, treat and prevent human diseases. Sweden's solid biomedical research foundation, its high quality health care system and health data registers make it one of the few places where such promises can be realized.

Sweden offers unique assets for development and follow-up of novel prevention and treatment technology: world-renowned clinical investigators, a high proportion of health care professionals with research training, strong clinical trials know-how, quality registers, patients that are keen to take part in research projects and a public health care system with universal access for all citizens.

Sweden is distinguished by high scientific standards and an outstanding capacity to track patients over time. Its credentials for clinical development also include one of the world's most respected medical products agencies. During the past five years Sweden has participated in 11 percent of all clinical trials initiated within the EU, a far higher share than its population would indicate (2 percent of the EU population). All the world's best selling medicines, both traditional chemical substances and new biopharmaceuticals, have been tested on Swedish patients during clinical development.

Sweden is particularly well suited for complex trials in phases I-II, involving novel compounds or medical technology and which require sophisticated regulatory advice. Population-based registers and healthcare databases offer great scope for drug assessment after market introduction (phase V).

Recognizing the importance of having a clinical research environment that benefits the industry, the health care system and patients alike, a number of national and regional initiatives are now underway to further strengthen Sweden's clinical research position. These are backed by the government and complemented by substantial increases in medical research spending.

Trust Sweden to deliver on promising life science.

<p>100 %</p> <p>Share of the world's ten best-selling medicines that have undergone clinical development in Sweden</p>	<p>No. 4</p> <p>Sweden's Medical Products Agency is one Europe's most preferred investigative authorities, measured as its share of investigations under the EU centralized procedure.</p>	<p>No. 6</p> <p>Sweden's ranking in a comparison of the world's most cited research publications in clinical medicine</p>	<p>"Clinical research in Sweden ... rightly deserves an excellent international reputation."</p> <p>Roger Bouillon, Professor, MD, PhD, Catholic University of Leuven, Belgium. Chair of the Panel evaluating clinical research in Sweden and Finland, May 2009</p>
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Good reasons to choose Sweden for Clinical Trials

Strong life science tradition

Sweden traces its life science roots to the early 1900s, when the pharmaceutical companies Astra and Pharmacia were founded. Seven Swedes have been Nobel Prize recipients and numerous important pharmaceutical and medical technology innovations are of Swedish origin.

Expertise in clinical research

Sweden maintains a strong international position in clinical research. It is the world's 12th largest producer of research results and placed 6th in the analysis of the most cited publications.

Strong skills in performing clinical trials

Qualified and experienced clinical trials professionals are found throughout; within the industry, at universities, hospitals, the Medical Products Agency and ethics review boards.

Outstanding regulatory advice

Sweden's Medical Products Agency is one of the EU's most frequently consulted authorities, under both centralized and mutual recognition procedures. It is widely recognized for its qualified advice.

Unique assets for biomedical research

Few places offer better prerequisites for longitudinal research approaches using electronic patient records, biobanks and the unique Swedish health care databases. The use of personal identity numbers enables linkage of exposure and outcome data dating back several decades.

High data quality

It is widely recognized that Swedish clinical data is of high quality, the result of both strong clinical trials know-how and a cultural trait of doing things in an orderly manner.

Patients willing to participate in studies

Due to patient willingness to participate and comply with studies, drop-out and lost to follow-up rates are very low.

High quality health care system

A health care system with universal coverage for all, common processes, treatment philosophies and routines for data collection is a major advantage. Registers and medical records are meticulously kept and of high quality.

Long-term use of personal identity numbers

All Swedes carry a unique number, composed of the date of birth plus four digits, which is always used for personal identification in public registers and records. Personal identity numbers have been in use for more than 60 years.

Insurance system adapted to industry needs

The Swedish Pharmaceutical Insurance Scheme covers claims related to adverse effects from participation in clinical trials. The scheme provides insurance cover also for multi-centre studies run from companies outside of Sweden.

Tradition of co-operation between industry and the health care system

Comprehensive and constructive co-operation between health care providers, universities and the pharmaceutical industry has been in place for decades, both during clinical development and following market introduction. Recently, SKL, the Swedish Association of Local Authorities and Regions, and LIF, the Swedish Association of the Pharmaceutical Industry, have agreed upon a national strategy for clinical trials. The agreement establishes a number of common objectives to be reached, relating for example to the quality, timeliness, ethical standard and cost for conducting clinical trials and non-interventional studies. The agreement has been ratified by all Swedish county councils.

Fluency in English

People in Sweden are exposed to the English language on a daily basis; in many of the larger companies English is the working language. The ease with which international companies can operate in Sweden is a considerable advantage.

Integrity & ethics

The Swedish culture, be it on a corporate, academic or public level, is founded on a strong sense of integrity, honesty and ethics. There is long experience from integrating ethical aspects in decision-making. With regards to clinical trials, Swedish ethics reviews committees are of a very high standard.

What the experts say

Professor Michael E. Porter, Harvard Business School, USA:

“With its strong tradition of quality registries, Sweden is poised to become the world's most advanced nation in measuring the actual outcomes of care across many diseases. This represents a major opportunity for Sweden to lead a global shift toward a new, value-based approach to health care delivery focused on improving patient health outcomes relative to cost.”

Dr. Sidney Goldstein, M.D., Henry Ford Hospital, Detroit, USA:

“The close relationship of academic medical centers and industry, so characteristic of Sweden, provides a unique opportunity to move innovation forward in medical science. In addition, the strong clinical research environment in Swedish medical centers accelerates the translation of basic research to the bedside. This broad spectrum of expertise in both basic and clinical science makes Sweden an integrated environment well suited to initiate and conduct clinical research.”

Professor emeritus Bertram Pitt, M.D., University of Michigan, USA

“I have long been an admirer of the cooperation between the cardiovascular researchers at the major Swedish universities and the Swedish pharmaceutical industry. The close collaboration, particularly in the areas of heart failure and hypertension, over the years has resulted in the development of new drugs and a number of major clinical trials that have helped to guide current clinical practice around the world.

CLINICAL RESEARCH POSITION

Clinical research position

Swedish clinical research enjoys a prominent international position. Emphasizing the link between the laboratory and the patient has yielded a solid track record of delivering patient benefits.

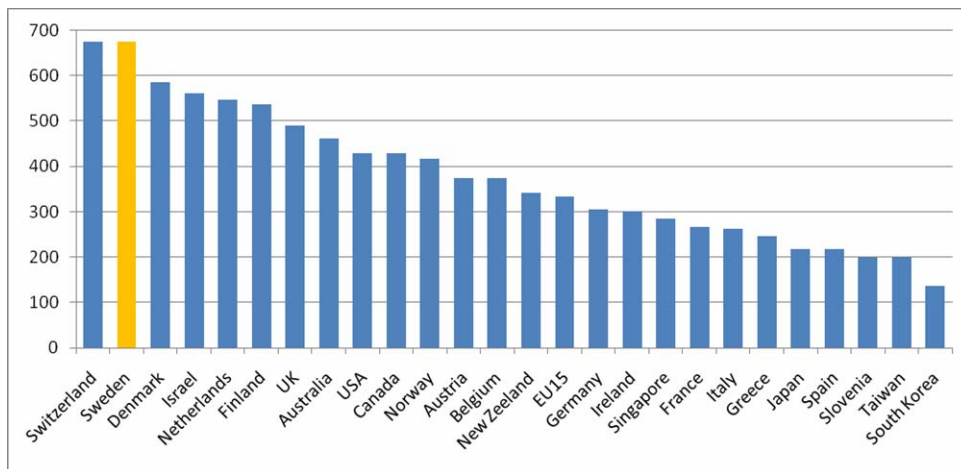
Swedish clinical research among world's top ten

A high proportion of health care professionals with research training; assets in the form of health data registers; quality registers and biobanks; patients that are keen to take part in research projects – these are some of Sweden's advantages. Sweden also has a long clinical research tradition. At an early stage, Sweden built an advanced healthcare system open to trying new technologies and treatments. This has contributed to the strong position of the Swedish life science industry.

A global bibliometric analysis of research productivity in 54 countries shows that Sweden is the world's 2nd largest per capita producer of medical publications and placed an overall 6th in the analysis of research quality based on citations. Sweden's 6th position is maintained whether or not citations are analyzed in total or calculated as the top 10 or top 1 percent of the most cited medical publications.

World's largest per capita producers of medical publications

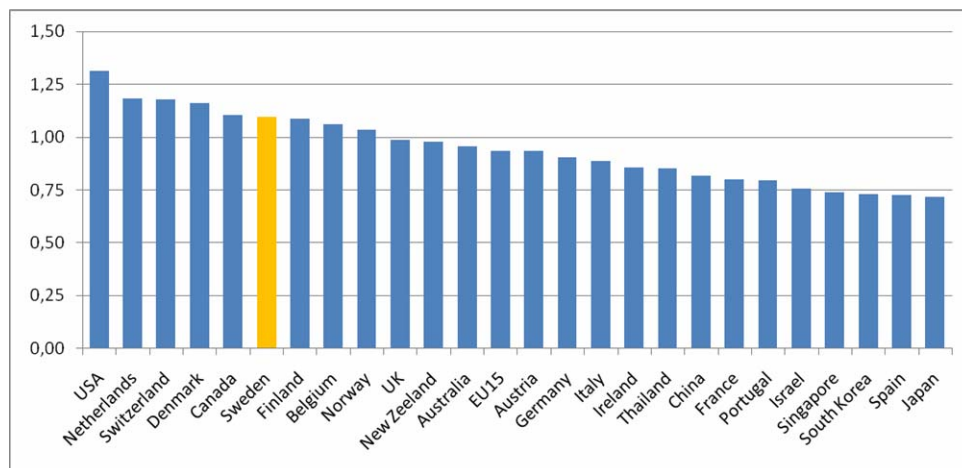
Publications per year and million inhabitants



Source: "Clinical Research in Finland and Sweden", Academy of Finland and Swedish Research Council, 2009

The 25 most highly cited countries in Clinical Medicine

Field normalised citation rate



High levels of internationalization

Swedish medical universities are noted for a high degree of internationalization in their research activities, both in terms of co-operation with other researchers, as coordinators for international research programs and as funding recipients.

Karolinska Institutet in Stockholm, Sweden's largest medical university, is a good example:

- In 2008, Karolinska Institutet had about 80 general international cooperation agreements on PhD level education and research.
- Nearly 60 percent of its publications had at least one co-author outside of Sweden.
- The Institute participated in 260 EU-funded projects. A Karolinska researcher was the coordinator in 41 of these projects.
- 33 percent of doctoral candidates that began the doctoral research program in 2007 were of foreign origin.

KI is also one of the main recipients of American research grants in Europe. In 2008, KI coordinated 14 projects financed with U.S. federal funds and was a partner in over 25 other federally financed projects. The National Institutes of Health (NIH) is KI's most important partner outside Europe.

High levels of international research collaborations are characteristic of all major Swedish medical universities. At the Sahlgrenska Academy in Göteborg, over 40 percent of research publications have at least one international co-author. In 2008, researchers at Sahlgrenska Academy participated in 50 research projects under the 6th and 7th Framework Programmes; some 10 of these were coordinated by Sahlgrenska researchers.

The Lund University Faculty of Medicine had over 80 international cooperation agreement contracts in 2008, including education and research. In addition, researchers at the departments are involved in international cooperations built on partnerships between individuals on top level research.

- Nearly 55 percent of the research publications had at least one co-author outside of Sweden for 2008.
- The Faculty participated in 64 EU 6th framework contracts including approximately 893 partners in 47 countries within and outside Europe. From funding agencies outside Europe the faculty has received, among others, 28 projects from NIH.

The largest producers of clinical research

The universities and university hospitals dominate clinical research activity. The largest publisher is Karolinska Institutet in Stockholm, the world-renowned medical university and Sweden's largest centre for medical training and research.

Swedish publications in Clinical Medicine			
Per year, 2004-2006			
Medical school	Number of publications	Share (%)	Mean citation rate
Karolinska Institutet, Stockholm	1098	28	1.25
Lund University	642	16	1.00
Göteborg University	542	14	1.19
Uppsala University	399	10	1.08
Umeå University	225	6	1.16
Linköping University	219	6	0.94
Other organisations	816	21	1.02
Total	3940	100	1.12

* Field normalised

Source: Academy of Finland, Swedish Research Council "Evaluation of clinical research in Finland and Sweden", May 2009

Largest research fields, Clinical Medicine and Biomedicine	
Publication volume per year, average for 2004-2006	
Subject field	Mean citation rate
Biochemistry & Molecular Biology	491.4
Oncology	329.6
Neurosciences	278.2
Endocrinology & Metabolism	270.3
Public, Environmental & Occupational Health	267.8
Immunology	228.8
Pharmacology & Pharmacy	218.8
Surgery	162.4
Cell Biology	161.8
Clinical Neurology	151.0

Source: Academy of Finland, Swedish Research Council "Evaluation of clinical research in Finland and Sweden", May 2009

**Most highly cited Swedish subject fields (>20% above world average)
2004-2006**

Subject field (Clinical Medicine & Biomedicine)	Mean citation rate
Medicine, General & Internal	1.92
Rheumatology	1.84
Anesthesiology	1.53
Dermatology	1.51
Clinical Neurology	1.43
Surgery	1.33
Dentistry, Oral Surgery & Medicine	1.32
Pharmacology & Pharmacy	1.22
Orthopedics	1.22
Toxicology	1.21

Source: Academy of Finland, Swedish Research Council
"Evaluation of clinical research in Finland and Sweden", May 2009

Health care system

Sweden has among the world’s best performing health care systems. A fundamental principle is that all citizens have the right to good health care on equal terms, regardless of where they live and what their economic circumstances are.

Decentralized system

The Swedish healthcare system is characterized by extensive decentralization and financing primarily through regional/local taxation. 20 county councils and regions supply their citizens with health care services, including hospital care, primary care and psychiatric care.

Health care services are provided by both public and private health care providers. The county councils own all emergency hospitals, but health care services can be outsourced to contractors. For pre-planned care there are several private clinics from which county councils can purchase certain services to complement care offered within their own units.

The organization of Swedish health services			
Central government		Local government	
Ministry of Health and Social Affairs	20 county councils	6 university hospitals 65 county/district hospitals 1,000 health centers	<i>Swedish Association of Local Authorities and Regions, SKL, represents county councils and municipalities</i>
National Board of Health and Welfare	290 municipalities	Housing, care and social support services for the elderly and disabled	
Responsibilities: * legislation * supervision * evaluation		Responsibilities: * finance * organization * follow-up	

Free for all

Health care is financed primarily by a county council tax supplemented by a state grant. Small user fees are also paid at the point of use. Long term care for the elderly is financed and organized by the municipalities. Patient fees are highly affordable and typically in the range of SEK 100 to 300 (EUR 10 to 30) per visit, depending on the type of care received. To limit costs for the individual there is a high-cost ceiling. After a patient has paid a total of SEK 900 (EUR 90), medical consultations in the twelve months following the date of the first consultation are free of charge. A similar ceiling exists for prescribed medication, set at SEK 1,800 (EUR 180) per twelve-month period.

Uniform treatment methods

The role of central government is to establish principles and guidelines for care and to set the political agenda for health and medical care. This is achieved by means of laws and ordinances or by reaching agreements with the Swedish Association of Local Authorities and Regions (*Sveriges Kommuner och Landsting, SKL*), which represents the county councils and municipalities.

The National Board of Health and Welfare (*Socialstyrelsen*) plays a fundamental role as the central government's expert and supervisory authority. The Board sets goals and outlines norms by issuing provisions, guidelines and general advice. The Swedish Council on Technology Assessment in Health Care (*Statens beredning för medicinsk utvärdering, SBU*) is a knowledge resource mandated by the government to evaluate methods and technology used to prevent, diagnose and treat health problems.

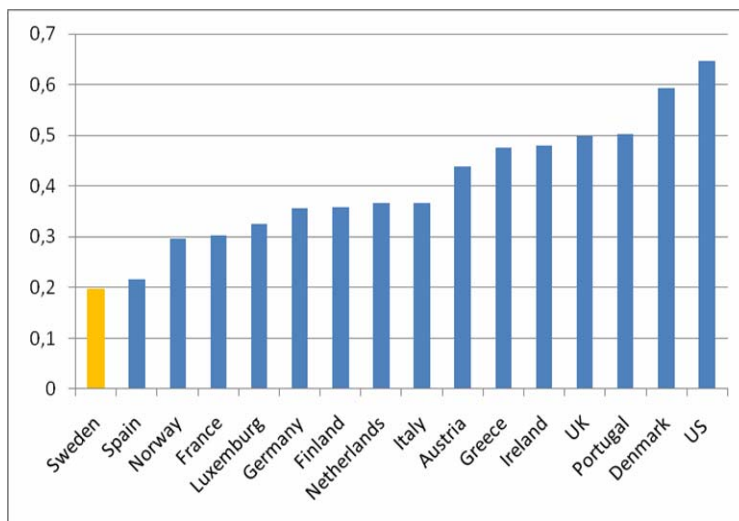
The Medical Products Agency (*Läkemedelsverket*) is responsible for regulation and surveillance of the development, manufacturing and marketing of drugs and other medicinal products. The Dental and Pharmaceutical Benefits Agency (*Tandvårds- och Läkemedelsförmånsverket, TLV*) is responsible for determining whether a pharmaceutical product or dental care procedure shall be subsidized by the state.

A peer in health care system quality

The quality of the Swedish healthcare system has been validated in numerous comparisons. In an analysis of medical outcomes in 17 European countries and the US, Sweden was placed first (see chart below). The analysis was based on 18 indicators including number of deaths from cancer, lung cancer, breast cancer, ischaemic heart disease and stroke. A lower index indicates better outcome.

European health care quality

Results index, 18 indicators*



Source: "The Swedish Healthcare System: How does it compare with other EU countries, the United States and Norway", Swedish Association of Local Authorities and Regions, 2008.

Continuous performance improvements

Healthcare quality and efficiency in the county councils and regions are benchmarked annually using a set of national performance indicators. The purpose is both to stimulate public debate on healthcare quality and efficiency and to support local and regional efforts to improve healthcare services.

High data quality

Generating high quality data in clinical trials is a complex exercise in which Sweden excels, thanks to its well-functioning health care system and highly qualified clinical investigators and study personnel with solid clinical trials experience and good insights into the regulatory aspects of clinical trials.

Outstanding ability to track patients

Sweden introduced the use of personal identity numbers (PINs) in 1948, an invaluable tool for record-keeping and cross-referencing between population registers and health registers. Swedish PINs consist of six digits for the birth date (year-month-day), followed by three digits that identify the individual and a tenth digit which is a check digit.

Medical products agency

As one of the EU's most frequently consulted regulatory authorities, the Medical Products Agency strongly influences recommendations related to medicines and medical devices. The MPA is recognized both for high quality scientific advice and approach to industry collaboration.

One of Europe's foremost regulatory authorities

Sweden's regulatory agency, the Medical Products Agency (MPA) is a modern, efficient authority that ranks among the best in Europe and is commonly used as a best-practice example for regulatory agencies within the EU. The MPA takes an active role in European regulatory affairs – several MPA staff holds the chair and vice-chair posts in EMEA scientific committees, for example.

A preferred partner for scientific advice

The MPA is one of the pharmaceutical industry's most preferred partners for scientific advice, a result of its highly competent staff and track-record of delivering qualified advice. Almost 80 percent of the MPA's staff have university degrees; some 20 percent have doctorates. Staff mainly comprise pharmacists and doctors, but also include veterinary surgeons, biologists, physicists, chemists, lawyers, IT specialists and statisticians.

Leading investigative authority

In 2008, the MPA's share of allocated investigations as a rapporteur or co-rapporteur country under the EU centralized procedure was 19 percent. The MPA's share of investigations for new chemical entities, new active substances and other types of complex investigations was 17 percent. The MPA was also allocated 11 percent of the EU's centralized scientific and regulatory advice projects. (Source: Medical Products Agency, Annual Report 2008)

Consistent quality

The MPA's process for handling clinical trials applications – with each application having to pass specific quality assurance groups, independent of the individual specialist assigned the application – contributes to the consistent and high quality of MPA's reviews.

Rapid processing times

The MPA shows strong compliance with the requirements for handling times under the EU Clinical Trials Directive. Between 2005 and 2008, 99 percent of applications were handled within 60 days. 90 percent of applications were handled within 30 days (2005-2007).

Introducing a European first for collaboration with pricing authority

In 2009, the MPA and Sweden's pricing authority, the Dental and Pharmaceutical Benefits Agency (TLV), began offering joint scientific advice meetings to the pharmaceutical industry. The purpose is both to contribute to a rational and cost-effective use of pharmaceutical products and to render applications processes more efficient for the pharmaceutical industry.

Clinical trials – Required approvals

Prior authorization from the Medical Products Agency, a favorable opinion from a regional ethical review board and in certain cases approval from a radiation protection committee is required before clinical trials can begin in Sweden. If the trial includes genetic analysis, notification must also be made to the Swedish Data Inspection Board. A patient that is to be included in a trial must receive both verbal and written information and sign a document of informed consent.

Research ethics review

Since January 2004, the Swedish research ethics review system is regulated by law. The legislation takes into account both the European convention on human rights and biomedicine and the EU directive on good clinical practice in the conduct of clinical trials on medicinal products for human use.

Two-tier system

The review is undertaken within six separate regional ethical review boards (*Regionala etikprövningsnämnder, REPN*) involving at least two separate units for review. Each unit includes ten experienced scientists, five persons representing the public and a chairman. The chairman and the chairman's substitute must be a judge or a former judge. All members and their substitutes are appointed by the government for a fixed period of time. Appeals on decisions taken by a regional ethical review board can be made to the Central Ethical Review Board (*Centrala Etikprövningsnämnden, CEPN*) at no extra cost.

Regional boards situated at the largest nodes for research

The regional boards are situated at the universities of Göteborg, Linköping, Lund, Umeå and Uppsala and at the Karolinska Institutet in Stockholm. Throughout 2005-2008, all regional ethical committees met the required processing time requirements.

Rapid approval process

Swedish ethical review boards are noted for their rapid approval process: Throughout 2005-2008, all regional ethical committees met the required processing time requirements of 30 days. As applications for regulatory and ethics approval can be made in parallel in Sweden, this means total processing time for both regulatory and ethics approval is normally under 30 days.

Insurance

Sweden offers unique and cost-efficient insurance to cover claims related to adverse effects from participation in clinical trials. The Swedish Pharmaceutical Insurance Scheme (LFF) has been adapted to provide insurance cover also for multi-centre studies run from companies outside of Sweden.

About the insurance

The pharmaceutical insurance covers all patients who have been treated with prescribed pharmaceutical products, who have received their pharmaceuticals at a hospital, who have legally purchased non-prescribed pharmaceuticals at a Swedish pharmacy or other retailers, or who are suffering adverse reactions or effects owing to participation in clinical trials. For clinical trials, insurance cover is dependent on the study having obtained scientific and ethical approval.

The Swedish Pharmaceutical Insurance Scheme (LFF) was created 30 years ago for companies and organisations that work with pharmaceuticals in Sweden. Today the scheme is administrated by LFF Service AB, a company owned by pharmaceutical companies that manufacture, sell or have clinical trials in Sweden. The scheme ensures patients using any pharmaceutical product the right to get his/hers injury investigated and paid for from the scheme.

Virtually all companies involved in the development, manufacturing and marketing of medical products in Sweden are participating, as well as contract research organizations and distributors of medicines.

All claims are handled by an independent body and its assigned claims investigator. Final claims decisions are typically made within a 4-5 months time frame. Approximately one third of claims receive reimbursement.

The scheme differentiates between companies with and without net pharmaceutical sales in Sweden. Participating companies with net sales in Sweden pay an annual service fee and premium directly related to the size of their operations. For companies with small or no net sales the minimum fee for 2009 is SEK 55,640 (EUR 5,564). This fee covers 50 patients; the premium for each additional patient is SEK 214 (EUR 21).

Adapted to multi-centre studies

If a multi-centre study is run from a company outside Sweden, the study is automatically insured in the Swedish scheme if a mother/sister company with net sales in Sweden is a shareholder in LFF Service AB. No separate reporting is needed to LFF. However, if a claim is made the sponsor company must provide research results, documentation, know-how and similar items available for claim adjustment.

Assets for clinical research

Sweden's use of personal identity numbers and the existence of national health data registers, population registers and health care quality registers make Sweden uniquely placed for longitudinal studies around cause of disease and disease prognosis as well as for studies of effects, side effects and health economics.

The National Board of Health and Welfare has historically supported the collection of health and quality information through epidemiological and quality registers. Epidemiological registers focus mainly on the collection and reporting of epidemiological data while quality registers seek to understand the process and results of care delivery by collecting information on process compliance and health outcomes. Increasingly, the registers are moving beyond medical data to include patient-perceived quality and quality of life.

Registers are based on personal identification numbers (PINs), which have been in use since 1948. The PIN can be used as a search code and makes it possible to link data on exposure or treatment to outcomes.

The availability of epidemiological and quality registers make Sweden particularly well prepared to contribute to the development of new therapies, including individualized care.

What the experts say

Anders Ekblom, Executive Vice-President, Development, Astra Zeneca:

"Sweden's health care registers bring unique advantages to the development of new therapies, also towards more individualized care."

Epidemiological registers

National health data registers are kept at the Center for Epidemiology at the National Board of Health and Welfare to monitor the development of health and diseases and health care utilization patterns.

The National Patient Register

The Swedish National Patient Register was started in 1964, initially covering inpatients in six county councils in Sweden. From 1987 it covers all public inpatient care and since 2001 all outpatient visits. The medical data includes main and secondary diagnoses and surgical procedures. Statistics about the register is presented in the table below.

Swedish Patient Registry			
Registry for inpatient care		Registry for specialized outpatient care	
Total number of visits, 1964-2007	52.4 million	Total number of visits, 1997-2007	71.7 million
Total number of visits, 2007	1.5 million	Total number of visits, 2007	9.7 million
<i>whereof:</i>		<i>whereof:</i>	
- Somatic care	1.2 million	- Somatic care	8.1 million
- Psychiatric care	0.1 million	- Psychiatric care	0.7 million
- Geriatric care	0.1 million	- Geriatric care	0.1 million
- Surgical procedures	0.2 million	- Surgical procedures	0.9 million
Diagnosis registered, share of total visit:	99%	Diagnosis registered, share of total visits	80%
Source: National Board of Health and Welfare, 2009			

The Swedish Medical Birth Register

Established in 1973. Includes individual data on previous gestation, smoking habits and drug use during pregnancy, medication, family situation, hospital, length of gestation, type of delivery, diagnoses of mother and child, etc. 85,000-120,000 new entries per year.

The Causes of Death Register

Swedish statistics on causes of deaths date back to 1749, when a nationwide report system was first introduced. Register includes underlying cause of death, information on surgery, diabetes, use of tobacco, alcohol and narcotics, etc.

The Swedish Cancer Register

Registers newly detected cases from all health care providers, both public and private. The national register is created annually at the National Board of Health and Welfare by merging data from six regional cancer registers. Both clinicians and pathologists/cytologists are required by law to notify the regional cancer register whenever a malignant condition is diagnosed (also autopsy). Approximately 45,000 new malignant cancer cases are reported every year.

The Twin Register

The Swedish Twin Register, maintained by Karolinska Institutet, is an invaluable tool for studying the relation between disease, genes, and environment. It was established in the 1960s by two Karolinska researchers, who were among the first to show that smokers acquire lung cancer more frequently than non-smokers. With information on approximately 85 000 twin pairs, both monozygotic and dizygotic, the register is the world's largest.

Population registers

Of importance are also the registers kept by Statistics Sweden, primarily the Population Register and the Multi-Generation Register.

The Total Population Register

The Total Population Register is the basis for all official population statistics and includes name, personal identity number, place of birth, civil status, spouse, children, parents, address, immigration data etc. Sweden has accumulated population statistics since 1749.

The Multi-Generation Register

The Multi-Generation register enables the identification of first-degree relatives of all Swedish residents born in 1932 or later and makes it possible to study hereditary influences on disease, using not only sibships and nuclear families but also wider family structures.

National health care quality registers

There are some 60 disease- and/or intervention-specific nationally sponsored health care quality registers in Sweden, all containing individual-based data on problems or diagnoses, treatment interventions and outcomes. Each register is managed by a group of professionals usually located at one of Sweden's university hospitals. Several registers receive support from the industry.

The local authorities and regions (e.g. county councils) have the primary responsibility for the operation, development, and financing of the registers. The registers are jointly administered via the Executive Committee for National Quality Registers, which includes representatives from the county council, the Swedish Association of Local Authorities and Regions (SALAR), the National Board of Health and Welfare, the Swedish Society of Medicine and the Swedish Society of Nursing.

Spearheading models for drug assessment

Swedish quality registers have played an instrumental role in providing intelligence on drug effectiveness in everyday clinical practice. For example, the ARTIS register (Anti-Rheumatic Therapies in Sweden) has demonstrated benefits and risks correlated with a certain class of biologic drugs – the TNF-alpha antagonists (see separate article).

The Register on Cardiac Intensive Care (RIKS-HIA) has contributed to knowledge of a number of treatments and interventions in the management of acute myocardial infarction. For the past few years, the RIKS-HIA system has also been the model for Internet-based registration and quality development in health care, and it is currently used as a platform for a large number of national and international registries.

National Healthcare Quality Registers

Respiratory Diseases

Swedevox – Respiratory Failure Register
Swedish Quality Register of Otorhinolaryngology

Childhood and Adolescence

BORIS – Childhood Obesity Register in Sweden
SWEDIABKIDS – The Swedish Childhood Diabetes Register
PNQn – Perinatal Quality Register/Neonatology
SÖK – National Register of Suspected/Confirmed Sexual Abuse in Children and Adolescents

Circulatory Diseases

Riksvikt – Heart Failure Register
SCAAR – Swedish Coronary Angiography and Angioplasty Register
Swedish Heart Surgery Register
RIKS-HIA – Register on Cardiac Intensive Care
National Register on Out-of-Hospital Cardiac Arrest
Riks-Stroke – National Quality Register for Stroke
Swedvasc – Vascular Register in Sweden
GUCH – Grown-Up Congenital Heart Disease Register
SEPHIA – Register on Secondary Prevention in Cardiac Intensive Care
National Catheter Ablation Register
Auricula – National Register of Atrial Fibrillation and Anticoagulation

Endocrine Diseases

NDR – National Diabetes Register
Scandinavian Quality Register for Thyroid and Parathyroid Surgery
SOReg – Swedish Obesity Surgery Register

Gastrointestinal Disorders

Swedish Hernia Register
GallRiks – Swedish Quality Register on Gallstone Surgery
Swedish Quality Register for Ventral Hernia

Musculoskeletal Disorders

RIKSHÖFT – National Hip Fracture Register
Swedish National Hip Arthroplasty Register
Swedish Knee Arthroplasty Register
National Pain Rehabilitation Register
Swedish Rheumatoid Arthritis Register
Followup in Back Surgery
Swedish Shoulder Arthroplasty Register
Swedish Cruciate Ligament Register – X-base
Swedish National Elbow Arthroplasty Register (SAAR)

Diseases of the Nervous System

SMS – Swedish Multiple Sclerosis Register
CPUP – Quality Register for Children with Cerebral Palsy
WebRehab Sweden – Quality Register in Rehabilitation Medicine
SveDem – Swedish Dementia Register

Genitourinary Disorders

GYNOP – National Quality Register for Gynecological Surgery
SRR – Swedish Renal Register

Cancer

National Prostate Cancer Register
National Breast Cancer Register
National Quality Register for Esophageal and Stomach Cancer (NREV)
Swedish Rectal Cancer Register
Swedish Gyn-Oncology Register
Swedish Colon Cancer Register

Eye Disorders

Swedish National Cataract Register
Swedish Corneal Transplant Register
Macula Register

Other

RIKSÅT – National Quality Register for Specialized Treatment for Eating Disorders
SIR – Swedish Intensive Care Register
PsoReg – Swedish Psoriasis Register
InfCare HIV
Swedish Therapeutic Apheresis Register
SKaPa – Swedish Quality Register in Caries and Periodontitis
Swedish National Register of Palliative Care
Senior Alert – National Register on Nutrition, Fall Prevention and Pressure Sores
Quality Register for Emergent Care

Source: "National Healthcare Quality Registries in Sweden 2007",
Swedish Association of Local Authorities and Regions

The ARTIS register – a success story for drug effectiveness follow-up

The ARTIS register (Anti-Rheumatic Therapies in Sweden) documents the outcome of treatment with biologic pharmaceuticals, potent compounds for the treatment of rheumatoid arthritis, other arthritic conditions, inflammatory bowel disease and psoriasis. The register was a key contributor to the success of TNF-alpha antagonists and today provides follow-up data on all biological compounds targeting rheumatoid arthritis.

Back in 1998, when the TNF-alpha antagonists were introduced, their targeted mechanism of action represented a new therapeutic approach. Their subsequent long-term effectiveness was essentially unknown and approval by the European Medicines Agency, EMEA, was made on condition that the manufacturers would make long-term follow-up on their safety.

Data from the ARTIS register could clearly show the benefits and risks correlated with the new compounds. For example, the risks for lymphoma and other cancer forms, infections and cardiovascular diseases associated with different treatments and correlated to different patient groups.

Complementary health economics analysis showed that the new compounds, in spite of their higher cost, led to significantly reduced costs to society due to the improved health of patients. The ARTIS clinical network, population-based outcome registers and regulatory support were the key factors contributing to success.

The ARTIS register currently comprises 14,000 patients, corresponding to 22,000 treatments. The model for assessing the long-term effectiveness of the pharmaceuticals in the register has yielded benefits for all stakeholders, including patients, health care professionals, clinical researchers and regulatory agencies.

For drug developers, the ARTIS model helps to improve compliance with legislative demands during the market introduction of a new medicinal product. Moreover, companies can fulfill their assessment obligations.

In Sweden, the ARTIS register serves as a role model for the development of other national registries for the assessment of medicinal products. There is a register already in place for new multiple sclerosis (MS) medicinal products. Another is being set up for inflammatory bowel diseases.

A preferred location for clinical trials

Pharmaceutical companies and medical technology firms have long since turned to Sweden for high quality clinical data. According to LIF, the Swedish Association of the Pharmaceutical Industry, 40 companies currently perform R&D in Sweden, e.g. conduct clinical trials or have employed researchers or other R&D expenses in Sweden.

World's best-selling medicines tested in Sweden

Best-selling pharmaceuticals, 2007	Trial in Sweden	Best-selling biopharmaceuticals, 2008	Trial in Sweden
1 Lipitor (atorvastation)	Yes	1 Enbrel (etanercept)	Yes
2 Plavix (clopidogrel)	Yes	2 Remicade (infliximab)	Yes
3 Nexium (esomeprazol)	Yes	3 Epogen/Procrit/Eprix/ESPO (epoetin alfa)	Yes
4 Seretide/Advair (fluticasone+salmeterol)	Yes	4 Rituxan/Mab Thera (rituximab)	Yes
5 Enbrel (etanercept)	Yes	5 Humira Pen (adalim-mab)	Yes
6 Zyprexa (olanzapine)	Yes	2 Avastin (bevacizumab)	Yes
7 Risperdal (reperidone)	Yes	7 Herceptin (trastuzumab)	Yes
8 Seroquel (quetiapin)	Yes	8 Aranesp/NESP (darbepoetin alfa)	Yes
9 Singulair (montelukast)	Yes	9 Neulasta (pegfilgrastim)	Yes
10 Aranesp (darbepoetin alfa)	Yes	10 Lantus (insulin glargine)	Yes

Clinical trials were performed in Sweden and several other countries.

Source: IMS Health, La Merie Business Intelligence, Trial Form Support

Proactive public support

The Swedish Government strongly supports life science, manifested for example in the recent and significant budget increases for medical research. A number of initiatives are directly targeting clinical research, serving to reinforce Sweden's position as a preferred location for clinical research.

Legislation that makes clinical research mandatory

Public health care providers in Sweden are required by law to assist the pharmaceutical industry in developing new treatments and technology.

Boost to medical research and innovation in 2008 Government bill

The Government research bill "A Boost to Research and Innovation", presented in 2008 and covering the period 2009-2012 provides the largest, single extra investment ever to have been made in Swedish research. Among strategic medicine fields to receive additional funds are molecular bioscience, stem cells and regenerative medicine, diabetes, neuroscience, cancer and epidemiology.

Several initiatives directly targeting clinical research

The government launched a public inquiry which began its work in 2007 and presented its interim and final reports with action plan proposals in 2008 and 2009. Several of the measures proposed in the interim report were included in the 2008 Government Bill on research and innovation. The final report stressed the following:

- Strengthen the link between education and clinical research and create more positions at university hospitals that combine research and clinical work.
- Form University Medical Centres (UMC) that integrate education, research and health care, under the joint management of local and central government.
- Provide increased infrastructure support to facilitate the use of biobanks and health care quality and patient data registers.

Agreement between industry and health care providers – common objectives for clinical trials established

The Swedish health care providers, medical faculties and the Swedish pharmaceutical industry have jointly agreed on a national strategy to promote Sweden as an attractive location for clinical trials and non-interventional studies. The main agreement signed by the Swedish Association of the Pharmaceutical Industry and SKL, the Swedish Association of Local Authorities and Regions, establishes a number of common objectives to be reached. These relate, for example, to the quality, timeliness, ethical standard and cost for conducting clinical trials and non-interventional studies. The agreement has been ratified by all Swedish county councils.

Delegation for Cooperation in Clinical Research

The Delegation for Collaboration in Clinical Research started work in the spring of 2007, to proactively support clinical research collaboration in Sweden. This has been achieved through conferences and workshops targeted at collaborating parties within health care providers, universities and the industry, among other things.

Clinical research sites

Stockholm: Karolinska Trial Alliance

The Karolinska Trial Alliance (KTA) works to coordinate and stimulate clinical research in Stockholm County. KTA acts as a knowledge and resource centre for conducting and coordinating clinical trials as well as providing advice and training. KTA has two own wards for carrying out clinical trials on Karolinska University Hospital.

www.karolinskatrialliance.se

Uppsala: Uppsala Clinical Research Center

The Uppsala Clinical Research Center (UCR) is an independent unit connected to both the disciplinary domain for medicine and pharmacy at Uppsala University and the Uppsala University Hospital. UCR is engaged in projects under the leadership of and in collaboration with clinical investigators at Uppsala University and at other universities and hospitals in Sweden and the world.

www.ucr.uu.se

Göteborg: Gothia Forum

Gothia Forum is a research collaboration that aims to strengthen clinical research in the Göteborg Region. Partners are Region Västra Götaland, the Sahlgrenska Academy, the Chalmers University of Technology and the clinical research industry.

www.vgregion.se/gothiaforum

A European life science leader

Sweden is renowned for its ability to apply research progress in clinical practice. Innovative medicines and technology have sprung from successful collaboration between corporate and academic research, public healthcare and other institutions.

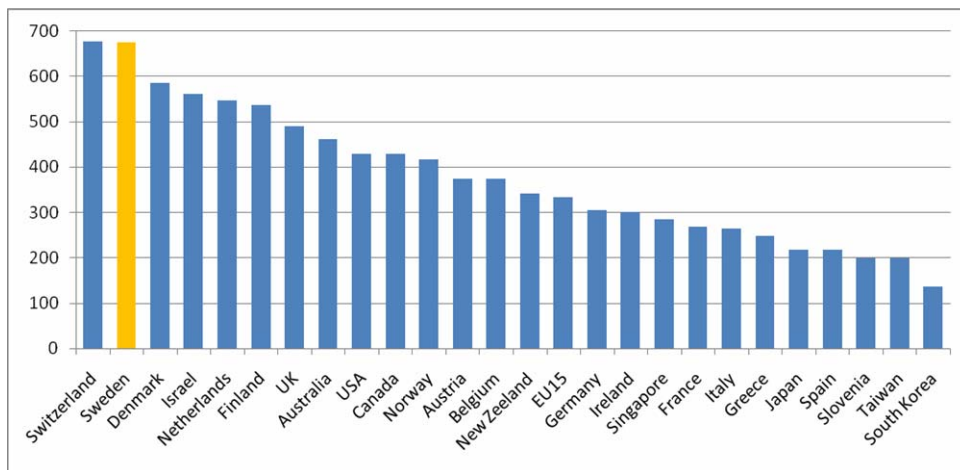
Strong scientific asset base

Sweden is the base for international leading researcher in numerous fields, including oncology, neurology and metabolic/cardiovascular diseases. The strongest research nodes are centered around Stockholm/Uppsala (Karolinska Institutet, Royal Institute of Technology, Uppsala University), Malmö/Lund (Lund University) and Göteborg (Sahlgrenska Academy, Chalmers University of Technology). Karolinska Institutet has been named among the world's best biomedical universities and among the best academic workplaces.

High quality life science research is also performed in Linköping and Umeå. Swedish researchers and institutions boast strong ties with the international scientific community, through direct and active participation in global networks and collaborative relationships.

World's largest per capita producers of medical publications

Publications per year and million inhabitants



Source: "Clinical Research in Finland and Sweden", Academy of Finland and Swedish Research Council, 2009

42,000 employees in life science

Sweden's life science companies are found throughout the value chain, with particular strengths in drug discovery and development and medical technologies. In all, the life science sector comprises 830 companies and 41,700 employees (2007). Sweden is also home to two of Europe's most distinguished biotech clusters, the Stockholm Uppsala Bioregion and Medicon Valley in Malmö/Lund/Copenhagen.

Industry innovation, now spanning more than half a century, has often been performed in close co-operation with universities and affiliated hospitals. Academic research, an advanced healthcare system and industry-applied development continues to drive life science industry growth in Sweden.

Life science companies in Sweden, a selection			
Pharmaceutical companies	Medical device, cont.	Largest companies 2007	Employees*
Abbott	Astra Tech	AstraZeneca (including Astra Tech)	10,206
Amgen	Elekta	GE Healthcare	2,011
Astellas Pharma	Fresenius Kabi	Getinge	1,161
AstraZeneca	Gambro	Pfizer	1,269
Baxter Medical	Gambro BCT	Gambro	1,071
Bayer	GE Healthcare	Fresenius Kabi	909
Biogen Idec	Getinge	St. Jude Medical	702
Biovitrum	HemoCue	Recip/Recipharm	548
Bristol-Myers Squibb	Mölnlycke Health Care	Biovitrum	539
Eisai	Nobel Biocare	Phadia	528
GlaxoSmithKline	Octapharma	Octapharma	516
H. Lundbeck	Phadia	Nobel Biocare	470
Janssen-Cilag	Q-Med	BectonDickinson Infusion Therapy	449
Merck Serono	Sangtec Molecular Diagnostics	Q-Med	445
Merck Sharp & Dohme	St Jude Medical	* In Sweden	
Novartis		Source: Vinnova, the Swedish Governmental Agency for Innovation	
Novo Nordisk	Biotechnology		
Nycomed	Active Biotech		
Otsuka Pharma	Artimplant		
Pfizer	Bioinvent		
Roche	Biovitrum		
Sanofi Pasteur MSD	Cell Therapeutics		
Sanofi-aventis	Doxa		
Schering-Plough	Entific		
Solvay Pharma	Integration Diagnostics		
Wyeth	Integrum		
	Karo Bio		
Medical device	Medivir		
Air Liquide	Mölnlycke Health Care		
Alcon	Nobel Biocare		
Allergan	Orexo		
Allergon	Q-sense		

Source for breakthrough medicines and medtech innovation

The pharmaceutical companies Astra and Pharmacia (now part of AstraZeneca and Pfizer) have been instrumental to Sweden's industrial position in life science and the development of a wide range of innovative medicines. AstraZeneca's global R&D head office and some 40 percent of the R&D staff are located in Sweden.

Using Sweden as a source for drug discovery and development is popular, as demonstrated by the number of in-licensing deals and international partnerships with academic research institutions. Today, Swedish developers of medicines have 74 projects in clinical phases I-III, excluding AstraZeneca projects. Neurological disorders and cancer-related conditions are dominating the pipeline.

Inventions have also been important to the medical device sector. Swedish companies commercialized the implantable pacemaker, the artificial kidney, the first blood test for allergy diagnostics and the radiating-beam surgery knife, among others. More recently, Swedish companies have been behind innovative systems for protein separation and protein interaction analysis.

Close ties with universities and hospitals

Industry innovation, now spanning more than half a century, has often been performed in close cooperation with universities and affiliated hospitals. Academic research, an advanced healthcare system and industry-applied development continues to drive life science industry growth in Sweden.

Drug development breakthroughs	Medtech innovation
Bricanyl, selective beta 2 stimulator	Artificial kidney
Dextran, Macrodex, blood plasma substitutes	Biosensors
Fragmin low-molecular-weight heparin	Brånemark implant systems
Genotropin, human growth hormone	DNA sequencing technology
Healon, ophthalmic device	Gamma knife
L-dopa	IgE allergy diagnosis
Losec/Prilosec, ulcer medicine	Implantable pacemaker
Nexium, proton pump inhibitor	Respirator
Pulmicort	Sephadex, gel filtration chromatography
Rheomacrodex, blood plasma substitutes	
Salazopyrin, anti-inflammatory	
Seloken, selective beta 1 blocker	
Xalatan, glaucoma drug	
Xylocain, local anesthetics	

Source: Invest in Sweden Agency, 2009