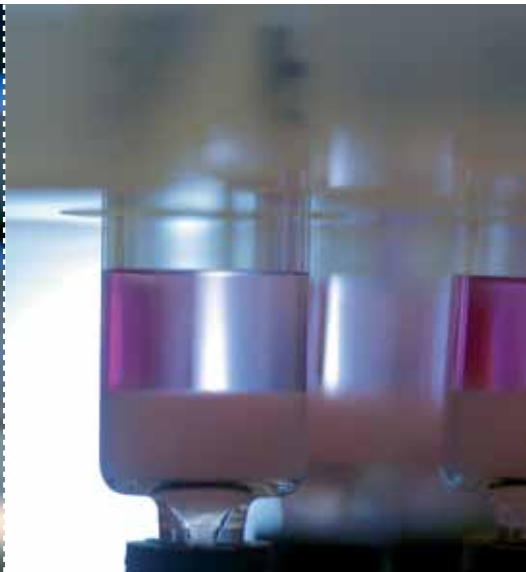




ANNUAL REPORT | 04



*Statens  
Serum  
Institut*

---

## MISSION STATEMENT

Statens Serum Institut prevents and controls infectious diseases and congenital disorders. Our expertise includes:

- Monitoring, advising and teaching on the incidence, prevention and treatment of infectious diseases and congenital disorders
- Specializing in the diagnosis of infectious, autoimmune, congenital and genetic diseases
- Ensuring the supply of vaccines, other biological products and diagnostic services through production and procurement
- Preparedness against biological terrorism
- Research and development in the Institute's areas of activity at an international level

Statens Serum Institut aims to ensure advanced control of infectious diseases, including new infections and biological threats. The Institute also strives to be a highly regarded and recognized national and international research, production and service enterprise.

---

# CONTENT



Management's Review .....	4
Research and Development .....	8
Avian Influenza .....	8
Center for Vaccine Research.....	10
Outbreak of Hepatitis A .....	12
Increased Occurrence of MRSA.....	14
Knowledge Report .....	16
Employees .....	20
Environment .....	24
Financial Statements.....	26
Statement of Management Board and Institute Council .....	32
Auditors' Report .....	33
Significant Accounting Policies.....	34
Income Statement, Balance Sheet, Statement of Cash Flows .....	40
Notes to the Income Statement and Balance Sheet ..	43
Publication List .....	46
Management Board and Institute Council .....	51
Organization Chart .....	52
Contact .....	53



# MANAGEMENT'S REVIEW



## Financial results for 2004

In 2004 Statens Serum Institut's revenue increased 8% to DKK 980m and exports totaled DKK 250m, up 13%. The government funding for the Institute's management of research-based monitoring, advisory, prevention and control functions totaled DKK 93m, corresponding to a 5% increase. External funding of research via foundations and EU funds increased 37% to DKK 58m.

Statens Serum Institut achieved a profit of DKK 12m in 2004 compared with DKK 4m in 2003. The profit for the year is carried forward to next year.

The results are better than expected and satisfactory. The positive variance reflects primarily the following developments:

An unusually high incidence of respiratory and gastrointestinal infections in the autumn resulted in increased activity in the diagnostics area.

In the plasma-derived drugs area, statutory amendments and a public tender in 2003 meant that the Institute was to cease supplying these products to the Danish health service as of January 1, 2004. However, the supply was continued until September.

The Institute has also proved able to establish itself faster than expected as a supplier to the pharmaceutical industry of biological analyses and controls as well as services such as bottling of drugs in compliance with the high quality standards set by the American Food and Drug Administration (FDA). In addition, export sales of tuberculosis vaccine (BCG) were higher than expected.

No events that materially affect the operations of the Institute have occurred since the end of the fiscal year.

## Financial outlook for 2005

For 2005 the Institute expects a moderate loss due to continued expenses for optimizing and commercializing the Institute's research portfolio in the plasma area, and to the fact that the polio vaccine plant is in its final and most costly stage of validation and control production required before commercial production can start. Both have a short-term negative impact on results. The Institute also expects to invest in the construction of a production plant for whooping cough vaccine in 2005.

In 2004 an interministerial working group analyzed various models for the future operations of the Institute. Based largely on the need to ensure adequate Danish emergency preparedness, it recommended that the Institute continues to operate on the general principles currently applied. The Institute therefore does not expect the analysis to result in significant changes in its operations in 2005.

## The year's main events

In 2004 the world's focus was on avian (bird) influenza. It was feared that the outbreak in Asia would result in the transmission of infection from animals to humans, creating the risk of an influenza pandemic. The threat still exists and it renewed the focus on the need for emergency preparedness plans to deal with such a pandemic. The Institute was granted DKK 6m for intensifying the emergency preparedness functions, and for expanded epidemiological monitoring and further development of methods for rapid identification of the influenza virus.

This was the year in which, despite a restrictive practice for prescribing antibiotics, the problem of antibiotic-resistant bacteria neared Denmark. The Institute has given the area higher priority and is participating in work on a national action plan to intensify controlling the spread of antibiotic-resistant staphylococcus in particular, which is a serious and growing problem.

On the research front, the Institute has documented that childhood vaccines do not cause other diseases such as autism and diabetes. This is of great importance to childhood vaccination programs world-wide.

Over Christmas the world was shaken by the tsunami in South and Southeast Asia. With only a few hours' notice, Statens Serum Institut sent off supplies of tetanus vaccines and immunoglobulin to prevent and treat tetanus among the many injured. The Institute also sent out an epidemiological expert to the disaster area.

In 2004 the Office of the Auditor General in Denmark completed a major administrative analysis of Statens Serum Institut. It was positive that the analysis concluded that the Institute is ensuring a satisfactory supply and quality of vaccines and diagnostic services.

It further concluded that the Danish system of prevention and control of infectious diseases is generally at a higher level than in our neighboring countries. The report noted that prices of a few of the Institute's vaccines are somewhat higher than prices in our neighboring countries, but this is due mainly to the Institute's additional public health and preparedness functions and its research, development and production activities for a smaller domestic market.

Because the exchange of information, in particular with the stakeholders in the health services, is a vital element, the Institute is increasingly using its website [www.ssi.dk](http://www.ssi.dk). Therefore the Institute is pleased that the website received the Danish Ministry of Science, Technology and Innovation's "Best on the Internet" award in 2004 among 180 research, advisory and educational institutions. In addition, approximately 1 million visitors to the website each year indicate that relevant information is disseminated in this way. The Institute is continually improving and developing the website as a web-based communications tool.

### **Diagnostics**

Revenue in the diagnostics area totaled DKK 242m, up 8%, due mainly to a high incidence of respiratory and gastrointestinal infections. In 2004 more than 30 new analyses were introduced, as well as package solutions where a sample from one patient can be analyzed for several possible respiratory infections.

Statens Serum Institut is trying to optimize diagnostic work processes so that the Institute can continue to offer analyses of the highest technology and quality at competitive prices.

### **Diagnostic media and reagents etc.**

In 2004 the revenue in this area increased 11% to DKK 76m. Since the establishment of the joint-venture company, Harlan Scandinavia ApS, the Institute has focused on phasing out the breeding of small test animals as an activity area. Harlan Scandinavia ApS is developing as expected and plans to start isolator breeding of special mice in 2005.

The Institute's efforts to quality assure and optimize production of diagnostic sera and diagnostic media and reagents are beginning to pay off through increased sales in Denmark and abroad, a trend that is expected to continue.

### **Vaccines**

The vaccine area continues its positive development. Exports rose 10% due mainly to our success in establishing the Institute as supplier of tuberculosis vaccine (BCG) to a number of countries in Europe. And the Institute's new booster childhood vaccine against diphtheria, tetanus, whooping cough and polio was approved in Denmark. The vaccine for revaccination against diphtheria and tetanus was approved for use in Ireland, Portugal, Spain and Greece. This is a good platform for further growth in exports.

The Institute's new high-tech plant for producing serum-free polio vaccine has now started producing vaccine for clinical documentation. The comprehensive documentation is expected to be completed in 2005 so that the Institute can start selling polio vaccine produced at the plant in 2006.

### **Plasma-derived products**

The Institute's obligation to secure the supply of plasma-derived drugs to the Danish health service ended at the beginning of the year. Due to ZLB, which won the tender, not being able to supply the products until September 2004, the Institute ensured the supply until then by buying and reselling products etc. At the same time, the Institute has been working on strengthening and commercializing its research and development portfolio.

### **R&D**

The Institute's R&D remains at a high international level. Besides continuous development of new diagnostic services for the Danish health service, the Institute published 238 scientific publications in 2004, 92% of which appeared in international journals with an impact factor. The average impact factor of the scientific publications was 4.0, which is very high. Eleven PhD theses were completed, six new patents



were obtained and four patent applications were submitted. The Institute therefore continues to be one of Denmark's largest research institutions in the health sector.

The Institute's vaccine research is recognized internationally. To further strengthen the area, the Institute established a Center for Vaccine Research in 2004, representing research in vaccines against tuberculosis, malaria and HIV that together cause 50% of all deaths world-wide. Research is also carried out in vaccines against Chlamydia, which is the most common venereal disease that can lead to sterility. It will be possible to control these diseases if the Institute succeeds in developing effective vaccines. The first promising vaccine candidates are now being tested in humans. Research in these areas is supported by a total of DKK 120m for some years from the EU, WHO and the Bill and Melinda Gates Foundation.

### **The year ahead**

Statens Serum Institut is in the middle of a challenging period. Growth in revenues is expected to be limited in the short term, until the launch of a range of new products. The Institute is still facing heavy expenses for the trials of the new polio vaccine and expected investments in a new production plant for whooping cough vaccine.

Statens Serum Institut still needs to focus on the international spread of pandemic diseases occurring naturally or through terrorism. To pool and intensify epidemiological monitoring and research, and biological preparedness functions, a Division of Epidemiology was established with Professor Mads Melbye as Executive Vice President. In collaboration with national authorities, the new division will work to further strengthen the Danish preparedness against infectious diseases.

Following the Danish Structural Reform, the Institute will strive to enter into collaboration agreements with the regions that will replace Denmark's counties and take over their tasks in the health sector. Statens Serum Institut aims to ensure that the Danish population has diagnostic products and services of the highest technology and quality for the fast and

targeted treatment of diseases. The Institute also aims to ensure the best possible national monitoring of serious infectious diseases and of the expansion of antibiotic-resistant bacteria, and will continue to assist local and regional health services in dealing with the outbreaks of such diseases.



*Nils Strandberg Pedersen  
President, CEO*

# AVIAN INFLUENZA

*Steffen Glismann, MD, DMSc, Department of Epidemiology*

In 2004 an outbreak of avian (bird) influenza type A led to much discussion, particularly about the risk of spread to other parts of the world. The infection has spread to a hitherto unseen extent in poultry in Cambodia, Indonesia, Japan, China, South Korea, Thailand and Vietnam. Furthermore, at least 17 persons in Thailand and 33 in Vietnam have been directly infected by poultry. In all, 37 of the patients died.

Transmission to humans has come in two waves, in which most were sick from January to March 2004. The large-scale destruction of sick poultry was presumably the main reason that the disease was not reported in humans until August, when deaths were again reported in Thailand and in September also in Vietnam. The recurrence of transmission to humans must be attributed to the fact that the interventions were not sufficiently effective.

The situation in South East Asia raised the question of the risk and seriousness of an influenza pandemic and stressed the need for Statens Serum Institut's competencies with respect to outbreak handling and prevention, including risk analysis, diagnostics and advice.

## Why avian influenza is dangerous

Avian influenza occurs all over the world and is caused by influenza virus type A, which can cause high morbidity and mortality among poultry. Avian influenza virus is found in nature among wild birds, particularly sea birds, which do not become sick, but all bird species can be infected. Transmission to humans occurs by direct contact with infected poultry and droppings.

Human influenza type A virus occurs in the winter periods in the northern and southern hemispheres and leads to millions of people being infected in Europe, Japan and the USA alone. It is these viruses that are prevented by yearly influenza vaccinations. On simultaneous infection, the human and avian influenza virus can exchange genetic material (antigen shift) and a new virus occurs. Pigs can act as intermediate host because they are receptive to both human and avian influenza

virus type A. The same applies to humans in the case of direct transmission from birds. Exchange of genes thus gives rise to a risk of a new influenza virus causing widespread infection among humans, and a pandemic can occur. Historically, influenza pandemics occur two to four times in a hundred years and in the worst case on a scale as in the influenza pandemic in 1918-19, the Spanish flu, from which 20-40 million people died.

## Outbreak of avian influenza

Fortunately, influenza pandemics like the Spanish flu occur very rarely, but it is naturally this dreaded scenario that sets the agenda with respect to handling and prevention. Apart from the outbreak in question, there have been several world-wide outbreaks of avian influenza among poultry since 1997, and three of them have involved transmission to humans:

- Hong Kong 1997: 18 people fell ill and six of them died. The outbreak was contained and halted by culling about 1.6 million chickens over a few days
- Hong Kong February 2003: Three people fell ill and two of them died. They were all from the same family and are thought to have been infected by poultry during a visit to Southern China
- The Netherlands, Belgium and Germany spring 2003: Outbreak of avian influenza type H7N7 among poultry. In the Netherlands, the virus was isolated in 89 people, of whom one died. The outbreak led to about 31 million poultry being culled

Besides the seriousness of transmission to humans, such outbreaks of avian influenza are an immense economic burden, particularly in countries with development-like status as in South East Asia.

## The current situation

A very large number of people have been exposed to transmission from poultry in connection with the outbreak in South East Asia. On the other hand, only relatively few patients have been reported, but the mortality has been high among young patients. This



may well be due to the fact that the virus in question has circulated earlier, so older people have achieved immunity and less risk of falling sick.

Influenza pandemics occur precisely where there are large numbers of birds, pigs and humans and close contact between them. The global population has tripled in the last 100 years. Half the population lives in urban areas, with the greatest growth in Asia in particular. At the same time, the global domestic animal population has multiplied many times over. Together with the great mobility in the world and the experience from the SARS outbreak in 2003, it must be assumed that a new influenza virus could spread to all parts of the world in just a few days.

In a risk analysis it is important that, unlike the avian influenza virus circulating in South East Asia at present, which is highly pathogenic to poultry, earlier pandemics have been caused by avian influenza with low mortality among poultry (low pathogenic). The immense media attention makes the situation in South East Asia highly visible, but it must be presumed that a new pandemic influenza virus could just as easily arise from an avian influenza virus with low virulence, which kills poultry on a less visible scale. In handling the current outbreak and preventing new epidemics it is therefore important to bear this fact in mind and aim for the worst imaginable scenario, which is a pandemic with high morbidity and mortality. Among other things, this calls for coordinated international action on surveillance, developing diagnostics and treatment and taking preventive measures and active intervention.

### **Globalization and handling of infectious diseases**

Globalization and population growth, the outbreak of avian influenza in 2004 and SARS in 2003 have led to day-to-day work at Statens Serum Institut becoming more international. The Institute participates in the international surveillance and prevention of influenza in an EU and WHO context, and besides developing fast diagnostic tests for both human and avian influenza viruses, Statens Serum Institut participates both nationally and internationally in the work of improving



the supply situation of a pandemic vaccine. Statens Serum Institut also contributes to the implementation of the Danish National Board of Health's pandemic plan.

To summarize, the international aspect must be expected to have a permanent place in the handling of infectious diseases. It is therefore important that Statens Serum Institut continues to develop already established and available competencies with respect to preventing and handling outbreaks both nationally and internationally.

# CENTER FOR VACCINE RESEARCH

*Michael Theisen, Manager, Mark Doherty, Senior Researcher, Department of Infectious Disease Immunology, Anders Fomsgaard, MD, MDSc, Department of Virology, and Peter Andersen, Director of the National Center for Vaccine Research*

Statens Serum Institut has extensive experience in all aspects of vaccine research and development, with particular focus on the development of vaccines against tuberculosis, malaria and HIV/AIDS. In 2004, considerable scientific progress was made, with vaccine candidates giving promising results in clinical studies. In recognition of this work, Statens Serum Institut has received large external grants in these areas, including DKK 120m from, e.g., the Bill and Melinda Gates Foundation, the European Malaria Vaccine Initiative and the EU.

To further strengthen activities within these three important vaccine research and development areas, Statens Serum Institut has established a Center for Vaccine Research (CfV) which currently has around 60 employees. CfV also has projects on the development of a vaccine for Chlamydia and the development of new adjuvant systems that can increase the immune response after vaccination.

Within the next ten years, the Institute intends to have developed and tested vaccines against the world's most serious diseases, tuberculosis and malaria, whereas a vaccine for HIV/AIDS lies some years ahead.

## **Tuberculosis, malaria and HIV/AIDS**

Tuberculosis, malaria and HIV/AIDS are large and growing global health problems. Together, these three diseases kill more than 5 million people annually worldwide. Besides the vast human suffering they cause, the economic consequences for society are enormous. The three diseases are therefore among the biggest obstacles for positive socio-economic development in much of the developing world and especially Africa.

The global health problems caused by these three infectious diseases are growing, partly because the treatment is costly and partly because of increasing resistance to the drugs used. Complete control can be achieved

only if the efforts to develop effective vaccines succeed. Development of vaccines against the three infectious diseases is an enormous scientific, technological and economic challenge that calls for broad international collaboration with the best research centers, industry and public and private investors. Diseases respect no borders – the development of safe and effective vaccines is important for the entire world and would directly help to reduce poverty in developing countries.

## **New vaccine against tuberculosis**

Research on the development of a new and improved vaccine against tuberculosis has high priority at CfV, and the first vaccine candidate will be tested in humans in the Netherlands in the summer of 2005. Preclinical studies in mice, guinea pigs and monkeys have shown that this vaccine gives significant protection against an experimental tuberculosis infection. It has also proven suitable for boosting the immune response against the Institute's current tuberculosis vaccine (BCG).

The aim is to combine the new vaccine with the existing BCG vaccine for children in order to improve their immune responses. When the effect of this vaccine diminishes at the age of 10-12 years, the new vaccine is intended to boost immune responses and thus help to protect the population of 15-40-year-olds against pulmonary tuberculosis.

## **Vaccine against malaria**

Another project at CfV aims to develop a vaccine against malaria. Malaria is an infectious disease caused by the parasite *Plasmodium falciparum*, which is transmitted by infected mosquitoes. Various efforts to control malaria have focused mainly on insecticides to eliminate the mosquito vector and on drugs to kill the parasite. However, with the emergence of insecticide-resistant mosquitoes and the increasing prevalence of multi-drug resistant *P. falciparum* parasites, the malaria problem has increased in recent years.

It is therefore important to develop a safe and effective malaria vaccine. Our research team has found a protein – GLURP – from *P. falciparum* which is a promising candidate for inclusion in a malaria vaccine.

The hope is to vaccinate newborn children in Africa to induce an immune response that is as strong as that found in immune adult Africans.

The first vaccine candidate has already been tested in humans in the Netherlands. The results show that the vaccine is safe, i.e. there are few or no side-effects, and it elicits a strong immune response in healthy people. This response is characterized by very high levels of antibodies – several times higher than the levels normally found in immune adult Africans.

New clinical studies are commencing in Africa in the summer of 2005. With a view to improving this vaccine still further, the research team has developed a “2nd generation vaccine”, in which GLURP is combined with a protein, MSP3, which is found on the surface of the parasite. This vaccine is being tested in Europe this year and is expected to be ready for testing in Africa at the beginning of 2006.

### Vaccine against HIV/AIDS

A third project at CfV involves research and development of vaccines against HIV/AIDS. The vaccine in question is a so-called “DNA-vaccine”, which codes for two components. One codes for surface proteins from clinically relevant HIV strains and produces new antibodies in tests on monkeys. The other codes for several small, constant areas of HIV which the cells of the immune system can be made to react. These activated immune cells (T cells) can eradicate already-infected HIV cells. The new vaccine can thus potentially be used both for prevention and treatment of persons infected with HIV (therapeutic vaccination). The project aims to run clinical trials of the therapeutic vaccine in selected persons infected with HIV in Denmark. If the vaccine has a therapeutic effect, it will indicate that there is also a preventive effect.

*Speeches on the global importance of tuberculosis, malaria and HIV were given by Oli Fruth of WHO (top) and Paul Henri Lambert of Center of Vaccinology (bottom)*





# OUTBREAK OF HEPATITIS A

Anne Mazick, EPIET fellow, MD, and Michael Howitz, MD, Department of Epidemiology

## Increase in cases of hepatitis A

At the beginning of 2004 Statens Serum Institut recorded an increase in cases of hepatitis A (infectious hepatitis). From 1 January 2004 to 1 January 2005 a total of 162 cases of hepatitis A were recorded among men over the age of 17. Of these, 107 were from Greater Copenhagen and at least 68 of them were men who had sex with men (MSM).

In addition, the Department of Epidemiology was informed of more patients from Skåne, Sweden, with hepatitis A, who had probably been infected in MSM saunas in Copenhagen. Besides general precautions in the case of a hepatitis A outbreak, such as strict hygiene and use of immunoglobulin for close contact with patients, it was recommended that MSMs who were not living in a monogamous relationship should be vaccinated. STOP AIDS, the Danish National Association of Gays & Lesbians and the medical health officers in Copenhagen carried out information campaigns in the spring of 2004 to promote prevention of hepatitis A.

When the outbreak continued during the summer a decision was taken to carry out a case-control study in collaboration between clinicians from the State University Hospital and Hvidovre Hospital and STOP AIDS. The purpose was to clarify risk factors and target preventive measures.

## Hepatitis A as a disease

Hepatitis A has gradually become a rare disease in Denmark. The disease breaks out about 4 weeks after infection, and the symptoms are typically a fever, nausea, stomach pains and jaundice. The urine becomes dark, and the stool pale. In adults, the symptoms last for one or several weeks, after which the patient is immune. The patients are rarely seriously ill, but some are hospitalized, and most are fatigued and have reduced working capacity for a long time after their illness.

The virus that causes the disease is excreted in the stool and, in the event of poor hygiene, can be



transferred to food and drink. Receptive persons are thus infected by ingesting contaminated food and water or by contact with stool, e.g. infants wearing diapers, who excrete the virus. In Denmark, hepatitis A is seen particularly as an imported disease and in connection with outbreaks among children in institutions.

The disease can be prevented effectively and safely by vaccination, which is recommended for children and adults before traveling to exotic destinations where there is a risk of hepatitis A.

### Case-control study

In the period June 1 to mid-August 2004, all MSMs with hepatitis A who lived in Greater Copenhagen were invited to participate in the study. Control persons were selected among MSMs who participated in Copenhagen Pride Festival on August 14, 2004. Saliva was collected from all control persons for serological investigation, and only persons that were receptive to hepatitis A and lived in Greater Copenhagen participated. Information was collected on a number of risk factors via a questionnaire. The study comprised 18 cases and 64 controls.

Among other things, the study showed that sex in Copenhagen saunas and sex with casual partners were associated with an increased risk of infection with hepatitis A. Most of the control persons were willing to be vaccinated against hepatitis A; however, only one quarter of them were willing to pay for the vaccination.

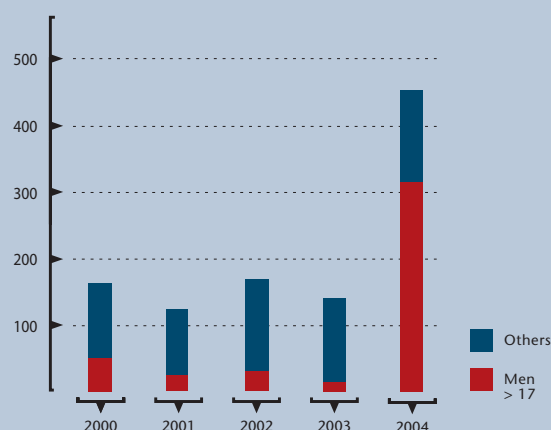
### What can we learn?

The MSM milieu's saunas have previously been connected with outbreaks of both hepatitis A and sexually transmitted diseases, e.g. syphilis. Since the mid-90s, outbreaks of hepatitis A have circulated between European cities and have been connected with the sauna milieu in other places. The largest Copenhagen sauna has 700-1,000 visitors a week. The sauna milieu is popular both with Danish MSMs and visitors from abroad. The increased risk of infection is probably related to the fact that there is a possibility of sex with several partners in the space of a short time. The study shows that it is important to inform people of the possibility for prevention by vaccination. This infor-

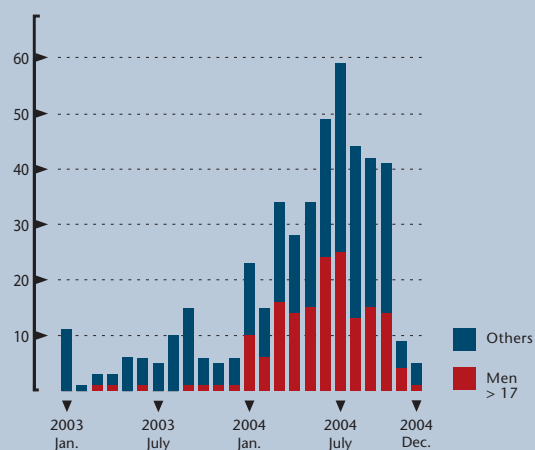
mation should be addressed particularly to MSMs connected with saunas and other milieus with frequent changing of sexual partners, since they are at particular risk of infection with hepatitis A. However, the price can be a barrier to vaccination.

Besides giving the possibility of targeting prevention, the study contributed to increased insight into parts of the MSM milieu, which may promote prevention of other diseases. Lastly, it must be stressed that we live in an age in which the panorama of infectious diseases is developing and changing. New diseases appear, and old ones occur in new forms or with a different spread. It is therefore important to examine outbreaks and regard them as an opportunity to practice epidemiological methods and increase the collaboration with relevant partners.

Notified cases of hepatitis A, 2000-2004



Notified cases of hepatitis A, 2003-2004





## INCREASED OCCURRENCE OF MRSA



*Robert Leo Skov, MD, and Niels Frimodt-Møller, MD,  
DMSc, Department of Antibiotic Resistance and Hospital  
Hygiene*

*Staphylococcus aureus* – also called the yellow staphylococcus – is one of the most common pathogenic bacteria in humans and the most frequent cause of hospital-acquired infections. MRSA are *Staphylococcus aureus* bacteria that are resistant to all  $\beta$ -lactam antibiotics, i.e. penicillins, cephalosporins and carbapenems. This is a problem as  $\beta$ -lactam antibiotics are the most effective for treating staphylococcus infections.

Partly for that reason, MRSA infections are linked to considerably increased morbidity and mortality. To prevent these bacteria from spreading, patients with MRSA infections are kept isolated during their stay in hospital. The longer confinement in bed, added to isolation, longer reconvalescence and more expensive treatment with antibiotics, mean that MRSA infections are connected with serious inconvenience for the individual patient and heavy costs for society.

The occurrence of MRSA has been increasing in Denmark. An MRSA epidemic is a threat to any country's health service, as besides causing suffering and death, it is very costly for both hospitals and the primary health service. Therefore the earlier the epidemic can be stopped, the better.

Experience shows that combating MRSA is a resource-intensive task that can be solved only in close cooperation between the doctors treating it, nursing personnel, the clinical microbiological departments, Statens Serum Institut and other central health authorities.

## Historically low incidence of MRSA in Denmark

Staphylococcus infections have been monitored in Denmark in close collaboration between the clinical microbiology departments and the Staphylococcus Laboratory, Statens Serum Institut, since 1957. Because of a high occurrence in the 1960s, a targeted effort was made to combat MRSA at that time. As a result, the number of MRSA infections fell from about 20% of all staphylococcus infections in the mid-1960s to less than

1% in the mid-1970s – the level at which it has remained. In other countries (apart from the Nordic countries and the Netherlands), the number of MRSA infections has risen steadily for the last 20 years and now constitutes up to 80% of all staphylococcus infections.

### New types of MRSA give a higher frequency

In recent years, however, there has been a worrying increase in cases of MRSA in Denmark (figure 1). The increase is due to the introduction of new types of MRSA bacteria that survive better outside hospitals and therefore spread more easily. This has led to a change in the epidemiology of staphylococcus infections. In Denmark, MRSA previously occurred most frequently in patients who had been hospitalized abroad; today, MRSA is most often contracted in Denmark and often occurs outside hospitals.

### Improved surveillance at Statens Serum Institut

The Staphylococcus Laboratory has consequently intensified both its surveillance and research regarding MRSA. Typing of bacteria is an important tool for identifying modes of transmission and describing the disease characteristics of the individual types of MRSA. In 2004 the Staphylococcus Laboratory therefore obtained the possibility of reprioritizing funds for introducing modern (DNA) sequence-based typing methods. By using these methods it is possible to compare isolates found in Denmark with isolates from other countries. Considerable new knowledge has thereby been obtained regarding the strains that are at present causing the alarming rise in cases of MRSA – knowledge that improves the targeted control of these strains.

The new MRSA strains have also proven difficult to detect in the laboratory. In the past two years the Staphylococcus Laboratory has played a central role in testing and introducing a new method for identifying MRSA in patient specimens. MRSA is detected by means of paper discs containing antibiotics or tablets on an agar plate. For many years this has been done with the substances methicillin or oxacillin, but these antibiotics are less than efficient at catching the new MRSA strains. Research collaboration between the

Staphylococcus Laboratory, Danish and international laboratories has shown that another antibiotic, ceftioxin, is far better at this task, and the method has now become standard in Denmark, Sweden and the USA.

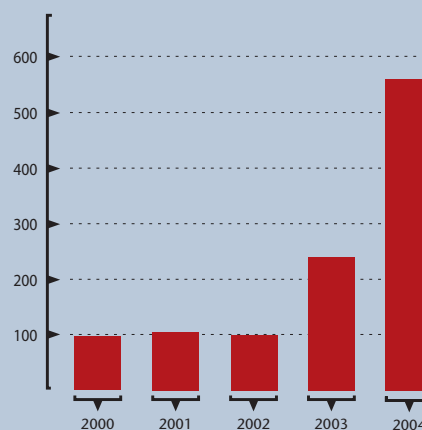
### Nationwide action

In 2004 the health authorities in Denmark initiated a focused nationwide campaign. An expert group with representatives from clinical microbiology, infection control nurses, infectious diseases, medical health officers, general practitioners and Statens Serum Institut will develop national guidelines for controlling MRSA. The guidelines must cover conditions both in and outside hospitals, including isolation procedures, tracing and treatment of disease carriers. MRSA will also soon become a notifiable disease.

### International cooperation

The rise in cases of MRSA and the change in the epidemiology have also been observed in other Scandinavian countries, which, like Denmark, have otherwise had a stable and low number of cases. The Scandinavian Society for Antimicrobial Chemotherapy (SSAC) has set up a working group, chaired by Statens Serum Institut, to reveal similarities and differences in the different countries' guidelines and ways of handling the epidemic and use this information to identify potential joint-Nordic action areas.

### MRSA isolates, 2000-2004



Knowledge building, research and development, skilled, motivated and specially trained employees and good relations with customers and the community in general are vital to Statens Serum Institut's operations, results and future development possibilities.

## **Statens Serum Institut – the enterprise**

Statens Serum Institut's objective is to prevent and control infectious diseases and congenital disorders. The Institute is organized as a state enterprise under the Ministry of the Interior and Health, and takes care of:

- Control of infectious diseases: surveillance, prevention, control of and advice on infectious diseases and congenital disorders
- Specialized diagnosis of infectious, autoimmune, congenital and genetic diseases
- Ensuring the supply of vaccines, other biological products and diagnostic media and reagents
- R&D at an international level within the Institute's areas of activity

Prevention and control of infectious diseases involve a number of assignments of an official nature and related research. The assignments are technologically and financially defined in a number of service contracts between the Ministry and the Institute. The Institute also undertakes research activities financed via foundation grants.

The activities are widely oriented towards social needs, and the results form a central part of the professional basis for the decisions made by the politicians and the health service. The Institute also supplies scientific advice and assistance to international authorities.

The Institute's other activity areas (diagnostics, diagnostic media and reagents, vaccines and plasma-derived products), all independent business units, must ensure a high level of professional competence and financial profitability. This is achieved through research, development, production, marketing and the sale of products and services.

Independent business units are not isolated from the prevention and control activities. Both diagnostics and the diagnostic media and reagent activities contri-

bute directly and indirectly, and are therefore essential for performing the Institute's central assignments.

The Institute is managed by a Management Board comprising the President and CEO, the CFO and the Executive Vice Presidents. Statens Serum Institut has an advisory Institute Council, called upon and consulted on all questions and issues considered to be of strategic importance. The Council members have general knowledge of the Institute's operations and activities with special emphasis on commercial experience and knowledge of pharmaceutical work and research.

## **R&D**

Innovative R&D is essential for Statens Serum Institut to be able to solve the tasks concerning prevention and control of infectious diseases and congenital disorders.

The Institute must ensure modern control of infectious diseases that covers current infection problems and can identify and respond to so far unknown infections and biological threats. This requires continuous knowledge building, research and international collaboration. It also requires close collaboration with the Institute's other activities so that scientific, information and technological synergies are used to best advantage.

Independent business units must have product-oriented R&D that supports the prevention and control of infectious diseases and helps maintain a strong market position. The R&D must be at the level of comparable enterprises.

The Institute's R&D remains at a very high international level, which is emphasized by the substantial grants obtained each year from national and international foundations. These grants cover all the research-intensive activities at the Institute, which reflects the wide scope of the Institute's research.

#### R&D in the period 2000-2004 in DKKm/% of revenue

Year	2000	2001	2002	2003	2004
Funded by the Institute	80.4/10.6	85.1/10.5	107.6/12.0	120.3/13.2	147.9/15.1
Government-funded	41.5/5.5	33.6/4.2	29.4/3.3	30.6/3.4	32.7/3.3
Non-government-funded	49.1/6.5	49.5/6.1	50.8/5.6	42.2/4.6	57.6/5.9
<b>Total</b>	<b>171.0/22.5</b>	<b>168.2/20.8</b>	<b>187.8/20.9</b>	<b>193.1/21.3</b>	<b>238.2/24.3</b>

The R&D activities are prioritized continuously. With a view to achieving optimal performance, the Institute currently focuses on the following areas in particular:

- Diagnosis and surveillance of gastrointestinal and respiratory infections
- Research and surveillance of hospital-acquired infections, antibiotic resistance of bacteria and the resistance of virus to antiviral drugs
- Research on vaccines against tuberculosis, malaria, Chlamydia and HIV, including DNA vaccines
- Research on and diagnosis of congenital diseases
- Research on plasma-derived drugs

#### Scientific publications

The quality of the Institute's research and knowledge building is reflected in the number and the level of the scientific articles that are published. In 2004 the Institute published 238 articles, which is in line with 2003.

#### Scientific publications, 2000-2004

	2000	2001	2002	2003	2004
Publications, number*	250	231	232	238	238
In international journals, %	86	87	87	91	92
In Danish journals, %	14	13	13	9	8
Authors from SSI only, %	28	26	26	20	19
Authors from SSI and others, %	72	74	74	80	81
First author from SSI, %	54	54	59	45	47
PhD theses, number	7	4	7	12	11
<b>Medical doctoral theses, number</b>	<b>2</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>0</b>

\* These figures do not include lectures, conference papers, newspaper articles, teaching materials, PhD theses and medical doctoral theses, etc.

The quality of the Institute's publication activity can also be measured by means of an impact factor analysis. An impact factor reflects how often, on average, an



article can be expected to be cited over a two-year period if published in a given journal.

#### Impact factor analysis

Area of activity	Impact factor 2004/2003	Number of publications* with impact factor 2004/2003
Infectious diseases	3.0/2.8	53/59
Hospital hygiene and antibiotic resistance	3.1/2.9	20/11
Congenital diseases	3.5/2.9	19/13
Vaccine research	3.5/4.6	26/20
Plasma proteins	1.8/3.0	4/24
Epidemiological research	5.3/5.4	77/63
<b>All areas</b>	<b>4.0/3.9</b>	<b>199/190</b>

\*Some articles were published in new journals that have not yet been assigned an impact factor, which is why the number is less than 238.

Both the total impact factor and the number of publications with an impact factor are slightly higher in 2004 than in 2003. The very high level in both Danish and international contexts has therefore been maintained, which is very satisfactory.

## Knowledge sharing

Statens Serum Institut's competitiveness depends on individual employees being well informed and able to retrieve existing data and further develop existing knowledge. It is also important for communication and exchange of information with the Institute's stakeholders to be efficient and flexible. As a state-owned enterprise, the Institute is under an obligation to communicate relevant knowledge.

In 2004 the Institute continued the focused task of using the Institute's website, [www.ssi.dk](http://www.ssi.dk), as an active communications tool to exchange knowledge, data etc. The efforts have paid off as [www.ssi.dk](http://www.ssi.dk) was chosen in 2004 as the best website ("Best on the Internet") among 180 research, advisory and educational institutions, and had more than one million visitors.

One example of [www.ssi.dk](http://www.ssi.dk) being used as an active communications tool is the launch of an interactive e-learning module on hand hygiene, which is the single most important factor in our efforts to reduce the incidence of hospital-acquired infections. See the module on hand hygiene on: [www.ssi.dk/haandhygiejne](http://www.ssi.dk/haandhygiejne).

In 2004 most of the Institute's research, development, prevention and control projects have been registered in our R&D database, which is designed as a tool for individual project groups and the management. The project groups can use the platform to collect, exchange and share knowledge about individual projects. It is the project managers that grant access to the information to relevant persons. For management use, it is possible to draw up a number of different status reports with selected information across projects. In 2004 this has strengthened the control of the Institute's total project portfolio and thereby contributed to ensuring optimal use of resources. Increasingly strict requirements are made externally and in-house on project management and follow-up, and the database platform is intended to support and increase the efficiency of the related work processes.

One of the activity areas that receives large grants from foreign foundations such as the Bill and

Melinda Gates Foundation, the European Malaria Vaccine Initiative and the EU is the Institute's vaccine research on tuberculosis, malaria and HIV. To strengthen and intensify efforts, the Institute has pooled these activities in a joint research network – Center for Vaccine Research.

Statens Serum Institut holds regular scientific briefing meetings at all organizational levels. The Polymorphy is a forum for scientific debate in which new knowledge and ideas are regularly disseminated and discussed.

## Customers and users

The buyers of Statens Serum Institut's products and services are the Danish health service and a number of Danish and international companies, institutions and organizations.

The users of the Institute's products and services, most of whom have medical expertise, demand the right quality and price. To be able to satisfy the demand for services and products, the Institute must know the users' needs and be innovative, ready for change, quality-minded and service-minded. The Institute has an active dialog with customers and users, and conducts regular user and customer satisfaction surveys in selected areas.



## BEDST PÅ NETTET • FORSKNINGS-, RÅDGIVNINGS- OG UDDANNELSESINSTITUTIONER

PRISEN BEDST PÅ NETTET GIVES TIL EN HJEMMESIDE, DER I SÆRLIG GRAD  
HAR FORMÅET AT SÆTTE BORGEREN I CENTRUM OG VÆRE ET EKSEMPEL TIL EFTERLEVELSE



STATENS SERUM INSTITUT • WWW.SSI.DK

PRISMODTAGER



STEEN ØRSKOV (FORMAND)  
Kommunalrådsformand i Hvidovre Kommune

METTE REJSMANN  
Folkebibliotekslæser, Folkebibliotek i Hvidovre

SØREN R. THIESEN  
Informationsrådgiver, Amtsbiblioteket i Hvidovre

CARSTEN LØSCH  
Projektleder, Den Digitale Tænkning

BJARNE VETTER-ANDERSEN  
Læge og  
De Samvirkende Institutorganisationer

DOMMERPANELET ER UDPEJET AF VIDENSBESKEDNINGEN HJØRGE SANDER



# EMPLOYEES



Through our human resource and management policies Statens Serum Institut's objectives are to:

- Attract, develop and retain professional and qualified staff
- Create a working environment in which the employees thrive and develop
- Help to ensure flexible and efficient job performance of high quality

### A new human resource policy in the pipeline

As follow-up on the new management policy adopted in 2003, the Institute has looked more closely at our human resource policy in 2004. Focus has been on defining key competencies for the employees that can be linked with the Institute's managerial values:

- Recognition
- Competence development
- Change

Based on a number of focus group meetings, a list of key competencies has been drawn up for employees at Statens Serum Institut that are to be implemented in the Institute's human resource policy. In addition, in 2005 the Institute will look at various areas, such as smoking, working hours and outdoor areas.

### Training and competence development

Statens Serum Institut finds an active training policy essential to attract and retain highly qualified staff. In 2004 the Institute invested 2.2% of its payroll in retraining employees.

The Institute also contributes to training courses for human biologists in microbiology and provides specialist training in clinical microbiology and hygiene nursing.

### Center for Management and Competence Development

In 2004 the Institute set up a Center for Management and Competence Development that offers training for managers and other employees as well as consultancy

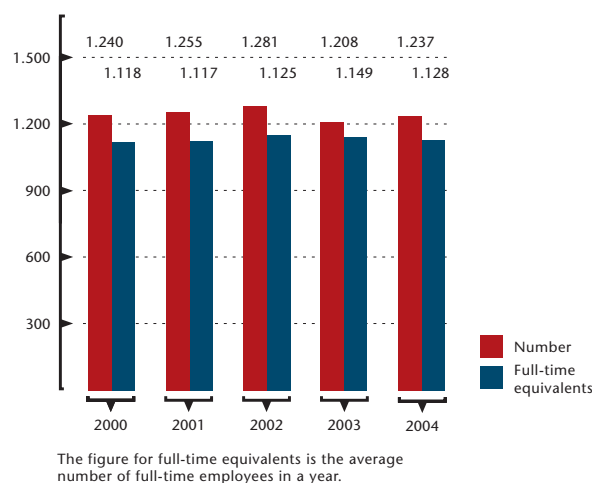
services e.g. coaching of managers, conflict resolution, career advice and tests in connection with staff recruitment.

The center is the result of the past ten years' work on employee and managerial development at the Institute. We are working with a wide range of theories and tools, including appreciative inquiry, systematic theory, emotional intelligence as well as coaching and dialog as conflict resolving method.

### Strategic competence development for laboratory assistants

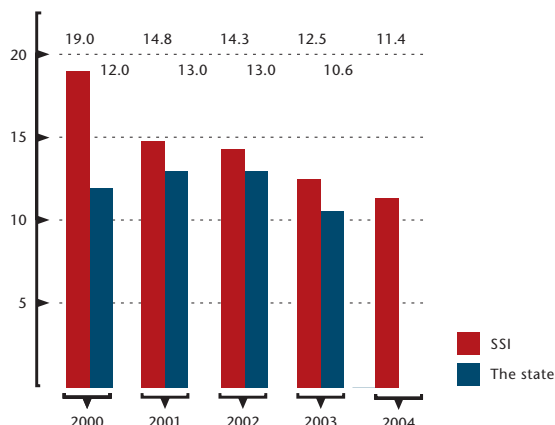
In 2004 a project to ensure general strategic competence development for the division's laboratory assistants was implemented in the Division of Microbiology & Diagnostics. With approximately 420 employees the laboratory assistant group is the Institute's largest group, which is why it is important to ensure that they have the necessary competencies to perform present and future tasks.

### Personnel consumption, 2000-2004



In the period 2000-2004, the number of employees and the figure for full-time equivalents were largely stable and resulted in increased revenue. Revenue per full-time employee equivalent therefore increased 32% from DKK 680,000 in 2000 to DKK 869,000 in 2004.

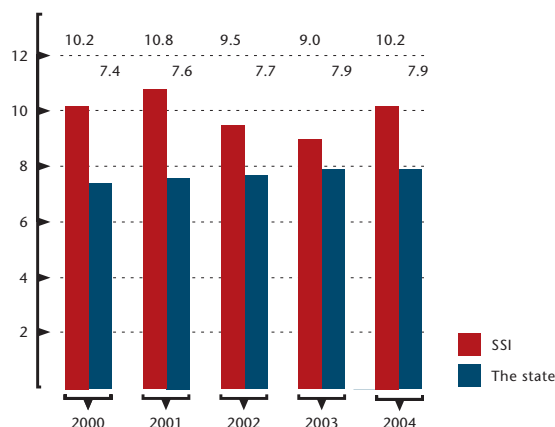
### Staff turnover, 2000-2004 (%)



As in previous years, staff turnover showed a slight fall in 2004 and is approaching staff turnover within the state.

### Absence due to illness

#### Average absence due to illness (days/employees), 2000-2004



The Institute must be expected to have more absence due to illness than the state in general because it is a manufacturing company. It is, however, unsatisfactory that the reduction in absence due to illness over the past few years has turned. The Institute will continue to focus on reducing absence to meet our aim of less than eight days of absence per employee.

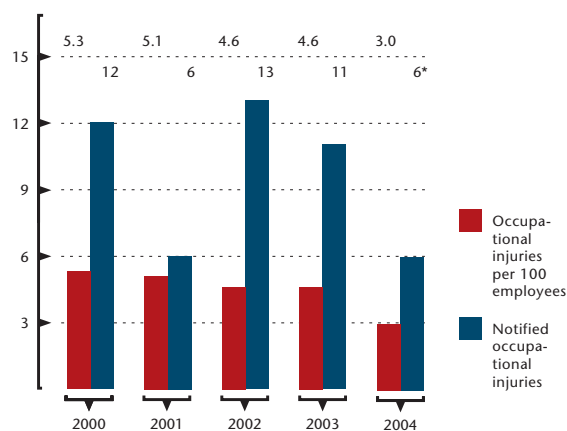
### Health and safety

For several years the Institute has taken systematic action to improve our work environment.

Besides the statutory health and safety training, the Institute has drawn up and implemented a supplementary training scheme for the members of the safety organization in 2004. The aim is to acquire more knowledge and competence and focus more clearly on high-priority action areas within health and safety. The training scheme covers a number of courses, including evaluation of work places, ergonomics, notification of injuries, mental working environment, how to handle chemical substances and biological agents.

In 2004 the accident frequency decreased from 4.6 to 3.0 per 100 full-time employee equivalents, which is satisfactory. Six of the occupational injuries were notified to the Working Environment Authority.

### Occupational injuries, 2000-2004



\* There may be cases notified to the Working Environment Authority of which the Institute is not aware – for instance, cases reported late or cases reported by the injured employee's doctor.

### Social responsibility

Statens Serum Institut has been a member of the Association for Integration of New Danes on the Labour Market since 1998. Through systematic action, the Institute wishes to ensure against discrimination of employees or applicants on grounds of race, religion, ethnic origin, philosophy, etc.





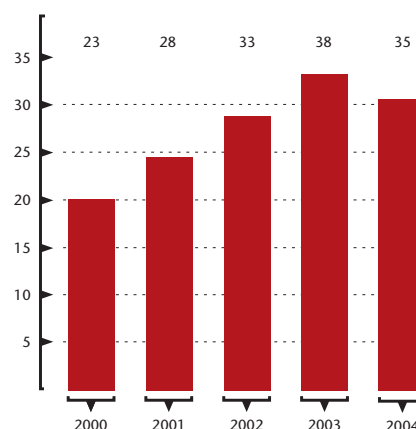
Accordingly, it must be ensured at the Institute that a person's suitability for a position is based only on his or her qualifications and ability to meet the Institute's needs in the given position.

Under the auspices of the Danish Ministry of the Interior and Health, Statens Serum Institut has been given the role of "ethnic ambassador" with a view to spreading to the Ministry's other areas the Institute's good results with recruiting and keeping employees with a different ethnic background. In 2004, the proportion of employees with a different ethnic background was 7.1%.

#### Social chapter

The creation of a more flexible labor market is an integral element of the Institute's human resource policy. The Institute therefore endeavors to keep its own employees when their capacity for work has been reduced owing to illness etc. It also strives to give unemployed people from outside the Institute the possibility of job training/rehabilitation when relevant work can be found for them.

**Number of employees in job training, (flex jobs, etc.), 2000-2004**





## Environmental management

Statens Serum Institut takes systematic action to reduce its impact on the surrounding environment. For this purpose an environmental manual was prepared in 2004, which is available to all employees. The manual covers subjects such as correct waste handling, awareness of current legislation and safe handling of chemical substances.

The internal audit, of which 15 were carried out in 2004, is an important tool for control and improvement in the environmental management system. It is a valuable basis for assessing the Institute's environmental, health and safety area achievements. It also provides an opportunity to give guidance on and discuss specific problems.

## Phasing out dangerous chemicals

All laboratories at the Institute use dangerous chemical substances to some degree. However, irrespective of the extent, the individual laboratories are striving to find alternatives.

Different substitution methods are applied according to the work methods used at the individual work places. Some employees co-operate on chemicals in interorganizational experience-exchange groups. Some work processes are so specific that only chemists with insight into them can assess which less dangerous substances may be used instead. The experience has been excellent, and the work will continue.

## A quiet enterprise

Statens Serum Institut is situated in an area with housing and day-care centers and is therefore subject to restrictive requirements concerning noise impact on its surroundings.

The Institute is continuously adopting measures to reduce its noise emission. In 2004 control measurements showed that the average daytime noise emission had decreased from 52.5 dB (in 2000) to 49 dB. During the night the noise emission measured in 2004 was only approximately 46.5 dB on average – that is not much more than the noise emitted from an automatic dishwasher.

However, since the Institute has still not fully reached its goals for all measuring points, further noise-reducing measures will be taken in the coming years to ensure that the Institute remains a good neighbor.

## Environmental impact

Increased production normally necessitates similarly increased consumption. However, at Statens Serum Institut, energy management resulted in energy consumption rising by only 20% from 1999 to 2004, despite a 29% rise in revenue in the same period. A similar trend can be seen in water consumption, which rose only 13% in the period in question.

Waste production has fallen considerably over the past years. The Institute's activities are continuously made more efficient, and in just three years our waste volumes have been reduced from 970 tons to 626 tons. It is mainly the volume of combustible waste that has been reduced. Instead there has been a slight increase in recyclable waste fractions: cardboard, paper and glass.

## Plans for 2005

The Institute is aiming for environmental certification under the current ISO standard in 2006. The time until then will be used to ensure that the Institute's employees have the necessary knowledge of the Institute's environmental policy and environmental manual.

In 2005 all facilities handling genetically modified microorganisms will undergo an environmental and health and safety audit, partly to ensure compliance with current requirements and partly to achieve overview and consensus and try to create a "best practice" in the area.

## Selected environmental data, 2000-2004

	2000	2001	2002	2003	2004
Energy (GWh)	27.7	28.6	30.6	31.6	33.3
Water (m <sup>3</sup> )	73,500	89,000	77,050	86,000	83,000
Waste (tons)	873	970	873	760	626



# FINANCIAL STATEMENTS

Statens Serum Institut is a state-owned enterprise under the Ministry of the Interior and Health with the objective of preventing and controlling infectious diseases and congenital disorders.

## Results for 2004

In 2004 the Institute achieved net income of DKK 11.7m, an increase of DKK 7.6m compared with 2003 and higher than expected.

The development in comparison with 2003 relates primarily to:

- Higher income from export sales of tuberculosis and DT vaccines (a positive DKK 23.6m)
- One-time sale of vaccines in 2003 (a negative DKK 18.7m)
- Higher expenses for running in the new IPV plant (a negative DKK 13.7m)
- Increased sales of diagnostic analyses due primarily to a mycoplasma epidemic at the end of the year (a positive DKK 14.1m)
- Increased income from diagnostic media and reagents sold to hospitals after they have started performing analyses themselves (a positive DKK 3.0m)

Readers are referred to the segment information in note 1 to the Income Statement.

## Results for 2004 compared with expectations

Overall results are better than estimated in the Annual Report 2003 due partly to a more efficient discontinuation of the plasma production than expected, partly to improved results within diagnostics due to a mycoplasma epidemic at the end of the year in 2004 and because the county hospital laboratories have performed fewer analyses themselves.

## Selected financial and operational data

Developments compared with previous years are shown in the table below.

### Selected financial and operational data

DKKm	2000	2001	2002	2003	2004
Net revenues	759.4	807.1	899.9	907.8	979.9
Operating income	29.9	(7.7)	43.7	14.2	18.8
Net income	21.0	(15.5)	31.8	4.1	11.7
Year-end equity	446.9	431.5	463.3	467.4	479.2
Investments for the year	53.4	131.0	63.2	50.5	82.3
Balance sheet total, end of year	763.9	910.6	1,020.4	1,020.6	1,039.6
Share of commercial revenue					
Diagnostics	30%	30%	30%	29%	29%
Vaccines	48%	50%	51%	51%	52%
Plasma-derived products	12%	11%	11%	11%	10%
Diagnostic media and reagents etc.	10%	9%	8%	9%	9%
Operating profit margin	3.9%	(1.0)%	4.9%	1.6%	1.9%
Return on invested capital (ROIC)	5.5%	(1.3)%	6.4%	2.1%	2.6%
Return on equity	4.8%	(3.5)%	7.1%	0.9%	2.5%
Equity ratio	58.5%	47.4%	45.4%	45.8%	46.1%
R&D in % of revenue	10.6%	10.5%	12.0%	13.3%	15.1%
Number of full-time equivalents	1,117	1,125	1,149	1,139	1,128
Revenue per full-time equivalent (DKK '000)	680	717	783	797	869
Share of exports	22%	25%	29%	28%	30%

The operating profit margin should be considered against a backdrop of revenue of DKK 150.9m in 2004 (DKK 131.2m in 2003) relating to non-profit activities for grants and external funds. The operating profit margin for commercial activities (adjusted for extraordinary write-down of the plasma assets) was 1.9% in 2004 compared with 3.9% in 2003.

In 2004 ROIC was slightly higher than the average cost of the Institute's long-term loan capital, amounting to 2.2% in 2004.

The equity ratio is again increasing moderately after it continued decreasing until 2002.

Commercial R&D expenses' share of revenue increased in 2004 compared with 2003, due primarily to expenses for running in and registering the new serum-free verocell polio vaccine, plus increased expenses for R&D within the tuberculosis area.

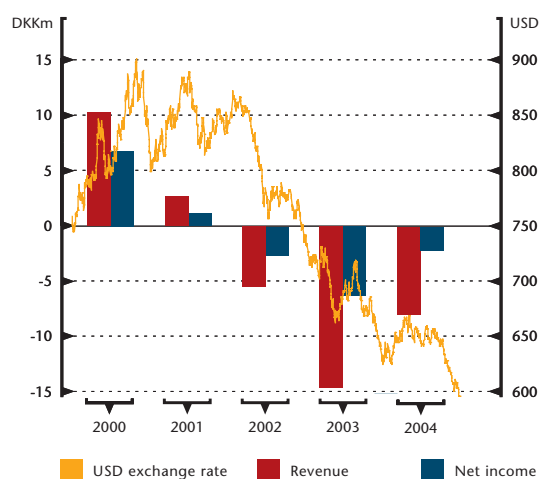
Compared with 2003, the Institute's share of exports increased, and at the same time the export mix has shifted from merchandise (2004: DKK 40.2m, 2003: DKK 42.2m) to own production (2004: DKK 209.7m, 2003: DKK 178.8m) with higher profit margins.



## Foreign currency impact

The average USD exchange rate fell from 659 in 2003 to 599 in 2004. This development adversely affected revenue by DKK 7.9m and operating income by DKK 2.2m.

## Impact of USD exchange-rate fluctuations



The above graph illustrates the impact on revenue and operating income of the change in the average USD exchange rate compared with 2003.

## Five-year summaries

DKKm	2000	2001	2002	2003	2004
Net revenues	759.4	807.1	899.9	907.8	979.9
Production costs	(539.2)	(618.5)	(639.5)	(646.4)	(676.6)
R&D expenses	(80.5)	(85.1)	(107.6)	(120.3)	(147.9)
<b>Gross profit</b>	<b>139.7</b>	<b>103.5</b>	<b>152.8</b>	<b>141.1</b>	<b>155.4</b>
Selling and distribution expenses	(43.7)	(42.4)	(36.5)	(43.1)	(55.2)
Administrative expenses	(66.5)	(69.9)	(73.1)	(84.8)	(82.5)
Other income and expenses	0.4	1.2	0.5	1.0	1.1
<b>Operating income</b>	<b>29.9</b>	<b>(7.7)</b>	<b>43.7</b>	<b>14.2</b>	<b>18.8</b>
Income before income taxes					
from investments					
in associated enterprises				(0.2)	(0.8)
Financing expenses, net	(8.8)	(7.8)	(11.9)	(9.8)	(6.3)
Special government taxes	(0.1)				
<b>Net income</b>	<b>21.0</b>	<b>(15.5)</b>	<b>31.8</b>	<b>4.1</b>	<b>11.7</b>

## Revenue overview

Revenue increased DKK 72.1m to DKK 979.9m equivalent to 8% compared with 2003. The increase in revenue stems mainly from commercial sales.

## Revenue overview

DKKm	2000	2001	2002	2003	2004
Denmark	491.6	505.0	543.5	555.6	579.1
Exports	142.0	170.8	217.7	221.0	249.9
<b>Total commercial revenue</b>	<b>633.6</b>	<b>675.8</b>	<b>761.2</b>	<b>776.6</b>	<b>829.0</b>
Privately-funded research	49.1	49.5	50.8	42.2	57.7
Government funding	76.7	81.8	87.8	89.0	93.2
<b>Total</b>	<b>759.4</b>	<b>807.1</b>	<b>899.9</b>	<b>907.8</b>	<b>979.9</b>

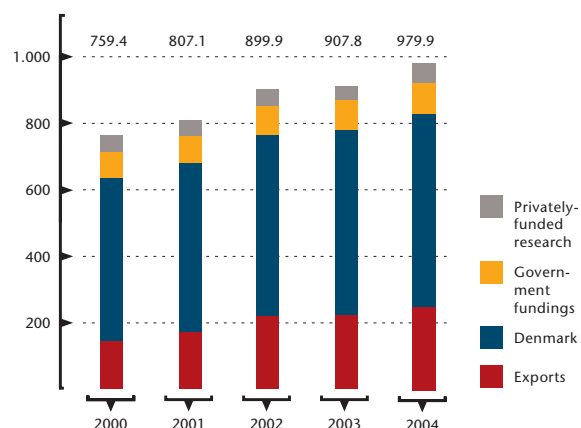
The growth in revenue in the period 2000-2004 was achieved primarily in the commercial part of our activities (Denmark and exports).

Domestic commercial revenue increased 4% compared with 2003. Exports grew 13% from 2003 to 2004.

Private funds increased 37% from 2003 to 2004, due mainly to the unusually low income following deferred income relating to a major research project carried out in collaboration with a number of foreign partners in 2003.

Government funding increased in the period 2000-2004 due to the Institute's establishment of a Center for Biological Defense and a Center for Anti-microbial Resistance and Hospital Infections. In 2004 the Institute received a special grant for improving the influenza pandemic preparedness.

## Development in revenue 2000-2004, DKKm



## Commercial revenue

The table shows commercial revenue broken down into business areas.

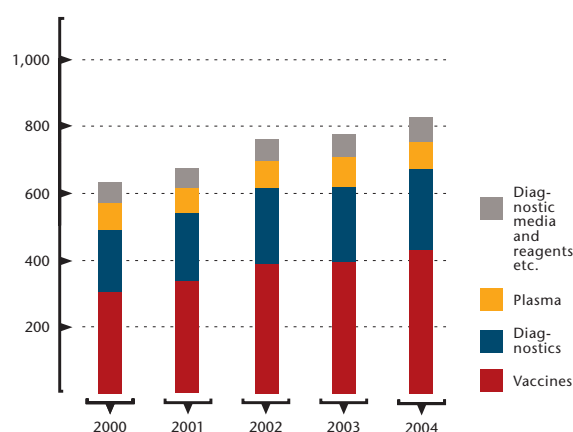
### Commercial revenue broken down into business areas

DKKm	2000	2001	2002	2003	2004
Diagnostics	182.2	197.5	219.1	217.2	235.4
Vaccines	192.0	192.1	196.9	203.9	219.7
Plasma-derived products	73.1	70.4	80.3	87.6	71.4
Diagnostic media and reagents etc.	44.3	45.0	47.3	46.9	52.6
<b>Total domestic revenue</b>	<b>491.6</b>	<b>505.0</b>	<b>543.5</b>	<b>555.6</b>	<b>579.1</b>
Diagnostics	6.0	7.2	6.8	5.7	6.3
Vaccines	112.9	143.9	191.8	191.2	211.0
Plasma-derived products	6.5	4.6	2.7	2.7	9.7
Diagnostic media and reagents etc.	16.5	15.1	16.5	21.4	22.9
<b>Total exports</b>	<b>142.0</b>	<b>170.8</b>	<b>217.7</b>	<b>221.0</b>	<b>249.9</b>
<b>Total</b>	<b>633.6</b>	<b>675.8</b>	<b>761.2</b>	<b>776.6</b>	<b>829.0</b>

Compared with Annual Report 2003, revenue for 2000 and 2001 have been reclassified between the business areas.

The increase in commercial revenue was achieved primarily in the vaccine and diagnostics areas. In 2004 the vaccine area alone accounted for 52% of commercial revenue. The revenue of the plasma-derived products area was lower in 2004 following the discontinuation of the supply at the end of August.

### Commercial revenue 2000-2004, DKKm

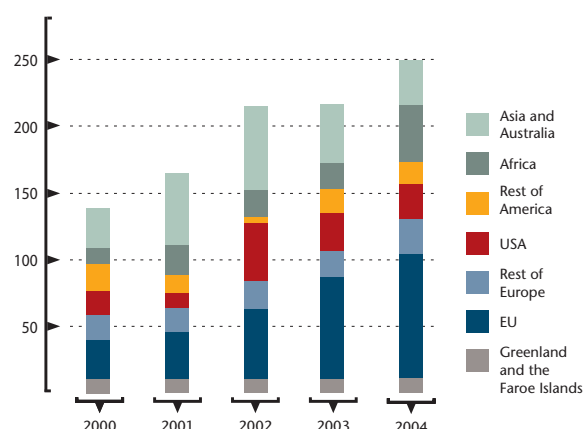


The increase in domestic sales of DKK 23.5m from 2003 to 2004 was achieved mainly within diagnostic analyses and diagnostic media and reagents.

The DKK 28.9m increase in exports in 2004 relates primarily to sales of BCG vaccines to the UK and diphtheria and tetanus booster vaccine in Scandinavia.

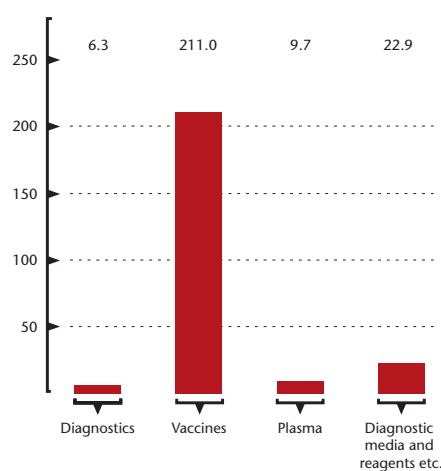
In 2003 exports included the one-time sale of vaccines of DKK 18.7m, net. The chart shows the geographical distribution of exports in 2000-2004.

### Development in exports 2000-2004, DKKm



In 2004 exports included primarily own-produced vaccines and diagnostic media and reagents.

### Exports allocated on business activities 2004, DKKm

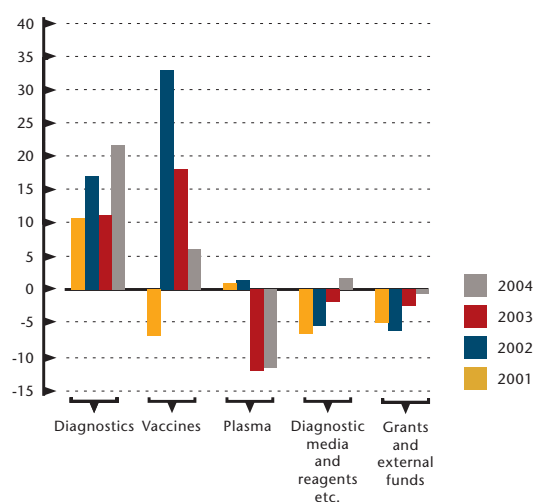




## Operating income

The chart shows the development in operating income in 2001-2004.

### Operating income 2001-2004, DKKm



In 2003 royalties and license fees of DKK 3.4m were transferred from Diagnostics to Diagnostic media and reagents etc. (the comparative figures for 2002 and previous years are unchanged).

## Diagnostics

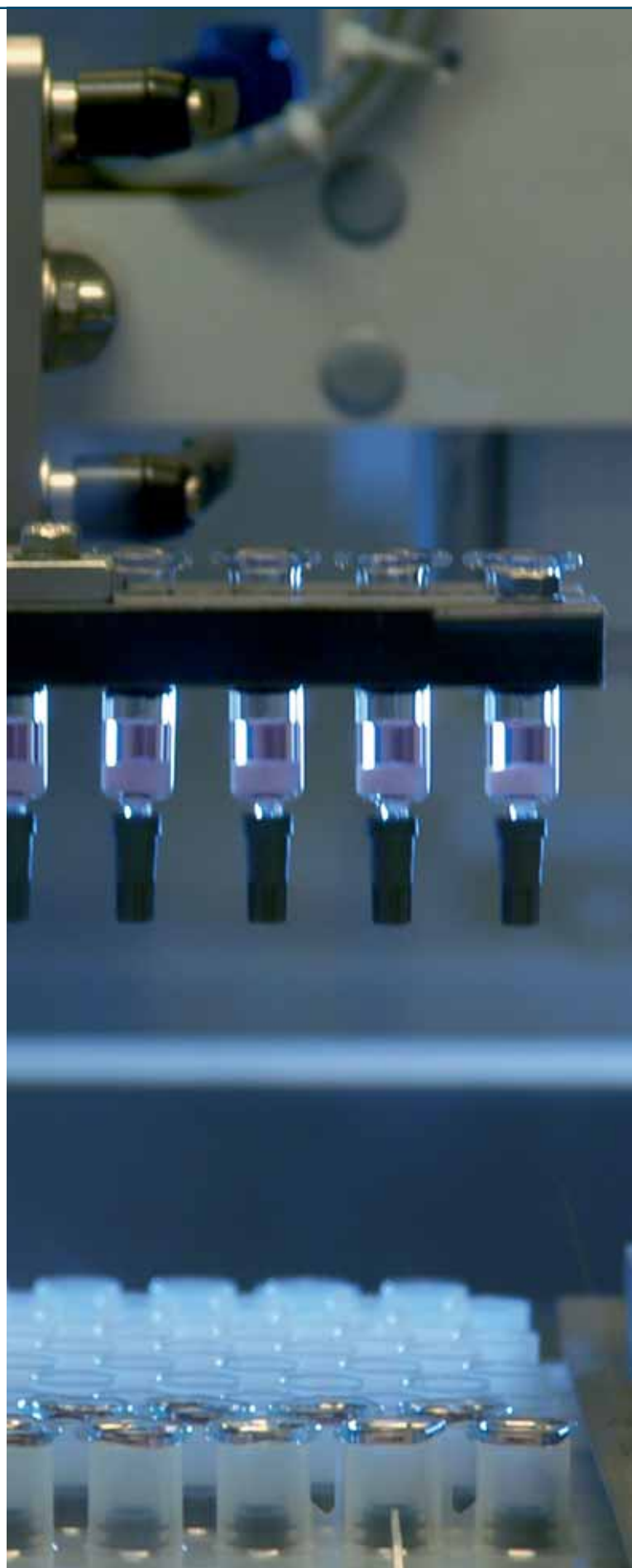
Diagnostics expenses do not increase proportionally with increasing activity but in stages, which means that changes in revenue will heavily impact operating income.

The net revenue increase in 2004 stemmed mainly from:

- A mycoplasma epidemic at year-end
- An increased number of tests regarding pneumococcus antibodies because vaccination is not recommended if a patient has formed antibodies
- More analyses concerning herpes vira as one county has not been able to handle the tests itself
- Increased sales of double and triple tests

## Vaccines

Particularly the product groups DT-booster, T-toxoids, Di-Te-Ki-Pol/Hib and contract work, together with



domestic sales of commercial vaccines, contributed to the results for 2004.

The results declined in 2004 compared with 2003 and related mainly to the anticipated expenses for running in and registering the new serum-free verocell polio vaccine as well as the impact in 2003 from one-time sales of vaccines.

### Plasma-derived products

The decline in results is partly due to the loss of the right to fraction Danish donor plasma as of January 1, 2004. At the request of the counties, the Institute continued the obligation to supply plasma-derived products to the Danish health service until August 31, 2004. The continuation of the supply with own and purchased plasma-derived products, and a more efficient discontinuation of the plasma production contributed to a reduction of total costs in the product area of approximately DKK 11m in 2004.

In 2003 the area's production plant was written down to the value that the plant will constitute in respect of future activities. The write-down amounted to DKK (13.1m).

### Diagnostic media and reagents etc.

As the county hospitals are now performing more diagnostic analyses themselves, our sale of diagnostic media and reagents for these analyses has increased. As a result of this and the discontinuation of the unprofitable production of test animals, the business area is now showing positive results.

### Government and privately funded activities

Results improved in 2004 compared with 2003 so that grants and consumption balance.

### Financing expenses

At year-end 2004 the Institute's interest-bearing debt totaled DKK 392.6m, mainly denominated in euro. The lending rate is fixed for periods of three months for most of the long-term debt. At year-end 2004, the euro rate was 2.15% per annum.

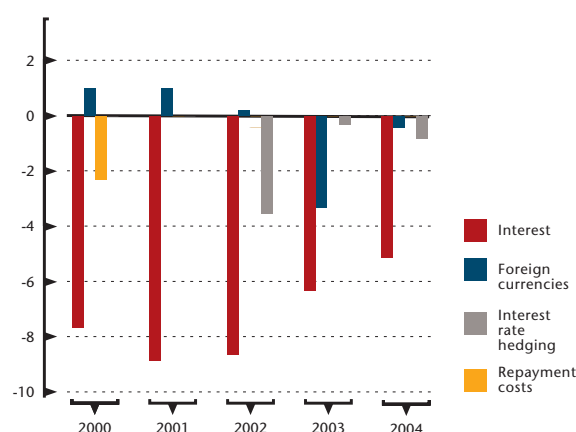
Despite largely unchanged debt, the incurred interest expenses were somewhat lower compared with 2003. This is due to a further fall in short-term interest rates in 2004.

In step with falling interest rates, value adjustment was made for forward-rate agreements, which will be effective until 2007.

Gains and losses relating to foreign currency transactions are more or less balanced by forward contracts.

The chart shows the development of net financing expenses.

Interest and other financial expenses 2000-2004, DKKm



## RISKS

### Vaccines

As a biological production, vaccine production, which is the main pillar in the development of revenue, is sensitive. For example, cultivation problems can occur as a consequence of quite small changes in the cultivation conditions. Some problems often emerge late in the production process, so rejects include not only raw materials but also the supplies and the work input.

### Employees

The development of new products and the production of vaccines are very dependent on personnel. Changes in the employee composition could have a significant adverse impact on the Institute's future earnings and activity. The Institute's ability to ensure future growth

and to manage and handle day-to-day operations efficiently therefore depend on our ability to attract and retain qualified employees.

### Credit risks

The credit risk on the Institute's non-public customers is limited because sales are distributed over a considerable number of customers. In addition to a stable home market, the customers are distributed over large parts of the world and cover both production and distribution enterprises. In Management's view, apart from the amounts for which allocation for uncollectibles has been made, no unusual credit risk is associated with the Institute's receivables from sales.

### Interest-rate risks

Most of the long-term debt is in euro and accrues interest at an interest rate fixed for periods of three months. The Institute is therefore exposed to fluctuations in short-term interest rates. To counter this risk, the Institute entered into CAP agreements ensuring that the interest rate on long-term debt will not exceed 5.5% up to mid-2007.

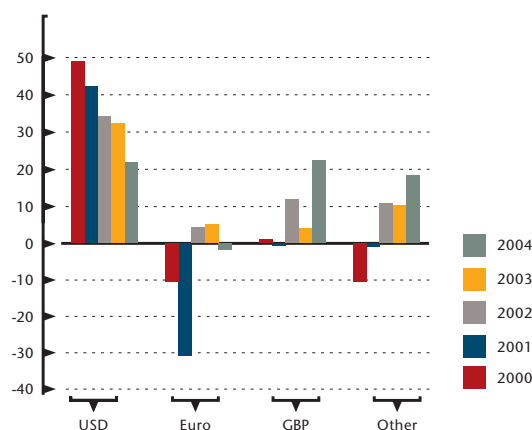
### Exchange-rate risks

With rising exports, Statens Serum Institut has increased its focus on foreign currency exposure. The Institute regularly calculates its foreign currency exposure on the basis of expected net payments in the principal currencies. The currency exposure is hedged in part by forward contracts.

The Institute hedges foreign currency risks to even out the impact of exchange rates on operating results and gain time to react to lengthy changes in exchange rates.

The increase in other currency movements shown in the chart below stems from increased transactions in SEK and NOK. Sales in GBP and USD are currently hedged in part by forward contracts.

### Net movements prior to hedging, DKKm



### Cash flow

In 2004 the Institute's cash flow from operating activities amounted to DKK 61.6m, compared with DKK 41.6m in 2003.

The significant increase is due mainly to the improved performance, higher trade accounts payable as a result of the construction of a new building for animals, lower trade accounts receivable and higher inflow of external funds in 2004 compared with previous years.

For a number of years, capital expenditures have been financed by long-term loans raised in the European Investment Bank.

Only a few repayments on capital expenditure loans were made in 2004 because large parts of the investments, which are financed by loans obtained in the past few years, have not been commissioned yet.

### Investments

In 2004 investments amounted to DKK 82.3m compared with DKK 50.8m in 2003.

In 2004 investments of DKK 57.3m were higher than in 2003 due to the construction of a new building for animals.

# STATEMENT OF MANAGEMENT BOARD AND INSTITUTE COUNCIL

Today, the Institute Council and Board of Management approved the Annual Report for the fiscal year January 1 – December 31, 2004 of Statens Serum Institut. The Annual Report has been drawn up in accordance with the Danish Financial Statements Act and Danish Accounting Standards.

In our opinion, the accounting policies applied are appropriate and the Annual Report gives a true and fair view of the Institute's assets, equity and liabilities, financial position, results, and cash flows.

Copenhagen, March 10, 2005

## Management Board



Nils Strandberg Pedersen  
President, CEO



Lars Birkjær



Pia Lading



Frank Espersen



Mads Melbye

## Institute Council



Mogens Bundgaard-Nielsen  
Chairman



Poul Rasmussen



Gunna Christiansen



Erik Juhl



Court Pedersen



Paul Bennett



Lisbeth Holm Petersen



# AUDITORS' REPORT



We have audited the Annual Report of Statens Serum Institut for the fiscal year January 1 – December 31, 2004, pages 4 to 45, prepared in accordance with the Danish Financial Statements Act.

The Annual Report is the responsibility of the Management Board and the Institute Council. Our responsibility is to express an opinion on the Annual Report based on our audit.

## Basis of opinion

We conducted our audit in accordance with Danish Auditing Standards. These standards require that we plan and perform our audit to obtain reasonable assurance that the Annual Report is free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the Annual Report. An audit also includes assessing the accounting policies used and significant estimates made by the Management Board and the Institute Council, as well as evaluating the overall Annual Report presentation. We believe that our audit provides a reasonable basis for our opinion.

Our audit did not give rise to any qualifications.

## Opinion

In our opinion, the Annual Report presents fairly, in all material respects, the Institute's assets, liabilities and financial position at December 31, 2004 and the results of the Institute's operations and cash flows for the fiscal year January 1 – December 31, 2004 in accordance with the Danish Financial Statements Act.

Copenhagen, April 8, 2005

The Office of the Auditor General in Denmark

*Henrik Otbo*  
Henrik Otbo

*Henning Madsen*  
/Henning Madsen



# SIGNIFICANT ACCOUNTING POLICIES



### **Statens Serum Institut is a state-owned enterprise**

The Annual Report 2004 of Statens Serum Institut has been prepared in accordance with the provisions of the Danish Financial Statements Act of 2001 for large enterprises in reporting class C and current Danish Accounting Standards.

The accounting policies are unchanged from last year. The recognition of government funding has been specified.

The Annual Report 2004 is presented in thousands of Danish kroner.

### **Recognition and measurement**

Income is recognized as earned in the Income Statement upon completion of delivery before the end of the fiscal year, including value adjustments of financial assets and liabilities measured at fair value or amortized cost. Furthermore, as a result of changed accounting estimates, all expenses incurred to generate earnings for the year are recognized in the Income Statement, including depreciation, amortization, impairment losses and provisions as well as reversals because of changed accounting estimates of amounts that were previously recognized in the Income Statement.

Assets are recognized in the Balance Sheet when it is probable that future economic benefits will flow to the Institute and the value of the assets can be measured reliably.

Liabilities are recognized in the Balance Sheet when it is probable that future economic benefits will flow out of the Institute and the value of the liabilities can be measured reliably.

Assets and liabilities are measured at cost on initial recognition. Subsequently, assets and liabilities are measured as described for each individual item below.

On recognition and measurement, anticipated losses and risks that arise before the time of preparation of the Annual Report and that prove or disprove affairs and conditions existing on the balance sheet date are taken into consideration.

### **Foreign currencies**

Transactions in foreign currencies in 2004 are translated

at the transaction-date exchange rates. Foreign exchange gains and losses arising from the date of transaction to the date of payment are recognized in the Income Statement as net financials.

Accounts receivable and payable in foreign currencies and other foreign currency monetary items not settled on the balance sheet date are translated at the balance-sheet-date exchange rates. The difference is recognized in the Income Statement as net financials.

### **Derivative financial instruments**

On initial recognition, derivative financial instruments are included in the Balance Sheet at cost and subsequently at fair value. Positive and negative fair values of derivative financial instruments are included as "Other receivables" under assets and as "Other accounts payable" under liabilities.

Changes in the fair values of derivative financial instruments that are designated and qualify as fair value hedges of a recognized asset or liability are recognized in the Income Statement together with any changes arising in the fair value of the hedged asset or the hedged liability.

Changes in the fair values of financial instruments that are designated and qualify as hedges of forecast future transactions are recognized in equity under retained earnings as regards the effective portion of the hedging. The ineffective portion is recognized in the Income Statement. If the hedged transaction results in an asset or a liability, the amount deferred under equity is transferred from equity and recognized in the cost of the asset or liability. If the hedged transaction results in an income or an expense, the amount deferred under equity is transferred from equity to the Income Statement for the period in which the hedged transaction is recognized. The amount is recognized under the same item as the hedged transaction.

### **Segment information**

Information is disclosed on the Institute's income and risks in business segments and geographical markets. Information on business segments and geographical

markets is based on statements from the internal financial reporting systems.

Geographical markets are regarded as secondary segments and, in pursuance of the executive order on exemptions from the Danish Financial Statements Act, information on geographical segment areas only concerns net revenues.

Items included under "Operating income" are distributed if they are directly or indirectly attributable to the segments. Items distributed both by direct and indirect statements include "Production costs", "R&D expenses", "Selling and distribution expenses", and "Administrative expenses". Items distributed by indirect statement are allocated on the basis of the segments' use of key resources.

Fixed assets in the segment cover fixed assets used directly in the operating activities of the segments, including intangible assets and property, plant and equipment.

Liabilities have not been allocated.

## Income Statement

**Net revenue** from finished goods and merchandise is recognized in the Income Statement provided the general criteria are met: Delivery and transfer of risk must have occurred before the end of the fiscal year, the amount can be calculated reliably and payment thereof can be expected with reasonable certainty. Net revenue is stated excluding VAT and taxes and less price reductions in the form of discounts and returned goods.

Income originating from external funds and government funding related to government-funded research as well as surveillance and control services is recognized as income in step with expenses incurred by the projects concerned and therefore has no effect on results.

**Production costs** comprise the costs incurred in order to achieve the net revenue for the year. These costs consist of raw materials, supplies, direct payroll costs and indirect production costs such as maintenance,

depreciation and amortization etc., operation and administration and plant management.

Production costs also cover amortization of capitalized development expenses.

Besides actual production costs, production costs include costs incurred to obtain and maintain FDA approval and to comply with GMP requirements.

Expenses incurred for research, surveillance and control services and covered by private funds and grants are included in production costs.

**Selling and distribution expenses** comprise expenses incurred in connection with the sale, distribution and marketing of the Institute's products, including salaries, depreciation, and commission paid to agents.

**R&D expenses** comprise expenses attributable to the Institute's commercial R&D activities, including salaries, amortization, registration and maintenance of patents.

**Administrative expenses** comprise expenses relating to the administrative functions of the Institute, including salaries, and depreciation.

**Other operating income and other operating expenses** consist of income and expenses, respectively, of a secondary nature in relation to the core activities of the Institute.

## Income from investments in associated enterprises

The proportionate share of income before income taxes less amortization of goodwill and R&D expenses is recognized under the item "Income from investments in associated enterprises".

**Net financials** comprise interest income and expenses, realized as well as unrealized foreign exchange gains and losses, forward-rate agreements and amortization of fixed-rate loans.



## Balance Sheet

### Intangible assets

#### Development projects, patents and licenses

Development project expenses comprise salaries, amortization and other expenses that are directly or indirectly attributable to the Institute's development activities.

For product-related development projects that are clearly defined and identifiable, where the level of technical exploitation, sufficient resources and a potential future market or business opportunity for the Institute can be demonstrated, and where the intention is to manufacture, market or exploit the results of the project, expenses are recognized as intangible assets where sufficient certainty exists that the future earnings cover not only production, selling and administrative expenses but also development expenses.

Development projects concerning the Institute's electronic information systems are recognized as intangible assets where sufficient certainty exists that future economic benefits flowing to the Institute will cover the development expenses.

Development projects that do not meet the criteria for recognition in the Balance Sheets are recognized as expenses in the Statements of Income.

Capitalized development expenses are measured as cost less accumulated amortization and write-downs or recoverable value, if this is lowest.

Capitalized development expenses are amortized after completion of the development work on a straight-line basis over the period in which it is expected to result in economic benefits.

Amortization period:

- Further development of standard systems ..... 5 years
- Own-developed standard system ..... 8 years

Acquired patents and licenses are measured at the lower of cost, less accumulated amortization and write-downs, and value in use.

The amortization period is:

- Patents ..... the remaining patent period
- Licenses ..... the contract period, although not exceeding ten years due to the notoriously rapid development in applied technologies

**Property, plant and equipment** are measured at cost less accumulated depreciation and write-downs.

Cost includes purchase price and expenses incurred in connection with the acquisition until the time at which the asset is ready to be taken into use. The cost of internally generated assets includes direct and indirect payroll costs and expenses for materials, components and subcontractors.

The basis for depreciation, calculated as cost less any residual value, is provided on a straight-line basis over the estimated useful lives of the assets, which are:

- Office and administration buildings ..... 40 years
- Production buildings ..... 25 years
- Building installations ..... 15 years
- Plant and machinery ..... 5-10 years
- Other plant, machinery, and equipment ..... 3-5 years
- Leasehold improvements ..... 10 years

Some of the plant and machinery and other plant, machinery and equipment acquired before 1997 are measured at assessed values in use less accumulated depreciation, taking into account the original time of acquisition of the assets.

Profit and loss arising from replacement of property, plant and equipment at regular intervals are recognized in the Income Statement under the individual functions to which the assets belong. Small assets below DKK 100,000 are expensed in the year of acquisition.

On commencement of use of a fixed asset financed in whole or in part by special grants, the grant is offset against the carrying value of the plant.

#### Write-down for impairment losses on fixed assets

The carrying values of both intangible assets and property, plant and equipment are tested on an annual

basis to determine whether there are any indications of impairment in excess of what is expressed in amortization and depreciation of assets. Where that is the case, write-down is made to the lower recoverable amount. The recoverable amount of assets is calculated as the higher of net selling price and value in use. If it is not possible to determine the recoverable amount of an individual asset, the need to write down the smallest group of assets for which it is possible to calculate the recoverable amount is assessed.

**Investments in associated enterprises** are recognized and measured under the equity method in the Financial Statements.

Investments in associated enterprises are recognized in the Balance Sheet at the proportionate share of the enterprises' net asset value calculated on the basis of the fair value of the identifiable net assets less deduction/with addition of unrealized Group internal profits or losses.

**Inventories** are measured at the lower of cost using the FIFO formula and net realizable value.

The net realizable value of inventories is calculated as the sum of future sales income that inventories are expected to fetch in the ordinary course of business and determined in accordance with marketability, obsolescence and development of expected selling price, less the estimated expenses necessary to effect the sale at the balance sheet date.

Cost of merchandise as well as raw materials and supplies covers purchase price and expenses incurred in bringing the inventories to their present location and condition.

Cost of finished goods, semi-finished products and work in progress covers the cost of raw materials, supplies, direct payroll costs and indirect production costs. Indirect production costs comprise indirect materials and payroll costs as well as maintenance and depreciation of the machinery, plant and equipment used in the production process and expenses for plant administration and management. Any borrowing costs incurred in the production period are not included.

**Accounts receivable** are measured in the Balance Sheet at the lower of cost and net realizable value, which in this case equals nominal value less write-downs on allowances for uncollectibles. Write-downs on losses are based on an individual assessment of the individual accounts receivable.

**Financial debts** are measured at amortized cost, which materially equals nominal value.

#### **Prepaid expenses and deferred income**

Prepaid expenses recognized as assets cover incurred prepaid wages and salaries, rent, insurance premiums, subscriptions and interest.

Deferred income recognized as liabilities comprise payments received covering income in subsequent years.

#### **Statement of Cash Flows**

The Statement of Cash Flows shows the Institute's cash flows for the year broken down into operating, investing and financing activities, changes in cash and cash equivalents for the year and the Institute's cash and cash equivalents at the beginning and end of the year.

**Cash flows from operating activities** are presented as net income adjusted for non-cash operating items such as depreciation, amortization and write-downs, provisions and changes in working capital. Working capital covers current assets less short-term debt.

**Cash flows from investing activities** include cash flows from the purchase and sale of intangible assets, property, plant and equipment as well as investments and other assets.

**Cash flows from financing activities** comprise changes in long-term debt.

**Cash and cash equivalents** include cash.

The Statement of Cash Flows cannot be deduced solely from the published Financial Statements.

## Definitions of key figures and financial ratios

**Operating profit margin =**

Operating income x 100

---

Net revenue

**Return on invested capital =**

Operating income x 100

---

Average assets excl. cash and cash equivalents less  
average short-term debt excl. credit institutions

**Return on equity =**

Net income/(loss) for the year x 100

---

Average equity

**Equity ratio =**

Year-end equity x 100

---

Total assets

**R&D in % of revenue =**

R&D x 100

---

Net revenue

**Number of full-time equivalents =**

Number of full-time equivalents reduced by  
reimbursement for illness and maternity, etc.

**Revenue per full-time equivalent =**

Net revenue

---

Full-time equivalents

**Share of exports =**

Export revenue x 100

---

Commercial revenue

# INCOME STATEMENT

DKK '000	Note	2004	2003
Net revenue	1	979,913	907,816
Production costs	5,13	(676,626)	(646,435)
R&D expenses	5,13	(147,922)	(120,282)
<b>Gross profit</b>		<b>155,365</b>	<b>141,099</b>
Selling and distribution expenses	5,13	(55,193)	(43,129)
Administrative expenses	5,13	(82,505)	(84,762)
<b>Income from ordinary operations</b>		<b>17,667</b>	<b>13,208</b>
Other operating income		1,120	973
<b>Operating income</b>		<b>18,787</b>	<b>14,181</b>
Income/(loss) from investments in associated enterprises	6	(756)	(219)
Interest and other financial income	2	7,054	7,341
Interest and other financial expenses	3	(13,339)	(17,159)
<b>Net income</b>		<b>11,746</b>	<b>4,144</b>

## Proposed distribution of income

DKK '000	2004	2003
Retained earnings	11,746	4,144



# BALANCE SHEET

DKK '000	Note	End of year 2004	End of year 2003
Patents and licenses	4	1,874	2,267
<b>Total intangible assets</b>		<b>1,874</b>	<b>2,267</b>
Land and buildings		438,728	450,395
Plant and machinery		112,440	108,330
Other plant, operating machinery, fixtures and fittings		8,341	12,371
Leasehold improvements		4,539	7,736
Property, plant and equipment under construction		82,218	28,251
<b>Total property, plant and equipment</b>	<b>5</b>	<b>646,266</b>	<b>607,083</b>
Investments in associated enterprises		400	131
<b>Total investments and other assets</b>	<b>6</b>	<b>400</b>	<b>131</b>
<b>Total fixed assets</b>		<b>648,540</b>	<b>609,481</b>
Raw materials and supplies		36,796	37,692
Contract work in process		46,876	41,702
Finished goods and merchandise		31,131	36,742
<b>Total inventories</b>		<b>114,803</b>	<b>116,136</b>
Trade accounts receivable		105,742	117,222
Amounts owed by associated enterprises		265	273
Other receivables	7	15,758	5,462
Prepaid expenses	8	10,388	6,435
<b>Total accounts receivable</b>		<b>132,153</b>	<b>129,392</b>
<b>Cash</b>	<b>9</b>	<b>144,112</b>	<b>165,621</b>
<b>Total current assets</b>		<b>391,068</b>	<b>411,149</b>
<b>TOTAL ASSETS</b>		<b>1,039,608</b>	<b>1,020,630</b>
<b>Equity</b>		<b>479,181</b>	<b>467,435</b>
Credit institutions	10	389,773	392,907
<b>Total long-term debt</b>		<b>389,773</b>	<b>392,907</b>
Credit institutions	10	2,796	2,612
Prepayments from customers		21,087	28,023
Trade accounts payable		53,872	46,264
Amounts owed to associated enterprises		425	103
Other accounts payable	11	74,430	73,793
Deferred income	12	18,044	9,493
<b>Total short-term debt</b>		<b>170,654</b>	<b>160,288</b>
<b>Total debt</b>		<b>560,427</b>	<b>553,195</b>
<b>TOTAL LIABILITIES AND EQUITY</b>		<b>1,039,608</b>	<b>1,020,630</b>
Contractual obligations	15		
Contingent liabilities	16		
Financial instruments	17		
Related parties	18		

# EQUITY AND STATEMENT OF CASH FLOWS

## Equity

DKK '000	2004	2003
Equity at transition to the Danish Company Accounts Act at Jan. 1, 1997	415,275	415,275
Retained earnings from previous years	52,160	48,016
Net income	11,746	4,144
Retained earnings at Dec. 31, 2004	63,906	52,160
Equity	479,181	467,435

## Statement of Cash Flows

DKK '000	Note	2004	2003
Net income		11,746	4,144
Unrealized gains and losses on currency translation adjustments, end of year		(338)	1,320
Changes in provisions for stocks		(708)	6,284
Depreciation, amortization and impairment losses		40,713	46,257
Income from investments in associated enterprises		756	219
Cash flow before change in working capital		52,169	58,224
Decrease/increase in accounts receivable		11,480	(8,632)
Increase/decrease in other accounts receivable		(14,241)	5,389
Increase/decrease in inventories		2,042	(4,702)
Increase/decrease in trade accounts payable		7,930	(12,944)
Decrease in prepayments from customers		(6,936)	(6,388)
Increase in other operating debt		9,188	10,661
Change in working capital		9,463	(16,616)
<b>Cash flows from operating activities</b>		<b>61,632</b>	<b>41,608</b>
Intangible assets		0	(228)
Property, plant and equipment		(81,255)	(50,298)
Investments and other assets		(1,025)	(350)
Sale/scraping of plant		1,751	748
<b>Cash flow from investing activities</b>		<b>(80,529)</b>	<b>(50,128)</b>
Repayment of credit institution loans		(2,612)	(2,441)
<b>Cash flows from financing activities</b>		<b>(2,612)</b>	<b>(2,441)</b>
<b>Change in cash and cash equivalents</b>		<b>(21,509)</b>	<b>(10,961)</b>
Cash and cash equivalents at Jan. 1, 2004		165,621	176,582
<b>Cash and cash equivalents at Dec. 31, 2004</b>	<b>9</b>	<b>144,112</b>	<b>165,621</b>

# NOTES FOR THE INCOME STATEMENT AND BALANCE SHEET

## 1. Segment information

DKK '000	2004		2003	
Commercial revenue, domestic		579,118		555,597
Commercial revenue, exports		249,931		220,997
Government funding	98,500		89,200	
Use of government funding transferred from last year	1,405		2,940	
Government funding carried forward to next year	(6,706)	93,199	(3,093)	89,047
Privately-funded research	57,665			42,175
<b>Total</b>	<b>979,913</b>		<b>907,816</b>	

## Business segments DKK '000

		Diagnostics	Vaccines	Plasma-derived products	Diagnostic media and reagents etc.	Grants and external funds	Non-distributed	Total
2004	Revenue	241,651	430,697	81,170	75,531	150,864	0	979,913
	Operating income	23,862	6,752	(13,007)	1,851	(671)	0	18,787
	Fixed assets	132,002	349,490	32,696	75,722	58,230	400	648,540
	Liabilities	0	0	0	0	0	555.434	555.434
2003	Revenue	222,965	395,062	90,295	68,291	131,203	0	907,816
	Operating income	12,289	19,953	(13,386)	(2,009)	(2,666)	0	14,181
	Fixed assets	121,848	300,848	43,112	87,244	56,298	131	609,481
	Liabilities	0	0	0	0	0	553.195	553.195

## Geographical markets

2004	Domestic revenue	235,398	219,704	71,429	52,587	0	0	579,118
	Revenue from exports	6,253	210,993	9,741	22,944	0	0	249,931
	Non-distributed revenue					150,864	0	150,864
	<b>Total revenue</b>	<b>241,651</b>	<b>430,697</b>	<b>81,170</b>	<b>75,531</b>	<b>150,864</b>	<b>0</b>	<b>979,913</b>
2003	Domestic revenue	217,224	203,872	87,585	46,935	0	0	555,616
	Revenue from exports	5,741	191,190	2,710	21,356	0	0	220,997
	Non-distributed revenue					131,203	0	131,203
	<b>Total revenue</b>	<b>222,965</b>	<b>395,062</b>	<b>90,295</b>	<b>68,291</b>	<b>131,203</b>	<b>0</b>	<b>907,816</b>

## 2. Interest and other financial income

DKK '000	2004	2003
Interest income	3,658	3,737
Currency translation adjustments	3,185	3,529
Other financial income	211	75
<b>Total</b>	<b>7,054</b>	<b>7,341</b>

## 3. Interest and other financial expenses

DKK '000	2004	2003
Interest expenses	8,746	10,013
Currency translation adjustments	3,753	6,874
Other financial expenses	840	272
<b>Total</b>	<b>13,339</b>	<b>17,159</b>

## 4. Intangible assets

DKK '000	2004	2003
Cost at Jan. 1, 2004	2,352	2,124
Additions during the year	0	228
Disposals during the year	0	0
Cost at Dec. 31, 2004	2,352	2,352
Amortization and impairment losses at Jan. 1, 2004	85	0
Amortization and impairment losses for the year	393	85
Disposals during the year	0	0
Amortization and impairment losses at Dec. 31, 2004	478	85
<b>Carrying value at Dec. 31, 2004</b>	<b>1,874</b>	<b>2,267</b>

Intangible assets comprise acquired patents and licenses as well as electronic monitoring programs.

## 5. Property, plant and equipment

DKK '000	Land and buildings	Plant and machinery	Other plant, operating machinery, fixtures and fittings	Leasehold improvements	Property, plant and equipment under construction	Total
Cost at Jan. 1, 2004	532,821	177,543	20,697	24,781	28,251	784,093
Additions during the year					81,255	81,255
Disposals during the year		2,255				2,255
Transfers to/(from) other items	9,615	16,745	928		(27,288)	0
Cost at Dec. 31, 2004	542,436	192,033	21,625	24,781	82,218	863,093
Depreciation and impairment losses at Jan. 1, 2004	82,426	69,213	8,326	17,045		177,010
Depreciation and impairment losses for the year	21,282	10,883	4,958	3,197		40,320
Disposals during the year		503				503
Depreciation and impairment losses at Dec. 31, 2004	103,708	79,593	13,284	20,242		216,827
<b>Carrying value December 31, 2004</b>	<b>438,728</b>	<b>112,440</b>	<b>8,341</b>	<b>4,539</b>	<b>82,218</b>	<b>646,266</b>

The cost of plant and machinery, other machinery and equipment at January 1, 1997 is calculated at actual costs/value in use less accumulated depreciation taking into account the dates on which the assets were originally acquired.

Buildings are measured on the basis of a value in use assessed externally in 1997. The value in use is understood to mean the value of the property and individual buildings publicly assessed if Statens Serum Institut were to lease the property/buildings at market rent. Market rent is the rent that Statens Serum Institut would be expected to be willing to pay following prior free negotiations between the Institute and a lessor in a new leasing or re-leasing situation.

According to the latest public property assessment the value of the Institute's land and buildings was DKK 429,700 thousand. Depreciation and amortization are included in the Income Statement by function as follows:

### Depreciation and amortization relating to notes 4 and 5

DKK '000	2004	2003
Intangible assets	393	85
Property, plant and equipment	40,320	46,172
<b>Total</b>	<b>40,713</b>	<b>46,257</b>
Recognized as follows:		
Production costs	35,022	43,192
R&D expenses	1,787	1,511
Selling and distribution expenses	930	179
Administrative expenses	2,974	1,375
<b>Total</b>	<b>40,713</b>	<b>46,257</b>

## 6. Investments in associated enterprises

DKK '000	2004	2003
Cost at Jan. 1, 2004	350	0
Additions during the year	1,025	350
Disposals during the year	0	0
Cost at Dec. 31, 2004	1,375	350
Write-downs at Jan. 1, 2004	(219)	0
Net income	(756)	(219)
Write-downs at Dec. 31, 2004	(975)	(219)
<b>Carrying value at Dec. 31, 2004</b>	<b>400</b>	<b>131</b>

### Associated enterprises:

Name	Domicile	Ownership interest and voting share
Harlan Scandinavia ApS	Allerød, Denmark	35%
Culture Screening ApS	Copenhagen, Denmark	40%

## 7. Other accounts receivable

DKK '000	2004	2003
VAT	4,761	177
Other taxes	747	559
Grants	6,042	200
Reimbursements	1,721	1,866
Outlays and advances for travel expenses	674	364
Deposits	651	595
Derivative financial instruments	211	939
Outstanding settlements, foundations etc.	951	762
<b>Total</b>	<b>15,758</b>	<b>5,462</b>

## 8. Prepaid expenses

DKK '000	2004	2003
Prepaid wages and salaries	2,517	2,499
Insurance	2,751	2,512
Retirement schemes	0	800
Prepaid rent	1,032	0
Other	4,088	624
<b>Total</b>	<b>10,388</b>	<b>6,435</b>

## 9. Cash and cash equivalents

DKK '000	2004	2003
Cash and cash equivalents	129,438	116,144
Reserved for investments	0	25,000
Reserved for privately-funded research	14,674	24,477
<b>Total</b>	<b>144,112</b>	<b>165,621</b>



#### 10. Credit institutions

Repayments due within one year are presented under short-term debt.  
Long-term debt due more than five years after the balance sheet date amounted to DKK 386,781 thousand.

#### 11. Other accounts payable

DKK '000	2004	2003
Personal income taxes etc. payable	7,047	2,049
Holiday pay liability	55,813	53,972
Provisions, utilities	1,607	1,438
Accrued expenses	9,963	16,334
<b>Total</b>	<b>74,430</b>	<b>73,793</b>

#### 12. Deferred income

DKK '000	2004	2003
Undrawn grants	18,044	9,493

#### 13. Employee matters

Staff costs constitute the following amounts:

DKK '000	2004	2003
Wages and salaries	375,136	372,600
Pension contributions	50,207	44,996
Other social security costs	9,854	10,635
<b>Total</b>	<b>435,197</b>	<b>428,231</b>

and are expensed as follows:

DKK '000	2004	2003
Production costs	304,736	308,923
R&D expenses	58,707	50,024
Selling and distribution expenses	22,857	19,030
Administrative expenses	46,288	44,382
Plant costs	2,609	5,872
<b>Total</b>	<b>435,197</b>	<b>428,231</b>

DKK '000	2004	2003
Remuneration and pension for the Management Board	4,293	4,678
Remuneration for the Institute Council	138	210

The Management Board at Statens Serum Institut, which can be compared with the registered managing directors of a company consists of: Nils Strandberg Pedersen, Pia Lading, Frank Espersen, Lars Birkjær and Mads Melbye. Lars Birkjær joined the Management Board as Executive Vice President at May 1, 2004 and Mads Melbye joined as Executive Vice President at November 1, 2004.

In 2004 the average number of full-time equivalent employees totaled 1,128 compared with 1,139 in 2003.

#### 14. Auditors' remuneration

Statens Serum Institut is a state-owned enterprise, which the Auditor General audits in accordance with Section 2 of the Danish Auditor General's Act on the Audit of State Accounts etc., cf. Executive Order no. 3 of January 7, 1997.

#### 15. Contractual obligations

Statens Serum Institut has rent obligations until 2013 of DKK 11,065 thousand plus indexation relating to rented premises.

#### 16. Contingent liabilities

At December 31, 2004 Statens Serum Institut has provided performance guarantees for the delivery of goods at a total value of DKK 956 thousand.

At December 31, 2004 the Institute had two ongoing disputes that may end in lawsuits, but for which the Institute does not expect to incur any losses.

#### 17. Financial instruments

The extent and nature of the enterprise's financial instruments appear from the Income Statement and Balance Sheet in accordance with the Significant Accounting Policies. Information is given below on conditions that can affect amounts, time of payment or reliability of future payments where such information does not appear directly from the Institute's Financial Statements or does not follow normal practice:

DKK '000	Dec. 31, 2004	Payment flow	Terms and conditions
Fixed-rate loans	5,788	Term to maturity: 2 years	6.91% interest
Floating-rate loans	386,781	Term to maturity: 6-8 years	Current interest 2.15%, determined quarterly
Forward-rate agreement (CAP)		Term to maturity: 2 1/2 years	5.50%
Forward contracts, GBP	4,392	Matures in 2005	exchange rate 1,075.3
Forward contracts, USD	26,051	Matures in 2005	Average exchange rate 542.76

The Institute's foreign currency balances and related hedging transactions at Dec. 31, 2004 are composed as follows:

Currency	Payment/ maturity	Receivables in DKK '000	Liabilities in DKK '000	Net position
USD	0-12 months	6,242	595	5,647
GBP	0-12 months	5,643	152	5,491
NOK	0-12 months	3,769	(251)	4,020
SEK	0-12 months	2,877	107	2,770
EUR	0-12 months	9,859	2,479	7,380
EUR	More than 12 months		386,781	(386,781)

#### 18. Related parties and ownership

Transactions with related parties are made on a statutory or arm's length basis.

Statens Serum Institut is a state-owned enterprise under the Ministry of the Interior and Health. Transactions with the Ministry of the Interior and Health comprise mainly government funding.

Transactions with the 35% owned Harlan Scandinavia ApS comprise mainly purchase of test animals and animal feed. Transactions with the 40% owned Culture Screening ApS comprise mainly sale of contract work.

# PUBLICATION LIST

## PHD THESES

**Ahlgren, M.** Birth weight and growth during school years and risk of cancer. Ph.d.-afhandling. Københavns Universitet. December 2004.

**Dragsted, D.** Pertussis in Denmark – Laboratory, Clinical and Epidemiological Aspects. Ph.d.-afhandling. Københavns Universitet. September 2004.

**Haargaard, B.** Childhood cataract in Denmark: Incidence and risk factors. Ph.d.-afhandling. Københavns Universitet. Oktober 2004.

**Hjalgrim, L.** Aspects of the natural history of childhood leukaemia. Ph.d.-afhandling. Københavns Universitet. Marts 2004.

**Jensen, H.D.** Cranberry juice and urinary tract infections. Ph.d.-afhandling. Danmarks Farmaceutiske Universitet og Statens Serum Institut, København. August 2004.

**Kæstel, P.** Micronutrient supplementation and other predictors of birth size and perinatal mortality in Guinea-Bissau. Ph.d.-afhandling. Den Kgl. Landbohøjskole, Frederiksberg. Marts 2004.

**Madsen, K.M.** Vaccinationer og autisme. Ph.d.-afhandling. Aarhus Universitet. Maj 2004.

**Mikkelsen, T.B.** Validation of the food questionnaire used in the Danish National Birth Cohort. Ph.d.-afhandling. Københavns Universitet. Maj 2004.

**Rehm, D.** Hierarchical modelling of bioassays. Ph.d.-afhandling. DTU. Juli 2004.

**Roldgaard, B.B.** Verocytotoxin-producing *Escherichia coli* in Denmark. Ph.d.-afhandling. Det Sundhedsvidenskabelige Fakultet, Københavns Universitet og Afd. for mikrobiologisk sikkerhed, Fødevaredirektoratet, København. Januar 2004.

**Roth, A.** Specific and non-specific effects of BCG - implications for routine immunisation. Ph.d.-afhandling. Københavns Universitet. Oktober 2004.

## GRADUATE THESES ETC.

**Arendrup, M.C.** Seminalt overvågning af invasive svampeinfektioner. 1. maj 2003 – 15. april 2004. Speciesfordeling og resistensforhold. Rapport udsendt til de Klinisk Mikrobiologiske Afdelinger i DK.

**Axelsen, N.H.** Misconduct in research. How to best teach bioethics. In: Report from a workshop March 2003 organised by The Nordic Committee on Bioethics and NorFA. 2004;519:89-94.

**Boisen, N.** Molekylær karakterisering af *Campylobacter*. Specialerapport, Biocentrum, Danmarks Tekniske Universitet. November 2004.

**Bruun, B., Justesen, T., Heltberg, O., Frederiksen, W., Poulsen, L., Christensen, J.J.** Referenceprogram for identifikation af klinisk vigtige bakterier, herunder nomenklatur. www.dskm.dk/rapporter (oprettet juli 2004).

**Dalby, T.** Development of ELISA for detection of *Salmonella* antibodies in human serum. Specialerapport for biokemi, Naturvidenskabeligt Fakultet, Københavns Universitet. Juli 2004.

**Folsing, C.** Verotoksin-producerende *Escherichia coli* (VTEC): Subtypning af verotoksin 1 og association til kliniske symptomer i mennesker. Specialerapport, Institut for Farmakologi, Danmarks Farmaceutiske Universitet. September 2004.

**Frimodt-Møller, N., Fris-Møller, A., Kristiansen, J.E., Pedersen, S., Schumacher, H., Siboni K., Skov, R.** Dansk Selskab for Klinisk Mikrobiologi's Referencegruppe vedrørende Antibiotika Resistensbestemmelse – Klaringssrapport. April 2004.

**Hammerum, A.M., Brandt, C., Muscat, M., Frimodt-Møller, N., Monnet, D.L.** Bidrag vedrørende de humane data i DANMAP 2003 – Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. ISSN 1600-2032, 2004.

**Hansen, C.E., Vinter, T.N.** Undersøgelse af tranebærjuices effekt på urinvejsinfektioner med *E. coli* kliniske isolater samt deres ekspresion af type 1 fimbriae. Speciale-rapport, diplomering. (kemi), BioCentrum, Danmarks Tekniske Universitet. Juni 2004.

**Holt, J.** Speciale ved Danmarks Pædagogiske Universitet – cand.pæd.pæd: Håndhygiejne. En handling mellem anstændighed og krænkelse. Juni 2004.

**Hougaard, D.** Antibiotikaresistens i *Salmonella* Stanley. Institut for Veterinær Patologi, Den Kongelige Veterinær- og Landbohøjskole, Frederiksberg. Levnedmiddel bachelorprojekt udført i Afdelingen for Antibiotikaresistens og Sygehushygiejne februar-juli 2004.

**Kirkegaard, U.S.** Verotoksinproducerende *E. coli* (VTEC): Effekten af antibiotika på bakterieekstraktets cytotoxicitet over for veroceller. Specialerapport, Institut for Farmakologi, Danmarks Farmaceutiske Universitet. Oktober 2004.

**Larsen, L.S.** Genekspressionsanalyser af *Helicobacter pylori*. Specialerapport, civ. ing. (kemi), BioCentrum, Danmarks Tekniske Universitet. September 2004.

**Mortensen, N.P.** Impact of *Campylobacter jejuni*'s virulence factors on clinical outcome. Specialerapport for biologi, Naturvidenskabeligt Fakultet, Københavns Universitet. April 2004.

**Møller, A.** Role of *Escherichia coli* lipopolysaccharide in colonization of the mouse large intestine of streptomycin-treated mice. Specialerapport, cand.scient. (biologi), Naturvidenskabeligt Fakultet, Københavns Universitet. Maj 2004.

**Møller, J.** Mannosederivatets indflydelse på *E. coli* infektionsevne ved urinvejsinfektioner. Specialerapport, Institut for Farmakologi, Danmarks Farmaceutiske Universitet. Oktober 2004.

**Pedersen, L., Abelha, S., Andersen, S.** Influence of the F-plasmid on the ability of a *Klebsiella pneumoniae* strain and its capsule mutant to colonise the gastrointestinal and urinary tracts. Midtvejsprojekt, civing.-studiet, BioCentrum, Danmarks Tekniske Universitet. Marts 2004.

**Pedersen, M.K.** Effect of different hapten-carrier conjugation ratios and molecular orientations on the antibody affinity. Specialerapport. Januar 2004.

**Raaby, B.** CNA som virulensfaktor i *Staphylococcus aureus*. Danmarks Tekniske Universitet. Ingeniørpraktik. Specialerapport udarbejdet i Afdelingen for Antibiotika-resistens og Sygehushygiejne 30. september 2003 - 19. januar 2004.

**Schjørring, S.** Undersøgelse af det konjugative plasmid RP4's indflydelse på *E. coli* stammers koloniseringsvne i tarmen. Specialerapport, civ. ing. (kemi), BioCentrum, Danmarks Tekniske Universitet. Februar 2004.

**Schultz, L., Jørgensen, K.N.** *Campylobacter* antistofmåling ved hjælp af ELISA. Rapport fra obligatorisk afgangsprøve, diplomering. (kemi), BioCentrum, Danmarks Tekniske Universitet. Juni 2004.

**Skardi, J., Wong, M.** Sammenhæng mellem forekomst af fimbriae og virulens hos *K. pneumoniae* samt identifikation ved real-time PCR. Specialerapport, diplomingeniørstudiet, BioCentrum, Danmarks Tekniske Universitet. Juni 2004.

**Sørensen, K.M.** Troponin T and other candidate genes in hypertrophic cardiomyopathy – Genetic screening and RNA analysis. Specialeafhandling. Københavns Universitet. Marts 2004.

**Sørensen, M.** Udvikling af 16S rDNA real-time PCR og sekventering til påvisning af bakteræmi. Specialerapport. Københavns Universitet. Marts 2004.

**Østergaard, J.** Undersøgelse af serin-aspartat repeat proteiner i *Staphylococcus aureus*, herunder SdrC, SdrD og SdrE. Institut for anvendt kemi, Danmarks Tekniske Universitet. Diplom- Kemiingeniør Eksamensprojekt udført i Afdelingen for Antibiotikaresistens og Sygehushygiejne. September 2004.

## PAPERS

**Abildstrøm, H., Christiansen, M., Rasmussen, L., Siersma, V., Hanning, C., Kui-pers, H.M., Korttila, K., Houx, P.J., Grimsmo, B., Kristensen, D., Vila, P., Ernlund, M., Johnson, T.W., Pandin, P., Hamiotaki, E., Nielsen, I.K., Silverstein, J., Sneyd, J.R., Møller, J.T. and the ISPOCD2 group.** Apolipoprotein E genotype and cognitive dysfunction after noncardiac surgery. *Anesthesiology*. 2004;101:855-861.

**Ahlgren, M., Melbye, M., Wohlfahrt, J., Sørensen, T.I.A.** Growth patterns and the risk of breast cancer in women. *N Engl J Med*. 2004;351:1619-1626.

**Albrich, W.C., Monnet, D.L., Harbarth, S.** Antibiotic selection pressure and resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*. *Emerg Infect Dis*. 2004;10:514-517.

**Andersen, P.S., Havndrup, O., Bundgaard, H., Larsen, I.A., Vuust, J., Pedersen, A.K., Kjeldsen, K., Christiansen, M.** Genetic and phenotypic characterization of mutations in myosin-binding protein C (MYBPC3) in 81 families with familial hypertrophic cardiomyopathy: total or partial haploinsufficiency. *Eur J Hum Gen*. 2004;12:673-677.

**Andersen, P.S., Larsen, L.A.** High-throughput Mutation Screening. *Mol Anal Geno Disc*. 2004;5:71-100.

**Andersen-Ranberg, K., Høier-Madsen, Wilk, A., Jeune, B., Hegedüs, L.** High prevalence of autoantibodies among Danish centenarians. *Clin Exp Immunol*. 2004;138:158-163.

**Ariyoshi, K., Berry, N., Cham, F., Jafar, S., Schim van der Loeff, M., Jobe, O., N'Gom, P.T., Larsen, O., Andersson, S., Aaby, P., Whittle, H.** Quantification of human T-lymphotropic virus type 1 (HTLV-I) provirus load in a rural West African population: no enhancement of human immunodeficiency virus type 2 pathogenesis, but HTLV-I provirus load relates to mortality. *J Infect Dis*. 2003;188:1648-1651

**Bager, P., Nielsen, N.M., Bihrmann, K., Frisch, M., Hjalgrim, H., Wohlfahrt, J., Koch-Henriksen, N., Melbye, M., Westergaard, T.** Childhood infections and risk of multiple sclerosis. *Brain*. 2004;127:2491-2497.

**Bang, D.D., Borck, B., Nielsen, E.M., Scheutz, F., Pedersen, K., Madsen, M.** Detection of seven virulence and toxin genes of *Campylobacter jejuni* isolates from Danish turkeys by PCR and Cytolethal Distending Toxin production of the isolates. *J Food Protect*. 2004;67(10):2171-2177.

**Baquero, M.R., Nilsson, A.L., Turrientes, M. del C., Sandvang, D., Galan, J.C., Martinez, J.L., Frimodt-Møller, N., Baquero, F., Andersson, D.I.** Polymorphic mutation frequencies in *Escherichia coli*: emergence of weak mutators in clinical isolates. *J Bacteriol*. 2004;186:5538-5542.

**Belleville, E., Duiva, M., Aamand, J., Bruun, L., Clausen, L., Christensen, C.B.** Quantitative microarray pesticide analysis. *J Immunol Methods*. 2004;286(1-2):219-229.

**Benn, C.S., Böttcher, M.F., Pedersen, B.V., Filleul, S.M., Duchén, K.** Mammary epithelial permeability in atopic and non-atopic mothers versus childhood atopy. *Ped Allergy Immunol*. 2004;15(2):123-126.

**Benn, C.S., Melbye, M., Wohlfahrt, J., Björkstén, B., Aaby, P.** Cohort study of sibling effect, infectious diseases, and risk of atopic dermatitis during first 18 months of life. *Brit Med J*. 2004;328:1223-1226.

**Benn, C.S., Wohlfahrt, J., Aaby, P., Westergaard, T., Benfield, E., Michaelsen, K.F., Björkstén B., Melbye, M.** Breastfeeding and risk of atopic dermatitis, by parental history of allergy, during the first 18 months of life. *Am J Epidemiol*. 2004;160:217-223.

**Bizzaro, N., Wilk, A.** Appropriateness in anti-nuclear antibody testing: from clinical request to strategic laboratory practice. *Clin Exp Rheumatol*. 2004;22:349-355.

**Bjørnelli, E., Jensen, J.S., Lidbrink, P.** Conjunctivitis associated with *Mycoplasma genitalium* infection. *Clin Infect Dis*. 2004;39:e67-69.

**Boesen, T., Madsen, C., Pedersen, D.S., Nielsen, B.M., Petersen, A.B., Petersen, M.A., Munk, M., Henriksen, U., Nielsen, C., Dahl O.** Preparation and antiviral properties of new acyclic, achiral nucleoside analogues: N-1 or N-9 [3-hydroxy-2-(hydroxymethyl) prop-1-ethyl]nucleobases and N-1 or N-9-[2,3-dihydroxy-2-(hydroxymethyl)propyl]nucleobases. *Org Biomol Chem*. 2004;2:1245-1254.

**Bohlin, M., Kogutowska, E., Blomberg, L., Heegaard, N.H.H.** Capillary electrophoresis-based analysis of phospholipid- and glycosaminoglycan-binding by human  $\alpha_2$ -glycoprotein I. *J Chromatogr A*. 2004;1059:215-222.

**Bornman, L., Campbell, S.J., Fielding, K., Bah, B., Silah, J., Gustafson, P., Manneh, K., Lisse, I., Allen, A., Sirugo, G., Sylla, A., Aaby, P., McAdam, K.P.W.J., Bah-Sow, O., Bennett, S., Lienhardt, C., Hill, A.V.S.** Vitamin D receptor polymorphisms and susceptibility to tuberculosis in West Africa: A case-control and family study. *J Infect Dis*. 2004;190:1631-1641.

**Brandt, C.T., Lundgren, J.D., Lund, S.P., Frimodt-Møller, N., Christensen, T., Benfield, T., Espersen, F., Hougaard, D.M., Østergaard, C.** Attenuation of the bacterial load in blood by pretreatment with granulocyte-colony-stimulating factor protects rats from fatal outcome and brain damage during *Streptococcus pneumoniae* meningitis. *Infect Immun*. 2004;72:4647-4653.

**Breiting, V.B., Hölmich, L.R., Brandt, B., Fryzek, J.P., Wolthers, M.S., Kjoller, K., McLaughlin, J.K., Wilk, A., Friis, S.** Long-term health status of Danish women with silicone breast implants. *Plast Reconstr Surg*. 2004;114:217-226; discussion 227-28.

**Broek, I., Weldingh, K., Leyten, E.M.S., Arend, S.M., Ravn, P., Andersen, P.** Specific T-cell epitopes for immunoassay-based diagnosis of *Mycobacterium tuberculosis* infection. *J Clin Microbiol*. 2004;42:2379-2387

**Broek, I., Weldingh, K., Lillebaek, T., Follmann, F., Andersen, P.** Comparison of tuberculin skin test and new specific blood test in tuberculosis contacts. *Am J Resp Crit Care Med*. 2004;170(1):65-69.

**Brodin, P., Rosenkrands, I., Andersen, P., Cole, S.T., Brosch, R.** ESAT-6 proteins: protective antigens and virulence factors? *Trends Microbiol*. 2004;12:500-508.

**Brydensholt, H.H., Axelsen, N.H.** Forskeretik. *Ugeskr Laeger*. 2004;166(24):2335-2336.

**Carvalho, L.J.M., Oliveira, S.G., Theisen, M., Alves, F.A., Andrade, M.C.R., Zanini, G.M., Brigido, M.C.O., Oeuvray, C., Póvoa, M.M., Muniz, J.A.P.C., Drulhe, P., Daniel-Ribeiro, C.T.** Immunization of *Saimiri sciureus* Monkeys with Plasmodium falciparum Merozoite Surface Protein-3 and Glutamate-Rich Protein Suggest that Protection is Related to Antibody Levels. *Scand J Immunol*. 2004;59:363-372.

**Chang, E.T., Smedby, K.E., Zhang, S.M., Hjalgrim, H., Melbye, M., Öst, A., Wolk, A., Adami, H.O., Glimelius, B.** Alcohol intake and risk of non-Hodgkin lymphoma in men and women. *Cancer Causes Control*. 2004;15:1067-1076

**Christiansen, J.J., Gravholt, C.H., Fisker, S., Svenstrup, B., Bennett, P., Veldhuis, J., Andersen, M., Christiansen, J.S., Jørgensen, J.O.L.** Dehydroepiandrosterone supplementation in women with adrenal failure: impact on twenty-four hour GH secretion and IGF-related parameters. *Clin Endocrinol*. 2004;60:461-469.

**Christensen J.J., Skov R.** *Aerococcus urinae*. Chapter in: Antimicrobial Therapy and Vaccines (Ed. VL Yu, R Weber, D Raoult). 1. edition 1998, 2. edition 2002. Published by Lippincott, Williams and Wilkins. Internet version revised in 2004 ([www.antimicrobe.org](http://www.antimicrobe.org)).

**Christiansen, M., Larsen, S.O., Oxvig, C., Qin, Q-P., Wagner, J.M., Overgaard, M.T., Gleich, G.J., Sottrup-Jensen, L., Nørgaard-Pedersen, B.** Screening for Down's syndrome in early and late first and second trimester using six maternal serum markers. *Clin Genet.* 2004;65:11-16.

**Cosin-Sales, J., Christiansen, M., Kaminski, P., Oxvig, C., Overgaard, M.T., Cole, D., Holt, D., Kaski, J.C.** Pregnancy associated plasma protein-A (PAPP-A) and its endogenous inhibitor, the proform of eosinophil major basic protein are related to complex stenosis morphology in patients with stable angina pectoris. *Circulation.* 2004;109:1724-1728.

**Cowan, S.A.** Kviksolv i influenzavaccine. *Ugeskr Laeger.* 2004;166(38):3289-3291.

**Damborg, P., Olsen, K.E.P., Nielsen, E.M., Guardabassi, L.** Occurrence of *Campylobacter jejuni* in pets living with human patients infected with *C. jejuni*. *J Clin Microbiol.* 2004;42(3):1363-1364.

**Danielsen, A.G., Weismann, K., Jørgensen, B.B., Heidenheim, M., Fugleholm, A.M.** Incidence, Clinical Presentation and Treatment of Neurosyphilis in Denmark 1980 – 1997. *Acta Derm Venereol.* 2004;84:1-4.

**Demissie, A., Abebe, M., Aseffa, A., Rook, G., Fletcher, H., Zumla, A., Weldingh, K., Brock, I., Andersen, P., Doherty, T.M., VACSEL Study Group.** Healthy individuals that control a latent infection with *Mycobacterium tuberculosis* express high levels of Th1 cytokines and the IL-4 antagonist IL-4delta2. *J Immunol.* 2004;172:6938-6943.

**Doherty, T.M.** New Vaccines Against Tuberculosis. *Trop Med Int Health.* 2004;9(7):818-826.

**Dragsted, D.M., Dohn, B., Madsen, J., Jensen, J.S.** Comparison of culture and PCR for detection of *Bordetella pertussis* and *Bordetella parapertussis* under routine laboratory conditions. *J Med Microbiol.* 2004;53:749-754.

**Eiberg, H., Nørgaard-Pedersen, B., Nielsen, I.-M.** Cholestasis Familiaris Groenlandica/ Byler-like disease in Greenland – A population study. *Circumpolar Health* 2003. *Int J Circumpolar Health* 2004; 63,(Suppl 2):189-191.

**Ekelund, K., Lemcke, A., Konradsen, H.B.** Evaluation of gastrointestinal symptoms as primary sign of severe invasive group A streptococcal infections. *Indian J Med Res.* 2004;119(Suppl):179-82.

**Elliott, J.A., Thompson, T.A., Facklam, R.R., Slotved, H.C.** Increased sensitivity of a latex agglutination method for serotyping group B streptococcus. *J Clin Microbiol.* 2004;42(8):3907.

**Engberg, J., Neimann, J., Nielsen, E.M., Aarestrup, F.M., Fussing, V.** Quinolone-resistant *Campylobacter* in Denmark: Risk factors and clinical consequences. *Emerg Infect Dis.* 2004;10(6):1056-1063.

**Ethelberg, S., Lisby, M., Torpdahl, M., Sørensen, G., Neimann, J., Rasmussen, P., Bang, S., Stamer, U., Hansson, H.B., Nygård, K., Baggesen, D.L., Nielsen, E.M., Mølbak, K., Helms, M.** Prolonged restaurant-associated outbreak of multidrug-resistant *Salmonella* Typhimurium among patients from several European countries. *Clin Microbiol Infect.* 2004;10(10):904-910.

**Ethelberg, S., Olsen, K.E.P., Gerner-Smidt, P., Mølbak, K.** Household outbreaks among culture confirmed cases of bacterial gastrointestinal disease. *Am J Epidemiol.* 2004;159(4):406-412.

**Ethelberg, S., Olsen, K.E.P., Scheutz, F., Jensen, C., Schiellerup, P., Engberg, J., Petersen, A.M., Olesen, B., Gerner-Smidt, P., Mølbak, K.** Virulence factors for hemolytic uremic syndrome, Denmark. *Emerg Infect Dis.* 2004;10:842-847.

**Falk, L., Fredlund, H., Jensen, J.S.** Symptomatic urethritis is more prevalent in *Mycoplasma genitalium* than in *Chlamydia trachomatis* infected men. *Sex Transm Infect.* 2004; 80:289-293.

**Fenger, M., Wiik, A., Høier-Madsen, M., Lykkegaard, J.J., Rozenfeld, T., Hansen, M.S., Samsøe, B.D., Jacobsen, S.** Detection of Antinuclear Antibodies by Solid-Phase Immunoassay and Immunofluorescence Analysis. *Clin Chem.* 2004;50:2141-2147.

**Fischer, T.K., Bihrmann, K., Perch, M., Koch, A., Wohlfahrt, J., Mølbak, K., Melbye, M.** Intussusception in early childhood: a cohort study of 1.7 million children. *Pediatrics.* 2004;114:782-785.

**Fischer, T.K., Gentsch, J.** Rotavirus typing methods and algorithms. *Rev Med Virol.* 2004;14(2):71-82.

**Fletcher, H.A., Owiafe, P., Jeffries, D., Hill, P., Rook, G., Zumla, A., Doherty, T.M., Brookes, R., VACSEL Study Group.** Increased expression of mRNA encoding interleukin (IL)-4 and its splice variant IL-4delta2 in cells from contacts of *Mycobacterium tuberculosis*, in the absence of in vitro stimulation. *Immunology.* 2004;112:669-673.

**Fomsgaard, A., Grauballe, P.C., Gilsman, S.O.** Risiko for en ny influenzapandemi? *Ugeskr Laeger.* 2004;166(10):912-915.

**Frederiksen, M.S., Brenøe, E., Trier, J.** Erythema multiforme minor following vaccination with paediatric vaccines. *Scand J Infect Dis.* 2004;36:154-155.

**Friborg, J., Koch, A., Stenz, F., Wohlfahrt, J., Melbye, M.** A population-based registry study of infant mortality in the the Arctic – Greenland and Denmark, 1973-1997. *Am J Public Health.* 2004;94:452-457.

**Frimodt-Møller, N.** Microbial Threat-The Copenhagen Recommendations initiative of the EU. *J Vet Med B Infect Dis Vet Public Health.* 2004;51:400-402.

**Frisch, M.** Health needs of women who have sex with women (letter). *Lancet.* 2004;328:464.

**Garly, M.L., Jensen, H., Martins, C.L., Balé, C., Balde, C., Balde, M.A., Lisse, I.M., Aaby, P.** Hepatitis B vaccination associated with higher female than male mortality in Guinea-Bissau: An observational study. *Pediatr Infect Dis J.* 2004;23(12):1086-1092.

**Gerner-Smidt, P.** Listeriose og Listeria monocytogenes. *Alimenta.* 2004;5:8-9.

**Gilsman, S.O.** Rubella in Denmark. *Eurosurveillance.* 2004;9(2):12-13.

**Gronskov, K., Larsen, L.A., Rendtorff, N.D., Parving, A., Nørgaard-Pedersen, B., Brøndum-Nielsen, K.** GJB2 and GJB6 mutations in 165 Danish patients showing non-syndromic hearing impairment. *Genet Test.* 2004;8(2):181-184.

**Gustafson, P., Gomes, V., Vieira, C.S., Rabna, P., Seng, R., Johansson, P., Sandström, A., Norberg, R., Lisse, I., Samb, B., Aaby, P., Nauciler, A.** Tuberculosis in Bissau: Incidence and risk factors in an urban community in sub-Saharan Africa. *Int J Epidemiol.* 2004;33:163-172.

**Haargaard, B., Wohlfahrt, J., Fiedelius, H.C., Rosenberg, T., Melbye, M.** A nationwide study of 1,027 cases of congenital/infantile cataract. Etiological and clinical classifications. *Ophthalmology.* 2004;111:2292-2298.

**Haargaard, B., Wohlfahrt, J., Fiedelius, H.C., Rosenberg, T., Melbye, M.** Incidence and cumulative risk of childhood cataract in a cohort of 2.6 million Danish children. *Invest Ophthalmol Vis Sci.* 2004;45:1316-1320.

**Haastrup, E., Thierry-Carstensen, B., Jensen, A.M., Stellfeld, M., Heilmann, C.** Safety and immunogenicity of a booster dose of inactivated poliovirus vaccine produced in vero-cells. *Vaccine.* 2004;22:958-962.

**Hammerum, A.M., Lester, C.H., Neimann, J., Porsbo, L.J., Olsen, K.E.P., Jensen, L.B., Emborg, H.D., Wegener, H.C., Frimodt-Møller, N.** A vancomycin-resistant *En-terococcus faecium* isolate from a Danish healthy volunteer, detected 7 years after the ban of avoparcin, is possibly related to pig isolates (letter). *J Antimicrob Chemother.* 2004;53(3):547-549.

**Hammerum, A.M., Nielsen, H.U., Agerø, Y., Ekelund, K., Frimodt-Møller, N.** Detection of tet(M), tet(O) and tet(S), and Transfer Studies of these Genes, in Tetracycline/Minocycline Resistant Group A Streptococcal Bacteraemia Isolates. *J. Antimicrob. Chemother.* 2004;53:118-119.

**Hanberger, H., Monnet, D.L., Nilsson, L.E., Intensive care unit.** In: Gould IM & van der Meer JWM. Antibiotic Policies: Theory & Practice. Heidelberg: Springer. 2004;261-279.

**Hansen, D.S., Aucken, H.M., Abiola, T., Podschun, R.** Recommended test panel for differentiation of *Klebsiella* species on the basis of a trilateral interlaboratory evaluation of 18 biochemical tests. *J Clin Microbiol.* 2004;42(8):3665-3669.

**Hansen, H.S., Olsen, S.F.** Sleep patterns, docosahexaenoic acid and gestational age (letter). *Am J Clin Nutr.* 2004;79:334.

**Helms, M., Simonsen, J., Mølbak, K.** Quinolone resistance is associated with increased risk of invasive illness or death during infection with *Salmonella* serotype Typhimurium. *J Infect Dis.* 2004;190(9):1652-1654.

**Helms, M., Vastrup, P., Gerner-Smidt, P., Mølbak, K.** Dødsfald efter fødevarerborne bakterielle mave-/tarminfektioner. *Ugeskr Laeger.* 2004;166(6):491-493.

**Hjalgrim, H., Rasmussen, R., Rostgaard, K., Nielsen, N.M., Koch-Henriksen, N., Munksgaard, L., Storm, H.H., Melbye, M.** Familial clustering of Hodgkin's lymphoma and multiple sclerosis. *J Natl Cancer Inst.* 2004;96:780-784.

**Hjalgrim, L., Rostgaard, K., Hjalgrim, H., Westergaard, T., Thomassen, H., Forester, E., Gustafsson, G., Kristinsson, J., Melbye, M., Schmiegelow, K.** Birth weight and risk for childhood leukemia in Denmark, Sweden, Norway, and Iceland. *J Natl Cancer Inst.* 2004;96:1549-1556.

**Hofman-Bang, J., Christiansen, M.** Single temperature endonuclease enhanced SSCP/HD mutation analysis: evaluation of the method. *Scand J Clin Lab Invest.* 2004; 64:605-608.

**Hofman-Bang, J., Jespersen, T., Grunnet, M., Larsen, L.A., Andersen, P.S., Kanters, J.K., Kjeldsen, K., Christiansen, M.** Does KCNE5 play a role in long QT syndrome? *Clin Chim Acta.* 2004;345:49-53.

**Hölmich, L.R., Vejborg, I.M., Conrad, C., Stetting, S., Høier-Madsen, M., Fryzek, J.P., McLaughlin, J.K., Kjoller, K., Wiik, A., Friis, S.** Untreated silicone breast implant rupture. *Plast Reconstr Surg.* 2004;114(1):204-214.

**Holt, J., Skifte, T., Koch, A.** Infection control in day-care centers in Greenland. *Int. J. Circumpolar Health* 2004;(Suppl. 2):256-260.

**Holt, J.** Hygiejne i almen lægepraksis. *Månedsskr Prakt Lægern.* 2004;82: 1315-1319.

**Holt, J.** Hygiejne i almen lægepraksis II. *Månedsskr prakt lægegern.* 2004;82:1433-1438.

**Holten-Andersen, L., Doherty, T.M., Korsholm, K.S., Andersen, P.** Combination of the cationic surfactant dimethyl dioctadecyl ammonium bromide and synthetic mycobacterial cord factor as an efficient adjuvant for tuberculosis subunit vaccines. *Infect Immun.* 2004;72:1608-1617.

**Hougaard, D.M., Larsson, L.-I.** Carboxypeptidase E in rat antropeyrotic mucosa: distribution in progenitor and mature endocrine cell types. *Histochem Cell Biol.* 2004;121:55-61.

**Hutchinson, J.M., Patrick, D.M., Marra, F., Ng, H., Bowie, W.R., Heule, L., Muscat, M., Monnet, D.L.** Measurement of antibiotic consumption: A practical guide to the use of the Anatomical Therapeutic Chemical classification and Defined Daily Dose system methodology in Canada. *Can J Infect Dis.* 2004;15:29-35.

**Hviid, A., Melbye, M.** Association between thimerosal-containing vaccine and autism (reply). *JAMA.* 2004;291(180):181.

**Hviid, A., Melbye, M.** Impact of routine vaccination with a conjugate *Haemophilus influenzae* type b vaccine. *Vaccine.* 2004;22:378-382.

**Hviid, A., Stellfeld, M., Andersen, P., Wohlfahrt, J., Melbye, M.** Impact of routine vaccination with a pertussis toxoid vaccine in Denmark. *Vaccine.* 2004;22:3530-3534.

**Hviid, A., Stellfeld, M., Wohlfahrt, J., Melbye, M.** Childhood vaccination and type 1 diabetes. *N Engl J Med.* 2004;350:1398-1404.

**Hylenius, S., Andersen, A.M.N., Melbye, M., Hviid, T.V.F.** Association between HLA-G genotype and risk of pre-eclampsia: a case-control study using triad families. *Mol Hum Reprod.* 2004;10(4):237-246.

**Jensen, B., Wittrup, I.H., Wiik, A., Friis, S., Bliddal, H., Thomsen, B., McLaughlin, J.K., Danneskjold-Samsøe, B., Olsen, J.H.** Antipolymer antibodies in Danish women with silicone breast implants. *J Long Term Eff Med Implants.* 2004;14:73-80.

**Jensen, E.S., Lundbye-Christensen, S., Samuelsson, S., Sørensen, H.T., Schonheyder, H.C.** A 20-year ecological study of the temporal association between influenza and meningococcal disease. *Eur J Epidemiol.* 2004;19(2):181-187.

**Jensen, H., Benn, C.S., Lisse, I.M., Aaby, P.** Non-specific beneficial effects of vaccinations in Burkina Faso: Survival bias? (E-letter). *Brit Med J.* 2004;<http://bmj.bmjjournals.com/cgi/eletters/329/7478/1309#e6939>

**Jensen, J., Langkilde, A., Fenst, C., Nicolaesen, M.S., Rode, H.G., Christiansen, M., Selleberg, E.** CD4 T cell activation and disease activity at onset of multiple sclerosis. *J Neuroimmunol.* 2004;149:202-209.

**Jensen, J.S., Bjørnelli, E., Dohn, B., Lidbrink, P.** Comparison of first void urine and urogenital swab specimens for detection of *Mycoplasma genitalium* and *Chlamydia trachomatis* by Polymerase Chain Reaction in patients attending a sexually transmitted disease clinic. *Sex Transm Dis.* 2004;31(8):499-507.

**Jensen, J.S., Bjørnelli, E., Dohn, B., Lidbrink, P.** Use of TaqMan 5' nuclease real-time PCR for quantitative detection of *Mycoplasma genitalium* DNA in males with and without urethritis who were attendees at a sexuality transmitted disease clinic. *J Clin Microbiol.* 2004;42(2):683-692.

**Jensen, L., Heilmann, C., Smith, E., Wantzin, P., Peitersen, B., Weber, T., Krosgaard, K.** Effektiviteten af selektiv antenatal screening for hepatitis B blandt gravide kvinder i Danmark. *Ugeskr Laeger.* 2004;166(38):3303-3305.

**Jensen, J.S.** *Mycoplasma genitalium*: the aetiological agent of urethritis and other sexually transmitted diseases. *J Eur Acad Dermatol Venereol.* 2004;18:1-11.

**Jensen, S.T., Madsen, J.** Estimation of proportional covariances in the presence of certain linear restrictions. *The Annals of Statistics.* 2004;32(1):219-213

**Jensen, T.G., Gahrn-Hansen, B., Arendrup, M.C., Bruun, B.** Fusarium fungemia in four Danish haematological patients. *Clin Microbiol Infect.* 2004;10:499-501.

**Jensen, V.F., Neimann, J., Hammerum, A.M., Mølbak, K., Wegener, H.C.** Does the use of antibiotics in food animals pose a risk to human health? An unbiased review? *J Antimicrob Chemother.* 2004;54:274-275.



- Jensen, V.F., Neimann, J., Hammerum, A.M., Mølbak, K., Wegener, H.C. Does the use of antibiotics in food animals pose a risk to human health? An unbiased review? *J Antimicrob Chemother.* 2004;54(1):274-275; Author reply 276-278.
- Jeppesen, D.L., Hasselbalch, H., Lisse, I.M., Ersbøll, A.K., Engelmann, M.D.M. T-lymphocytes subsets, thymic size and breast feeding in infancy. *Pediatr Allergy Immunol.* 2004;15:127-132.
- Johansen, I.S., Lundgren, B., Tabak, F., Petri, B., Hosoglu, S., Saltoglu, N., Thomsen, V.Ø. Improved sensitivity of nucleic acid amplification for rapid diagnosis of tuberculous meningitis. *J Clin Microbiol.* 2004;42(7):3036-3040.
- Johansen, I.S., Thomsen, V.Ø., Forsgren, A., Hansen, B.F., Lundgren, B. Detection of Mycobacterium tuberculosis complex in formalin-fixed, paraffin-embedded tissue specimens with necrotizing granulomatous inflammation by strand displacement amplification. *J Mol Diagn.* 2004;6(3):231-235.
- Johansen, I.S., Thomsen, V.O., Marjamäki, M., Sosnovskaja, A., Lundgren, B. Rapid, automated, nonradiometric susceptibility testing of Mycobacterium tuberculosis complex to four first-line antituberculous drugs used in standard short-course chemotherapy. *Diagn Microbiol Infect Dis.* 2004; 50(2):103-107.
- Johansen, J.K., Sehested, A., Myrholm, T., Ladefoged, K., Krogh, K.A. Helicobacter pylori infection in Greenlandic patients with dyspepsia. *Int J Circumpolar Health.* 2004;63(Suppl):213-214.
- Jørgensen, C.S., Christiansen, M., Norgaard-Pedersen, B., Østergaard, E., Schiødt, F.V., Laursen, I., Houen, G. Gc globulin (vitamin D-binding protein) levels: an inhibition ELISA assay for determination of the total concentration of Gc globulin in plasma and serum. *Scand J Clin Lab Invest.* 2004;64:157-166.
- Jørgensen, C.S., Jagd, M., Sørensen, B.K., McGuire, J., Barkholt, V., Højrup, P., Houen, G. Efficacy and compatibility with mass spectrometry of methods for elution of proteins from sodium dodecyl sulfate-polyacrylamide gels and polyvinylidene difluoride membranes. *Anal Biochem.* 2004;330:87-97.
- Juul, K., Tybjaerg-Hansen, A., Marklund, S., Heegaard, N.H., Steffensen, R., Sillesen, H., Jensen, G., Nordestgaard, B.G. Genetically reduced anti-oxidative protection and increased ischemic heart disease risk: The Copenhagen City Heart Study. *Circulation.* 2004;109:59-65.
- Kanaujia, G.V., Motzel, S., Garcia, M.A., Andersen, P., Gennaro, M.L. Recognition of ESAT-6 sequences by antibodies in sera of tuberculous nonhuman primates. *Clin Diagn Lab Immunol.* 2004;11:222-226.
- Kanters, J.K., Fanoe, S., Larsen, L.A., Bloch-Thomsen, P.E., Tøft, E., Christiansen, M. T-wave pattern morphology analysis distinguishes between KvLQT1 and HERG mutations in Long QT syndrome. *Heart Rhythm.* 2004;1:285-292.
- Karp, B.E., Engberg, J. Comment on: Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. *J Antimicrob Chemother.* 2004;54(1):273-274; author reply 276-278. 2004 May 12.
- Kemp, M., Andresen, K., Sørensen, M., Christensen, J.J. Molekylærbiologisk bakteriologisk diagnostik: Påvisning af bakteriel DNA med PCR og identifikation ved DNA sekventering. *Ugeskr Laeger.* 2004;166:4351-4354.
- Kern, M.B., Frimodt-Møller, N., Espersen, F. Urinary concentrations and urine ex-vivo effect of mecillinam and sulphamethizole. *Clin Microbiol Infect.* 2004;10:54-61.
- Kjoller, K., Hölmich, L.R., Fryzek, J.P., Jacobsen, P.H., Friis, S., McLaugh, J.K., Lipworth, L., Henriksen, T.F., Høier-Madsen, M., Wilk, A., Olsen, J.P. Self-reported Musculoskeletal Symptoms Among Danish Women With Cosmetic Breast Implants. *Ann Plast Surg.* 2004;52(1):1-7.
- Knudsen, V.K., Orozova-Bekkevold, I., Rasmussen, L.B., Mikkelsen, T.B., Michaelsen, K.F., Olsen, S.F. Low compliance with recommendations on folic acid use in relation to pregnancy: is there a need for fortification? *Public Health Nutr.* 2004;7:843-850.
- Kotoed, P.E., Aldrangis, M., Poulsen, A., Rodrigues, A., Gjedde, S.B., Ronn, A., Rombo, L. Genetic markers of resistance to pyrimethamine and sulphonamides in Plasmodium falciparum, parasites compared with the resistance patterns in isolates of E. coli from the same children in Guinea-Bissau. *Trop Med Int Health.* 2004;9(1):171-177.
- Kotoed, P.E., Rodrigues, A., Co, F., Hedegaard, K., Rombo, L., Aaby, P. Which children come to the health center for treatment of malaria? *Acta Trop.* 2004;90:17-22.
- Kovats, R.S., Edwards, S.J., Hajat, S., Armstrong, B.G., Ebi, K.L., Menne, B., The Collaborating Group. The effect of temperature on food poisoning: a time-series analysis of salmonellosis in ten European countries. *Epidemiol Infect.* 2004;132(3):443-453.
- Kremer, K., Glynn, J.R., Lillebaek, T., Niemann, S., Kurepina, N.E., Kreiswirth, B.N., Bifani, P.J., van Soelingen, D. Definition of the Beijing/W lineage of Mycobacterium tuberculosis on the basis of genetic markers. *J Clin Microbiol.* 2004;42(9):4040-4049.
- Kroman, N., Holtveg, H., Wohlfahrt, J., Jensen, M., Mouridsen, H.T., Blichert-Toft, M., Melbye, M. Effect of breast-conserving therapy versus radical mastectomy on prognosis for young women with breast carcinoma. *Cancer.* 2004;100:688-693.
- Landgren, O., Björkholm, M., Konrad, H.B., Söderqvist, M., Nilsson, B., Gustavsson, A., Axedorp, U., Kalin, M., Grimfors, G. A prospective study on antibody response to repeated vaccinations with pneumococcal capsular polysaccharide in splenectomized individuals with special reference to Hodgkin's lymphoma. *J Int Med.* 2004;255:664-673.
- Larsen, J.S., Pedersen, E.B. and Nielsen, C. Synthesis of N-1-Alkylated 6-Benzyluracil-5-carboxylic Esters as Potential Non-Nucleoside Reverse Transcriptase Inhibitors. *Synthesis.* 2004;11:1874-1878.
- Lauenborg, J., Hansen, T., Jensen, D.M., Vestergaard, H., Mølsted-Pedersen, L., Hommes, P., Loch, H., Pedersen, O., Damm, P. Increasing Incidence of Diabetes After Gestational Diabetes. *Obstet Gynecol Surv.* 2004;59(10):696-697.
- Lauenborg, J., Hansen, T., Møller Jensen, D., Vestergaard, H., Mølsted-Pedersen, L., Hommes, P., Loch, H., Pedersen, O., Damm, P. Increasing incidence of diabetes after gestational diabetes. A long-term follow-up in a Danish population. *Diabetes Care.* 2004;27:1194-1199.
- Lauritzen, L., Jørgensen, M.H., Mikkelsen, T.B., Skovgaard, I.M., Straarup, E-M., Olsen, S.F., Høy, C-E, Michaelsen, K.F. Maternal fish oil supplementation in lactation: Effect on visual acuity and n-3 fatty acid content of infant erythrocytes. *Lipids.* 2004;39:195-206.
- Laustrop, H., Heegaard, N.H.H., Voss, A., Green, A., Lillevang, S.T., Junker, P. Autoantibodies and self-reported health complaints in relatives to SLE patients. A community based approach. *Lupus.* 2004;13:792-799.
- Lei, U., Wohlfahrt, J., Christens, P., Westergaard, T., Lambe, M., Pedersen, B.N., Melbye, M. Reproductive factors and extreme levels of maternal serum alpha-fetoprotein – a population-based study. *Acta Obstet Gynaecol Scand.* 2004;83:1147-1151.
- Lemcke, A., Rasmussen, E., Glismann, S.O., Krogfelt, K.A. Leptospirose i Danmark 1980-2002. En relevant diagnose for danske læger? *Ugeskr Laeger.* 2004;166(32):2659-2663.
- Lemming, L., Holt, H.M., Petersen, I.S., Østergaard, C., Bruun, B. Bactec 9240 blood culture system: to preincubate at 35o or not? *Clin Microbiol Infect.* 2004;10:1089-1091.
- Lerbæk, A., Kristiansen, T.B., Katzenstein, T., Mathiesen, L., Gerstoft, J., Nielsen, C., Larsen, K., Nielsen, J.O., Obel, N., Laursen, A.L., Nielsen, S.D. Tenofovir treatment in an unselected cohort of highly antiretroviral experienced HIV positive patients. *Scand J Infect Dis.* 2004;36:280-286.
- Lester, C.H., Frimodt-Møller, N., Hammerum, A.M. Conjugal Transfer of Aminoglycoside, Macrolide Resistance between Enterococcus faecium isolates in the Intestine of Streptomycin-Treated Mice. *FEMS Microbiol Lett.* 2004;235:385-391.
- Lillebaek, T., Dirksen, A., Kok-Jensen, A., Andersen, A.B. A dominant Mycobacterium tuberculosis strain emerging in Denmark. *Int J Tub Lung Dis.* 2004;8(8):1001-1006.
- Linneberg, A., Petersen, J., Gronbak, M., Benn, C.S. Alcohol during pregnancy and atopic dermatitis in the offspring. *Clin Exp Allergy.* 2004;34:1678-1683.
- Lizeng, Q., Nilsson, C., Sourial, S., Andersson, S., Larsen, O., Aaby, P., Ehnlund, M., Björling, E. Potent neutralizing serum immunoglobulin a (IgA) in human immunodeficiency virus type-2-exposed IgG seronegative individuals. *J Virol.* 2004;78:7016-7022.
- Loksha, Y.M., El-Babary, A.A., El-Badawi, M.A., Nielsen, C., Pedersen, E.B. Synthesis of 2-Hydroxymethyl-1H-imidazoles from 1,3-Dihydroimidazole-2-thiones. *Synthesis.* 2004;1:116-120.
- López-Lozano, J.M., Monnet, D.L., Campillos Alonso, P., Cabrera Quintero, A., Gonzalo Jiménez, N., Yagüe Muñoz, A., Thomas, C., Beyaert, A., Stevenson, M., Riley, T.V. Applications of time series analysis to antibiotic resistance and consumption data. In: Gould IM & van der Meer JWM. Antibiotic Policies: Theory & Practice. Heidelberg: Springer. 2004;447-463.
- Lopman, B., Vennema, H., Kohli, E., Pothier, P., Sanchez, A., Negro, A., Buessa, J., Schreier, E., Reacher, M., Brown, D., Gray, J., Iluriza, M., Gallimore, C., Böttiger, B., Johnsen, C., Hedlund, K-O., Torvén, M., von Bonsdorff, C-H., Maunula, L., Poljsak-Prijatelj, M., Zimsek, J., Reuter, G., Szics, G., Melegh, B., Svensson, L., van Duinhoven, Y., Koopmans M for the European Food-borne Viruses Network: Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of a new Norovirus variant. *Lancet.* 2004;363(9410):682-688.
- Lyashchenko, K., Whelan, A.O., Greenwald, R., Pollock, J.M., Andersen, P., Hewinson, R.G., Vordermeier, H.M. Association of tuberculin-boosted antibody responses with pathology and cell-mediated immunity in cattle vaccinated with Mycobacterium bovis BCG and infected with M. bovis. *Infect Immun.* 2004;72:2462-2467.
- Madsen, K.M., Lauritsen, M.B., Pedersen, C.B., Thorsen, P., Plesner, A.M., Andersen, P.H., Mortensen, P.B. Thiomersal og forekomsten af autisme. Negativ økologisk evidens fra danske registerdata. *Ugeskr Laeger.* 2004;166(38):3291-3293.
- Madsen, K.M., Storgaard, M., Krogfelt, K.A., Obel, N. Rickettsiose efter ophold i det sydlige Afrika. *Ugeskr Laeger.* 2004;166(10):902-904.
- Martin-Casabona, N., Bahrmand, A.R., Bennedsen, J., Thomsen, V.O., Curcio, M., Fauville-Dufaux, M., Feldman, K., Havelkova, M., Katila, M.L., Koksalan, K., Pereira, M.F., Rodrigues, F., Piyffer, G.E., Portales, E., Urgell, J.R., Rusch-Gerdes, S., Tortoli, E., Vincent, V., Watt, B.; Spanish Group for Non-Tuberculosis Mycobacteria. Non-tuberculous mycobacteria: patterns of isolation. A multi-country retrospective survey. *Int J Tuberc Lung Dis.* 2004;8(10):1186-1193.
- Masmas, T.N., Jensen, H., da Silva, D., Co, A.O., Høj, L., Sandström, A., Aaby, P. Survival among motherless children in rural and urban Guinea-Bissau. *Acta Paediatr.* 2004;93:99-105.
- Masmas, T.N., Jensen, H., da Silva, D., Co, A.O., Høj, L., Sandström, A., Aaby, P. The social situation of motherless children in rural and urban areas in Guinea-Bissau. *Soc Sci Med.* 2004;59:1231-1239.
- Mens, H., Højlyng, N., Arendrup, M.C. Disseminated Penicillium marneffe sepsis in a HIV-positive Thai woman in Denmark. *Scand J Infect Dis.* 2004; 36(6-7):507-509.
- Meraldi, V., Nebié, I., Tiono, A.B., Diallo, D., Sanogo, E., Theisen, M., Drullhe, P., Corradin, G., Moret, R., Sirima, B.S. Relation between antibody response and malaria episodes Natural antibody response to Plasmodium falciparum Exp-1, MSP-3 and GLURP long synthetic peptides and guidelines for vaccination with protection. *Parasite Immunol.* 2004;26:265-272.
- Meyer, C.N., Samuelsson, S., Galle, M., Bangsbo, J.M. Adult bacterial meningitis. Aetiology, penicillin susceptibility, risk factors, prognostic factors, and guidelines for empirical antibiotic treatment. *Clin Microbiol Infect.* 2004;10(8):709-717.
- Mogensen, J., Perrot, A., Andersen, P.S., Handrup, O., Klausen, I.C., Christiansen, M., Bross, P., Egeblad, H., Bundgaard, H., Osterziel, K.J., Haltern, G., Lapp, H., Reinecke, P., Gregersen, N., Borglum, A.D. Clinical and genetic characteristics of  $\alpha$  cardiac actin gene mutations in hypertrophic cardiomyopathy. *J Med Genet.* 2004;41:E10.
- Mølbak, K. Spread of resistant bacteria and resistance genes from animals to humans – the public health consequences. *J Vet Med B Infect Dis Vet Public Health.* 2004;51(8-9):364-369.
- Mølbak, K., Scheut, F. Verocytotoxin-producing Escherichia coli and other diarrhoeagenic E. coli, pp 213-27. In: Cotruvo, J.A., Dufour, A., Rees, J., Bartram, J., Carr, R., Cliver, D.O., Craun, G.F., Fayer, R., Gannon, V.P.J. (Eds.) Waterborne Zoonoses. WHO, IWA Publishing, London 2004.
- Møller, M., El Maghrabi, R., Olesen, N., Thomsen, V.O. Safe inoculation of blood and bone marrow for liquid culture detection of mycobacteria. *Occur Med.* 2004;54:540-543.
- Monnet, D.L. Antibiotic development and the changing role of the pharmaceutical industry [background paper]. The Global Threat of Antibiotic Resistance: Moving Towards Concerted Action. Uppsala (S): Dag Hammarskjöld Foundation, 2004. Available from: URL: <http://soaping.iccube.snowfall.se/stopresistance/industry.pdf>
- Monnet, D.L., Frimodt-Møller, N. Only percentage within species; neither incidence, nor prevalence: demographic information and representative surveillance data are urgently needed to estimate the burden of antimicrobial resistance. *Int J Antimicrob Agents.* 2004;24:622-623.
- Monnet, D.L., MacKenzie, F.M., López-Lozano, J.M., Beyaert, A., Camacho, M., Wilson, R., Stuart, D., Gould, I.M. Antimicrobial drug use and methicillin-resistant Staphylococcus aureus, Aberdeen, 1996-2000. *Emerg Infect Dis.* 2004;10:1432-1441.
- Monnet, D.L., Mölstad, S., Cars, O. Defined daily doses of antimicrobials reflect antimicrobial prescriptions in ambulatory care. *J Antimicrob Chemother.* 2004;53:1109-1111.
- Müller-Pebody, B., Muscat, M., Pelle, B., Klein, B.M., Brandt, C.T., Monnet, D.L. Increase and change in pattern of hospital antimicrobial use, Denmark, 1997-2001. *J Antimicrob Chemother.* 2004;54:1122-1126.
- Munksgaard, L., Obitz, R., Goodlad, J.R., Davidson, M.M., Ho-Yen, D.O., Hamilton-Dutoit, S., Hjalgrim, H. Demonstration of B. burgdorferi-DNA in two cases of nodal lymphoma. *Leuk Lymphoma.* 2004;45:1721-1723.
- Nébié, I., Cuzin-Ouattara, N., Dially, D.A., Couens, S.N., Theisen, M., Corradin, G., Traoré, A.S., Esposito, F. Humoral responses to defined malaria antigens in children living since birth under insecticide treated curtains in Burkina Faso. *Acta Tropica.* 2004;88:17-25.

- Newport, M.J., Goetghebuer, T., Weiss, H.A., The MRC Gambia Twin Study Group (Aaby, P.), Whittle, H., Siegrist, C.-A., Marchant, A. Genetic regulation of immune responses to vaccines in early life. *Genes Immun.* 2004;5:122-129.
- Nielsen, E.M., Skov, M.N., Madsen, J.J., Lodal, J., Jespersen, J.B., Baggesen, D.L. Verocytotoxin-producing *Escherichia coli* in wild birds and rodents in close proximity to farms. *Appl Environ Microbiol.* 2004;70(11):6944-6947.
- Nielsen, H.U., Hammerum, A.M., Ekelund, K., Bang, D., Pallesen, L.V., Frimodt-Møller, N. Tetracycline and macrolide co-resistance in *Streptococcus pyogenes*: co-selection as a reason for increase in macrolide-resistant *S. pyogenes*? *Microb Drug Resist.* 2004;10(3):231-238.
- Nielsen, J., Valentiner-Branth, P., Martins, C., Cabral, F., Aaby, P. Malnourished children and supplementary feeding during the war emergency in Guinea-Bissau in 1998-99. *Am J Clin Nutr.* 2004;80:1036-1042.
- Nielsen, N.M., Rostgaard, K., Askgaard, D., Skinhøj, P., Aaby, P. Life-long morbidity among Danes with poliomyelitis. *Arch Phys Med Rehabil.* 2004;85(3):385-391.
- Nordberg, P., Monnet, D.L., Cars, O. Antibacterial drug resistance [background paper]. Priority Medicines for Europe and the World "A Public Health Approach to Innovation". Geneva (CH): World Health Organization, 2004. Available on CD-ROM (WHO/EDM/PAR/2004.7) and from: URL: <http://mednet3.who.int/prioritymeds/report/background/antibacterial.doc>
- Oakeshott, P., Hay, P., Taylor-Robinson, D., Hay, S., Dohn, B., Kerry, S., Jensen, J.S. Prevalence of *Mycoplasma genitalium* in early pregnancy and relationship between its presence and pregnancy outcome. *BJOG.* 2004;111:1464.
- Obriest, P., Spizzo, G., Ensinger, C., Fong, D., Brunhuber, T., Schäfer, G., Varga, M., Margreiter, R., Amberger, A., Gastl, G., Christiansen, M. Aberrant tetranectin expression in human breast carcinomas as predictor of survival. *J Clin Pathol.* 2004;57:417-421.
- Oken, E., Kleinman, K.P., Olsen, S.F., Rich-Edwards, J.W., Gillman, M.W. Associations of seafood and elongated n-3 fatty acid intake with reduced fetal growth and length of gestation: results from a US pregnancy cohort. *Am J Epidemiol.* 2004;160:774-783.
- Okkels, L.M., Andersen, P. Protein-protein interactions of proteins from the ESAT-6 family of *Mycobacterium tuberculosis*. *J Bacteriol.* 2004;186:2487-2491.
- Okkels, L.M., Müller, E.C., Schmid, M., Rosenkrands, I., Kaufmann, S.H., Andersen, P., Jungblut, P.R. CFP10 discriminates between nonacetylated and acetylated ESAT-6 of *Mycobacterium tuberculosis* by differential interaction. *Proteomics.* 2004;4:2954-2960.
- Olsen, A.W., Brandt, L., Agger, E.M., van Pinxteren, L.A.H., Andersen, P. The Influence of Remaining Live BCG Organisms in Vaccinated Mice on the Maintenance of Immunity to Tuberculosis. *Scand J Immun.* 2004;60:273-277.
- Olsen, A.W., Williams, A., Okkels, L.M., Hatch, G., Andersen, P. Protective Effect of a Tuberculosis Subunit Vaccine Based on a Fusion of Ag85B and ESAT-6 in the Aerosol Guinea Pig Model. *Infect Immun.* 2004;72:6148-6150.
- Olsen, S.F. Is supplementation with marine omega-3 fatty acids during pregnancy a useful tool in the prevention of preterm birth? *Clin Obstet Gynecol.* 2004;47:768-774.
- O'Neill, A.J., Larsen, A.R., Henriksen, A.S., Chopra, I. A fusidic acid-resistant epidemic strain of *Staphylococcus aureus* carries the *fusB* determinant, whereas *fusA* mutations are prevalent in other resistant isolates. *Antimicrob Agents Chemother.* 2004;48:3594-3597.
- Overgaard, M.T., Glerup, S., Boldt, H.B., Rodacker, V., Olsen, J.M., Christiansen, M., Sottrup-Jensen, L., Giudice, L.C., Oxvig, C. Inhibition of proteolysis by the proform of eosinophil major basic protein (proMBP) requires covalent binding to its target protease. *FEBS Lett.* 2004;560:147-152.
- Paget, J., Meijer, A., Fleming, D., Samuelsson, S., Schweiger, B. Further reductions of influenza activity reported in Europe in week 02/2004: an update from EISS. *Eurosurveillance Weekly* 2004; 8(4).
- Painter, J.A., Mølbak, K., Sonne-Hansen, J., Barrett, T., Wells, J.G., Tauxe, R.V. Salmonella-based rodenticides and public health. *Emerg Infect Dis.* 2004; 10(6):985-987.
- Patrick, D.M., Marra, F., Hutchinson, J., Monnet, D.L., Ng, H., Bowie, W.R. Per capita antibiotic consumption in populations: how does a North American jurisdiction compare with Europe? *Clin Infect Dis.* 2004;39:11-17.
- Patrick, M.E., Christiansen, L.E., Waino, M., Ethelberg, S., Madsen, H., Wegener, H.C. Effects of climate on incidence of *Campylobacter* spp. in humans and prevalence in broiler flocks in Denmark. *Appl Environ Microbiol.* 2004;70(12):7474-7480.
- Perch, M., Kofoed, P.E., Fischer, T.K., Cø, F., Rombo, L., Aaby, P., Eugen-Olsen, J. Serum levels of soluble urokinase plasminogen activator receptor is associated with parasitemia in children with acute *Plasmodium falciparum* malaria infection. *Parasite Immunol.* 2004;26:207-211.
- Pietkiewicz, H., Hiszczynska-Sawicka, E., Kur, J., Petersen, E., Nielsen, H.V., Stankiewicz, M., Andrzejewska, I., Myjak, P. 2004. Usefulness of *Toxoplasma gondii*-specific recombinant antigens in serodiagnosis of human toxoplasmosis. *J Clin Microbiol.* 42:1779-1781.
- Pottel, H., Wiik, A., Loch, H., Gordon, T., Roberts-Thomson, P., Abraham, D., Dobbels, C., Bosschere, K., Hulstaert, F., Meheus, L. Clinical optimization and multicenter validation of antigen-specific cut-off values on the INNO-LIA ANA update for the detection of autoantibodies in connective tissue disorders. *Clin Exp Rheumatol.* 2004;22(5):579-588.
- Purcell, B., Samuelsson, S., Hahne, S.J., Ehrhard, I., Heuberger, S., Camaroni, I., Charlett, A., Stuart, J.M. Effectiveness of antibiotics in preventing meningococcal disease after a case: systematic review. *Brit Med J.* 2004;328(7452):1339.
- Rasmussen, L.S., Poulsen, M.G., Christiansen, M., Jansen, E.C. Biochemical markers of brain damage after carbon monoxide poisoning. *Acta Anaesth Scand.* 2004;48:469-473.
- Ravn, P., Munk, M.E., Andersen, A.B., Lundgren, B., Nielsen, L.N., Lillebaek, T., Soerensen, L.J., Andersen, P., Weldingh, K. Reactivation of tuberculosis during immunosuppressive treatment of a patient with a positive QuantiFERON-RD1 test. *Scan J Infect Dis.* 2004;36(6-7):499-501.
- Roldgaard, B.B., Scheutz, F., Boel, J., Aabo, S., Schultz, A.C., Cheasty, T., Nielsen, E.M., Olsen, K.E.P., Christensen, B.B. VTEC O157 subtypes associated with the most severe clinical symptoms in humans constitute a minor part of VTEC O157 isolates from Danish cattle. *Int J Med Microbiol.* 2004; 294(4):255-259.
- Roth, A., Jensen, H., Garly, M.L., Djana, Q., Martins, C.L., Sodemann, M., Rodrigues, A., Aaby, P. Low birth weight infants and Calmette-Guérin bacillus vaccination at birth: community study from Guinea-Bissau. *Pediatr Infect Dis.* 2004;23:544-550.
- Sahly, H., Aucken, H., Benedi, V.J., Forestier, C., Fussing, V., Hansen, D.S., Ofek, I., Podschun, R., Sirot, D., Tomas, J.M., Sandvang, D., Ullmann, U. Increased serum resistance in *Klebsiella pneumoniae* strains producing extended-spectrum beta-lactamases. *Antimicrob Agents Chemother.* 2004;48:3477-3482.
- Sahly, H., Aucken, H., Benedi, V.J., Forestier, C., Fussing, V., Hansen, D.S., Ofek, I., Podschun, R., Sirot, D., Tomas, J.M., Sandvang, D., Tomas, J.M., Ullmann, U. Impairment of respiratory burst in polymorphonuclear leukocytes by extended-spectrum beta-lactamase-producing strains of *Klebsiella pneumoniae*. *Eur J Clin Microbiol Infect Dis.* 2004;23:20-26.
- Scheutz, F., Cheasty, T., Woodward, D., Smith, H.R. Designation of O174 and O175 to temporary O groups OX3 and OX7, and six new *E. coli* O groups that include verocytotoxin-producing *E. coli* (VTEC): O176, O177, O178, O179, O180 and O181. *APMIS.* 2004;112(9):569-584.
- Schiellerup, P., Dyhr, T., Rolain, J.M., Christensen, M., Damsgaard, R., Ethelberg, S., Fisker, N., Andersen, N.F., Raoult, D., Krogfelt, K.A. Low seroprevalence of *Bartonella* species in Danish elite orienteers. *Scand J Infect Dis.* 2004;36(8): 604-606.
- Schiellerup, P., Krogfelt, K.A., Andersen, A.B. *Bartonella henselae* causing severe and protracted illness in an otherwise healthy person. *Scand J Infect Dis.* 2004;36(4):316-318.
- Shams, H., Klucar, P., Weis, S.E., Lalvani, A., Noonan, P.K., Safi, H., Wizel, B., Ewer, K., Nepom, G.T., Lewinsohn, D.M., Andersen, P., Barnes, P.F. Characterization of a *Mycobacterium tuberculosis* peptide that is recognized by human CD4+ and CD8+ T cells in the context of multiple HLA alleles. *J Immunol.* 2004;173:1966-1977.
- Siemer, B.L., Harrington, S.C., Nielsen, E.M., Borck, B., Nielsen, N.L., Engberg, J., On SLW. Genetic relatedness among *Campylobacter jejuni* serotyped isolates of diverse origin as determined by numerical analysis of amplified fragment polymorphism (AFIP) profiles. *J Appl Microbiol.* 2004;96(4):795-802.
- Singh, S., Soe, S., Mejia, J.P., Roussillon, C., Theisen, M., Corradin, G., Drulibe, P. Identification of a conserved region of *Plasmodium falciparum* MSP3 targeted by biologically active antibodies to improve vaccine design. *J Infect Dis.* 2004;190:1010-1018.
- Slotved, H.C., Kalfolt, M., Skovsted, I.C., Kern, M.B., Espersen, F. Simple, rapid latex agglutination test for serotyping of pneumococci (Pneumotest-Latex). *J Clin Microbiol.* 2004;42(6):2518-2522.
- Smith, E. Dawning Answers: How the HIV/AIDS Epidemic has helped to strengthen public health. In: Ronald O Valdiserri (ed). *J. Epidemiol. Community Health.* 2004;(58):355.
- Sodemann, M., Veirum, J.E., Bial, S., Nielsen, J., Balé, C., Jakobsen, M., Gustafson, P., Aaby, P. Reduced case fatality among hospitalized children during a war in Guinea-Bissau: a lesson in equity. *Acta Paediatr.* 2004;93:959-964.
- Soe, S., Theisen, M., Roussillon, C., Khin-Saw-Aye, Drulibe, P. Association between protection against clinical malaria and antibodies to merozoite surface antigens in a hyper-endemic area of Myanmar: complementarity between responses to MSP3 and GLURP. *Infect Immun.* 2004;72:247-252.
- Srikantiah, P., Lay, J.C., Hand, S., Crump, J.A., Campbell, J., Van Duyn, M.S., Bishop, R., Middendor, R., Currier, M., Mead, P.S., Mølbak, K. *Salmonella enterica* serotype Javiana infections associated with amphibian contact, Mississippi, 2001. *Epidemiol Infect.* 2004;132(2):273-281.
- Steino, A., Jorgensen, C.S., Laursen, I., Houen, G. Interaction of C1q with the receptor calreticulin requires a conformational change in C1q. *Scand J Immunol.* 2004;59:485-495.
- Steinsland, H., Valentiner-Branth, P., Aaby, P., Mølbak, K., Sommerfelt, H. Clonal relatedness of enterotoxigenic *Escherichia coli* strains isolated from a cohort of young children in Guinea-Bissau. *J Clin Microbiol.* 2004;42(7):3100-3107.
- Steinsland, H., Valentiner-Branth, P., Gjessing, H.K., Aaby, P., Sommerfelt, H., Mølbak, K. Beskyttelse mod infektioner med enterotoksigene *Escherichia coli*. (Protection against enterotoxigenic *Escherichia coli* infections). *Ugeskr Laeger.* 2004;166(45):4051-4053.
- Stellfeld, M. Dukoral. Peroral vaccine mod kolera. *Ugeskr Laeger.* 2004;166(47):4251-4253.
- Stensballe, L., Poulsen, A., Nante, E., Jensen, I.P., Kofoed, P.E., Jensen, H., Aaby, P. Mothers may transmit RSV infection more easily to sons than daughters: community study from Guinea-Bissau. *Scand J Infect Dis.* 2004;36:291-295.
- Stensballe, L., Poulsen, A., Nante, E., Jensen, I.P., Kofoed, P.E., Jensen, H., Aaby, P., Storgaard, M., Tarp, B., Ovesen, T., Vinter, B., Andersen, P.L., Obel, N., Jensen, J.S. The occurrence of *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and herpesviruses in otitis media with effusion. *Diagn Microbiol Infect Dis.* 2004;48:97-99.
- Stralin, K., Kalfolt, M.S., Konradsen, H.B., Olcen, P., Holmberg, H. Comparison of two urinary antigen tests for establishment of pneumococcal etiology of adult community-acquired pneumonia. *J Clin Micro biol.* 2004;42(8):3620-3625.
- Struve, C., Krogfelt, K.A. Pathogenic potential of environmental *Klebsiella pneumoniae* isolates. *Environ Microbiol.* 2004;6(6):584-590.
- Theisen, M., Soe, S., Brunstedt, K., Follmann, F., Bredmose, L., Israelsen, H., Madsen, S.M., Drulibe, P. A *Plasmodium falciparum* GLURP-MSP3 chimeric protein; expression in *Lactococcus lactis*, immunogenicity and induction of biologically active antibodies. *Vaccine.* 2004;22:1188-1198.
- Thierry-Carstensen, B., Stellfeld, M. Iching Nodules and hypersensitivity to aluminium after the use of adsorbed vaccines from SSI. *Vaccine.* 2004;22:1845.
- Thierry-Carstensen, B., Frederiksen, M.S., Andersen, P.H., Stellfeld, M. Spontaneously reported adverse reactions after diphtheria-tetanus revaccination at 4 to 6 years of age – a comparison of two vaccines with different amounts of diphtheria toxoid. *Vaccine.* 2004;23(5):668-671.
- Thomsen, V.Ø., Lillebaek, T., Stenz, F. Tuberculosis in Greenland – current situation and future challenges. *Int J Circumpolar Health.* 2004;63,(Suppl 2):225-229.
- Thorell, H.D., Beyer, N.H., Heegaard, N.H.H., Ohman, M., Aasa, R., Nilsson, T. Comparison of native and recombinant chlorite dismutase from *Ideonella dechloratans*. *Eur J Biochem.* 2004;271:3539-3546.
- Thyssen, J.P., Lillebaek, T., Andersen, P.A., Kok-Jensen, A., Thomsen, V.O. Tuberculosis not verified by culture in a low incidence country. *Scand J Infect Dis.* 2004;36(10):1-4.
- Torpdahl, M., Ahrens, P. Population structure of *Salmonella* investigated by amplified fragment length polymorphism. *J Appl Microbiol.* 2004;97(3):566-573.
- Valdimarsson, H., Vikingsdottir, T., Bang, P., Saevarsdottir, S., Gudjonsson, J.E., Oskarsson, O., Christiansen, M., Blou, L., Laursen, I., Koch, C. Human plasma-derived mannose-binding lectin: a phase I safety and pharmacokinetic study. *Scand J Immunol.* 2004;59(1):97-102.
- Valvatne, H., Steinsland, H., Grewal, H.M., Mølbak, K., Vuust, J., Sommerfelt, H. Identification and molecular characterization of the gene encoding coli surface antigen 20 of enterotoxigenic *Escherichia coli*. *FEMS Microbiol Lett.* 2004;239(1):131-138.



Vandamme, A.-M., Sønnerborg, A., Alt-Khaled, M., Albert, J., Asjo, B., Bacheler, L., Banhegyi, D., Boucher, B., Brun-Vézinet, F., Camacho, R., Clevenbergh, P., Clumeck, N., Dedes, N., De Luca, A., Doerr, H.W., Faudon, J.-L., Gatti, G., Gerstoft, J., Hall, W.W., Hatzakis, A., Hellmann, N., Horban, A., Lundgren, J.D., Kempf, D., Miller, M., Miller, V., Myers, T.W., Nielsen, C., Opravil, M., Palmisano, L., Perno, C.F., Phillips, A., Pillay, D., Pumarola, T., Ruiz, L., Salminen, M., Schapiro, J., Schmidt, B., Schmit, J.-C., Schuurman, R., Shulze, E., Soriano, V., Staszewski, S., Vella, S., Youle, M., Ziermann, R., Perrin, L. Updated European recommendations for the clinical use of HIV drug resistance testing. *Antiviral Therapy*. 2004;9:829-848.

Vervenne, R.A.W., Jones, S.L., van Soelingen, D., van der Laan, T., Andersen, P., Heidt, P.J., Thomas, A.W., Langermans, J.A. TB diagnosis in non-human primates: comparison of two interferon- $\gamma$  assays and the skin test for identification of *Mycobacterium tuberculosis* infection. *Vet Immunol Immunopathol*. 2004;100:61-71.

Vestergaard, H., Johnsen, C.K., Böttiger, B. An unusual enterovirus outbreak in Denmark: Clinical characteristics and molecular epidemiology. *Scand J Infect Dis*. 2004;36:840-847.

Vestergaard, M., Hviid, A., Madsen, K.M., Wohlfahrt, J., Thorsen, P., Schendel, D., Melbye, M., Olsen, J. MMR vaccination and risk of febrile seizures. *JAMA*. 2004;292:351-357.

Vestergaard, M., Madsen, K.M., Olsen, J., Hviid, A., Wohlfahrt, J., Melbye, M., Thorsen, P., Schendel, D. MMR vaccination and febrile seizures (reply). *JAMA*. 2004;292(17):2083-2084.

von Linstow, M.-L., Larsen, H.H., Eugen-Olsen, J., Koch, A., Winther, T.N., Meyer, A.-M., Westh, H., Lundgren, B., Melbye, M., Høgh, B. Human metapneumovirus and respiratory syncytial virus in hospitalized Danish children with acute respiratory tract infection. *Scan J Infect Dis*. 2004;36:578-584.

Wamberg, M., Pedersen, E.B., Nielsen, C. Synthesis of Furoannelated Analogues of Emiirine (MKC-442). *Arc Pharm Med Chem*. 2004;337:148-151.

Wamberg, M., Pedersen, E.B., El-Brollosy, N.R., Nielsen, C. Synthesis of 6-arylvinyl analogues of the HIV drugs SJ-3366 and Emivirine. *Bioorg Med Chem*. 2004;12:1141-1149.

Waters, W.R., Palmer, M.V., Bannantine, J.P., Whipple, D.L., Greenwald, R., Esfandiari, J., Andersen, P., McNair, J., Pollick, J.M., Lyashchenko, K.P. Antigen recognition by serum antibodies in white-tailed deer (*Odocoileus virginianus*) experimentally infected with *Mycobacterium bovis*. *Clin Diagn Lab Immunol*. 2004;11:849-855.

Westh, H., Zinn, C.E., Rosdahl, V.T., the SARISA study group. An international multicenter study of antimicrobial consumption and resistance in *Staphylococcus aureus* isolates from 15 hospitals in 14 countries. *Microb Drug Resist*. 2004;10:169-176.

Weyer, K., Overgaard, M.T., Laursen, L.S., Nielsen, C.G., Schmitz, A., Christiansen, M., Sottrup-Jensen, L., Giudice, L.C., Oxvig, C. Cell surface adhesion of pregnancy-associated plasma protein-A is mediated by four clusters of basic residues located in its third and fourth CCP module. *Eur J Biochem*. 2004;271:1525-1535.

Wiik, A. Guidelines and approaches to autoantibody testing. In: Conrad K, Bachmann MP, Chan EKL, Fritzler MJ, Humbel RL, Sack U, Shoenfeld Y (Eds.). *Autoantigens, autoantibodies, autoimmunity*, vol. 4, 2004, Pabst Science Publishers, Berlin. pp.441-447.

Wiik, A. Systemic small vessel vasculitis: pathophysiological aspects of anti-neutrophil cytoplasm antibodies (ANCA). A review on recent findings. *Autoimmun Rev*. 2004;3(Suppl 1):51-53.

Wiik, A., Gordon, T.P., Kavanaugh, A.F., Lahita, R.G., Reeves, W., van Venrooij, W.J., Wilson, M.R., Fritzler, M., IUIS/WHO/AF/CDC Committee for the Standardization of Autoantibodies in Rheumatic and Related Diseases. Cutting edge diagnostics in rheumatology: the role of patients, clinicians, and laboratory scientists in optimising the use of autoimmune serology. *Arthritis Care Res*. 2004;51:291-298.

Wohlfahrt, J., Rank, F., Kroman, N., Melbye, M. A comparison of reproductive risk factors for CIS lesions and invasive breast cancer. *Int J Cancer*. 2004;108:750-753.

Zhang, H., Raji, A., Theisen, M., Hansen, P.R., Marconi, R.T. BdrF2 of the Lyme disease spirochetes is co-expressed with a series of cytoplasmic proteins 1 and produced specifically during early infection. *J. Bacteriol*. 2004;187:175-184.

Zinn, C.E., Westh, H., Rosdahl, V.T., the SARISA study group. An international multicenter study of antimicrobial resistance and typing of hospital *Staphylococcus aureus* isolates from 21 laboratories in 19 countries or states. *Microb Drug Resist*. 2004;10:160-168.

Østergaard, C., Benfield, T., Lundgren, J.D., Eugen-Olsen, J. Soluble urokinase receptor is elevated in cerebrospinal fluid from patients with bacterial meningitis and is associated with fatal outcome. *Scand J Infect Dis*. 2004;36:14-19.

Østergaard, C., Brandt, C., Konradsen, H.B., Samuelsson, S. Differences in survival, brain damage, and cerebrospinal fluid cytokine kinetics due to meningitis caused by 3 different *Streptococcus pneumoniae* serotypes: evaluation in humans and in 2 experimental models. *J Infect Dis*. 2004;190(7):1212-1220.

Aaby, P., Jensen, H., Gomes, J., Fernandes, M., Lisse, I. The introduction of diphtheriatetanus-pertussis and child mortality in rural Guinea-Bissau: An observational study. *Int J Epidemiol*. 2004;33:374-380.

Aaby, P., Jensen, H., Rodrigues, A., Garly, M.L., Benn, C.S., Lisse, I. Divergent female-male mortality ratios associated with different routine vaccinations among female-male twin pairs. *Int J Epidemiol*. 2004;33:367-373.

Aaby, P., Rodrigues, A., Biai, S., Martins, C., Veirum, J.E., Benn, C.S., Jensen, H. Oral polio vaccination and low case fatality at the paediatric ward in Bissau, Guinea-Bissau. *Vaccine*. 2004;22:3014-3017.

Aaby, P. Uses of error: Being wrong in the right direction. *Lancet*. 2004;364:984.

Aaby, P. Vet vi vad vi gör när vi vaccinerar? *Lakartidningen*. 2004;101:294-297.

Aagaard, C., Brock, I., Olsen, A., Ottenhoff, T.H.M., Weldingh, K., Andersen, P. Mapping immune reactivity toward Rv2653 and Rv2654: two novel low-molecular-mass antigens found specifically in the *Mycobacterium tuberculosis* complex. *J Infect Dis*. 2004;189:812-819.

Aamand, J., Bruun, L., Christensen, C.B. Immunological analysis of pesticides: a new tool in groundwater testing. *Geological survey of Denmark and Greenland Bulletin* 2004;4:29-32.



# MANAGEMENT BOARD

Nils Strandberg Pedersen

President, CEO (from left)

Lars Birkjær

Executive Vice President, CFO

Pia Lading

Executive Vice President, Division of Vaccine

Frank Espersen

Executive Vice President,

Division of Microbiology & Diagnostics

Mads Melbye

Executive Vice President, Division of Epidemiology



# INSTITUTE COUNCIL

The Institute Council is intended to support the Management Board in the commercial development of the Institute. The Institute Council consists of five members appointed by the Ministry of the Interior and Health and two members elected by the Institute's employees.

The Institute Council is represented by:

Court Pedersen

(Professor, MD, DMSc, Odense University Hospital)

*(front row from the left)*

Gunna Christiansen (Professor, Aarhus University)

Lisbeth Holm Petersen

(Laboratory Assistant, elected by the employees)

Paul Bennet (MSc, elected by the employees)

*(back row from the left)*

Mogens Bundgaard-Nielsen (Chairman)

Erik Juhl (Director of Research, MD, DMSc,

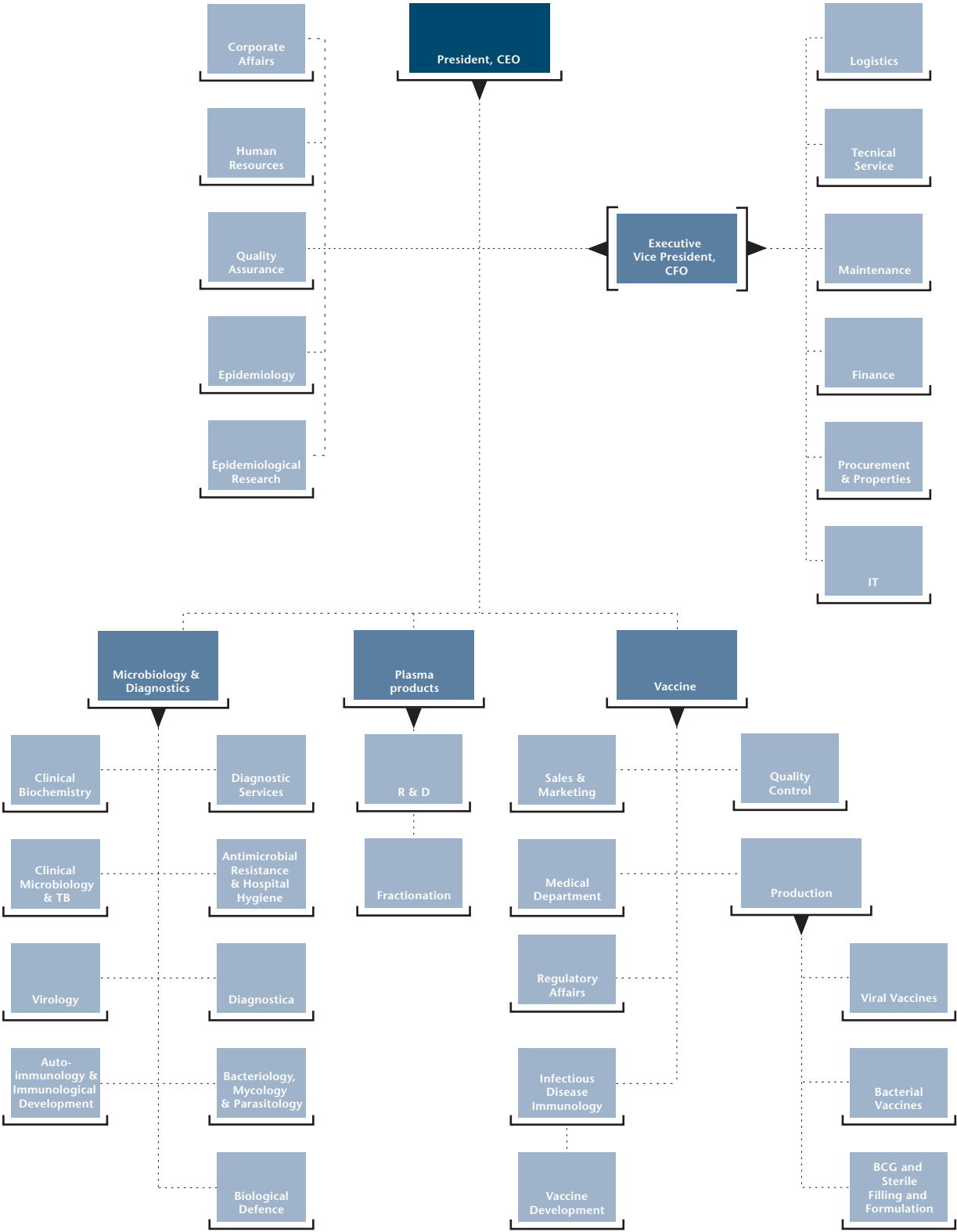
The Lundbeck Foundation)

Poul Rødbroe Rasmussen

(Executive Vice President, R&D, LEO Pharma A/S)



# ORGANIZATION CHART





# CONTACT



## HEAD OFFICE

■ Statens Serum Institut  
5, Artillerivej  
2300 Copenhagen S  
Denmark  
Tel: +45 3268 3268  
Fax: +45 3268 3868  
serum@ssi.dk  
www.ssi.dk

## SALES ORGANIZATION

■ Diagnostics  
Tel: +45 3268 3326  
Fax: +45 3268 8124  
diagnostik@ssi.dk

■ In Vitro Diagnostics  
Tel: +45 3268 8378  
Fax: +45 3268 8179  
microbiology@ssi.dk

■ Vaccine  
Tel: +45 3268 3918  
Fax: +45 3268 3167  
vaccine@ssi.dk

## INTERNATIONAL OFFICES

### VACCINE

■ SSI Polska  
ul. Grójecka 22/24 m. 53  
02-021 Warszawa  
Poland  
Tel: +48 22 668 8673  
Fax: +48 22 668 7587  
hak@ssi.pl

■ SSI Sweden  
Slagthuset  
211 20 Malmö  
Sweden  
Tel: +46 40 699 8890  
Fax: +46 40 699 8891  
ekblad@telia.com



---

ANNUAL REPORT 2004

PUBLISHED BY STATENS SERUM INSTITUT

APRIL 2005

EDITED BY OLE ØSTERGAARD JENSEN,

ANNE-METTE SKOVHUS AND HELLE RAITH

3,000 COPIES PRINTED

DESIGN AND LAYOUT BY KROGH & CO

PHOTO: PHOTO & CO, BJØRN WENNERWALD AND OTHERS

PRINTED BY PRINFO RINGSTED

ISBN 87-89148-89-4

THE FINANCIAL STATEMENTS ARE AVAILABLE IN DANISH AND ENGLISH.

IN CASE OF DOUBT, THE DANISH VERSION SHALL APPLY.

---



STATENS  
SERUM  
INSTITUT

*prevention and control  
of infectious diseases  
and congenital disorders*



STATENS SERUM INSTITUT | 5, ARTILLERIVEJ | DK-2300 COPENHAGEN S | DENMARK | TEL +45 3268 3268 | SERUM@SSI.DK | WWW.SSI.DK