



Research Strategy of Statens Serum Institut

1st edition | 2024

Table of Contents

Introduction	3
Our Vision	4
Our Mission	4
General Research Strategy	4
Strategic Research Areas	5
Vaccine Research.....	5
Early Life Health.....	6
Infectious Disease Preparedness.....	7
Antimicrobial Resistance.....	7
Scientific Approaches	9
Precision Public Health.....	9
One Health.....	9
Pathogen, Patient, Population.....	10
Organizational approaches	11
Strengthening Data Organization, Accessibility and Infrastructure.....	11
The Danish National Biobank as a Research Partner.....	11
Using Historical and Contemporary Samples.....	12
Making Optimal Use of Laboratory Facilities and Equipment.....	12
Establishing Legal Frameworks to Support Research.....	12
Providing Research Support.....	13
Attracting and Retaining Research Talent.....	13
Cultivating Networks, Collaboration and Academic Exchange.....	13
Strengthening Intersectoral and Multidisciplinary Collaborations.....	13



Introduction

Statens Serum Institut (SSI) is a research institute under the auspices of the Danish Ministry of the Interior and Health dedicated to preventing and combatting infectious diseases and congenital disorders through research, surveillance, diagnostics, and guidance. To achieve our mission, SSI emphasizes qualities such as being prepared, professional, useful, innovative and collaborative. Research at SSI is integrated in our surveillance and diagnostic activities, ensuring scientifically rooted services. This research strategy document outlines the objectives, ambitions, and goals for SSI's research strongholds, which include (molecular) epidemiology, disease understanding and surveillance, antimicrobial resistance (AMR), One Health, and data science. In addition, it defines our overarching approach to research, including scientific and organizational approaches and ambitions.

Today's societies need to be prepared to confront the complexities presented by infectious disease threats, including new pandemics, to safeguard public health and ensure the resilience of our healthcare systems. As a One Health institute, the research forms the foundation for the methods used, and the advice provided, performing diagnostics, surveillance and counselling within the health care system, for governmental- and international authorities and stakeholders as well as the public, within both human and veterinary areas. This holistic approach is a distinctive advantage of SSI, enabling us to address the full entirety of infectious disease preparedness.

This new research strategy emphasizes that research is an integral part of SSI's responsibilities and thus, a substantial proportion of employees are involved in research. That also includes employees providing critical indirect support such as e.g. laboratory, data and human resources. We acknowledge that a robust infrastructure combined with a strategic research portfolio is essential for the successful completion of the core mission of SSI.

SSI's commitment to - and involvement in - research distinguishes SSI from other Danish governmental health institutions. It is our strategic objective to maintain and foster a broad spectrum of research activities. This will be done by providing even better research support and guidance in the future through a continuous focus on research by the SSI management. Simultaneously, this strategy points to research areas of strategic significance that will serve as focal points for achieving scientific excellence. This strategy will be updated yearly and complemented by an implementation plan to ensure its realization and contribution to the achievement of our mission and vision.

Henrik Ullum



Our Vision

It is our vision to be an internationally leading research and preparedness organization with the overall aim of strengthening the health of humans and animals.

As such, One Health is an integrated part of our identity, influencing our scientific research, infectious disease control, and vaccine development. The SSI vision is focused on achieving excellence through innovative research and strategic planning, with the goal of advancing health outcomes for populations across the globe. Overall, SSI's vision underscores the importance of research and preparedness in promoting health and wellbeing and emphasizes the need for collaboration and innovation in the field of public and veterinary health.

Our Mission

It is our mission to prevent and fight infectious and congenital diseases through research, surveillance, diagnostic developments, and scientific guidance.

SSI was established in 1902 by the Danish State as the principal Danish authority for microbiological and epidemiological medical research. Since then, SSI has developed into a unique and highly respected scientific institution that has been at the forefront of medical research, diagnostics and public health surveillance for more than a century.

General Research Strategy

We conduct high-quality research that contributes to preventing and combatting diseases. To pursue high standards, research must integrate with our diagnostics and surveillance efforts. Consequently, each and all scientific departments and their employees must dedicate time and resources for research to ensure that the advice, diagnostics and surveillance we provide to national authorities and partners are always scientifically sound and in accordance with the latest scientific advancements. This also means that SSI must prioritize research-supporting infrastructures, such as efficient and secure data access, state-of-the-art laboratory facilities, legal and fund-raising support. All academic departments must work to ensure a positive research culture characterized by, for example, publications with high impact on science and society, a significant degree of external funding, a daily work-life characterized by stimulating scientific discussions and productive national and international collaborations. In conclusion, SSI aims to foster a working culture, where research is present everywhere and where everyone is given a chance to contribute.

To contribute significantly additional focus is needed on key strategic research areas, defined by scientific and societal impact matched with SSI competences and strategic interests. The strategy's ambition is to attract research leaders and scientific staff and strengthen the strategic research areas further.

To ensure the inclusivity of our research efforts, SSI recognize the importance of research that contributes to addressing health disparities, ensuring that our work benefits all segments of society equitably.

The research strategy harmonizes with other strategic documents encompassing initiatives to enhance the working environment, an integrated data strategy and to expand collaborations both nationally and internationally.

Strategic Research Areas

SSI has a long track-record of innovative and effective programs, which promote public health nationally and globally. This includes efforts to curb the spread of infectious diseases, most recently demonstrated during the COVID-19 pandemic, surveying and combating antimicrobial resistance (AMR), screening for and preventing congenital diseases, and developing new vaccines.

The purpose of the strategic research areas is to strengthen existing strongholds further and enhance research capabilities, develop innovative approaches, and strengthen our contribution to global health. Intersectoral collaboration with national healthcare providers, veterinary professionals, environmental agencies, academic institutions, and international organizations should amplify the impact of SSI's research efforts and promote the translation of scientific evidence into practice. Through these strategic initiatives, we strive to fulfill our mission of preventing and combating diseases for the benefit of both the individual and the society, nationally and globally.

Vaccine Research

Immunization is one of the big public health success stories in recent history and its development is key to further improve global health outcomes. Discovering and developing vaccines lie at the historical heart of SSI. Serum to curb diphtheria and the development of the tuberculosis vaccine BCG in the 1920s and 1930s are all part of our track-record in this area. Today, SSI does research into the interplay between host and microorganism to obtain information that can help develop new vaccines against a number of serious infectious diseases, including tuberculosis, malaria, and chlamydia. Our vaccine research is rooted in the detailed understanding of protective immunological mechanisms combined with tailored molecular adjuvant systems and platform technologies designed to fit adaptive immune responses to the targeted pathogen.

SSI has the capability to facilitate development of vaccine candidates, adjuvants, and biologicals suitable for clinical phase 1 and 2 evaluation according to Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), and Good Clinical Practice (GCP) requirements. Our competences include cloning into bacterial systems, process and analytical development for subunit proteins, formulation with adjuvants, and coordination of toxicology studies and clinical trials. SSI has the infrastructure to conduct animal experiments with Bio Safety Level (BSL) class 1-3 and Gene Modified Organisms (GMO) I-II organisms, as well as perform Quality Control (QC), Good Manufacturing Practice (GMP) services for vaccines. The strategic mission for vaccine research is to conduct translational vaccine research and for 2024-2030 we will:

- Develop new vaccines for mucosal pathogens for which AMR is important
- Explore novel strategies to induce and evaluate mucosal immunity, using novel delivery systems and advanced animal models and early clinical trials
- Enable an R&D environment that collaborates with key stakeholders at universities, funders, policymakers and communities

Early Life Health

SSI examines all newborns in Denmark for 25 serious treatable disorders using neonatal dried blood spots. The measurement of predictive disease markers within the first week of life represents the first step towards diagnosis and preventive therapy for up to 1 in 1000 children who would otherwise have suffered severe health consequences. The newborn screening panel is subject to continuous research and new genetic and metabolic markers are regularly added to enable rapid diagnosis of a growing number of diseases.

The Danish Neonatal Screening Biobank contains all neonatal dried blood spots collected since 1982, giving unique opportunities for biomedical research, since all samples can be linked to the wealth of health-related, demographic, and social data contained in national Danish registries. An active research environment at SSI has pushed the boundaries for the types of analyses (DNA sequencing, array genotyping, methylation profiling, mRNA analysis, metabolomics, and immunoassays measuring proteins, peptides, and antibodies) that can reliably be performed on very small amounts dried blood spot sample material. These advances provide unprecedented possibilities for research in early life health and development of novel approaches to personalized diagnostics, prediction, and prevention of disease.

Early life health determinants may exert their effects before delivery, and pregnancy is a crucial period with implications for the future health of mother and child. Thus, SSI also has a long-standing focus on pregnancy research, e.g., being home to the Danish National Birth Cohort, a collection of almost 100,000 mother-child pairs with biological samples and 20+ years of extensive follow-up data. Other complementary resources include smaller pregnancy cohorts with deep molecular data, e.g. in blood and placental samples, from healthy pregnancies as well as pregnancies with complications such as preeclampsia and preterm birth.

Based on these foundations, our ambition is to:

- Prioritize research based on samples in the Danish Neonatal Screening Biobank towards projects that focus on conditions manifesting in early life and strengthen outreach efforts to inform the general population about the importance of research in early-life disease prevention and the benefits of neonatal screening.
- Strengthen research of reproductive health and pregnancy, including pregnancy complications and their consequences for later health of mother and child.
- Build a critical mass of data science talent and expertise to analyze a variety of omics data and to perform integrative analyses of multiple data modalities.
- Leverage the close proximity of research facilities and the neonatal screening program to continuously develop the screening panel and make research discoveries with a very immediate and direct impact on early life disease prevention and diagnostics.



Infectious Disease Preparedness

Preparedness against infectious diseases is challenged by the dynamic nature of pathogens (e.g., changes in the epidemiology and/or virulence of known pathogens and emergence of new pathogens) and by changes in the host populations (e.g., an aging human population). Moreover, domestic animals and wildlife can act as reservoirs for many infectious diseases. In the most extreme cases, zoonotic pathogens can become fully adapted to a new host, as exemplified by the SARS-CoV-2 virus which gave rise to the COVID-19 pandemic

SSI plays a central role in the Danish preparedness against pathogenic bacteria, viruses, parasites, and fungi in humans and animals under the auspices of the Danish Ministry of Health and the Ministry of Environment and Food of Denmark, respectively. This means that we are committed to strengthen both human and animal health in a One Health perspective. SSI has developed core capacities in several infectious disease areas, including prevention (e.g., infection hygiene, prevention and control strategies, and vaccines), pathogen diagnostics and strain characterisation (e.g., isolation, identification, and typing of pathogens, antigenicity, antimicrobial susceptibility testing, and detection of drug resistance genes), treatment and care (e.g., antimicrobial stewardship, use, and consumption), and epidemiology (e.g., surveillance, disease burden, and detection of drivers and burden of drug resistance).

We recognise that maintenance of an efficient infectious disease preparedness programme relies on evidence generated through basic and applied research activities involving national and international stakeholders from different disciplines and sectors in a One Health perspective. At SSI, we seek to strengthen national and global preparedness against infectious diseases by performing high-impact research in all the relevant infectious disease areas, including:

- Developing cutting-edge laboratory, whole-genome sequencing, bioinformatics, and epidemiological tools as well as big-data techniques (e.g., mathematical modelling, machine learning, and artificial intelligence) to facilitate surveillance of known and early detection of new pathogens, strain characterisation, real-time outbreak investigations (including source attribution), and early detection of host jumps.
- Using our large data repositories and strain collections in combination with these tools/techniques to trace the spread of pathogens within and between human and animal populations (e.g., through close or direct contact, food/feed, the environment, and vectors) and identify drivers and burden of disease.
- Developing alternative pathogen surveillance methods such as high-throughput sequencing of environmental DNA (e.g., from wastewater).
- Participating in the development of early warning and response systems against outbreaks and epidemics.

Antimicrobial Resistance

Antimicrobial resistance (AMR) in pathogenic bacteria and other microorganisms now poses one of the biggest threats to human and animal health, food security, sustainable economic growth and human development. At the same time, the pipeline for new antimicrobial drugs is running dry. To combat this double-barrelled threat, there is an urgent need for development of new drugs and a better understanding of the complex and interlinking drivers of AMR.

AMR can spread through transmission of resistant microorganisms or via horizontal transfer of resistance mechanisms between different microorganisms. As mentioned in the previous section (Infectious Disease Preparedness), SSI contains core capacities in several infectious disease areas (e.g., prevention, diagnostic methods, treatment and care, and epidemiology), all of which are also relevant for AMR. As part of SSI's central role in the Danish preparedness against infectious disease, we also monitor clinical use of antimicrobials and perform surveillance of AMR and resistance mechanisms in pathogens from humans and animals. In addition, SSI has state-of-the-art research laboratories and animal facilities for efficacy screening of new drugs in the discovery phase, proof of concept, as well as for pharmacokinetic and pharmacodynamic studies.

SSI is committed to bridging existing knowledge gaps in our understanding of AMR as a One Health problem through close collaborations with national and international stakeholders across the different AMR areas and thereby paving the way towards development of effective evidence-informed solutions. In addition to the research topics mentioned in the previous section (Infectious Disease Preparedness), SSI strives to perform high-impact research within several AMR areas, including:

- Developing rapid phenotypic and genotypic antimicrobial susceptibility testing methods to improve clinical decision-making and facilitate surveillance of known and early detection of new resistant pathogens and resistance mechanisms.
- Identifying drivers, sources, spread, and burden of AMR within and between human and animal populations using a multidisciplinary and cross-sectoral approach.
- Developing alternative AMR surveillance methods, including high-throughput sequencing of environmental DNA (e.g., from wastewater).
- Serving as a hub for developing new therapies against resistant pathogens in our state-of-the-art laboratories and animal facilities.



Scientific Approaches

To strengthen the institute's strategic research areas, SSI will use a variety of complementary scientific approaches outlined in the following.

Precision Public Health

Interventions are at the core of public health, and as a research-based institute SSI strives to provide the scientific guidance needed for the optimal planning, implementation and evaluation of health interventions. To fully realize this, we will need to move towards more targeted approaches that take the unique characteristics of individuals and subgroups better into account.

We will pave the way for this transformation by increasingly embracing a precision public health approach in our research at SSI. The goal of precision public health is to provide targeted interventions, in the form of treatment or prevention, with the best possible benefit-risk profile for individuals and subgroups of the population. This will facilitate improved health for all citizens together with reduced health disparities. At SSI, we understand the power of prevention and a key focus will be precision prevention.

Precision public health is only made possible by a solid foundation of data. Our research will take advantage of the unique and rich data sources available to Danish health researchers. From genomics, metabolomics, exposomics and epigenetics to social and environmental determinants of health, we are committed to research that incorporates the full extent of unique characteristics of individuals and subgroups. This is an ambitious approach and to be successful it must be accompanied by an increased focus on data science analytics, digital health solutions, and IT-infrastructures that are optimally suited to create and extract insights from complex and large-scale data. Together with the adoption of these methods comes the promise of predictive capabilities. We will increasingly complement our classical inferential research with predictive modeling of health outcomes for individuals and subgroups. Our hope is that this will translate our research more readily into policy.

We realize that precision public health is still in its infancy and that there are many challenges still to be overcome. The sensitive individual-level data needed for precision public health must be managed with great care, the public must be engaged on their concerns about misuse, and the policy implications of more targeted approaches should be considered in the research process.

One Health

One Health is an integrated, unifying approach that recognises the connectivity and interdependence of human, animal, and environmental health. The One Health approach relies on multisectoral and cross-disciplinary collaboration and can be used to address health challenges, including spread of known zoonotic pathogens and AMR mechanisms, emergence of new infectious diseases and AMR mechanisms, and environmental determinants of health.

The need for a holistic perspective on infectious diseases preparedness has been recognised both in Denmark and internationally. SSI – as a public health institute that also has veterinary preparedness functions – has developed and implemented surveillance systems to monitor the occurrence of specific pathogens and AMR in humans, production animals, food production systems, and wildlife. However, these frameworks do not always sufficiently consider the role of e.g. ecological drivers of disease emergence and further development is needed.

Climate change can significantly impact the dynamics of infectious diseases, alter the habitats of vectors and reservoirs, and influence the spread of pathogens. Recognizing and understanding these connections will enhance the effectiveness of our One Health initiatives, contributing to a more robust approach to addressing emerging health challenges.

To strengthen our One Health preparedness and response capacity against emerging infectious diseases and AMR mechanisms in an evidence-based manner, it is important to increasingly address the full range of One Health-related hazards in future research projects in collaboration with other national and international partners representing different sectors and disciplines. This way of thinking might also be relevant for other complex problems including non-infectious diseases such as congenital disorders caused by socioeconomic, infectious, nutritional, or environmental factors.



Pathogen, Patient, Population

SSI is uniquely positioned in the research space by being both a steward and a producer of rich data on pathogens, patients and populations. It is our ambition to continue to harness this advantage and conduct research that combines data from the microscopic level, the individual level and the macroscopic level for a better understanding of the dynamics and impacts of infectious diseases.

This is multidisciplinary and collaborative research that combines expertise in molecular biology, microbiology, immunology, clinical infectious disease medicine, and epidemiology. There are both current examples where integrative approaches have been effectively applied and future challenges that will benefit from integrative approaches. During the COVID-19 pandemic, sequencing became essential for the understanding of the clinical severity of disease at the patient level and the dynamics of spread at the population level. Future challenges that will benefit greatly from an integrative approach are AMR and One Health.

SSI also has a strong history of studying the associations between pathogens and non-communicable diseases. Many such associations are already well-established such as *Helicobacter pylori* and gastric cancer, human papillomavirus and cervical cancer, and Epstein-Barr virus and Hodgkin's lymphoma. There is also a growing body of evidence supporting a key role of the microbiome in both infectious and non-infectious diseases.

We believe that a unifying approach will provide more comprehensive insights and consequently more comprehensive solutions to societal health challenges. A unifying approach brings together diverse perspectives which fosters innovation, improves communication and understanding between research fields, and will have a much broader impact on a wider audience and in multiple fields.

Organizational approaches

In this chapter we delve into the organizational approaches that empower SSI's Research Strategy and enable us to respond effectively to evolving challenges and deliver impactful outcomes.

Strengthening Data Organization, Accessibility and Infrastructure

SSI collects and produces a remarkable amount of invaluable data for population-based public health research projects in a worldwide unique setup. To fully unlock the potential of this data wealth, SSI has the ambition that all its data live up to FAIR principles, which means that SSI's data must be available to a broad scientific community, must be searchable (Findable), accessible (Accessible), system-independent (Interoperable), and reusable (Reusable), both within SSI, nationally, and internationally. To this end a common data platform (data catalogue) across SSI needs to be established. Furthermore, SSI's researchers need to have easy access to a shared high-performance computing (HPC) facility, where diverse omics, wet and dry data can be stored and mined. Establishing such a common infrastructure and parallel access and data flows is complex and involves diverse collaborations with stakeholders within and outside the institute. SSI is therefore elaborating a dedicated data strategy, with the long-term goal of being able to collect, store, share and mine SSI's data on a common infrastructure including a shared data governance (a legal framework) to secure a safe, compliant and efficient access to health data for research purposes.

As such, SSI has an ambition to strengthen the data foundation and access to new registries to benefit researchers, policymakers, and public health practitioners by providing a more robust and comprehensive basis for evidence-based decision-making.

In line with these goals SSI plays an active role in the national initiative 'Vision for bedre brug af sundhedsdata', which aims at establishing a national framework and infrastructure for more efficient data access across Denmark. In addition, SSI is also member of the Danish ELIXIR node, a European life science infrastructure, enabling researchers to access and analyze life science data, to improve the value and impact of life science research on public health, the environment and the economy.

The Danish National Biobank as a Research Partner

Inaugurated in 2012, the Danish National Biobank (DNB) contains approximately 14 million biological samples in state-of-the-art storage facilities with adjacent high-throughput laboratories. To minimize sample and data errors, DNB has implemented fully automated laboratory procedures and is working towards accreditation with the ISO/DIS 20387 standard. SSI has also developed a national cohort explorer system, the Danish Biobank Register (DBR), providing researchers with a rapid overview of more than 30 million biological samples (from around 6.1 million Danish donors) stored at DNB and in other Danish biobanks linked to various national registries with diverse health related and demographic information. DBR provides much-needed support for register-based research and shortens from months to minutes the previously very laborious process of identifying pre-existing biological material to support new research projects.

As DNB creates the foundation of core activities at SSI, resources should be allocated to ensure DNB a position as the preferred collaboration partner for national as well as international projects, providing efficient and timely support and guidance to the researchers that would like to collect, store, and use samples. Since July 2023, The Danish National Biobank at SSI is responsible for national coordination of the Danish biobank network (as a Head of Node) within the European consortium – BBMRI-ERIC, a European research infrastructure for biobanking.



Using Historical and Contemporary Samples

As a longstanding national central laboratory, SSI has an extensive collection of both historical and contemporary samples from humans and animals, and clinical isolates of a broad range of pathogens. Metadata connected to the samples are collected and can be explored further in the Danish national registries, where data on all individuals are stored. This provides a unique collection of samples and pathogens with data that can be used in various research projects by partners to explore details at the pathogen, patient, and population level.

Making Optimal Use of Laboratory Facilities and Equipment

SSI has laboratory and animal experimental facilities to manage both human and veterinary pathogens as well as genetically modified organisms at different biosafety and biosecurity levels (BSL1 to 3, GMO1 to 2, OIE1 to 3*). The laboratories provide the infrastructure to support and collaborate with external partners on research projects where high containment is needed, allowing the opportunity to perform investigations of live-pathogen mechanisms on classified and emerging pathogens.

Establishing Legal Frameworks to Support Research

To conduct research within public health, SSI processes significant amounts of both confidential and sensitive personal data. It is a key task and prerequisite for SSI to maintain citizen trust in its research activities, as the consequences of loss of confidentiality, integrity, or availability of sensitive data can be extremely serious for both the organization and the data subjects. To ensure data security and privacy according to the highest standards, appropriate legal support and guidance is necessary. Institutional legal and ethical frameworks should be aligned with national policies, and legal assistance to researchers should always be flexible and easily accessible, and the processing time should always be as short as possible.

Providing Research Support

Effective research support contributes to the overall function and reputation of SSI. A well-supported research environment attracts talented researchers, collaborators, and funding partners, enhancing the institution's credibility and impact. Well-managed research support is essential for partnering with external funders, optimizing research outcomes, managing resources, complying with regulations, and fostering a productive and collaborative research environment.

Funding from public and private partners is a lifeline for research at SSI, as most ongoing research and collaborative projects are funded by external sources. As such, SSI is highly dependent on effective research support, to assist researchers in their pursuit of external funding and collaboration.

Attracting and Retaining Research Talent

To remain at the frontline of both human and veterinary medical research, surveillance, and preparedness and to strengthen the health of humans and animals, it is crucial that SSI attracts and employs nationally as well internationally leading researchers, provides unique career opportunities and a dynamic and stimulating research environment. To this end, SSI aims at establishing both Danish and English as working languages for external as well as internal communication. Furthermore, to strengthen recruitment and work environment clear career paths for scientists along with institutional support for hosting international symposia, conferences, and academic specialist courses will be established.

Cultivating Networks, Collaboration and Academic Exchange

Breakthroughs in human and veterinary medical research are typically characterized by interdisciplinary and international collaboration involving research groups with complementary fields of expertise. SSI aspires to be centrally involved in more breakthrough studies within the institution's strategic research areas by cultivating additional strong and extensive networks of collaboration with other leading research institutions. Important mechanisms to facilitate this development including establishing further possibilities for affiliation to relevant university departments at academic levels from postdoc to professor, attracting external researchers for shorter or longer research stays at SSI, development of programs for joint postdocs between Danish or foreign universities and SSI. As part of the SSI culture, we actively reach out to strong scientific partners to increase the research output.

Strengthening Intersectoral and Multidisciplinary Collaborations

Public health challenges are often complex and require a multi-faceted approach, where SSI is dependent on external partners. Intersectoral collaboration allows SSI to collaborate with partners from different sectors, bringing together diverse expertise, resources, and perspectives to address these challenges comprehensively. Furthermore, collaborating with experts from other sectors, such as academia, government agencies, and private industry, enables SSI to gain access to specialized knowledge and insights that can enhance its guidance and research further.

SSI aims to actively increase intersectoral collaboration with national and international partners, including government agencies, academic institutions, international institutions, and private sector partners in health. With this we increase institutional knowledge capacity and fulfill our mission to prevent and fight infectious and congenital diseases through research, monitoring, diagnostics and guidance and become a catalyst for transformative research, policy influence, and cross-sectoral cooperation.