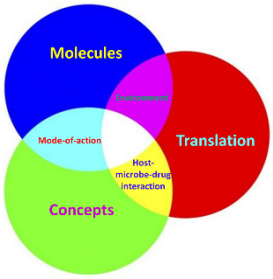
Centre for New Antibacterial Strategies (*CANS*) – A new strategic research initiative at UiT



Summary

The World Health Organization (WHO) considers antimicrobial resistance (AMR) to be one of the three most important global challenges to health. A working group appointed by the Faculty of Biosciences, Fisheries and Economics (BFE), Faculty of Science and Technology (NT) and Faculty of Health Sciences (Helsefak) is hereby presenting a proposal for a major strategic research initiative in AMR at UiT – the Arctic University of Norway (UiT). The initiative builds on existing strong research communities, which will be collectively enhanced and made more visible through a binding inter-faculty research effort. The aim is to develop an internationally recognized transdisciplinary centre for AMR research and education that will create added value for animal and human health through regional, national and international collaborations. CANS will target objectives outlined in the WHO global action plan, the European JPI-AMR initiative and the Norwegian National Strategy against Antibiotic Resistance 2015-2020. The complexity of the challenges that AMR presents requires an interdisciplinary approach. The proposal includes the recruitment of young researchers in tenure-track positions, new permanent positions and PhD/postdoctoral positions. These will be phased in to CANS' priority research areas over a period of time, in pace with CANS' success and access to external funding for research. The new tenure track-/permanent positions are suggested to support new complementary areas of knowledge [the human - (Helsefak), marine (BFE) microbiome and systems biology (NT)], and to strengthen ongoing research activities [synthetic capacity (NT), animal infection models (Helsefak), and bioprospecting (BFE)] relevant to the development of CANS. The current AMR-related research activities at UiT involves above 130 positions in 14 research groups, at 6 departments, with ongoing external research project funding of 230 MNOK. It is proposed that CANS start-up will take place in a number of phases, with the establishment of an organization structure in 2018 and the appointment of new positions from 2019.

Background

Antimicrobial resistance is a global threat to health – the role of research

Antibiotics have saved millions of lives and have underpinned the development of modern hospital medicine, including foreign body surgery, transplantation, neonatal medicine, and life-saving cancer treatment. However, antibiotics have become a victim of their own success. The extensive use and misuse of antibiotics on animals, humans and in the environment has led to the selection and spread of bacteria that have developed a resistance to antibiotics.

There is now evidence of resistance to all available antibiotics in pathogenic bacteria in humans. In addition, no new antibiotic classes have been developed for clinical use in the last 20 years. The combination of resistance development and the lack of new effective antibiotics means that WHO and the UN consider antibiotic resistance to be one of the three most important global health challenges. The Norwegian Minister of Health and Care Services describes antibiotic resistance as the health service's climate challenge. **WHO's global action plan on antimicrobial resistance** stipulates five strategic objectives (http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/) is:

1. Improve **awareness and understanding** of antimicrobial resistance through effective communication, education and training;
2. Strengthen the **knowledge and evidence base** through surveillance and research;
3. R**educe the incidence of infection** through effective sanitation, hygiene and infection prevention measures;
4. O**ptimize the use of antimicrobial medicines** in human and animal health; and
5. Develop the economic case for investment in **new medicines, diagnostic tools, vaccines** and other interventions.

Major research efforts are now underway with a view to strengthening the knowledge and evidence base vis-à-vis AMR. Norway is part of **the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)**, formed in 2011 by 15 European Countries with the support of the European Commission. JPIAMR is now a global platform (26 countries) for collaborative AMR-research, and has developed a strategic research agenda (JPIAMR; http://www.jpiamr.eu/) that focuses on six priority topics:

1. **THERAPEUTICS:** The development of new antibiotics and therapeutic alternatives to antibiotics – from basic research to market
2. **DIAGNOSTICS:** The development of novel diagnostics to improve treatment and prevent infections
3. **SURVEILLANCE:** The establishment of an international, standardized surveillance programme for AMR and antibiotic use
4. **TRANSMISSION:** Mechanisms for the selection and transmission of AMR at micro and macro levels
5. **ENVIRONMENT:** The role of the environment in the selection and development of AMR
6. **INTERVENTIONS:** The development and testing of interventions that focus on preventing the development/transmission of AMR and infections caused by AMR

The **Norwegian National Strategy Against Antibiotic Resistance 2015-2020** lays out the Government's goals for work over the coming years and the steps needed to achieve these (https://www.regjeringen.no/en/dokumenter/national-strategy-against-antibiotic-resistance/id2424598/). The strategy is anchored across sectors and describes overarching and sector-specific goals that are mutually reinforcing. The four overarching goals are to:

1. Reduce the total **use of antibiotics.**
2. More appropriate use of antibiotics.
3. **Improve knowledge** of what drives the development and spread of antibiotic resistance.
4. Be a **driver in international and normative work** to improve access, responsible use, and development of new antibiotics, vaccines and better diagnostic tools.

The sector-specific goals have been developed to be measurable and verifiable including goals for health (n=5), food producing animals and pets (n=6), fish (n=1) as well as climate and

environment (n=2). The implementation of the overall national plan has been further developed within the Health sector though a **governmental action plan against antimicrobial resistance in the health services (**https://www.regjeringen.no/contentassets/915655269bc04a47928fce917e4b25f5/handlingsplan-antibiotikaresistens.pdf) with an overarching aim to reduce the general use of antibiotics in humans by 30% from 2012 standards by 2020. The action plan describes specific objectives to strengthen the national organization of the AMR-work as well as specific measures towards the general population, the prescribers of antibiotics, hospital services, primary health care, and dental health services.

Status of AMR research, education and innovation at UiT

In collaboration with the University Hospital of North Norway (UNN), UiT has built up strong complementary research groups within antimicrobial resistance (AMR; Figure 1). At UiT, these expert communities are located at BFE, NT and Helsefak. A survey of AMR-relevant research communities/groups has been carried out at UiT. A supplementary description of the research groups involved at UiT and UNN, their priority research areas and expertise (Appendix 1), as well as their current external research funding (Appendix 2) are enclosed.

The main activity in the AMR community at **BFE** is marine bioprospecting, which entails the charting, identification and characterization of new antimicrobial compounds. This AMR community also served as the coordinator of one of the Centres for Research-based Innovation (SFI), *MabCent*. It has also invested in an associated modern research infrastructure.

At **NT**, the main focus of the Department of Chemistry (IK) is on the development (synthesis) of new antibiotics and their mechanisms of action, as well as molecules that inhibit clinically important resistance mechanisms in bacteria (carbapenemases). NT heads *BIOSnet*, a national network for the synthesis of bioactive natural products, including antibiotics, funded by BIOTEK2021, a major research programme in the Research Council of Norway (RCN). Like BFE, NT has also invested in a modern infrastructure to perform such activities, including a leading national expert community in structural biology.

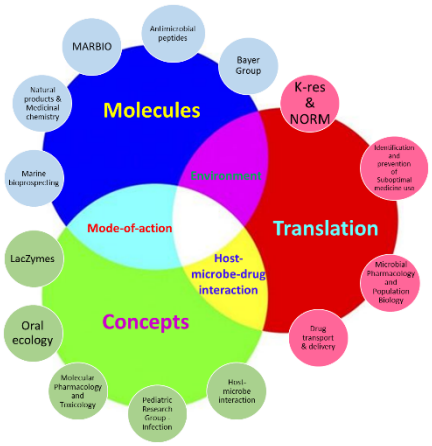


Figure 1. Research communities with expertise that form the basis for CANS

Primary activities within AMR at **Helsefak** are aimed at establishing a fundamental understanding of resistance biology, the molecular epidemiology of AMR (genes, mobile genetic elements and bacterial clones), and interactions between bacteria, antibiotics and humans. A close collaboration has also been initiated with UNN in methods for the detection and surveillance of resistance. The establishment of the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM) and the Norwegian National Advisory Unit on Detection of Antimicrobial Resistance (K-res) at UNN are good examples of this. The

Department of Medical Biology (IMB) at Helsefak is also a partner institution (project co-leader) for the new National Graduate School in Infection Biology and Antimicrobials (IBA), and hosts the associated PhD programme in AMR. In 2017, a research group at Helsefak's Department of Pharmacy (IFA) was confirmed as the coordinator of a research project funded by JPIAMR (*Collateral damage*). Another research group at UNN will be a partner in the JPIAMR project *PILGRIM* from 2018. In addition, an academic environment at IFA has overlapping activity with the NT faculty.

Several of the research activities are already being carried out in **a close interdisciplinary collaboration between research groups across the three faculties**. This can best be illustrated through three of the new inter-faculty thematic initiatives at UIT: *AntiBioSpec* (coordinated by NT), *AntifoMar* (headed by BFE), and *LEADScAMR* (coordinated by Helsefak), all three initiatives involve BFE, NT and Helsefak. *AntiBioSpec* had recently a major research application approved, *DigiBiotics*, as part of the RCN's Digital Life programme.

The academic environments at UiT also have a long tradition of **innovation and commercialization** within the antimicrobial field. The establishment of *Lytix Biopharma* (http://www.lytixbiopharma.com) and its subsidiary *Amicoat* (http://amicoat.com) are good examples of successful translation from basic research to commercial products. *DigiBiotics* is a research-based innovation project with two partners from industry. Furthermore, *LEADscAMR* has recently been awarded an *Exploratory pre-seed grant* by the Novo Nordisk Foundation. Similarly, the chemistry research community has also received support from Novo Nordisk for the development of beta-lactamase inhibitors in a collaboration with the University of Oslo (UiO). UiT has a well-established system for facilitating innovation and commercialization through Norinnova Technology Transfer.

Initiative

There is a general perception that UiT has strong, complementary academic environments in the field of AMR (Appendices 1 and 2). However, a binding inter-faculty approach would strengthen our work and make us more visible. The Rector has therefore called on the academic community to submit a proposal for an enhanced interdisciplinary strategic focus on AMR at UiT, to be rooted in *Health, Welfare and Quality of Life* – one of UiT's five strategic focus areas in "*Drivkraft I Nord: Strategy for UiT towards 2020"*. In collaboration with the three relevant faculties and the Vice Rector for Research and Development, a working group was set up in 2017 whose remit was to facilitate a proposal for a strategic AMR initiative. The main objective is to enhance quality and external competitiveness within AMR research at UiT.

Vision, main objective and secondary objectives

Vision and main objective

The *vision* is to develop an internationally recognized transdisciplinary centre for AMR research and education, which will create and disseminate new innovative knowledge based on basic, translational and clinical research. CANS will target objectives outlined in the WHO global action plan, the JPI-AMR initiative and the Norwegian National Strategy against

Antibiotic Resistance 2015-2020. The complexity of the challenges presented by AMR requires an interdisciplinary approach.

Within 3–5 years, CANS will have established binding international academic networks involving similar centres, and these academic environments will have been approved for new interdisciplinary research projects by the RCN, the EU and JPIAMR. Within 5 years, CANS's affiliated researcher(s) will have achieved the prestigious ERC-grant(s). Within 10 years the centre itself will have acquired the status Centre for Research-based Innovation and/or Norwegian Centre of Excellence (SFI/SFF) and have sustainable financial resources through externally funded research projects, philanthropic contributions and partnerships with affiliated institutions and industry.

The *main objective* is to develop new, innovative and sustainable antibacterial strategies anchored within objectives in the WHO global action plan and list of priority pathogens, the JPI-AMR strategy, and overarching goals in the Norwegian National Strategy against Antibiotic Resistance by:

- **Integrating** innovative basic, translational and clinical research, and **educate** the next generation of antibiotic-infection biology researchers in an interdisciplinary perspective.
- Providing a balanced research focus by **enhancing existing** strong academic environments and **appointing new researchers with relevant complementary expertise**.

Secondary objectives

MOLECULES – with antibacterial activity

MOLECULE-activities focus on objectives 2 and 4 in the WHO global action plan, priority topic 1 in the JPI-AMR strategy, and the 4th overarching goals in the Norwegian National Strategy against Antibiotic Resistance:

- Further develop and improve the efficacy of the pipeline for design, synthesis and modification of molecules/scaffolds based on knowledge of marine organisms.
- Use structural and systems biology methods as a tool in the search for or refinement of new antibacterial molecules.
- Create, develop and evaluate experimental and digital methods for determining the molecular structure of new potential antibiotics.
- Determine the antibacterial spectrum and mechanisms of action and predict resistance development of promising active molecules.
- Refine the structure of new molecules with a view to counteracting resistance development.
- Optimize pharmacokinetic properties (drug-likeness), and develop effective advanced formulations for drug delivery and *in vivo* animal studies.

CONCEPTS – for new antibacterial strategies

CONCEPT-activities focus on objectives 2 and 4 in the WHO global action plan, priority topic 1 and 4 in the JPI-AMR strategy, and the 3rd overarching goals in the Norwegian National Strategy against Antibiotic Resistance:

- Develop knowledge for new targets for antibacterial strategies.
- Develop structural and systems biology models to identify and evaluate new antibacterial strategies.
- Develop knowledge for microbiome-based strategies to combat antibacterial resistance.
- Develop knowledge and improve models for assessment, counteraction and reversal of resistance development.
- Develop infection model systems to evaluate new antibacterial strategies *in vitro* and *in vivo.*

TRANSLATION – from basic research to application

TRANSLATION-activities focus on objective 2 in the WHO global action plan, priority topic 1 and 4 in the JPI-AMR strategy, and the 1st, 2nd and 3rd overarching goals in the Norwegian National Strategy against Antibiotic Resistance:

- Evaluate new antibacterial strategies in the prevention and treatment of infections.
- Evaluate strategies to counteract and reverse resistance development.
- Evaluate microbiome-based strategies for the decolonization of unwanted bacteria.
- Evaluate strategies for combating biofilm related bacterial growth.

EDUCATION

EDUCATION-activities focus on objective 1 in the WHO global action plan, priority topic and the all four overarching goals in the Norwegian National Strategy against Antibiotic Resistance:

- Train UiT-based young researchers in cross-disciplinary skills in order to develop and propagate expertise in antibiotics, antibiotic resistance, treatment and development of new antibacterial strategies.
- Develop the National IBA-related PhD-programme in AMR hosted by UiT as an arena for international research network activities.
- Highlight the AMR problem in the existing education provision and student recruitment in a One Health perspective.
- Communicate the societal challenges of AMR and CANS activities through Internet and relevant social media platforms.

RESPONSIBLE RESEARCH AND INNOVATION (RRI)

RRI-activities focus on objective 1 in the WHO global action plan and all four overarching goals in the Norwegian National Strategy against Antibiotic Resistance:

- Instigate an inclusive dialogue with interest groups, decision makers and the general public with a view to developing socially responsible and sustainable research and innovation in the field of AMR.
- Contribute to insight and development of new strategies for combating AMR, infections and unwanted bacterial growth.
- Use a reflective approach to illuminate and evaluate ethical aspects and dilemmas of antibiotic use and resistance development.

Strategy and measures

CANS' strategic orientation is therefore based on an overarching understanding of the need for an interdisciplinary approach based on priorities given in the WHO global action plan, the JPI-AMR initiative and the Norwegian National Strategy against Antibiotic Resistance. The knowledge gaps within AMR are diverse and complex, and necessitate a credible binding interdisciplinary research environment. **Therefore, the individual measures must have a distinct interdisciplinary profile across** academic environments, departments and faculties - categorized as:

(i) **Identification of new complementary areas of knowledge relevant to the development of CANS:** In order for CANS to achieve its objectives, this measure is fundamental in the further development of the academic AMR-community at UiT. This will be done via international recruitment advertisements for three tenure-track positions as part of six-year start-up packages (postdoctoral, PhD, technician, operation). The working group has identified three essential new areas of knowledge in dialogue with the AMR-related research groups and department chairs: systems biology, marine microbiota and human microbiome. The working group proposes that these three new areas of knowledge are developed at NT, BFE and Helsefak respectively, due to the specific nature of each area and the relevant affiliated expert communities.

(ii) **Strengthening of existing academic environments relevant to the development of CANS:** This must take place in the form of permanent academic positions supported with start-up packages (postdoctoral, PhD and operation) and a pool of fixed-time positions (postdoctoral, PhD) in order to better equip CANS to achieve research objectives and compete for external research funds. An open process for selecting priority academic environments must be facilitated in collaboration with the institution's research strategy management at the rector, faculty and departmental level. Such processes will be based on academic merits and CANS' objectives. The supporting start-up packages and fixed-time positions must adjusted and filled in according to the overall needs/success of external research funding.

(iii) **Internationalization – networking:** It is essential to establish binding collaboration with other similar centres. Such collaborations may include the establishment of joint study programmes, agreements for the exchange of MSc/PhD/postdocs/established researchers, and the intent to submit joint project applications. Countries we wish to be compared with have established similar centres,[1] which currently collaborate with some units at UiT. This collaboration will be further strengthened through the establishment of CANS.

[1] To date, we are aware of the following relevant centres: Uppsala – Professor Dan Andersson; Gothenburg – Professor Joakim Larsson; Utrecht – Professor Marc Bonten; San Diego – Professor Victor Nizet; Durban – Professor Sabiha Essack.

(iv) **A stronger focus on AMR in study programmes:** Learning outcomes for AMR must be established in relevant bachelor and master's programmes, thus enabling students to select AMR as a theme in BSc/MSc dissertations within CANS' field of work.

(v) **Organizational infrastructure:** CANS must have the academic and administrative capacity required for the practical implementation, administrative management and operation of CANS. This will be described in more detail below.

(vi) **Infrastructure for scientific equipment:** Workshops have not identified a need for major investments in scientific equipment beyond the maintenance/renewal of existing core facilities at Helsefak (genomics platform, bioimaging, proteomics, the Preclinical PET/SPECT/CT unit), BFE (biodiscovery pipelines) and NT (synthesis equipment, high performance computing and the Norwegian Structural Biology Centre).

Academic focus areas

1. Strengthening of new complementary areas of knowledge relevant to the development of CANS

The working group has identified new areas of knowledge that need to be established in order for CANS to achieve its long-term objectives. These are competences that are dependent on, and thus complement, the interdisciplinarity that already exists in the current academic environments. The working group recommends strengthening three areas of knowledge with an orientation that necessitates interdisciplinary activities across faculties. The three areas of expertise will be established in the most relevant existing academic environments in order to facilitate integration within the field (Appendix 3).

Resources allocated to each faculty: (i) 1 tenure-track position: initially to be funded from the UiT board's strategic funds in collaboration with the Tromsø Research Foundation (TRF), and subsequently taken over by the faculty/department after 3–6 years if the contract is renewed, (ii) 1 postdoctoral position (3 years), (iii) 1 PhD position (4 years), (iv) purchase of services equivalent to 1 technician position (6 years), and (v) operation (TNOK 300/year). For all resources, it is a requirement that the orientation is in accordance with CANS' objectives and requirements for interdisciplinarity. Announcement and evaluation processes will be topic related, but otherwise in line with TFR-starting grant criteria. Jobs must be phased in as appropriate.

NT – systems biology: Systems biology is the recognition that the whole of a complex system is always greater than the sum of its parts. Systems biology is a holistic approach to the development of AMR and aims to decipher the complex networks of the system as a whole (microbe-patient-treatment) that create resistance. Systems biology is largely driven by big data generated in CANS, and its main purpose is to integrate information from all disciplines represented in CANS. Using a systems biology approach taking into account modern concepts in bacterial population biology, CANS wishes to create a holistic understanding of the system as a whole that will enable us to predict the mechanisms for how AMR might evolve. Ultimately, this knowledge could predict how the system (microbe-host- treatment) will change in response to the choice of antibiotics and how different antibacterial strategies can

be combined. This type of knowledge can be used to improve current prediction models for resistance development, new molecular targets for antibacterial activity and outcomes of interventions. Through the systems biology dimension, the research in CANS will contribute to the development of evidence-based treatment regimens that will largely minimize the risk for development of AMR. We proposes that the systems biology expertise in CANS is developed at the NT faculty, since systems biology – in addition to the biological dimension – integrates expertise and technologies from chemistry, physics, information technology, bioinformatics and chemistry informatics, all of which are currently represented at NT.

BFE – marine microbiota: Identification of novel antimicrobials from the marine environment requires a broader strategy than traditional bioprospecting focusing on extracts from invertebrates. A large proportion of marine microorganisms live in close symbiosis with animals, plants and algae. Within this relationship, marine microorganisms often are the major producers of bioactive molecules even though the same compounds can be isolated in small quantities from animal extracts. Thus, these microorganisms that represent a major potential source for discovery, production and development of new antibacterial molecules will therefore be the centre of attention in the novel approach. The biggest challenge associated with marine bacteria is that 99% of them are difficult to grow. It is therefore not easy to obtain good isolates through traditional cultivation and to isolate bioactive components. Whole-genome sequencing of some marine microorganisms has also shown that they have many silent gene clusters that encode new antibacterial molecules. It has proven difficult to clone and express these genes *in vitro* as long as the bacteria are cultivated as pure cultures. By understanding interactions in marine microorganisms in nature, it will be possible to see which chemical signals and interactions are relevant to the expression of antibacterial compounds. Genome sequencing of new marine microorganisms will be able to predict which ones have antibacterial potential. This knowledge will be important for selecting which marine microorganisms to work with, and will thereby increase the probability of inducing an expression of potentially new antibiotics. It will subsequently be necessary to use heterological expression systems with a view to producing gene products that can be assessed and further developed. The range of application may be clinical, but other applications in animal welfare (marine and land-based), antifouling and other industrial uses may also be relevant. We propose that this area of knowledge in CANS is developed at BFE, in close collaboration with the relevant AMR-related marine academic environment, and the systems and computational biology community at NT.

Helsefak – the human microbiome: Microbiome research is reshaping our understanding of human biology, health and disease development. The fast-paced development of next-generation sequencing technology, computational biology and model systems has led to new discoveries. The findings have also provided a greater understanding of/hypotheses about the importance of normal flora to homeostasis, including the protective effect against unwanted bacteria. A fundamental understanding of the normal composition and function of the microbiome is also a *conditio sine qua non* for the development of sustainable organic antibacterial strategies in order to oust/prevent colonization and infections with pathogenic bacteria, including multi-resistant strains. This knowledge requires a new expertise and resources, as well as the handling of big data, and has a kinship to a systems biology approach. This kind of expertise will also be sought in population surveys (the Tromsø Study). It is proposed that this area of knowledge in CANS is developed at Helsefak, where we have relevant academic environments with an understanding of human microbiology/immunology

and access to population surveys and clinical studies. This work should also take place in close collaboration with the systems and computational biology community at NT.

2. Strengthening of existing academic environments relevant to the development of CANS

Several AMR-research groups at BFE, NT and Helsefak are in a favourable situation with regard to research funding from regional, national and international sources. However, external funding is unpredictable and give rise to a great deal of uncertainty. In order to achieve ambitious goals in the development of new sustainable antimicrobial strategies, long-term work is necessary, with stability in expertise and more robust, predictable access to resources, including in current research environments. The working group recommends strengthening three academic environments/areas of expertise with a permanent academic position provided through a start-up package at each of the three faculties, where the orientation necessitates interdisciplinary activities across the faculty. A dynamic research environment needs a critical mass of PhD and postdoctoral positions. We therefore also propose that a pool of 12 PhD and 3 postdoctoral positions is allocated and phased in over a period of eight years. These positions will be advertised, externally reviewed and filled in line with the overall needs of the research environment of CANS within the focus areas of molecules, concepts and translation.

Resources allocated to each faculty: (i) 1 permanent academic position in the relevant environment: initially financed from new funding and continued after natural retirement, (ii) 1 postdoctoral position (3 years), (iii) 1 PhD position (4 years), (iv) operation over 5 years (NOK 300 000 per year), and (v) 12 PhD and 3 postdoctoral positions will also be advertised and externally reviewed in an open competition in the CANS-affiliated academic community. For all resources, it is a requirement that the orientation is in accordance with CANS' objectives and requirements for interdisciplinarity.

NT: Several activities at IK focus on antibiotics and resistance, in particular the development of beta-lactamase inhibitors (*LacZymes*) and the research group in digital discovery of antibiotic molecules (*DigiBiotics*). In addition, significant efforts are being made to develop synthesis methods for the production of antibiotic natural analogues, also in collaboration with BFE and Helsefak. These and other initiatives have either already developed or will develop an antimicrobial AMR pipeline, which is of major importance to several of the inter-faculty projects in CANS. These should be strengthened and coordinated in order to maximize CANS' access to high-quality molecules that can be tested in advanced model systems developed within CANS**.**

BFE: Targeted utilization of marine resources is an ongoing BFE activity with relevance to CANS. The aim is to acquire new basic knowledge about relevant marine molecules or genes derived from marine bacteria, plants, algae (micro and macroalgae) and invertebrates (bioprospecting). This knowledge will be used to define molecules that have a potential for the development of new antibiotics, anti-biofilm molecules (which prevent or remove/destroy biofilm) or molecules that can have antifouling properties (marine installations). Strengthening existing environments will be essential in order to develop new and smarter assays that i) test molecules under conditions of increased complexity, and ii) expand the understanding of the mode of action for each molecule. Pipelines have already been

established for separation, isolation of marine natural products and studies of bioactivities and mechanisms of action such as antibacterial and antibiotic activity (marbio + other facilities). This has been achieved through projects such as **MabCent-SFI, eXBioPepS, PharmaSea** and an ongoing strategic project at UiT (**AntifoMar**), where everyone is/has been involved in extensive collaborative efforts across the faculties. CANS will further strengthen this work.

Helsefak: The AMR environments at Helsefak and UNN carry out activities aimed at establishing a basic understanding of resistance evolution, the molecular epidemiology of AMR, and interactions between bacteria, antibiotics and humans. There is a robust research environment within host-microbe-drug interactions, with academically strong international relations and important complementary expertise for the development of CANS. A fundamental understanding of bacterial virulence factors, their function and interaction partners has the potential to engender new concepts in antibacterial strategies. Studies of host-microbe-drug interactions and potential interventions require advanced expertise and access to new experimental models and supervisory capacity that must be developed and maintained over time. Helsefak also coordinates *LEADScAMR,* which involves the design and synthesis of a new class of antibiotics and their microbe interactions, as well as the development of antibiotic formulations.

Organization and management

An appropriate organizational structure and management are needed to safeguard the practical implementation, administrative management and operation of CANS. Academic structures with defined scientific areas of responsibility also need to be in place.

Areas of responsibility and functions include:

- Drawing up a proposal for the necessary governing documents for CANS.
- Organizing AMR-related internal seminar series and discussion platforms to promote knowledge dissemination, project and interdisciplinary collaboration and application activities.
- Organizing AMR-related workshops and conferences to promote national and international collaboration.
- Raising awareness of UiT's overall AMR activities internally and externally.
- Public relations, including influencing research funding sources.
- Establishing collaboration agreements with similar centres and other relevant partners.
- Raising awareness of funding opportunities and providing administrative support for application processes.
- Preparing annual action plans and activity reports.

The following organizational structure will be established (Figure 2):

- The **Centre for New Antibacterial Strategies (CANS**) will be established under a department with AMR-research activity. The working group proposes IMB at Helsefak. The host faculty/department will be responsible for ensuring the necessary operational framework conditions.

- The post of **centre director** (50% FTE) based at IMB will be advertised. The post will be temporary during the start-up phase, and 50% will be funded by the host faculty and 25% by each of the other two faculties.
- A **project coordinator** (administrative resource, 50–75% FTE) will be linked to the centre head to deal with communication and provide administrative support to the centre head and other structures within CANS. This resource should be placed in an associated administrative environment at the host faculty. Each of the three faculties involved will provide one third of the funding for this position.

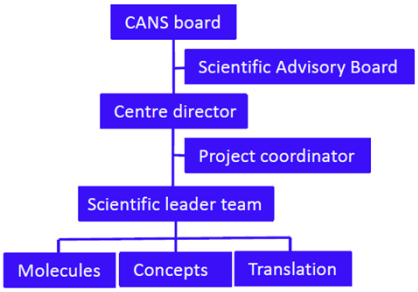


Figure 2. CANS' organizational structure.

- An internal operational **scientific leader team** will be set up, fronted by the centre head and otherwise consisting of an academic member of staff (established professor) from each of the three faculties. These three academics will hold a 20% operational role in CANS and provide academic support for the centre head (arrange academic discussion platforms, provide an overall assessment of external referee statements of advertised resources, support the centre head in internal and external communications, draw up proposals for annual action plans and activity reports, maintain a core dialogue with the respective faculty and department management boards, etc.).
- A **CANS board** will be made up of representatives from the three faculties and the Rector, who will oversee the activities and attainments, and process proposals for annual action plans and activity reports. The head of CANS will be the board secretary.
- A **scientific advisory board** will be established with representatives from similar centres. The council will meet annually to evaluate CANS' activity and provide strategic advice for future activities. Annual meetings will be coordinated with CANS board meetings and the annual academic CANS seminar.
- Provision should be made for **physical premises for the centre** facilitated by the host faculty which as a minimum should accommodate the centre head, project coordinator, academic council meetings and project-related activities.

Process and implementation plan

The working group envisages several phases in the development of a sustainable centre based on our vision, objectives and priority research areas. It is important to ensure a smooth start-up process and an appropriate sequence of events. A temporary centre head, project coordinator and a scientific leader team are in place for 2018. Following the interim period and institutional decisions, the next phases will ensue.

Phase 1: Start-up (2018)

- Recruitment and temporary employment of the centre head: 25% FTE from 1 January and 50% FTE from 1 August 2018
- Appoint project coordinator: 25% FTE from 1 January and 50% FTE from 1 August 2018

- Establish academic management team: 3 x 10% FTEs from 1 January and 3 x 20% FTEs from 1 August 2018
- Operating fund (travel, profiling, internal seminars): NOK 200 000
- Prepare governing documents, and internal/external networking
- Advertise new permanent academic and/or tenure-track positions
- Start-up seminar internally, and profiling of CANS

Phase 2: Establishment (2019–20)

- Appoint centre head
- Fill permanent academic and tenure-track positions
- Advertise postdoctoral and PhD positions
- Establish permanent meeting platforms (CANS board, academic management team, international academic council, CANS seminar)
- Arrange international start-up seminar

Phase 3: Operation and mid-way evaluation (2020–23)

- Operation: maintain and develop meeting platforms
- Focus on internal and external networking, academic development through research and study programmes, and positioning/quality in relevant research applications including SFI/SFF
- Mid-way evaluation

Phase 4: Work and positioning vis-à-vis SFI/SFF etc. (2023 –)

- Operation: maintain and develop meeting platforms
- Focus on internal and external networking, academic development through research and study programmes, and positioning/quality in research applications
- Positioning for further major research grants

Anchoring of the strategic framework and budget

The **strategic framework** of CANS has been developed and anchored in dialogue with the **AMR-related research environment** at UiT and UNN through interactive workshops and meeting activities (March and November 2017, January 2018), and the **UiT-leadership** through meetings in the temporary steering committee (Vice-Rector for research and innovation + Deans for BFE-, NT and Helsefak) and with the Rector throughout 2017-18. The **resources** are expected to be funded from strategic funds from UiT's board and the faculties, the departmental level through natural retirement, and the Tromsø Research Foundation.

On behalf of CANS - the temporary scientific leader team

Arnfinn Sundsfjord Klara Stensvåg John Sigurd Svendsen Johanna E. Sollid

Appendices

1. Overview of CANS-related research groups and CVs from group leaders and interim scientific leader team.
2. Overview of current external AMR-related research funding at UiT.
3. Description of the new areas of knowledge relevant to the development of CANS (tenure-track positions). In process.
4. Description of competences/capacities related to strengthening of existing academic environments relevant for the development of CANS (new academic positions). In process.

Table 1. Overview SANS-related reserach groups and their respective human resources

	Employe categories				
Research group	**Professor/ Ass. professor**	**Researcher/ PostDoc**	**PhD**	**Technical**	**Group leader**
HF - IKM – Pediatric - Infection	2,5	3	3	1	Trond Flagstad
HF - IMB – Molecular Pharmacology and Toxicology	2,5	0	2	0,5	Ingebrigt Sylte
HF - IFA – MicroPop	1,45	5	3	0	Pål J Johnsen
HF - IKO – Oral Ecology	1	1	1	1	Mohammad Al-Haroni
HF - IFA - Drug Transport and Delivery	4,2	1	0	2	Natasa Skalko-Basnet
HF – IMB - K-Res	0	3	0	3	Kristin Hegstad
HF - IFA – Natural Products and Medicinal Chemistry	4	0	3	2	Morten B. Strøm
HF - IFA – IPSUM	6	0	3	1	Lars Småbrekke
NT - Chemistry – LacZymes	1	1	1	0	Hanna-Kirsti Schrøder Leiros
NT - Chemistry– Bayer Group	1	1	1	0	Annette Bayer
NT – Chemsitry - Antimicrobial peptides	6	7	7	1	John Sigurd Mjøen Svendsen
HF - IMB – Host – Microbe - Interactions	5,6	2	7	2	Mona Johannessen
BFE – Marbio	1	3	6	3	Jeanette H. Andersen
BFE - Marine bioprospecting	4	0	6	2,5	Klara Stensvåg
Total	**40,25**	**27**	**43**	**19**	