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DART – the German strategy to fight antimicrobial resistance. Report on history and current state¹⁾

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Abstract

This report outlines the German strategy to fight antimicrobial resistance consisting of ten objectives: strengthening of surveillance systems on antibiotic resistance and antibiotic consumption, systematic feedback of data on antibiotic resistance and antibiotic consumption, promoting the use of guidelines to ensure the diagnosis, promotion of training, further education and training of health professionals, pharmacists, and natural scientists, national and international cooperation, promotion of assessment measures in human medicine, promotion of knowledge transfer in the field of antibiotic resistance, as well as networking and strengthening of science in the field of antibiotic resistance. The proposed draft legislation and questions concerning sustainable maintenance of good laboratory practice and the corresponding means are addressed.

Keywords: antibiotic resistance; consumption of antibiotics; German strategy to fight antimicrobial resistance; guidelines; infection protection act; microbial diagnosis; national and international cooperation; nosocomial infections; surveillance systems.

Introduction

In concert with the EU member states, Germany adopted a strategy to combat antibiotic resistance in 2008, also known by its German acronym DART (the German Antibiotic Resistance Strategy).

Courtesy of the communications staff of the Federal Ministry of Health (BMG), Berlin, on the basis of key

extracts from the interim report published in April 2011 on the German antibiotic resistance strategy, the ten national objectives and related proposed legislative changes are presented in this paper.

DART sets out in the medical part ten goals to reduce and control the spread of antibiotic resistance, to be implemented by a variety of measures by the end of 2013. The bill amending the Infection Protection Act and other laws is based on DART and strengthens key areas to reduce the spread of antibiotic resistance and reduce treatment-associated infections in Germany. The project is currently being discussed by the legislative bodies and is to enter into force in mid-2011.

Objective 1: Strengthening of surveillance systems for antibiotic resistance and antibiotic consumption

The ARS project – Antibiotic Resistance Surveillance in Germany – at the Robert Koch Institute was funded with departmental research resources of the BMG, which has led to the establishment of sustainable structures related to lab-based surveillance of antibiotic resistance in outpatient and inpatient care. The surveillance system currently covers around ten per cent of hospitals, but is not yet regionally representative. The data collected in the form of standardised reports on the situation and development of resistance is made publicly available through an interactive database (<https://ars.rki.de>).

The resistance surveillance, based on voluntary participation, was added as a statutory measure with the introduction of mandatory laboratory reporting regarding the detection of methicillin-resistant *Staphylococcus aureus* strains (MRSA) in blood or cerebrospinal fluid starting on 1 July 2009 [Regulation to adapt the reporting requirements under Section 7 of the Infection Protection Act (IfSG)].

Side by side with resistance surveillance, ARS is currently working on setting up a system to monitor the consumption of antibiotics. The data concerning outpatient care are available for the period 2007–2010. The Robert Koch Institute (RKI) receives these data from the Central Institute of the Evaluation Committee (ZI). The data are aggregated, anonymised evaluations of antibiotic prescriptions collected from prescription bills. The first data transfer is scheduled for the first quarter of 2011. To monitor inpatient care, a cooperation of RKI and the Department of Infectious Diseases at the University Hospital Freiburg continues, and continually expands, the established

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project “Anti-infective surveillance in hospitals”, in which currently around 50 hospitals participate.

With the publication of GERMAP 2008 – a report on the consumption of antibiotics and the spread of antibiotic resistance in human and veterinary medicine in Germany – the data generated throughout various projects were presented for the first time (<http://www.p-e-g.org/econtext/gemap2008>); a follow-up report is currently being prepared and supported by the BMG.

In addition, some German states carried out a study into the incidence of MRSA as part of prevalence screenings. These data were compiled with regional data from resistance monitoring systems in different states (e.g., Thuringia and Lower Saxony) in cooperation with microbiology laboratories and evaluated.

Objective 2: Systematic feedback of data on antibiotic resistance and antibiotic consumption

Suitable formats of feedback are currently being developed as part of ARS. In addition, an early warning system for the occurrence of new resistance types is being established. In this case, routine diagnostic laboratories and national reference centres (NRZ), which specialise in advanced diagnostic procedures and investigations on the spread of (multi-)resistant pathogens, cooperate with each other. Based on the data from routine diagnostics, the NRZ analyse the molecular-epidemiological background in connection with the timely detection of the occurrence and spread of new resistance types in close international cooperation and communicate their findings as part of an early warning system.

With the new appointment of the National Reference Centre for Gram-negative hospital pathogens, a gap in the NRZ system was closed, so that now additional capacity has been freed up. As well, through the network of NRZ and consulting laboratories, the network “Antimicrobial Resistance” was set up, which will facilitate the processing of cross-pathogen issues.

Moreover, the findings of the surveillance systems are implemented at the national, regional and local levels in conjunction with clinical-epidemiological background data in real time and used to expand existing, as well as to work out new, prevention recommendations on the part of the Commission for Hospital Hygiene and Infection Prevention (KRINKO) at RKI. The recommendations of KRINKO are applied directly (by way of recommendations for dealing with patients who are colonised by or infected with MRSA/MRP) and indirectly (recommendations for minimising overall nosocomial infections) to improve preventive measures at the national level. Currently the Commission deals with necessary public health measures in connection with Gram-negative problem pathogens and MRSA in rehabilitation facilities.

The ZI, in cooperation with physicians’ associations, is working on a further development in the drug info service (AIS) of the National Association of Statutory Health Insurance Physicians (KBV). This will soon be available as a feedback system for panel doctors, in addition to individual

prescription data (including data on prescriptions for antibiotics). The data are to be accessed either via an online portal or as a PDF document about two months after the end of the reporting period.

Finally, the issue of “nosocomial infections” will be addressed again as part of the cross-sector quality assurance effort of the Federal Joint Committee (G-BA). The German Hospitals Association is determined to accord special priority to (multi-)resistant pathogens and antibiotic resistance. The process of developing appropriate quality indicators was initiated by the G-BA.

Objective 3: Promoting the use of guidelines

To strengthen rational antibiotic therapy, the commission “Anti-infectives, resistance and therapy (ART)” is established at the Robert Koch Institute, which will inspect the existing recommendations on antibiotic therapy and initiate the preparation of independent, scientifically grounded recommendations in the event of shortcomings. The bill amending the Infection Protection Act and other laws bestows upon the ART commission a legal foundation. This additional measure, which builds upon DART, gives the commission the requisite status and thus supports the significance of the future commission work. In addition, the bill specifically requires medical facilities to comply with hygiene measures and to adhere to the principles of proper administration of antibiotics. The recommendations of the commissions for hospital hygiene and infection prevention (KRINKO) and ART thus become mandatory in nature. As well, to promote the implementation of recommendations, the bill creates a legal foundation and obligation for states to pass regulations to improve hygiene measures at hospitals and other relevant facilities, which also allows for the imposition of fines in case of contraventions. Through such regulations, medical facilities are to be obligated to put in place specific rules and regulations for necessary measures regarding the prevention, detection, registration and control of nosocomial infections and hospital pathogens in the context of resistance. This includes, for example, the responsibilities and composition of a public health commission, the requisite staffing with public health experts and hospital epidemiologists, as well as the appointment of public health officers, or the necessary qualification and training of staff with respect to infection prevention.

As part of the hospital infection surveillance system (KISS), three modules (MRSA-KISS, MRP components of ITS-KISS and DEVICE-KISS) will regularly collect and analyse also data on the occurrence of multi-resistant pathogens in patients infected non-nosocomially (also see current data at www.nrz-hygiene.de).

The national “Operation Clean Hands” campaign has been promoted by the BMG since 2008 and has been coordinated by the Institute of Hygiene and Environmental Medicine of Charité (Berlin). Since 2011 the focus of the campaign has been on outpatient care, such as nursing homes and long-term care facilities. At this time, 608 hospitals and 48 rehabilitation

clinics are part of the campaign. Current findings can be obtained from www.aktion-sauberehaende.de.

Objective 4: Securing the diagnosis

At the initiative of the BMG, remuneration for diagnostic services and the care of patients with (multi-)resistant pathogens who are in the care of panel doctors as well as the existing and potential application problems have been examined by the institute of the evaluation committee, and deficits in the area of reimbursement have been identified. Due to the existing reimbursement deficits, the bill to amend the Infection Protection Act and other laws initially provides, for a limited period of time, for an EBM code for diagnosis and rehabilitation of patients infected with MRSA or colonised by MRSA.

The German Hospitals Association supports this approach, since only one cross-sectoral strategy to combat resistant pathogens will be successful. It is also committed to achieving comparable funding regulations for hospitals as well. KBV and the Statutory Health Insurance Scheme (GKV), already prior to the draft bill, were planning an integrated approach for MRSA patient care, which included, for example, a separate fee scale item for the laboratory diagnostics of MRSA as well as the eradication of problem pathogens. Also, some states, within their regional networks for the prevention and control of antimicrobial resistance and other projects, cooperate with microbiological laboratories. The aim of such cooperation is to carry out a comparable and quality-assured diagnosis as well as to improve diagnostic quality.

Objective 5: Promotion of training, further education and professional development of health professionals, pharmacists and natural scientists

On the occasion of the second European Antibiotics Day in 2009, the BMG and RKI organised a workshop on the training, further education and professional development of health professionals, pharmacists and natural scientists. Initial proposals and measures were worked out, such as on how the issue of antibiotic resistance can be given more prominence in the curricula of various health-care professionals. At the workshop, a certified further education programme leading to a qualification as a NIP/ABS Consultant (NIP=nosocomial infection prevention, ABS=antibiotic stewardship) was presented that was funded by the BMG and conceived of by the German Society for Hygiene and Microbiology (DGHM) and the German Society for Infectious Diseases (DGI). This programme is to train experts in the field of administering of antibiotics and infection prevention in hospitals. A total of seven NIP courses with 174 participants and eleven ABS courses with almost 300 participants have taken place so far. The strong demand and positive feedback highlight the need for such professional development programmes that are not industry-specific.

Regular training courses with different areas of emphasis and for a variety of target groups also serve as the basis of exchange within the regional networks. By including the state medical associations in state boards, professional development can be offered as additional support even outside the scope of individual networks.

Objective 6: National cooperation

Cooperation among the actors in health care at a regional level is reinforced by the promotion of regional networks specialising in the prevention and control of antimicrobial resistance. The BMG supports the establishment of regional networks through the start-up funding of four groups of networks acting as model projects with different specialisations over a period of four years: The Berlin/Brandenburg network focuses on antibiotics consumption in connection with general practitioners and its effects on the prevalence of MRSA (ca-MRSA) contracted by outpatients. The Münsterland/Osnabrück network group specialises in the application of findings made by the EUREGIO project “MRSA-Net” to other pathogens (ESBL, *Clostridium difficile*) as well as in a nationwide perspective (EUREGIO MRSA-Net (<http://www.mrsa-net.org/indexDE1.html>)).

The Rhine-Main/Hesse/Saarland network deals with *Clostridium difficile* and the use of software in treating patients infected with (multi-)resistant pathogens.

The Freiburg/Baden-Württemberg network is primarily concerned with establishing comparisons of structures, resistance rates and antibiotics consumption in the region.

In addition to this, other regions too set up networks for the prevention and control of multi-resistant pathogens (MRP). In setting up the various networks, the significance of dovetailing local activities as well as of technical and political support became clear. Therefore, boards responsible for setting up networks were created at state level in parallel to local activities. This includes state associations, such as municipal associations, hospital associations, medical associations, panel physician associations, pharmacists and health insurance companies in addition to representatives of professional associations and societies. These boards are supported technically and in part scientifically by the integration of regional health authorities, laboratories, universities and colleges.

The central element within the networks established at regional and federal state level is a consensus on measures to be implemented uniformly. Through direct contact with practitioners as well as scientific institutes, the experience gained from the networks is also applied to the preparation and improvement of practical guidelines. Quality assurance measures are rendered mandatory for participating hospitals through a system of quality seals within the networks. This also includes the implementation of the KRINKO recommendations.

Furthermore, some states have realised cross-departmental cooperation with the veterinary sector. Additional studies allow for pathogens to be identified that are associated with agricultural farm animals (la-MRSA for “livestock-associated”).

In prevalence studies and also in public health approaches, potential risks of transmission to people and their role in human medicine are described at the state level.

The DGK established the first nationwide cross-hospital MRSA network in the Hamburg region through “MEDILYS 2004”, which records, analyses and evaluates in a differentiated and systematic manner all MRSA cases from seven hospitals. This instrument makes it possible to evaluate the quality of results relating to the handling of problem pathogens at a hospital. In close cooperation with health departments, the focus is also on referring medical facilities. Outpatient and inpatient care facilities have also shown themselves to be open to cooperation. As part of the European prevalence survey “HALT” (Health-care associated infections in European long-term care facilities), the incidence of infections, antibiotic use and resistance of bacterial pathogens in residents of inpatient care facilities have been examined.

Another example of successful cooperation at the regional level is the EUREGIO MRSA Net project of the panel of physicians' association of Westphalia-Lippe (KVWL). As part of the project, the KVWL has taken measures particularly in connection with the treatment of carriers of problem pathogens. The KBV competence centre on patient safety, which is part of the KVWL, has been able to ensure the transfer of the know-how gained into the health insurance system.

The RKI supports the formation of networks, for example, through regular meetings of the moderators of regional MRP networks in Germany for the purpose of presenting and sharing findings and experience. The second meeting of the moderators was held at the RKI in May 2010. An inter-ministerial working group on antibiotic resistance was established to ensure overall coordination at the federal level. The group meets regularly to plan, evaluate, adjust and expand the national antibiotic resistance policy.

Objective 7: International cooperation

Germany is a member of the European networks “European Antimicrobial Resistance Network” (EARS Net, http://www.ecdc.europa.eu/en/publications/Publications/1011_SUR_annual_EARS_Net_2009.pdf) and “European Surveillance of Antimicrobial Consumption” (ESAC). By strengthening the national surveillance systems in Germany, comparisons with European countries are more solid and more significant. Apart from those mandatory cooperation efforts, Germany is involved in a number of other EU projects on issues related to antibiotic resistance, such as the “European Network of Laboratories for Sequence-based Typing of Microbial Pathogens” (SeqNet) or the “Transnational Research on Combating Antimicrobial Resistance” (TROCAR).

The European funding initiative “European and Development Countries Clinical Trials Partnership” (EDCTP) supports and groups into networks existing research initiatives in Europe and Africa to combat the infectious diseases HIV/AIDS, malaria and tuberculosis.

Under the leadership of the initiative, clinical studies and capacity-building measures are carried out. Since June 2009,

and for a period of five years, it has funded an international research consortium to establish an African network for clinical studies on new tuberculostatics in the amount of EUR 7.7 million through the German Federal Ministry of Education and Research (BMBF). The German share provided from funds of the health research programme accounts for EUR 1 million (for more information: www.edctp.org).

ERA-NET PathoGenoMics (“Genome sequencing and functional genomics of humanpathogenic microorganisms”, 2004–2012) is a consortium of thirteen funding organisations in nine countries (eight EU member states and Israel). The cooperation in European research funding in the field of genome research on pathogenic microorganisms was launched in the 6th Framework Programme under the banner of the then-new “ERA-NET scheme”, and provided a successful forum for transnational cooperation, particularly in organising joint calls for tender. So far, PathoGenoMics has realised three transnational calls and has provided a total of over EUR 42 million in funding for transnational research projects. At approximately EUR 20 million, the BMBF shoulders the bulk of the initiative. German researchers were very successful in all three calls; thus, 15 out of a total of 34 subsidised collaborations are coordinated by German researchers.

All three calls focused on fundamental and applied aspects of the infection biology of pathogenic bacteria and fungi. Despite great advances in medicine in recent years, infectious diseases still pose a serious threat, which is due, for example, to the development of resistance to anti-infectives and the spread of pathogenic microorganisms as a result of global travel. The projects funded as part of PathoGenoMics are expected to make a significant contribution to countering this threat. The projects go far beyond traditional genome research and involve a number of practical topics, such as the formation of biofilm or the development of new diagnostics, all of which are also linked to the issue of antibiotic resistance.

Another European initiative is the Joint Programming Initiative “The Microbial Challenge – An Emerging Threat to Human Health” (JPI AMR), which is coordinated by Sweden. An interim secretariat has been established at the Swedish Research Council. A grant has been requested from the 7th Framework Programme to fund the initiative. Fifteen countries, including Germany (BMBF), participate in this initiative. A vision paper is to be completed by the end of 2011. The working programme of the proposed JPI AMR consists of three modules that are to be implemented in a corresponding set of work packages in the further course of the initiative.

1. Biology and dynamics of resistance: Identification of mechanisms that are essential for the evolution and spread of resistance mechanisms, typing of bacterial strains, predictions of resistance emergence and risk assessment with regard to the development and spread of antibiotic resistance;
2. Prevention of resistance development and innovative treatment options: Development of methods for rapid diagnosis of infectious microorganisms and their resistance

patterns, identification of new lead molecules for the development of new antimicrobial drugs, development of alternative treatment options;

3. Epidemiology and burden of disease: Study of the emergence and spread of resistance around the world, including the veterinary use of antibiotics and the emergence of antibiotic resistance in the food industry and in agriculture; clinical and economic impact of antibiotic resistance.

Objective 8: Promotion of evaluation measures in human medicine

The strategy aims at promoting the rational use of antibiotics. Consequently, studies on the factors influencing the prescription habits regarding antibiotics and on relevant patient attitudes have been carried out as part of DART even before the start of appropriate intervention in order to determine the initial situation. As part of the study “Influences on the prescription of antibiotics by doctors in Germany” in 2008, doctors working in outpatient and inpatient environments were surveyed on their prescription habits. To complement the study, an online survey was also conducted in 2008 to collect data on antibiotics as well as expectations concerning the prescription of antibiotics from a random sample of the general population. The analysis of the questionnaires showed that the focus of future measures would have to be primarily on doctors prescribing antibiotics, as they can exert substantial influence on the prevention and control of antibiotic resistance and nosocomial infections through their own prescription and hygiene habits.

Objective 9: Promotion of knowledge transfer regarding antibiotic resistance

The KBV funds quality circles and, as part of such work, supplies panel doctors with specific information. There are over 5000 moderated quality circles in Germany that have been accredited by associations of panel doctors. Participants are issued “scripts” on relevant topics, including rational drug therapy and accounting for antibiotic therapy.

In this context, it also bears mentioning the two issues of the journal “Wirkstoff aktuell” on the rational use of antibiotics in connection with infections of the upper respiratory tract and urinary tract infections, as well as the medical Centre of Quality (ÄZQ), whose web-based “medical library” also provides evidence-based current information on the topic of antibiotic therapy and resistances.

The regional networks of the states also include scientific facilities. This also establishes a link to practice, while ensuring the promotion of knowledge transfer and the interlinking of science. In addition to the professional development of medical staff, information for patients and their families is also generated and made available.

To educate and inform the population, the Institute for Quality and Efficiency in Health Care (IQWiG) has developed

the leaflet “The safe use of antibiotics” and published it via the platform Gesundheitsinformation.de.

The GKV, in a circular sent out to its members, has positioned itself on DART, the inadequate use of antibiotics and the resulting resistance problem as well as pointing to the measures that the GKV supports in this context.

Objective 10: Networking and strengthening of science in the field of antibiotic resistance

To identify deficiencies and gaps in the field of antibiotic resistance research in Germany, an expert workshop was organised under the leadership of the Joint Scientific Advisory Council (GWB) of the BMG. As a result, deficiencies were identified particularly in social science and public health studies, in clinical research, molecular epidemiology, clinical microbiology, in the area of molecular fundamentals and vaccine development against multi-resistant pathogens. Based on these recommendations, the BMG intends to issue an extensive call for tenders for the implementation of the research focus “Antimicrobial resistance and nosocomial infections”.

In addition, the Federal Ministry of Education and Research also strengthens, and provides networking support for, scientists working on antibiotic resistance through a number of initiatives.

The following are some selected examples:

Zoonoses

On 26 March 2009, the guidelines for the promotion of further research collaborations on select zoonotic infectious diseases with an explicit link to antibiotic resistance strategy were published: “In light of increasing antibiotic resistance found in bacteria, collaborating researchers can apply for projects on bacteria with antibiotic resistance that is transferred from animals to people. This will contribute to the implementation of the German antibiotic resistance strategy (DART) of the Federal Ministries of Education and Research (BMBF), of Health (BMG) and Nutrition, Consumer Protection and Agriculture (BMELV).” As a result of the assessment, two collaborative research efforts on the transmission of antibiotic resistance from animals to people will be funded, for three years, from 1 November 2011, in the amount of approx. EUR 5.6 million. The two collaborative projects consist of seven and eight partners, respectively, including the federal facilities – the Robert Koch Institute, the Federal Institute of Risk Assessment and the Friedrich Loeffler Institute.

Research association RESET: ESBL and fluoroquinolone resistance in Enterobacteriaceae

The research association RESET deals with resistance to antibiotics in a group of bacteria, enterobacteria. These include *Escherichia (E.) coli* and *Salmonella (S.) enterica*, which occur not only in people but also in animals and in the environment. Resistant bacteria in animals can be transmitted to people through food. To contribute to consumer health protection, the

research association looks at bacteria that are resistant to the crucial beta-lactam antibiotics and fluoroquinolones. RESET consists of various complementary studies on factors linked to the spread of emerging resistance characteristics in enterobacteria in people, animals and the environment.

The goal of this research association is the assessment of the influence of different bacteria, their origins and transmission routes relevant to people (for more information: www.reset-verbund.de).

Research association MedVetStaph: Interdisciplinary research network regarding the zoonotic significance of *Staphylococcus aureus*/MRSA

The research association MedVet-Staph deals with the incidence and spread of *S. aureus* bacteria, particularly MRSA, as zoonotic pathogens that can be transmitted between animals and people. The association investigates the potential virulence, pathogenicity, antibiotic resistance and host-cell interaction of these bacteria, as well as the mechanisms behind the transmission of *S. aureus* between animals and people. Moreover, evolutionary changes in these pathogens are detected. The impact of zoonotic transmission of *S. aureus*/MRSA on human and animal health is also studied. Furthermore, the mechanisms behind the spread of *S. aureus*/MRSA in animal reserves and health-care facilities as well as the introduction of pathogens into the food chain are examined. The objective is to utilise the knowledge gained from the findings of the research association for developing rational, evidence-based recommendations for the prevention and control of zoonotic *S. aureus*/MRSA. The website of the association (www.medvet-staph.org) is currently under construction.

Zoonoses platform

To coordinate and network cooperation among the subsidised projects on zoonotic infectious diseases in Germany, as well as to promote the broad-based horizontal networking of human and veterinary medicine, the BMBF has funded the national research platform for zoonoses since 1 January 2009, initially set for a period of three years (www.zoonosen.net). The national research platform for zoonoses is carried substantively and in a cross-departmental manner by the three federal ministries BMBF, BMG and BMELV, and supported by the government research institutes of the BMG and BMELV. Depending on the outcome of the interim assessment in October 2011, more funding is envisaged for another three years.

Competence network CAPNetZ

The goal of competence networks in medicine is the perpetuated horizontal and vertical networking of scientists, physicians and research institutes with respect to one specific clinical picture. In the field of infectious diseases, “CAPNetZ”, a competence network specialising in community-acquired pneumonia, received funding in the amount of approx. EUR 14.5 million from the BMBF for the period from 2001 to 2011. Its outstanding results include the varied

commitment of the network to fighting the unnecessary use of antibiotics as well as the development of S3 guidelines concerning community-acquired deep respiratory tract infections and pneumonia. One project that is still in the process of being completed is the multicentre randomised PENCAP study that compares the efficacy of antibiotics of the class of penicillins and fluoroquinolones, two types of antibiotics to which resistance in Germany has been on the rise. Of great relevance are also pharmacokinetic and pharmacodynamic studies of antibiotic efficacy in the elderly performed within the competence network. The development of resistance of different pathogens to different classes of antibiotics has also been examined. Still during the last BMBF funding phase, the CAPNETZ foundation was created in order to continue and expand the work by means of additional financial support. The network's success is based on its structure consisting of local clinical centres that provide access to outpatients as well as on an extensive patient material collection, which is also immensely attractive for commercial studies. This biobank has collected blood, urine and sputum as well as pathogens from over 9000 patients. For more information, see www.capnetz.de.

Health region Baltic Sea Coast-HIC@RE-action against multi-resistant bacteria

The health region Baltic Sea Coast, funded by the BMBF since early 2011 to the tune of EUR 7.5 million for the next four years, is seen as a model region for Germany to test successful containment of the spread of multi-resistant pathogens (MRP). The consortium HIC@RE (Health, Innovative Care and Regional Economy) will, in this context, develop and implement an innovative, population-based, integrated and evidence-based MRP intervention management, which will span the entire value chain from basic research and clinical intervention to health economic evaluation. This is supported by the development of a regional MRP information system. This approach, which covers a range of different types of pathogens, facilities and patients, allows the health region Baltic Sea Coast to strengthen the implementation of existing statutory regulations on infection protection and thus to act as a role model for other regions. The HIC@RE network combines 37 regional and national academic and corporate partners. This makes it possible to pool expertise with respect to health care, community medicine as well as supporting and service staff, complemented by competencies in health economics and qualification. One thematic focus is the improvement of patient care at different levels of health care (hospital, outpatient department, nursing home, residential care) by implementing a regional antibiotics guideline. Side by side with that, the use of anti-infectives and resistance trends are to be monitored at the participating clinics and in outpatient care.

Another area examined is the prevalence of MRSA strains acquired in the community and at hospital and coagulase-negative staphylococci in representative orthopaedic, trauma and cardiac surgery centres and cohorts, as well as their association with implant-associated infections. New types of spacer

cement in infected knee endoprostheses and antimicrobial-coated hip hemiarthroplasties are examined and the adjuvant systemic antibiotic therapy is evaluated. In addition, the efficacy and tolerance of the developed antibiotic-free rehabilitation regimen that is based on a special (containing octenidine) ointment preparation to decolonise the nose are to be examined as part of a clinical study. The use of special software in a clinical setting is to be examined in connection with the treatment and management of MRP carriers with chronic lesions. More information can be obtained from the website (www.hicare.de).

Clinical studies

The priority area “Clinical studies” has been funded since August 2009 in the amount of approx. EUR 1.2 million, for a period of three years, involving a clinical study on antibiotic resistance. The aim of the study is to determine the effectiveness of *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea (AAD) and *Clostridium difficile*-associated diarrhoea (CDAD) in adult hospitalized patients. The methodology consists of a randomised, double-blind, placebo-controlled, multicentre study involving 1525 patients at eight test centres. The experimental intervention consists of the twice-daily administration of *Saccharomyces boulardii* during antibiotic therapy until one week after cessation of antibiotic therapy. The control intervention involves the corresponding administration of a placebo. The non-prescription drug has not yet been approved for the indication of AAD prevention.

German Centre for Infection Research

In 2010 the BMBF published the notice on the establishment of a German Centre for Infection Research (DZIF). With the formation of DZIF, the most powerful German institutions of infection research are to be brought together to coordinate their work and to protect the population more effectively against bacterial, viral, parasitic and fungal infectious diseases. In particular, severe life-threatening infections or nosocomial infections are to be fought more effectively while containing the spread of drug resistant pathogens. But also globally important infections as well as neglected and poverty-associated infectious diseases are to be studied. After the preliminary selection of seven partner sites, the final assessment will be done by an international panel of experts in early April 2011. At present, the DZIF is to conduct a research programme on infections caused by resistant Gram-negative bacteria, as well as a research programme to search for new anti-infectives. Depending on the evaluation result, funding for the DZIF will be lined up from autumn 2011. The German Research Foundation (DFG), which is partially funded by the BMBF, also addresses the research field of antimicrobial resistance through different measures. For example, since 2009, the research group at the University of Bonn on “Post-genomic strategies for new antibiotic agents and target structures” has been funded, for the subsequent years, in the amount of approx. EUR 3 million. The

research group is to develop foundations for the development of effective new antibiotics through post-genomic concepts. The research concept follows a primarily biological approach and integrates in a complementary way microbiological, biochemical, chemical and pharmaceutical activities. For more information: www3.unibonn.de/forschung/forschungsprofil/dfg-gefoerderte-projekte/for854.

The federal government has referred to the Bundesrat (Upper House of the German Parliament), for the purpose of further funding for the implementation of DART, the bill contained in the federal printed matter 150/11 dated 17 March 2011 on amending the Infection Protection Act and other laws for further processing and approval.

Section 23 of the Infection Protection Act (IFSG) is to read as follows according to the bill:

Nosocomial infections; resistance; regulations by the states

1. The Robert Koch Institute will establish a Commission for hospital hygiene and infection prevention. The Commission shall adopt its rules of procedure, which shall require the approval of the Federal Ministry of Health. The Commission shall prepare recommendations for the prevention of nosocomial infections as well as operational and organisational and structural and functional measures of hygiene in hospitals and other medical facilities. The Commission's recommendations will be published by the Robert Koch Institute. The Commission members are appointed by the Federal Ministry of Health in consultation with the country's top health authorities. Representatives of the Federal Ministry of Health, the highest regional health authorities and the Robert Koch Institute will participate in the meetings in an advisory capacity.
2. The Robert Koch Institute will establish a Commission for anti-infectives, resistance and therapy. The Commission shall adopt its rules of procedure, which shall require the approval of the Federal Ministry of Health. The Commission shall draw up recommendations, general principles of diagnosis and antimicrobial therapy, particularly for infections with resistant pathogens. The Commission's recommendations will be published by the Robert Koch Institute. The Commission members are appointed by the Federal Ministry of Health in consultation with the country's top health authorities. Representatives of the Federal Ministry of Health, the highest regional health authorities, the Robert Koch Institute and the Federal Institute of Drugs and Medical Devices will participate in the meetings in an advisory capacity.
3. The heads of hospitals, facilities for outpatient surgery, prevention or rehabilitation facilities where medical care is comparable to hospitals, dialysis facilities, day clinics, maternity services, comparable treatment or care facilities, medical offices, dental offices and practices of other human medical health professionals to ensure that according to the state of medical knowledge necessary measures are taken to prevent nosocomial infections and the spread of pathogens, particularly those with resistance.

Compliance with the state of medical science in this area will be assumed if the recommendations published respectively by the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch Institute and the Commission for anti-infectives, resistance and therapy at the Robert Koch Institute are complied with.

4. The heads of hospitals and facilities for outpatient surgery shall ensure that the nosocomial infections and the occurrence of pathogens with special resistance and multi-resistance defined by the Robert Koch Institute in Section 4(2)(2)(b) are recorded continuously in a separate transcript and evaluated and that appropriate conclusions will be drawn with regard to necessary preventive measures. The necessary preventive measures shall be communicated to staff and be implemented. The records referred to in Sentence 1 shall be kept for ten years. The competent health authority shall be granted access to the records, evaluations and conclusions if so requested.
5. The heads of hospitals, prevention or rehabilitation facilities, facilities for outpatient surgery, dialysis facilities, day hospitals, maternity facilities and comparable treatment or care facilities shall ensure that internal procedures for infection hygiene are laid down in hygiene plans. These institutions are subject to infection hygiene monitoring by the health department.
6. Medical offices, dental offices and practices of other human medical health professionals where invasive procedures are performed can be monitored by the health department with respect to infection hygiene.
7. Inspectors shall be empowered to enter and inspect, during hours of operation and business, properties, business and operating premises, operation-related equipment and facilities as well as means of transportation, and to inspect the accounts or other documents, as well as to take copies, photographs or extracts thereof and to examine any other objects or to request or take samples for investigation where they deem it necessary to perform their tasks. Section 16(2) Sentence 2–4 shall apply accordingly.
8. The state governments shall, by regulation for hospitals, facilities for outpatient surgery, prevention or rehabilitation facilities that provide comparable medical care, as well as for dialysis facilities and day clinics, take all necessary measures to prevent, detect and control nosocomial infections and hospital pathogens with resistance. This shall, in particular, involve provisions on minimum hygienic requirements for construction, equipment and operation of facilities, the appointment, tasks and composition of health commissions, the required staffing with health professionals and hospital epidemiologists and the appointment of health officers, the tasks and requirements for continuing education of the necessary public health officers, health professionals and hospital epidemiologists, the necessary qualification and training of personnel in the prevention of infections, the structures and methods for the detection of nosocomial infections and resistant pathogens and for recording in the medical and nursing documentation requirements, the inspection necessary to fulfil their respective duties by persons

referred to under (4) of records of the respective facility, including patient records, the information given to staff on measures necessary for the prevention and control of nosocomial infections and pathogens with resistance, clinical-microbiological and clinical-pharmaceutical advice for the medical staff, the information provided to the receiving facilities and general practitioners in connection with the transfer, referral or discharge of patients on measures necessary for the prevention and control of nosocomial infections and pathogens with resistance.

The state governments can delegate this authority created by regulation to other agencies.”

Furthermore, for example, Social Security Code V is to be amended as follows:

1. Section 87 shall be amended as follows:

In paragraph 2a the following sentences shall be added:

“By 31 October 2011, a regulation shall be in place, with effect from 1 January 2012, pursuant to which medical services in connection with diagnosis and outpatient eradication therapy including electronic documentation of carriers of methicillin-resistant *Staphylococcus aureus* (MRSA) are compensated. The compensation agreement shall be limited to two years; a follow-up arrangement shall be realised by 31 October 2013. The National Association of Statutory Health Insurance Physicians shall report to the Federal Ministry of Health quarterly on assessment results from the provision under Sentence 3. The Federal Ministry of Health may specify the content of the report under Sentence 5 as well as the assessment of the anonymised documentation for the purpose of health care research; it may also mandate the evaluation committee with the presentation of the report. Moreover, the publication requirement under Section 136(1) Sentence 2 shall apply.”

In Paragraph 2d Sentence 1, “2a Sentence 3” shall be inserted in front of “2b and 2c”, and the words “services and” shall be inserted after the word “mentioned”. [Refers to the German text.]

Section 137 shall be amended as follows:

The following Paragraphs 1a and 1b shall be inserted after Paragraph 1:

- “(1a) The Federal Joint Committee shall, in its guidelines under Paragraph 1, define appropriate policies to ensure hygiene in health care and shall identify especially for the cross-facility quality assurance of hospitals indicators to assess hygienic quality. It shall decide on the requirements under Sentence 1 for the first time by 31 December 2012. The Federal Joint Committee shall take into account in the specifications established procedures for the collection, analysis and feedback of nosocomial infections, antimicrobial resistance and antibiotic consumption as well as recommendations commissions set up at the Robert Koch Institute pursuant to Section 23 (1) and (2) of the Infection Protection Act.

- (1b) The results measured with the indicators under Paragraph 1a Sentence 1 following the introduction and suitable for publication shall be presented in the quality reports under Paragraph 3 No. 4. The Federal Joint Committee shall include in the quality reports findings on the status of hygiene at hospitals already accessible to it immediately and shall set out additional requirements under Paragraph 3 No. 4 concerning the improvement of information on hygiene.”

At present, this raises the following questions for a microbiological laboratory doing practical work:

1. To what degree or intensity must medical services in connection with diagnosis and outpatient eradication therapy including electronic documentation of carriers of methicillin-resistant *Staphylococcus aureus* (MRSA) be performed?
2. What impact does this have on the compensation of mandatory additional services, such as the reimbursement of transportation costs?
3. How can one arrive at a medically fair and sustainable compensation for medical services commensurate with the services performed, also in consideration of the necessary investment costs, that would allow the facility to provide the services on a sustainable basis and with efficient management? How can such compensation ensure the necessary, real-time reporting chain patient-doctor-medical laboratory to ensure exclusively necessary antibiotic therapy?
4. How can colleagues be recruited who can fill the gap of those with lab-medical, microbiological and hygiene training who would be able to perform future responsibilities, particularly at the bedside?

Sources and related links

1. Antimicrobial resistance surveillance in Europe 2009. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) (http://www.ecdc.europa.eu/en/publications/Publications/1011_SUR_annual_EARS_Net_2009.pdf).
2. DART – Brochure of the Federal Ministry of Health (https://www.bundesgesundheitsministerium.de/fileadmin/dateien/Publikationen/GesundheitBBroschueren/Deutsche_Antibiotika_Resistenzstrategie_DART_110331.pdf).
3. DART – Interim Report of the Federal Ministry of Health (http://www.bmg.bund.de/fileadmin/dateien/Downloads/A/Antibiotikaresistenzstrategie/DART_Zwischenbericht_110407.pdf).
4. Epidemiological Bulletin 13/2011 of the Robert Koch Institute (RKI) dated 4 April 2011 (http://edoc.rki.de/documents/rki_fv/reAxcJrrLbHY/PDF/293U744uaZfzI.pdf).
5. European Center for Disease Prevention and Control ECDC (http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/Pages/index.aspx).
6. European Network of Laboratories for Sequence Based Typing of Microbial Pathogens (<http://www.SeqNet.org>).
7. EUREGIO MRSA-net (<http://www.mrsa-net.org/indexDE1.html>).
8. EurSafety Health-Net (www.eursafety.eu).
9. Bill to amend the Infection Protection Act and other laws (http://www.bundesrat.de/cIn_152/SharedDocs/Drucksachen/2011/0101-200/150-11,templateId=raw,property=publicationFile.pdf/150-11.pdf).
10. State Working Group on Multi-Resistant Pathogens (LARE) (<http://www.lgl.bayern.de/gesundheits/lare/index.htm>).
11. MRSA Network Lower Franconia (<http://www.mrsa-unterfranken.de>).