Die
Bundesregierung

DART 2030

German Antimicrobial Resistance Strategy

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Foreword

In implementing the measures required to combat antimicrobial resistance, the involvement of all relevant stakeholders is a vital prerequisite for long-term success. The good and constructive cooperation previously shown played a key role in achieving the results obtained in implementing the predecessor versions to this new strategy, DART 2030.

Our thanks go to everyone involved in the comments and input process. To the extent possible, the feedback received has been taken into account in devising this latest DART Strategy and/or will be taken up in the subsequent DART 2030 Action Plan.

Introduction

Antimicrobial resistance (AMR)[1] is increasing on a global scale, posing an ever-growing challenge in the treatment of patients in both human and veterinary medicine. Its impact means that only a few or in some cases no treatment options are available in treating bacterial infections that were previously treated with ease. In addition to the personal suffering of those affected, this means longer and significantly more serious courses of disease, and consequently more deaths. Also, many of the achievements attained in modern medicine, such as joint replacements, chemotherapy in treating cancer, immunotherapies for rheumatic disease, and neonatal care for premature babies, would be unthinkable without effective antibiotics. AMR is also a source of considerable additional costs. These arise, among other things, from the rising costs of treatment, prolonged hospital stays, absences from work and premature deaths.

The increasing prevalence of resistant pathogens also heightens the risk of emergency situations in treating animals in veterinary medical care. As our fellow creatures, all sick animals have a right to receive medical treatment. Where necessary, this also includes administering antibiotics prescribed by a veterinarian. And as animals are often kept in close proximity to humans, the transfer of resistant pathogens between animal keepers and their domestic animals and pets poses a growing problem.

The release of antibiotic substances and their metabolites (metabolic products) into the environment from human settlements and animal husbandry upsets the environmental balances in the biosphere and can promote the distribution of novel resistance mechanisms. The environment can thus be a source of resistant micro-organisms for humans and animals alike.

Preventing the further spread of AMR calls for a package of measures which are to be implemented in a wide range of areas. The Global Action Plan on Antimicrobial Resistance adopted by the World Health Assembly in 2015 calls upon member states to devise their own national action plans. Taking account of the goals set out in the Global Action Plan, these national actions plans are to contain measures which are aligned to the actual situation in each country. The plans also serve in achieving the UN Sustainable Development Goals (SDGs).

The first German Antimicrobial Resistance Strategy (DART) was adopted by the Federal Government back in 2008. Like its successor strategy, DART 2020 launched in 2015, it took the One Health approach, was jointly developed by the Federal Ministries of Health (BMG), Food and Agriculture (BMEL) and Education and Research (BMBF), and subsequently adopted by the Federal Cabinet. A Final Report on the implementation of DART 2020 was published in April 2022.[2] The report describes both the measures implemented to achieve the DART 2020 goals and the key outcomes – including in relation to resistance rates and antibiotic use. It also sets out the initial focal areas to be taken up in this successor strategy, DART 2030.

These focal areas include prevention, further promotion of appropriate use of antibiotics in human and veterinary medicine, and greater involvement of the environment sector in activities to combat AMR. The situation which has evolved in recent years has further highlighted this sector's increasingly important role.

In the area of human medicine, greater focus will be placed on sepsis – the most severe form of infection. In the past, measures were initiated under DART 2020 whose direct or indirect goal was to prevent both cases of sepsis and deaths due to sepsis. Via the funding

[1] While it uses the accepted international abbreviation AMR (antimicrobial resistance), the aim of DART 2030 is to reduce antibiotic resistance in bacterial pathogens. Also, for the purposes of this report the term 'antibiotics' refers to antibacterial substances only.

[2] https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/D/DART_2020/BMG_DART_2020_Abschlussbericht_bf.pdf

opportunities provided by the Innovation Fund of the Federal Joint Committee (G-BA), scientific studies were enabled on the epidemiology of sepsis, its long-term effects and the effectiveness of information campaigns for the prevention and early detection of sepsis. There have been repeated calls for a national sepsis plan which would set out a package of effective measures for the prevention and early detection of sepsis, and could be supplemented with additional activities at a later date. In order to make the most of the many interfaces and synergies, however, it was decided not to develop a standalone national sepsis plan. Targeted measures to combat sepsis will be taken up as part of DART 2030 instead.

The future AMR Strategy will also consider outpatient medical care. Given that it involves both the prescription of more than 80 percent of antibiotics used and the vast majority of patients being treated with respiratory and urinary tract infections, the outpatient healthcare sector represents an important area in the national AMR Strategy, among other things because its processes in diagnostics and treatment differ greatly from those involved in providing inpatient care. This is where the future development of an outpatient antibiotic stewardship strategy will play an important role by focusing on the specificities and needs of general practitioner and paediatric primary care, outpatient care and dental care.

DART 2030 was jointly developed by the Federal Ministry of Health (BMG), the Federal Ministry of Food and Agriculture (BMEL), the Federal Ministry of Education and Research (BMBF) and, new to the group, the Federal Ministry for Economic Cooperation and Development (BMZ). The Federal Ministry for the Environment, Nature Conservation, Nuclear Safety and Consumer Protection (BMUV) was also involved in the review. The main areas of focus in the predecessor version, DART 2020, remain valid and in place: expansion of the surveillance and monitoring systems on AMR and antibiotic use, improvements in infection prevention and appropriate use of antibiotics, raising public awareness, facilitating the acquisition of necessary knowledge among medical professionals, and intensifying R&D support – the One Health approach being taken into account in each case.

As the Strategy's planned lifecycle runs up to 2030 and it is impossible to say which measures and steps will be needed or require alignment to achieve its set goals, a two-step approach is taken. This report sets out both the goals to be achieved by the end of the Strategy's lifecycle, and from what starting points, in combating AMR – both at national level and through international cooperation. In a second step, an action plan to be published at a later date will set out the measures and steps required to achieve the DART 2030 goals. The action plan will be regularly reviewed and realigned as needed. It will also be used as the basis for reporting on the status of DART 2030 implementation. As with DART 2020, this will continue the tried and trusted process of issuing regular interim reports.

Reporting on the progress made in achieving the overarching goals for AMR reduction in human medicine is to be aided by the setting of suitable targets. In the course of Germany's G7 presidency in 2022, the G7 health ministers agreed to define measurable national-level AMR targets by the end of 2023 which also cover the use of antibiotics. By including targets in DART 2030, Germany has followed through on this commitment. It is envisaged that the targets will be presented with the action plan. Progress made in target achievement will also be addressed as part of the planned reporting process.

Action Area 1: Prevention

This action area takes in the prevention of infectious diseases requiring treatment using infection protection and control measures (as understood in their broadest sense) to reduce both the use of antibiotics and selection pressure in microorganisms. Prevention also includes containing the emergence and spread of AMR in and via the environment (such as through wastewater, waterbodies and soil) and preventing the spread of AMR along the food chain.

1.1. Human medicine and nursing care

In the human medicine sector, the Commission for Hospital Hygiene and Infection Prevention (KRINKO) at the RKI draws up recommendations aimed, among other things, at preventing nosocomial infections in medical facilities. The available recommendations cover all key thematic areas, thereby providing valuable guidance for the prevention of infectious diseases in medical facilities. They are subject to regular review, and are adapted and realigned as needed. The Act to strengthen the protection of the population and in particular vulnerable groups against COVID-19 (*Gesetz zur Stärkung des Schutzes der Bevölkerung und insbesondere vulnerabler Personengruppen vor COVID-19*), which entered into force in September 2022, expanded the area of responsibility of the new Commission for Infection Prevention in Medical Facilities and in Facilities and Companies of Care and Integration (*Kommission für Infektionsprävention in medizinischen Einrichtungen und in Einrichtungen und Unternehmen der Pflege und Eingliederungshilfe*). In the future, recommendations are also to be drawn up for such facilities and companies, and their needs adequately taken into account in measures to prevent infection.

Recommendations and guidelines on hygiene and infection prevention must be provided, observed, applied and evaluated in the facilities. Obstacles that hinder their implementation must be identified and eliminated. As part of this process, the findings of ongoing research projects are to be used as a basis on which to develop additional, targeted measures. As in promoting appropriate use of antibiotics in human medicine (see 3.1), the various medical associations also play an important role in improving both the implementation and acceptance of measures concerning hygiene and infection prevention.

Likewise, awareness of infection prevention and the resulting potential cost reduction must be secured at all levels in both medical and care facilities. Only then can a long-term, positive effect be expected as regards the rate of infections requiring treatment.

Vaccination is an important and effective means of preventing infection. Preventing infections and serious cases of infectious disease makes it possible to reduce antibiotic resistance. This also includes viral infections in which bacterial superinfections often lead to severe courses of disease. The National Vaccination Schedule sets out Germany's vaccination targets. The Schedule's consistent, determined implementation can also help to reduce both the emergence and spread of AMR. Vaccinations likewise play an important role in preventing sepsis infection and vaccines are available for certain pathogens that are known to cause sepsis. Worthy of note in this regard are pneumococcal and influenza vaccines. The aim is thus to further increase the number of people who are vaccinated, especially among risk patients and vulnerable groups.

1.2. Animal health

Animal husbandry conditions, systems and management all have a significant impact on the health of animals and livestock. Existing husbandry and management processes must thus be subjected to critical review to assess whether they foster infectious disease, thereby increasing the need to use antibiotics. To promote animals' resistance to disease and reduce the pressure of infection, animal husbandry and management processes are to be modified where necessary, taking prevailing animal health and welfare requirements into account.

Animal nutrition also has a significant impact on an animal's resilience to disease. The potential impact of needs-based animal nutrition containing both macro and micronutrients, a balanced supply of fibre and a suitable feed structure (which is essential) should not be

underestimated. Additional measures that can play a highly important role include feed hygiene (elimination/ reduction of antinutritive and toxic substances, and harmful organisms) and the use of feed components with beneficial effects on the physiological function of the digestive tract and its microbiome, and on animals' immune status.

In both animal husbandry and animal transport, consistent use of hygiene, animal welfare and biosafety measures is needed. This reduces the infection pressure in the animal environment, thereby reducing the risk of infection.

Vaccination measures serve not only direct prevention of infection with the specific pathogens they target – they also protect against secondary diseases, thereby improving animals' general immunity and reducing the frequency of bacterial infections that have to be treated with antibiotics.

Animal breeding can also help to improve the vitality and robustness of animals, and increase genetic diversity. This means that healthy, robust animals are less at risk of infection. Genetically heterogeneous populations are better able to resist pathogens. In animal breeding, functional traits such as health and robustness are gaining in importance, and can be included in the breeding value estimation of animals. Use of genomic selection in breeding value estimation, which has been practiced for some years, further promotes the breeding of improved functional traits.

1.3. Environmental release of antibiotics and antibiotic resistances

There are still considerable gaps in available knowledge regarding the extent and importance of the environmental release of antibiotic substances and their metabolites, and of antibiotic resistant bacteria and resistance genes via wastewater, household waste, stable dust, slurry, solid manure and fermentation substrate. Current knowledge must nonetheless be used to critically assess the existing practices applied in wastewater treatment, farming and commercial processing of food as to their role in the occurrence and especially the spread of AMR, with alternatives being developed as needed. In the area of livestock husbandry, when developing strategies to prevent the environmental release of antibiotics and resistances, other needs such as animal welfare, organic farming and sustainable management practices must also be considered.

1.4. Food chain

ESBL/AmpC-producing E. coli are also being detected in agricultural livestock (poultry, pigs and cattle). Sampling carried out during monitoring of zoonoses at retail level repeatedly detects foods contaminated with multidrugresistant pathogens (MDROss) being displayed on sale to consumers. It can thus be assumed that those pathogens can be transmitted via food. The importance of the role of food and livestock as sources of MDRO infections in humans cannot be adequately estimated using available data. It can be assumed that it differs between the different types of bacteria and is not particularly significant in a large number of cases. Further efforts are nonetheless needed in order to minimise their role.

Resistance determinants enter the food chain via livestock husbandry, humans and the environment, and can be either eliminated or further transmitted once in the chain. As well as foods of animal origin, this also affects plant-based foods. The release of resistance determinants into the food chain can be prevented among other things through the detection of survival and adaptation strategies of (antibiotic resistant) bacteria and their distribution paths, and any existing contamination of food can be reduced by means of suitable practices of processing and treatment.

Action Area 2: Surveillance and Monitoring

Standardised and uniform surveillance and monitoring of antibiotic use and AMR are needed to assess the situation in all healthcare sectors (including primary care, outpatient specialist care and dental care), identify changes, progresses and trends, and then use the findings to implement targeted measures and track their effects. The methods used, planning of targeted monitoring activities and both the evaluation and reporting of results are all subject to continuous development.

2.1. Systems used in human and veterinary medicine

In Germany, data on AMR in human medicine is collated in the antibiotic resistance surveillance system (ARS) established at the RKI. Via feedback reports, the participating laboratories receive an overview of resistance at the local level along with information concerning rare resistances. For antibiotic use in inpatient care, the RKI's antibiotic use surveillance system (AVS) can be used in addition to various other systems. The AVS also serves to assist inpatient facilities in implementing the legal requirements set out in the Protection Against Infection Act (IfSG) regarding documentation and evaluation of data on antibiotic use. Use of antibiotics in the outpatient setting is documented as a rule by the statutory health insurance funds. To further improve available data, efforts should be made to harmonise the surveillance systems. Also, to be able to arrive at more detailed conclusions on the prevalence and spread of AMR, the national surveillance systems for both the outpatient and inpatient settings should be further developed and enhanced. Resistance data on fungi should also be included. Additional data sources, including those available in the various Länder (Federal states) and those concerning specific pathogens – such as the national reference centres (NRC), the consulting laboratories (CL), scientific societies and projects – are also to be considered. In the future, the German Electronic Reporting and Information System for Infection Protection and Control (DEMIS) will play an important role in surveillance.

In particular with regard to reserve antibiotics under Section 35a (1c) of Book V of the German Social Code (SGB V), it is important – via the RKI's existing surveillance systems on antibiotic resistance and antibiotics use – to be able to obtain a general overview of resistance developments and trends (taking account of antibiotic use) in order to identify unfavourable trends at an early stage and implement the countermeasures needed.

Both the inclusion of clinical patient information and the nationwide collection of outpatient resistance data sorted by primary and secondary care is also to be promoted to aid the development of targeted recommendations for treatment.

In addition to improving the availability of data at national level, expanding the surveillance systems will enable Germany to better comply with reporting requirements in the EU's European Antimicrobial Resistance Surveillance Network (EARS-Net) and European Surveillance of Antimicrobial Consumption Network (ESAC-Net), and also in the Global Antimicrobial Resistance and Use Surveillance System (GLASS).

Molecular biological studies on pathogens are a key instrument used in, for example, detecting resistance genes in AMR and tracing infection chains – especially concerning (super-regional) outbreaks of disease. When establishing an integrated molecular surveillance system, i.e. linking genome data of pathogens with data from the reporting system in accordance with the IfSG, a molecular surveillance system is also to be established for antibiotic-resistant pathogens of special importance, including 4MRGN (multidrug-resistant gram-negative pathogens with resistance to four antibiotic groups) and MRSA (methicillin-resistant Staphylococcus aureus).

Conducting molecular studies using standardised and harmonised processes is a prerequisite for the collation of sequence data on resistant pathogens from the human, veterinary and environmental sectors. This approach enables both better tracing and verification of cross-sectoral infection chains, and subsequent conclusions to be drawn on the spread of resistances across sectors. Cross-sectoral cooperation and joint evaluation of data

from the surveillance and monitoring systems is to be gradually expanded.

Current antibiotic resistance monitoring along the food chain, in which the Länder (states), the Federal Institute for Risk Assessment (BfR) and the Federal Office of Consumer Protection and Food Safety (BVL) are involved, is to be continued. In addition to alignment to the new EU legislative requirements (Implementing Decision (EU) 2020/1729), supplementary national programmes will also be implemented, further developed and enhanced.

National antibiotic resistance monitoring of animal pathogenic bacteria will likewise be continued and further developed by the BVL. Efforts will also be made to centrally collect and analyse more data on AMR from diagnostic studies conducted by testing laboratories of the Länder and private laboratories. That data is intended to enable both early identification of specific resistance patterns and subsequent implementation of further targeted studies as needed.

With effect from 2023, Regulation (EU) 2019/6 on Veterinary Medicinal Products regulates EU-wide documentation of the quantities of antibiotics sold for use in animals (sales data) and of the actual quantities used. Germany already has documentation systems in place for both quantities and this must now be aligned with the provisions of the EU Regulation. In particular, the phased documentation required in the EU Regulation of the quantities used for all food-producing animals as well as horses, dogs and cats can only be implemented by means of a significant increase in the digital workload of veterinarians, animal keepers and competent authorities. This will enable data on antibiotic use in animals to be obtained separately according to animal species and type of production. In particular, the use and the effects of certain antibiotic substances that play an important role in human medicine, such as colistin, fluoroquinolones and third and fourth generation cephalosporins, are to be subjected to especially critical monitoring.

Data from both resistance monitoring programmes in the veterinary sector, the documented quantities of antibiotics and information on trends in the treatment frequencies in livestock farms subject to the national antibiotics minimisation concept are key sources of information that can be used in national-level risk assessment and in developing management measures. To make the findings more easily accessible, reporting and analysis systems for routine analysis of data and also web-based systems will be developed and implemented for use. Opportunities arising from increasing digitalisation will be leveraged in the process.

Currently, there remains a lack of systematically collected, representative data on the spread of AMR in and via the environment. This knowledge gap must be closed. When considering the establishment of an official system to monitor antibiotic resistance in the environment, the longstanding experience in resistance monitoring in the veterinary sector, the related cooperation between the Federal and Länder governments, and the collective experience gained in monitoring wastewater for SARS-CoV-2 must all be drawn upon and used.

2.2. Integrated One Health surveillance

Integrated analysis of resistance data from surveillance in environment, veterinary and human medicine is a key prerequisite for fact-based, cross-sectoral assessment of the resistance situation in Germany and plays an important role in the One Health approach to combating AMR.

Under Germany's G7 presidency in 2022, the G7 health and agriculture ministers agreed to establish and expand integrated surveillance systems on AMR and antibiotic use in the human and veterinary sectors as well as in agriculture and the environment. Establishing those systems calls for a phased approach in which, among other things, it is necessary to decide how to deal with differing data formats and comply with differing data protection provisions. Initial steps have already been taken in the course of research projects conducted over the past few years. The long-term goal is to link (molecular) data from the human, veterinary and environment sectors with epidemiological, social medicine and other subject-relevant data, and generate a broad data resource to aid targeted interventions.

2.3. Additional data collection

Targeted questions that go beyond standardised evaluation of surveillance and monitoring data can be addressed by means of dedicated studies and research projects. In the human medicine sector, this especially involves regular surveys initiated by the European Centre for Disease Prevention and Control (ECDC) – for example, the national part of an EU point prevalence study on, among other things, the incidence of nosocomial infections and antibiotic use in hospitals and long-term care facilities. In the food safety sector, it involves participation in studies coordinated by the European Food Safety Authority (EFSA) on the occurrence of resistant microorganisms in the food chain, such as MRSA in livestock and food. Germany will continue to participate in the EU surveys and use the resulting trends as a basis on which to adapt and align measures at national level.

Action Area 3: Appropriate Use of Antibiotics including Laboratory Diagnostics

Antibiotic stewardship (ABS) is designed to ensure both indication-appropriate use of antibiotics and the best possible antibiotic treatment, and help to reduce or prevent increasing development of resistance. ABS takes in reliable diagnostics, selection of a suitable antibiotic and its fastest-possible use (especially on suspicion of sepsis), and adequate recommendations concerning indication, treatment duration, antibiotic dosage, dosage form and reevaluation. The aim is to establish responsible use and handling of antibiotics by general practitioners, dentists and veterinarians – including regular reflection on their own actions and behaviours – and make these standard practice. Mandatory further training measures are to be reviewed along with adequate teaching of the topic in medical studies, including knowledge of alternative options for treatment. In some cases, it may also make sense to develop dedicated models for certain types of livestock farming.

3.1. Antibiotic use in human medicine

In ABS activities, data analyses that compare resistance rates with antibiotic use can be of great assistance and help identify how they influence each other. The Robert Koch Institute (RKI) has developed the ARVIA system for use in inpatient treatment and care. ARVIA is a German acronym for Integrated Antimicrobial Resistance and Consumption Analysis. It highlights potential dependencies between the resistance situation and antibiotic prescriptions, and can help in aligning treatment recommendations and treatment practices in the field. The aim now is to establish this system and gain a comprehensive, uniform overview of the data for Germany by means of constructive cooperation with the treating physicians, coordination with experts responsible for ABS and by merging data from the differing systems already in place.

Up-to-date, evidence-based guidelines on the diagnosis and treatment of infectious diseases and cases of sepsis which can be attributed to the resistance situation are a further prerequisite for ABS. Needs-oriented guidelines can only be developed if current and disaggregated care data is available. The aim is to have and keep up to date a catalogue of infectiological S3 guidelines for each care setting in the guidelines register of the Association of the Scientific Medical Societies in Germany (AWMF) – including explicitly for primary and secondary outpatient care and dental care. The respective treating disciplines and their institutions must be closely involved in developing the catalogue. An important contribution can be made here by the funding opportunities provided by the Innovation Fund of the Federal Joint Committee (G-BA) and by the issuing of evidence search requests to the Institute for Quality and Efficiency in Health Care (IQWiG) by the Federal Ministry of Health (BMG) at the recommendation of the AWMF. Additionally, it must be ensured that guidelines are actually applied and followed in practice. To aid this process, various forms of evaluation and also strategies must be developed in cooperation with relevant stakeholders. This also includes setting out the content of the guidelines in concise, user-friendly form. Adherence to the guidelines can be ensured by putting in place the prerequisites for implementation of ABS programmes (such as quality indicators and information technology), strategies to optimise prescribing behaviour (such as ABS rounds and further and continuous training), and strategies for treatment optimisation (such as evaluation of anti-infective treatments).

Data on AMR and on antibiotic use in human medicine, and also the guideline catalogue should be regularly provided to the Commission on Anti-Infectives, Resistance and Therapy (ART) at the RKI. In this way, priorities can be set in guideline development and alignment. The ART draws up recommendations, setting out basic principles for diagnostics and antimicrobial treatments, especially for infections involving resistance pathogens. It also reports on appropriate conditions for and on obstacles to implementation of appropriate anti-infective treatment, and proposes practical solutions. The ART's role and area of responsibility are to be reviewed, made clearer and better aligned to actual requirements in the future.

When it comes to appropriate use of antibiotics, the availability of sufficiently qualified personnel also plays an important role. At the 124th Medical Assembly held in

2021, it was decided to introduce stand-alone specialist further training in “Internal Medicine and Infectiology” within the field of internal medicine in Germany. Additional further training in infectiology is also open to all physicians who have successfully completed further training in an area involving immediate patient care or in microbiology, virology and infectious disease epidemiology or in hygiene and environmental medicine. The new further training opportunities will help to promote infectiology expertise in human medicine.

By means of intensive further training programmes offered by the specialist associations, it was ensured that all “ABS Representatives” or “ABS Experts” possess a very good and current level of knowledge. Given the differing conditions and requirements in hospitals, care facilities and medical practices, the various models already in place must be reviewed and optimised where needed. To improve ABS implementation, efforts should be made to expand the further training opportunities available in both inpatient and outpatient care. This also calls for the expansion of a nationwide network of infectiology expertise and with it the expansion of further training opportunities and capacities, especially in paediatric and adolescent infectiology.

Pharmacists with specialist training in infectiology or ABS-trained clinical pharmacists are an integral component of multidisciplinary ABS teams in German hospitals and play an important role in ensuring the appropriate use of antibiotics.

Another key factor in ensuring appropriate use of antibiotics comprises regular reviews of how ABS is implemented. The monitoring authorities must thus possess the knowledge needed. Training measures must be introduced.

To bridge the gap in the meantime, innovative, data protection compliant telemedicine communications processes must also be developed which ensure that the infectiology expertise available in university hospitals is also made available to non-university hospitals in rural regions.

By promoting infectiology expertise, positive effects can be expected with regard to early detection and treatment of sepsis. This could help in achieving a long-term reduction in the high sepsis mortality rates in hospitals in Germany compared with those in countries with similarly well-developed healthcare systems. In the future, the Federal Government and the Länder must introduce suitable measures to ensure adequate staffing of medical facilities with doctors and pharmacists who are trained in infectiology.

Outpatient care accounts for approximately 85 percent of antibiotic prescriptions. It thus plays a significant role in promoting appropriate use of antibiotics. To be effective, therefore, structures and measures must take account of the specific needs and requirements in outpatient care. Among other things, this calls for guidelines covering relevant diseases in outpatient care, hygiene, diagnostics and treatment options, and monitoring of antibiotic use via a feedback mechanism specially devised for the outpatient sector. This would enable a comparison to be drawn between a physician’s own prescription behaviour and that of other representatives of the same specialist discipline, and indicate areas where changes can be made. The aim is to expand antibiotic use surveillance to take in the entire outpatient care sector and enable facility-specific feedback. A system which has already been tried and tested as part of a feasibility study is to be established at the RKI and implemented nationwide.

Based on the results of a number of research projects that looked at the prerequisites for promoting appropriate use of antibiotics in outpatient care, further measures are to be introduced and established for the longer term. In the course of that process, national and regional specificities must be taken into account. Although antibiotic use in Germany is low, broad-spectrum and reserve antibiotics are prescribed comparatively frequently, and regional differences are also evident in the frequency of antibiotic prescription and the antibiotics chosen. Outpatient ABS should be developed and established that takes account of the specificities of outpatient care. The specific needs of paediatric care must also be considered.

The measures in the inpatient and outpatient sectors should be interconnected to eliminate problems of overlapping and, for example, to make better use of the benefits of outpatient parenteral antibiotic treatment. In addition, efforts should be taken to establish a joint, web-based continuing training platform for doctors.

Antibiotics are also frequently used in residential care homes. Suitable measures are thus needed to promote their appropriate use in the provision of primary care.

In recent years, various unforeseeable events have highlighted the vulnerability of global supply chains to bottlenecks in delivery and shortfalls in supply. The strong focus on production sites of older, generic but medically indispensable antibiotics in Asia meant that the supply of antibiotics was exponentially affected. There is a growing risk that, in the future, delivery bottlenecks

could result in the need for greater use of broad-spectrum antibiotics, which in turn would negatively impact resistance developments and trends. Measures to minimise this risk, such as relocating production sites of essential antibiotics to the EU, must be evaluated and pursued.

A general trend can, however, be observed whereby approvals of 'older' antibiotics used in human medicine which are essential in treating bacterial infections are being withdrawn because it no longer pays to market those drugs. Strategies must thus be developed which can be used to combat this trend while still ensuring both the availability of those antibiotics and their use in guideline-compliant treatment.

3.2. Antibiotic use in veterinary medicine

Taking account of the knowledge gleaned from its evaluation, the antibiotics minimisation concept for livestock farms is being continuously further developed and expanded to include other animal categories and production types. The express aim of the antibiotics minimisation concept revised at the end of 2022 is to help further reduce the quantity of antibiotics used in animals by 50 % between 2018 and 2030, as set out in the European Commission's Grean Deal and Farm to Fork Strategy. The Federal Government thus continues to pursue the goal of reducing the use of antibiotics in veterinary medicine to the medically necessary minimum while safeguarding animal health and welfare.

In the cases of fluorochinolones, third and fourth generation cephalosporines and colistin, the aim is to further reduce the quantities used in veterinary medicine to the unavoidable minimum. This objective is served, for example, by the inclusion of a legally-defined weighting factor which, when veterinary medicinal products containing these active substances are used in food-producing animals, is included in the calculation of the treatment frequencies for food-producing animals and increases its value compared to other antibiotics that are less critical for the treatment of humans. This provides an important incentive for veterinarians and livestock keepers to largely refrain from using these substances. The use in food-producing animals of veterinary medicinal products for oral administration which contain the active substance colistin is to be further restricted by means of a new provision in the Ordinance on Veterinary In-house Dispensaries (Verordnung über tierärztliche Hausapotheken).

The component of 'monitoring' antibiotic use in further animal populations is established in the antibiotics minimisation concept. On the one hand, these are areas in which, based on previous experience, low to moderate use of antibiotics can be assumed (e.g. in fattening cattle over the age of 12 months) or where high resistance rates have not been observed so far. On the other, the use will be documented in small farms where animals and animal groups are kept, which fall under the provisions of the national antibiotics minimisation concept, but are not included in the benchmarking due to the low numbers of animals kept. Thus, as part of the BfR reporting, developments and trends in antibiotic use in these animal populations will also be recorded and subsequently evaluated in terms of the total quantity used and any changes made in substance selection. This will enable early recognition of a need to include further livestock farms in the antibiotics minimisation concept.

The Federal Veterinary Surgeons' Association (Bundestierärztekammer, BTK) guidelines on the prudent use of antibiotics summarise the status of current veterinary medical science on responsible use of antibiotics. The guidelines are regularly reviewed for their currentness and revised as needed. Advancing digitalisation also provides an opportunity to develop easily accessible online tools which can assist the use of the guidelines in decisions on treating individual animals and livestock herds.

Linking slaughterhouse findings with animal-specific data from livestock farms, with laboratory diagnostics data (including data from susceptibility tests) and data from veterinary treatments (especially antibiotics) is a valuable tool in assessing animal health in livestock herds. It assists animal keepers in their decision-making regarding farm management, their own on-farm controls and adopting good farming practice. Linking of this data also gives the treating veterinarian important information to aid their decisions as regards treatment and adapting prevention and treatment plans. This also includes advising the farmer with the aim of improving general animal health and reducing antibiotic use. If the competent authority is also given access to this data, it could improve both the efficiency of and benefits to be had from official controls for authorities, animal keepers and veterinarians, particularly in connection with the antibiotics minimisation concept.

3.3. Laboratory diagnostics

Professional microbiological laboratory diagnostics equipped with adequate technology is essential in identifying infection-causing bacteria and their resistance traits. Knowledge on pathogens and antibiotic resistance enables targeted (as opposed to calculated) antimicrobial treatment. It serves as the basis for responsible antibiotic use. In addition to preventing resistance selection and

undesired side-effects, improved, targeted treatment in human medicine will also reduce the lethality of sepsis.

Laboratory diagnostics is also indispensable in surveillance and monitoring. Methodological gaps are to be closed yet further, existing methods enhanced and, in areas where methods are still lacking, evaluation criteria developed to enable their integration into routine diagnostics. Through the use of suitable instruments, it must also be ensured that rapid microbiological diagnostics are made widely available to healthcare institutions. This applies in particular to the further development of point of care testing (POCT), which can greatly assist rational antibiotic treatment in outpatient human medicine.

Digitalisation makes it possible to conduct centralised evaluations of the results of pathogen identification tests and antibiograms performed in routine diagnostics. This applies at the level of hospital, care facility, medical practice and livestock herd, as well as at regional and national level.

Therapeutic drug monitoring (TDM) plays an important role in targeted management of antibiotic treatment (preventing toxicity through overdosage and development of resistances through underdosage). Antibiotic level determination should thus be available to in-house hospital laboratory diagnostics for the purpose of treatment monitoring.

Collaboration between medical microbiology and clinical departments should also be further intensified to make the new molecular biological opportunities for improved treatments accessible in practice.

Action Area 4: Communication and Cooperation

This action area covers dissemination of knowledge to create and maintain fact-based public awareness of infections, the link between non-targeted antibiotic treatment and AMR, and the relationship between infectious disease and the development of sepsis as a complication. It also covers knowledge dissemination in and by specialist groups, including in medical training – primarily further and continuing training. Added to this is exchange between stakeholders in all participating sectors and interest groups. In addition to new findings from research and development, knowledge gaps and issues are also to be discussed, the aim being to create incentives for collaborative and transnational research with a focus on practical application. To ensure successful implementation of the Antimicrobial Resistance Strategy, cooperation between all stakeholders is of vast importance.

4.1. Cooperation and the One Health approach

At Federal Government level, the Interministerial Working Group on Antimicrobial Resistance (IMAG AMR) is responsible for cross-ministerial coordination, alignment and expansion of the AMR Strategy. The IMAG AMR comprises the ministries BMG, BMEL, BMBF, BMUV and BMZ, as well as authorities in those ministries' remits. Over time, the group of participants has been extended in the face of additional needs, for example in relation to the environment, the role of plants in addressing AMR, and research and development of new antibiotics. Cooperation between the members of the IMAG AMR has proven valuable and is to be continued. Their work will place even greater focus on coordinating DART 2030 measures and monitoring their implementation. Exchange is also to take place with the respective Länder-specific committees.

In a range of studies, new molecular methodologies have been used to investigate the roles played by human and veterinary medicine and by agriculture in the emergence and spread of AMR. In those studies, it became clear that the exchange of resistant pathogens between these three areas occurred less frequently than had previously been assumed, that the interrelationships are extremely complex and that each area has its own resistance problems. But in many cases, the interrelationships between the three areas remain characterised by insufficient insight into each other's needs. To improve this situation, a format for dialogue and exchange is to be developed and introduced. Because not only in state-run facilities, but also for doctors practicing in human and veterinary medicine, and the respective representative associations, communication as equal partners along the lines of "talking to rather than about each other" can foster understanding for the various activities, relationships and problems, eliminate prejudices and close knowledge gaps.

4.2. Specialist groups

In diverse projects, studies have looked at the measures deemed suitable in reducing inappropriate use of antibiotics in outpatient human medicine. As part of that work, informational material was developed for medical and pharmaceutical staff, and for patients. This is to be made readily available to a broad (specialist) public and kept current as part of the process. An assessment is also to be made as to whether the existing material should be supplemented with additional information. Along with content focusing on specific settings, such as patient-doctor consultations, informational material can also be useful which illustrates the interactions between human and veterinary medicine, agriculture and the environment in the emergence and spread of resistance, fostering mutual understanding as a result.

The development of additional materials, publications and training content should thus involve the respective specialist groups. These are key players in the transfer of knowledge to clinical inpatient and outpatient care. Communication should also be intensified between the various organ-specific specialist disciplines and infectiology.

With regard to 'older' antibiotics, activities have been pursued at EU level for a number of years to reevaluate and revise specialist information, especially where approved indications and dosages are concerned. The specialist information also describes the resistance situation in Germany concerning a range of approved

antibiotics, the aim being to simplify the choice of suitable antibiotics for calculated treatment in human medicine. The combination of current, reliable resistance data on antibiotics for frequent infectious diseases – and improved, digital access to that data – is intended to assist in shifting prescription behaviour among doctors towards more rational use of antibiotics. An assessment is thus needed as to how the current national resistance situation can be portrayed in the specialist information for all antibiotics and how that information can be used efficiently and effectively by prescribing physicians.

In "Regional MDRO Networks" coordinated by the public health administration, hospitals, rehabilitation centres, residential care homes and private medical practices collaborate with the aim of containing the further spread of multidrug-resistant pathogens by means of a coordinated regional approach. The networks also serve communication between the various stakeholders. Regional networks have been established in many parts of Germany. Given the central role they can play in dealing with MDRO and the use of antibiotics in a given region, their expansion should be further advanced. The Federal Government and the Länder must thus agree on measures to support that process. This will require clarification as to whether the regional networks should be expanded to take in additional stakeholders, such as specialised pharmacists, to ensure these goals are achieved.

Early detection of sepsis symptoms by medical and nursing staff at all levels of patient care, for example in rescue coordination centres and in outpatient and inpatient treatment of people requiring care, should be improved through the provision of materials for informational purposes and training. In the medium term, knowledge concerning inpatient care in Germany will be supplied by the Federal Joint Committee (G-BA) in the course of its consultations on the data-supported quality assurance process for the diagnosis, treatment and follow-up care of sepsis.

In light of the knowledge that animal keepers can significantly influence animal health and thus the use of antibiotics in their animals, communication and cooperation with this group has gained in importance. In this connection, the new EU Animal Health Law assigns veterinarians a communicative and cooperative role towards animal keepers. Through the provision of modern informational materials and communication training tools, veterinarians can be assisted in their mandate to sensitise animal keepers to the topic of AMR. Such materials can also be used in further training for animal keepers and veterinarians. But in addition to livestock keepers, pet owners must also be better reached, educated and informed about how they influence both their animals' health and the development and spread of AMR. The tried and tested communication resources and channels used by the Federal Centre for Health Education (BzgA) could be a constructive way of reaching private animal keepers. Improved communication on the successes achieved with existing strategies to reduce the use of antibiotics can promote the idea among animal keepers.

4.3. General public

Disseminating information to the general public about the treatment of infectious disease and appropriate use of antibiotics is to be improved. Ways in which these topics can be addressed include conducting media information campaigns, developing educational content/materials and disseminating information through doctors in private practices.

Germany's comparatively high number of sepsis-related deaths are due in part to knowledge gaps among medical staff and the general public about the early symptoms of sepsis. This can result in late detection and treatment of a sepsis. There are especially large knowledge gaps among people in general as regards infections and how sepsis develops, its long-term consequences and the importance of preventing infection by means of vaccinations and following basic hygiene rules. For this reason, people's health literacy, skills and sepsis awareness must be improved.

Developing communication strategies to publish the findings of surveillance and monitoring serves in providing informative scientific content for lay audiences and is directed at fostering better public awareness and understanding of such information.

4.4. Knowledge dissemination

Target group-appropriate dissemination of knowledge and information helps farmers, animal keepers, veterinarians, people working in the food processing industry, consumers, medical staff in human medicine, patients and their families to adopt the right behaviours in their respective environments and fields. When developing and providing modern, target group-appropriate informational material, allowance must also be made for changes in media use arising in the course of digitalisation. In addition to the target audience, people working in supervision, media representatives and the general public all benefit from targeted preparation and events-driven dissemination of information on the topics of antibiotics, AMR and hygiene.

When disseminating knowledge, both content and the chosen channels of communication must focus on the target group. Special needs should also be considered, such as when addressing risk groups, children and adolescents, and people who are visually impaired. One particularly important target group comprises people who are socially disadvantaged and elderly people who live alone. Evidence-based, lay person-friendly tools for use in infectiological self-assessment (e.g. fact sheets and a sepsis checklist) can improve people's health literacy concerning infections and thus result by way of self-empowerment in early and adequate treatment of emergency cases of infectious disease (e.g. meningitis and sepsis).

A system of disseminators can be used to enable broad-based sharing of specialist and target group-appropriate information, thereby informing those affected about changes in legal provisions as well as new requirements in a timely way.

Digital solutions can support the appropriate use of antibiotics (see Action Area 3). Among other things, this involves providing user-friendly access to current guidelines, national resistance data, data on antibiotic use and the resulting recommendations for calculated and targeted use of approved antibiotics via a dedicated, single-source website. Appropriate online services are to be further expanded at various levels.

When disseminating the results of resistance surveillance and monitoring, the quantities of antibiotics sold and used in veterinary medicine, and the use of antibiotics in human medicine, new forms of communication such as dashboards and interactive applications are also to be considered. Social media channels should also be used as a source of communication in order to reach the broadest possible audience.

Action Area 5: European and international Cooperation

AMR is a multidimensional global challenge that does not stop at borders. It is thus one which the international community must tackle together in a coordinated effort using the One Health approach. Global trade and travel result in a closely knit network encompassing all regions of the world. Resistances that develop in one place can lead to the global spread of pathogens that no longer respond to treatment. AMR poses a global health risk for humans and animals, and is a source of great pressure as regards the global economy and the security of food supply.

5.1. Cooperation to build capacity

Structurally weak regions are especially vulnerable to the risks of AMR and must be supported through the development of regulatory and monitoring systems, as well as improved national AMR prevention effort. Poverty also promotes the emergence and spread of AMR. In these structurally weak countries and regions, people living in poverty, marginalised groups, women and children are all greatly at risk from AMR. These groups are at risk from a high prevalence of infectious disease, inadequate access to high-quality antibiotics and healthcare facilities, and a lack of clean water and sanitation.

In terms of population, the largest share of antibiotics is used in the global North, while the greatest exposure to disease caused by antibiotic-resistant pathogens occurs in the global South – especially in Sub-Saharan Africa and South Asia. The quadripartite organisations – the World Health Organization (WHO), the World Organization for Animal Health (WOAH), the UN Food and Agriculture Organization (FAO) and the UN Development Programme (UNDP) – are key partners in the provision of support to other countries, and they collaborate closely as part of the One Health approach. In the form of the WHO Collaborating Centre for Antibiotic Resistance, Consumption and Healthcare-Associated Infections at the RKI, a structure is in place which draws on operational experience from collaboration in this particular area of AMR and is able to take on a coordinating role.

To contain the emergence and spread of AMR around the world, international coordination of targets and measures is needed. Strengthening healthcare systems (human and veterinary medicine) and preventing infection in humans, animals and plants are of key importance. The overarching objective of all associated measures is to maintain the efficacy of antimicrobial substances, provide sustainable and equitable access to them to ensure their responsible and appropriate use in human and veterinary medicine, and in agriculture as a contribution to achieving the SDGs, and to prevent the emergence of infection by means of improved hygiene.

Priority areas of intervention and focus in the course of Germany's international cooperation at both technical (including by higher federal authorities) and financial level are described below.

In the prevention of infectious disease, emphasis is placed on improving water and sanitation (WASH) as well as hygiene and infection prevention and control (IPC) in hospitals and other medical facilities. Vaccination programmes for both humans and animals can also play an important role. In animal husbandry, access to animal healthcare services, optimisation of husbandry conditions and feeding, and also biosafety are further pillars in the prevention of infectious disease. These are the most important instruments along with measures to underpin legal requirements and their enforcement.

To ensure the supply of essential medicines, investments must be made in building local capacities for vaccine and medicine production. It is thus important that environmental legislation be strengthened as regards consideration of AMR aspects in order to avoid localised development of resistance and its spread into the environment at production sites (e.g. in wastewater). With the help of social security systems, equitable access to healthcare facilities and medication is to be enabled, especially for women and children. Poor quality antimicrobial agents (counterfeit, wrongly labelled, expired or incorrectly stored) foster the emergence of resistances and pose a risk to the provision of effective treatment. This is why it is necessary to implement

systems to promote the standards of Good Manufacturing Practice (GMP) in production along with monitoring and regulation of supply chains in order to detect, trace and eliminate the occurrence of poor quality or counterfeit antimicrobials. In many places, antibiotics and other antimicrobial medicines are sold over-the-counter. Given this situation, medical, veterinary and pharmaceutical staff must be trained in appropriate use and dispensing of antibiotics, and the legal prerequisites created for restrictive dispensing.

To enable diagnostic and sensitivity testing, the establishment and expansion of laboratories along with training of laboratory personnel must be advanced, including beyond large towns and cities. Secure supply chains for diagnostic materials must also be promoted to facilitate local production. Data collected in the field provides the basis for appropriate use of antimicrobial substances in patient care and for AMR surveillance and monitoring. Existing surveillance structures are often only of a temporary nature, financed using project funds and limited to larger conurbations in many cases. They thus provide an inadequate picture of the resistance situation and the AMR load. Data on resistance development and on the use and sale of antimicrobial agents could be used locally and regionally in treatment management and for global level reporting. New surveillance systems must be able to collect both nationwide and cross-sectoral data. In line with the One Health approach, resistance data from human medicine, veterinary medicine, the environmental sector and food production must be integrated. The WHO Tricycle Protocol and Tripartite Integrated Surveillance System (TISSA) serve as examples. Surveillance and monitoring of wastewater also harbours vast potential for the collection of resistance data, especially in regions where no hospital laboratories exist.

At national level, coordinating structures that collate data on AMR and antibiotic use from various sectors, and then evaluate and forward it to regional and global systems (e.g. GLASS) are vital. To develop such structures, strengthening public health institutes and veterinary services, and developing a digital infrastructure are of huge importance.

5.2. Cooperation with organisations, committees and working groups

The work performed by international organisations, committees and platforms, including the definitions and standards they develop, is of key importance in combating AMR – also in Germany.

Over the past few years – among other things based on the recommendations of the Interagency Coordination Group (IACG) issued in 2019 – a range of, mostly intersectoral, international AMR structures and initiatives have been established and others are under development. There are also various working groups and projects in place at global level. Germany will continue its involvement and participation, and closely monitor international processes associated with AMR. This makes it possible to contribute German experience and standpoints, learn from others and share best-practice examples.

When it comes to global trade in animals, animal products and also food and feed, international standards are of vast importance – especially those of the WOAH and the Codex Alimentarius Commission (CAC), a joint instrument of the FAO and WHO. Through involvement in the quadripartite working groups and other international organisations, collaboration with the EU partners pursues the goal of achieving a global ban on the use of antibiotics to improve production and as a routine prophylaxis against infection. Also together with its European partners, Germany seeks to have language to this effect agreed in G20 and G7 summit declarations and ministerial statements.

In recent years, Germany has worked to ensure that the G7 and the G20 address AMR as a priority topic. For example, the Global AMR Research and Development (R&D) Hub was established following the G20 consultations under German presidency in 2017. The Hub is effectively a partnership of countries, non-governmental donor organisations and intergovernmental organisations. It serves the global coordination of research and development (R&D) priorities, funding instruments and incentive mechanisms related to AMR.

Yet further commitments on combating AMR and sepsis were secured under Germany's G7 presidency in 2022. These include the continuation of research and development of new, urgently needed antibiotics and improvements in the appropriate use of antibiotics and in the regulatory and economic conditions needed to secure the market for both existing and new antibiotics in the longer term. This calls, among other things, for national regulations which align with a common international framework. The Federal Government will continue to actively advance talks in the respective international forums, notably the G7 and G20.

Germany also continues to be involved in the various EU-level working groups and projects around AMR. This gives

the country's experts the opportunity to participate in overarching design of surveillance and monitoring systems, and in the analysis and interpretation of data, address issues related to AMR, nosocomial infections and infections that develop outside the healthcare system, and benefit from related networks.

Action Area 6: Research and Development

Research and innovation can contribute significantly to reducing AMR. This makes it necessary to support all relevant research areas in a One Health approach – from basic research to clinical research, healthcare research, research on public health issues, environmental and climate research, logistics research, and collaborative research with the health and food sectors, agriculture, the building and construction sector, the healthcare sector and media and communications. In all phases of research and development, an understanding must be reached regarding global needs and actual clinical practice, and these are to be given adequate consideration. Thus, in the course of associated projects, researchers, clinicians and stakeholders from practice are to be brought together via networks.

6.1. One Health research

One Health research aims to generate knowledge on the interdependence of human, animal and environmental health, and use it to derive and test measures for use in prevention and intervention. To effectively prevent the spread of AMR, the underlying mechanisms must be better understood. Among other things, this calls for meaningful data and mathematical models which can be used to describe the emergence and spread of bacteria and resistance-coding genetic elements. To create the conditions needed in devising such models, a comprehensive data repository must be made available in each sector. In addition, molecular mechanisms and the risk factors for traditional transmission events, transmission frequencies, and the dynamics involved in the spread of resistance between humans, animals and the environment must all be understood. Substantial findings are already available regarding the role played by the water cycle in the release and spread of antibiotic residues, resistant bacteria and resistant genes. This is where wastewater treatment plays a central role. Innovative and in some cases decentralised treatment methods harbour potential for the control of critical releases at source. The importance of environmental factors such as biofilms and the impact of the potential release of antibiotics and resistant microorganisms into soil via wastewater and slurry are not yet adequately understood and – along with measures to reduce the environmental release of antibiotics and resistances – require further development and research.

The aim of expanding One Health research at national, European and international level is to address these and many other research questions. At national level, research on open questions concerning infection epidemiology, molecular mechanisms of infection and pathogenesis, and pathogen-host-environment interactions (among other things) is to be conducted at two newly-established institutes – the Helmholtz Institute for One Health (HIOH) and the Institute of International Animal Health/One Health (IITG) at the Friedrich-Loeffler-Institute (FLI). The HIOH was founded in April 2022 by the Helmholtz Center for Infection Research (HZI) in conjunction with the University of Greifswald, Greifswald University Medicine and the FLI as founding partners.

The HZI and the German Centre for Infection Research (DZIF), which is funded by the Federal Government and the respective host Länder, play a focal role as Germany's central institutions of scientific research on infection. They provide key substantive and structural impetus for further development of the research area and for strengthening translational research.

Initial and further/continued training of a new generation of infection researchers also plays a vital role. Together with the host Länder, the Federal Governmentsupports the DZIF with the DZIF Academy, a comprehensive training and career development programme for students and graduates, and for scientists in clinical and translational research.

At international level, the European Partnership on One Health AMR enables an integrated research approach that covers the full pathogen spectrum, from bacteria to viruses, and from fungi to parasitic infections. The Partnership will build on existing initiatives such as the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) and its mandate will be to assist and promote the European One Health Action Plan against Antimicrobial Resistance. In terms of content and focus, this European Partnership aims to generate knowledge

on AMR, develop new treatments, vaccines and diagnostics, and devise innovative economic models.

In the area of animal health at international level, the European Partnership on Animal Health and Welfare will use both research and integrative activities to improve the status of knowledge on monitoring and intervention measures, diagnostics and alternatives treatment methods, and also improve animal husbandry, thereby supplementing and enhancing knowledge generated by the European Partnership on One Health AMR.

6.2. New diagnostics

In order to slow down the further spread of AMR new diagnostics tools are urgently needed which accelerate pathogen diagnostics. The prerequisite for targeted treatment is an accurate diagnosis of the infectious pathogen involved and its behavioural resistance. In recent years, a strong upward trend has been seen in point of care testing (POCT) and this now plays an increasing role in outpatient care. Molecular POCT processes bring significant time-saving benefits as there are no transport times involved. They are, however, limited to predefined purposes and known resistances, and cannot replace the use of pathogen cultures for comprehensive pathogen characterisation. These approaches and the linking of POCT and generic diagnostics must be further researched, developed and refined for use as coordinated diagnostic strategies, and then marketed and ultimately transferred into routine medical care. To promote the development of new diagnostics procedures, licensing and approval processes and also reimbursement models can provide important development incentives.

For initial diagnosis, rapid and easy-to-use diagnostics tools (ideally at the point of care) are needed which are able to differentiate between a bacterial and a viral infection, identify the pathogen involved and indicate existing, molecular-detectable, treatment-relevant resistances.

6.3. New antibiotics, alternatives to antibiotic treatments and vaccines

One of the focal areas of future research at national and international level will involve the development of novel antibiotics, other antimicrobial medicines and antimicrobial processes which, for example, address the bacterial pathogens prioritised by the WHO and for which there is a particularly great medical need. The aim here will be to fill the pipeline with innovative drug candidates which can ideally be clinically tested. Development of suitable drug candidates in late pre-clinical and early clinical phases will also be promoted in a targeted effort with the aim of subsequently finding an industry partner to develop them further. Collaboration between science and industry is to be sustained and expanded to strengthen translation and introduce new drugs into routine practice at a faster rate.

In addition to national funding measures for research institutes and small and medium-sized businesses (SMEs) in the medical biotechnology sectors, international initiatives – such as the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) and the Global Antibiotic Research & Development Partnership (GARDP) – are to be further pursued which drive the research and development of new antibiotics and alternative medicines and treatments. Complementary to this process, the international CARB-X and GARDP initiatives, which Germany also supports, serve to advance the development of new antibiotics from early pre-clinical research through to clinical development, approval and provision.

Successful development of innovative treatments requires scientific, regulatory and economic expertise. This is why both German approval authorities, the Federal Institute for Drugs and Medical Devices (BfArM) and the Paul-Ehrlich-Institute (PEI), assist the DZIF in clarifying issues of a regulatory and specialist/technical nature.

Development of natural substance-based antibiotics with innovative mechanisms of action is to be further intensified and the pipeline of new substances is to be further expanded.

Development of alternative and immune-modulatory treatment processes (such as phages and non-coding RNAs) represents a key strategic approach in the treatment of bacterial infections and sepsis. In basic research, a range of alternatives are already being explored, although their clinical efficacy has yet to be proven in many cases. Only when that proof has been provided companies will be able to develop new products up to the level of market maturity. In the case of promising candidates, their clinical efficacy is to be proven – both jointly with industrial partners and with regulatory advice from the BfArM, thereby paving the way for their use in inpatient and outpatient care.

Measures such as the development of bacteriophages for use as alternative forms of treatment, in the decontamination of surfaces and germ reduction in food, and also in creating the regulatory conditions needed for their future use are of interest in the human medicine, veterinary medicine, agriculture and food safety sectors. These measures involve the analysis of potential uses of

substances which, in addition to an antimicrobial effect, specifically address the underlying resistance mechanisms in AMR. Adopting this approach could foster the development of alternative treatment processes which make the range of established antibiotics usable again in clinical practice. Also, in the future, when developing vaccines against multiresistant pathogens, greater use is to be made of new technologies such as messenger RNA (mRNA), protective microbiota components and viral vectors.

As an alternative to antibiotics, known medicines which are currently used for other indications, such as antibacterial active monoclonal antibodies or immunoglobulins, can also be used – especially in prevention.

Stool transplants and synthetic microbiomes also harbour potential. Innovation in this area rests on the concept of using natural resilience and microbiome resistance as a form of treatment in which the use of antibiotics is reduced.

6.4. Prevention and public health

To prevent the spread of resistances it is important to understand the underlying economic, social and behavioural factors involved. For example, preventive design of workplaces and work processes must be scientifically monitored and evaluated with regard to ways in which pathogens are spread. To ensure preventive measures are adhered to, improving people's health literacy and skills is of central importance (see Action Area 4: Communication and Cooperation). This means, for example, developing and scientifically evaluating channels to access hard-to-reach groups.

To secure the financial feasibility of the healthcare system, accompanying health economics studies on public health and hygiene measures to combat AMR play an important role.

6.5. Further research questions

To track the use of antibiotics at the various levels of outpatient care, identify influencing factors, and sustainably implement and evaluate measures taken, point-of-care research is needed which looks at the respective conditions in primary care, including in (residential) care facilities, specialist outpatient care and dental care, and enables targeted measures to be taken.

Further research and development is required on many issues concerning antibiotics and AMR in the areas of agriculture, animal husbandry, veterinary medicine and food chain under the remit of BMEL that are mentioned in other action areas. Animal vaccines can, for example, play a key role in preventing infection, while innovations in slaughtering and butchering processes can reduce both the release and the spread of resistance determinants via meat production and processing.

To foster practical use of new knowledge and findings, and of known measures which are effective but little used, targeted investigation is required as to the communication measures needed to facilitate and promote the transition from knowledge into practice.

Conclusion

This AMR Strategy sets out the areas in which measures are to be introduced in the course of the DART 2030 lifecycle to achieve the overarching goal of maintaining effective forms of treatment for bacterial infections. In a second step, those measures will be further defined and set out in a dedicated action plan. They are then to be regularly reviewed, adapted and aligned as needed.

Combating AMR is a task in which everyone must play their part, from members of the general public to medical and pharmaceutical personnel working in human and veterinary medicine, from the agricultural sector to stakeholders along the entire food value creation chain, from science and research to product development and the legislator. The aim of DART 2030 is to collaborate with relevant stakeholders to create the structures and conditions needed at local level to facilitate responsible use of antibiotics and effective forms of treatment for bacterial infections.

The key action areas set out in DART 2030 build on the findings achieved with its predecessor, DART 2020. They focus on improving the availability of data through surveillance and monitoring, enhancing infection prevention, promoting appropriate use of antibiotics, improving communication and collaboration at all levels, building personnel capacities, developing more rapid diagnostic methods, innovative substances and treatment approaches, and conducting research into vaccines to prevent infections caused by resistant pathogens. Only through a combination of a range of measures and the willingness for collaboration at all decision-making levels and across all disciplines and sectors, can long-term success be achieved. Application of the One Health approach at all times is of central importance. Even though all of the action areas address human and veterinary medicine, agriculture and the environment, different approaches and their resulting measures are nevertheless needed in each area due to the differing requirements that must be met, such as those at EU level.

The AMR burden is greater in resource-poor regions due to serious gaps in data on AMR, inadequate access to vital antibiotics, and poverty-driven interactions which further promote the emergence and spread of AMR. In the coming years, therefore, the Federal Government will use a range of strategies and measures to address the problem of increasing AMR at many different levels – from regional to global – and take efforts to ensure that the issue remains on the global agenda.

Executive Summary

Antimicrobial resistance (AMR) is increasing on a global scale and poses an ever-greater challenge when treating patients in human and veterinary medicine. Its impact means that only a few or in some cases no treatment options are available in treating bacterial infections that were previously treated with ease.

Preventing the further spread of AMR calls for a package of measures which are to be implemented in a range of different areas. The Global Action Plan on Antimicrobial Resistance adopted by the World Health Assembly in 2015 calls upon member states to devise their own national action plans. Taking account of the goals set out in the Global Action Plan, these national action plans are to contain measures which are aligned to the actual situation in each country.

The first German Antimicrobial Resistance Strategy (DART) was adopted by the Federal Government back in 2008 and its successor strategy, DART 2020, followed in 2015. The approaches and measures used must nonetheless be consistently further developed and aligned to changing conditions and needs. This is where DART 2030 comes in, the aim being to further address the outcomes of its predecessor strategy, DART 2020.

In DART 2030, the major focus areas of DART 2020 will be retained: expanding the surveillance and monitoring systems on AMR and antibiotic use, improving infection prevention and promoting appropriate use of antibiotics, raising public awareness, facilitating the acquisition of necessary knowledge among medical professionals, and intensifying R&D support – at all times taking account of the One Health approach to human, animal and environmental health. This report sets out the strategic goals and focuses in six action areas for combating AMR at both national level and through international collaboration by the end of the DART 2030 lifecycle. Specific measures will follow as part of a future action plan to be published at a later date.

1. Prevention

This action area takes in the prevention of infectious diseases requiring treatment using infection protection and control measures (as understood in their broadest sense) to reduce the use of antibiotics. Prevention includes, for example, vaccinations and containing the emergence and spread of AMR in and via the environment (e.g. through wastewater, waterbodies and soil), and preventing the spread of AMR along the food chain.

2. Surveillance and Monitoring

Surveillance and monitoring of antibiotic use and AMR are necessary to determine the situation in all healthcare sectors in both human and veterinary medicine, detect changes, processes and trends, derive targeted measures and measure their effects. As part of this process, the methods used, planning of targeted monitoring activities and both the evaluation and reporting of results are all subject to continuous development. The systems already in place are to be continued, further developed and enhanced. The long-term goal is to establish an integrated surveillance and monitoring system with data on AMR and the use of antibiotics in human and veterinary medicine and in the environment, enabling that data to be analysed together.

3. Appropriate Use of Antibiotics including Laboratory Diagnostics

Antibiotic stewardship (ABS) is designed to ensure both indication-appropriate use of antibiotics and the best possible antibiotic treatment, and help reduce or prevent increasing development of resistances. ABS takes in reliable diagnostics, selection of a suitable antibiotic and its fastest-possible use, as well as recommendations on treatment duration, antibiotic dosage, dosage form and reevaluation. The aim is to establish responsible use and handling of antibiotics by general practitioners, dentists and veterinarians, including regular reflection on their own actions and behaviours, and make these standard practice.

4. Communication and Cooperation

Through the dissemination of corresponding knowledge, the aim is to raise public awareness to infections, the link between non-targeted antibiotic treatment and AMR, and the relationship between infectious disease and the development of sepsis as a complication. It also covers knowledge dissemination in and by specialist groups, including in medical training – primarily further and continuing training. Added to this is exchange between stakeholders in all participating sectors and interest groups. In addition to new findings from research and development, knowledge gaps and specific issues are also to be discussed to create incentives for collaborative and transnational research with a focus on practical application.

5. Cooperation in the EU and Beyond

AMR is a multidimensional global challenge that does not stop at borders. It is thus one which the international community must tackle together in a coordinated effort using the One Health approach. Global trade and travel result in a closely knit network encompassing all regions of the world. Resistances that develop in one place can lead to the global spread of pathogens that no longer respond to treatment. AMR poses a global health risk for humans and animals, and is a source of great pressure as regards the global economy and the security of food supply. To contain the emergence and spread of AMR on a global scale, international coordination of targets and measures is needed. Both cooperation in capacity building efforts and also collaboration with international organisations, committees and working groups are to be intensified and supported.

6. Research and Development

Research and innovation can contribute significantly in reducing AMR. This makes it necessary to support all relevant research areas in a One Health approach – from basic research to clinical research, healthcare research, research on public health issues, environmental and climate research, logistics research, collaborative research with the health, food, agriculture, building and construction, and healthcare sectors, as well as media and communications. In all research and development phases, knowledge and understanding of global needs and actual clinical practice are to be generated and taken into account.

List of Abbreviations

ABS	Antibiotic Stewardship
AMR	Antimicrobial Resistance
ARS	Antibiotic Resistance Surveillance
ART	Commission on Anti-Infectives, Resistance and Therapy
ARVIA	Antibiotika-Resistenz und -Verbrauch – integrierte Analyse (Integrated Antibiotic Resistance and Consumption Analysis)
AVS	Antibiotika-Verbrauchs-Surveillance (Antimicrobial Use Surveillance)
AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (Association of the Scientific Medical Societies in Germany)
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices)
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
BMBF	Bundesministerium für Bildung und Forschung (Federal Ministry of Education and Research)
BMEL	Bundesministerium für Ernährung und Landwirtschaft (Federal Ministry of Food and Agriculture)
BMG	Bundesministerium für Gesundheit (Federal Ministry of Health)
BMUV	Bundesministerium für Umwelt, Naturschutz, nukleare Sicherheit und Verbraucherschutz (Federal Ministry for the Environment, Nature Conservation, Nuclear Safety and Consumer Protection)
BMZ	Bundesministerium für wirtschaftliche Zusammenarbeit und Entwicklung (Federal Ministry for Economic Cooperation and Development)
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (Federal Office of Consumer Protection and Food Safety)
CAC	Codex Alimentarius Commission
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CL	Consultant Laboratory
DART	Deutsche Antibiotika-Resistenz-Strategie (German Antimicrobial Resistance Strategy)
DEMIS	Deutsches Elektronisches Melde- und Informationssystem für den Infektionsschutz (German Electronic Reporting and Information System for Infection Protection)
DZIF	German Center for Infection Research
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority

ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended Spectrum β-Lactamase
EU	European Union
R&D	Research and Development
FAO	Food and Agriculture Organization of the United Nations
FLI	Friedrich-Loeffler-Institute
G20	Group of Twenty
G7	Group of Seven
GARDP	Global Antibiotic Research & Development Partnership
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GMP	Good Manufacturing Procedures
HIOH	Helmholtz Institute for One Health
HIRI	Helmholtz Institute for RNA-based Infection Research
HZI	Helmholtz Center for Infection Research
IACG	Interagency Coordination Group
IfSG	Infektionsschutzgesetz (Protection Against Infection Act)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
IITG	Institut für Internationale Tiergesundheit/One Health (Institute of International Animal Health/One Health)
IMAG	Interministerielle Arbeitsgruppe (Interministerial Working Group)
IPC	Infection prevention and control
JMU	Julius-Maximilians-Universität of Würzburg
JPIAMR	Joint Programming Initiative on AMR
KRINKO	Kommission für Krankenhaushygiene und Infektionsprävention (Commission for Hospital Hygiene and Infection Prevention)
MDRO	Multidrug-resistant organisms
(m)RNA	Messenger ribonucleic acid
MRSA	Methicillin-resistant *Staphylococcus aureus*
NRC	National Reference Centre
PEI	Paul-Ehrlich-Institute
POCT	Point of Care Test
R&D	Research & Development
RKI	Robert Koch Institute
SARS-CoV-2	Severe acute respiratory syndrome coronavirus type 2
SDGs	Sustainable Development Goals
SGB V	Sozialgesetzbuch V (Social Code Book V)
SMEs	Small and Medium-Sized Enterprises

TDM	Therapeutic Drug Monitoring
TISSA	Tripartite Integrated Surveillance System
UNEP	UN Environment Programme
WASH	Water, Sanitation, Hygiene
WHO	World Health Organization
WOAH	World Organization for Animal Health

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