The
Federal Government

DART 2020

Fighting antibiotic resistance for the good of both humans and animals

DART 2020

With many infectious diseases, the health of humans and animals is very closely interwoven. Animals and people are often infected by the same pathogens, treated with the same antibiotics and thus have a mutual influence on the problems of resistance.

In order to protect the health of people and animals and to maintain the effectivity of antibiotics, cooperation between all those responsible across all sectors is essential. Only together can we successfully curb the development and spread of resistance to antibiotics. The increase in the number of bacterial pathogens that have become less susceptible or even completely resistant to antibiotics has become a major challenge worldwide. This affects human and veterinary medicine in equal measure. For the patients, this often means longer treatment times and additional stress caused by delays in the healing of infections, or complete failure of the infection to heal, often with fatal consequences.

In Germany, each year between 400,000 and 600,000 people become infected with pathogens in connection with inpatient medical treatment, and 10,000 to 15,000 die. Around a third of these infections could be avoided if suitable measures were taken. Resistant pathogens play a particularly important role here, since the treatment options are limited. It is not only the incorrect use of antibiotics in human and veterinary medicine that accelerates the development of resistance. Inadequate hygiene measures and, not least, commerce and tourism also help to spread resistant pathogens. Our common objective must be to prevent avoidable infections.

With the German Antimicrobial Resistance Strategy (DART), the German Federal Government presented a concept in 2008, which was subsequently implemented, aimed at reducing the further development and spread of antibiotic resistance. DART contains a number of measures for recognising, averting, and combatting antibiotic resistance in Germany.

This initiative has achieved a number of things. Many changes in the law, such as the amendment to the 2011 Infection Protection Act and the 2013 Medicinal Products Act, have made it possible to implement strategies and develop instruments. Cooperation between various groups and institutions that have each recognised their responsibility and made their contribution, combined with in-depth discussions, have heightened awareness of the problem amongst health professionals, those with political responsibilities, and the population at large.

Even if some initial successes are becoming apparent, we must increase our efforts and consistently further develop and expand the concepts and measures applied. The current situation shows that the fight against antibiotic resistance is still not being tackled with the necessary urgency and that awareness of the problem in various areas still needs to be improved. The revised DART will help here. The new focus has been developed in collaboration with all the relevant stakeholders.

We would like to thank everyone involved for the progress achieved to date in implementing and further developing DART. Close cooperation with all those responsible will also be essential in the future if we are to implement DART together. The Federal Government controls this process. We will be approaching the stakeholders in this.

In addition, the Federal Government has successfully campaigned for the development of a Global Action Plan for the Containment of Antibiotic Resistance by the World Health Organization. A central element of the Global Action Plan is the preparation of National Antibiotic Resistance Strategies. With DART 2020, the German Federal Government is meeting this requirement very promptly, clearly demonstrating the importance it attaches to the subject of antibiotic resistance nationally and internationally.

The Federal Government, together with other states, will also continue to step up efforts at international levels to expedite the necessary measures to contain the development of resistance. The aim is to expand monitoring systems, intensify preventive measures, establish regional, national and international cooperation in the long term, and support interdisciplinary collaboration in research and development so that new treatment opportunities can be made available in the future.

Contents

I. The problem: antibiotic resistance

Throughout the world, specialists, health officials, those working in health and veterinary care, and not least a concerned public are seeing the spread of bacterial pathogens which are less susceptible or completely resistant to common antibiotics. There is a risk that antibiotics are becoming less effective in treating infectious diseases and that the fear that infectious diseases evoked before the era of antibiotics might return.

The creation of antibiotic resistance is a natural process which is being accelerated by the excessive, inappropriate use of antibiotics and, furthermore, resistant pathogens are able to spread because of hygiene deficiencies in human and veterinary medicine. Alongside a lack of information on the part of doctors and veterinary surgeons, the wishes of patients and animal-owners are often the cause of the excessive, inappropriate use of antibiotics. In addition, and just as importantly, mistakes are made in the administration and application of antibiotics.

Bacteria which are naturally resistant to certain antibiotics or which have acquired resistance are no longer contained or killed by treatment. They can reproduce freely and also transmit their resistance genes to other bacteria, thus spreading the resistance. If bacteria take up various different resistance genes, they can resist several antibiotics, i.e. they become multi-resistant. Many antibiotics are ineffective in treating such multi-resistant pathogens.

The use of antibiotics affects the formation of the resistance: If susceptible bacteria are killed off, the resistant bacteria can reproduce freely and pass on their resistance factors.

Hospitals are of necessity places where pathogens repeatedly occur that are unsusceptible to many or sometimes even all antibiotics. The high rate of antibiotic use in clinics promotes their selection. If a lack of hygiene is added to this, these infectious agents can spread.

If antibiotic treatment fails, this can have severe or even fatal consequences for patients. Healing is delayed and further treatments are necessary. Alongside the personal suffering on the part of the patients affected, this also causes a considerable additional financial burden for the health system and for the economy. The costs per infection caused by resistant pathogens can be more than twice as much as for infections caused by susceptible pathogens.

The spread of antibiotic resistance is also causing problems in livestock farming and food production. It makes the treatment of animals suffering from bacterial infections more difficult, just as it does for people. This causes problems in animal welfare and also has a negative financial impact for the animal owners.

Resistant bacteria can be transmitted from animals to people or vice versa – from people to animals. Transmission is possible not only through contact with an infected animal, but also through contact with the meat of slaughtered animals that is contaminated with resistant pathogens, or through the consumption of contaminated foods. However, the impact that this method of transference has on the problem of resistance in human medicine seems to be relatively minor, as far as we can currently judge. In addition, the dissemination of resistant pathogens through raw vegetables and salad should not be ignored.

Resistant pathogens are not just transferrable from animals to people and vice versa, they can also move into the environment. They also occur naturally here, and can be transmitted from the environment to humans.

Resistance has increased steadily since antibiotics were first used in medicine in the 1940s. Studies comparing

What are antibiotics?

Antibiotics are naturally occurring defence and signalling substances that keep the coexistence of micro-organisms in balance. Fungi and bacteria produce various antibiotics in order to defend themselves against other micro-organisms. Alongside these antibiotics in the narrower sense, synthetically manufactured chemotherapeutic drugs are also described as antibiotics. Even in small quantities, these substances curb the growth of bacteria or kill them.

Antibiotics as medicines

The Scottish scientist Alexander Fleming discovered the effect of penicillin – and thus the great significance of such substances for medicine – in 1928. Antibiotics have been used to treat bacterial infections since then. Some come from nature, others are produced synthetically or partly synthetically. There are different groups which differ in the way they work and in the effect they have on various types of bacteria.

What is antibiotic resistance?

Bacteria have the natural ability to protect themselves against antibiotics of other microorganisms. This resistance is caused by certain genes in the genetic makeup of the bacteria. These genes are sometimes formed by natural mutations. In addition, bacteria can also swap genes between each other and thus pass on resistance genes. Bacteria can take up several resistance genes which will protect them against different antibiotics. This results in multi-resistant bacteria, which are resistant to a large number of antibiotics.

present-day soils with soils from the Netherlands archived in 1940 have shown that some resistance genes have shown a more than 15-fold increase. The environment harbours a pool of resistance factors, the dynamic of which is so far insufficiently understood by scientists. Experts are assuming that resistance factors can also be transmitted from this pool to animal or human pathogenic bacteria. If resistant micro-organisms or resistance factors form in the environment and are spread and selected there, this represents a danger to the health of humans and animals and may possibly contribute to the observed deterioration in the effectiveness of antibiotics.

Gram-positive pathogens
Staphylococci and streptococci are amongst the normal bacterial flora of humans and animals. Listeria and clostridia are also widespread and occur naturally in living beings. Some species of these families of bacteria can also cause illness, however. Staphylococcus aureus, for example, is the most common cause of wound infections. Some streptococci species cause septic tonsil inflammations, lung inflammations or scarlet fever. Pathogenic clostridia are the cause of botulism or lockjaw (tetanus). One species of listeria causes food poisoning.

Gram-negative pathogens
Klebsiella pneumoniae, although it normally inhabits the gastrointestinal tract, can cause lung inflammations in people with weakened immune systems. Pseudomonas aeruginosa, a widespread soil and water bacterium, is one of the most significant hospital bacteria. E. coli is normally a harmless producer of vitamins in the human intestinal flora. However, there are also pathological strains.

The pathways via which antibiotics can get into the environment vary considerably. An organism only partly metabolises antimicrobial substances and excretes a considerable proportion of the active substance. Antibiotics therefore pass via sewage treatment plants into water and through sewage sludge into the soil. This means that waste from hospitals or private households may also contribute to the problem of resistance. From surface water and soil, they can be transported further and enter the ground water.

In exactly the same way, antibiotics that are used in veterinary medicine pass into the environment with the excrements of the treated animals. Antibiotics can be transferred to soils and into surface and ground water in areas used for agriculture via slurry and dung used as farmyard manure and also through the direct excrements of animals kept in the open. An additional transmission route is created by aquacultures, waste water and waste produced in the manufacture of antibiotics and by their incorrect disposal.

The lack of (rapid) diagnostic test methods to identify (multi-)resistant pathogens prevents adequate diagnosis, and the absence of new antibiotics or alternative therapy options makes the treatment of infectious diseases difficult. In recent years, the pharmaceutical industry throughout the world has increasingly withdrawn from researching and developing antibiotics. The reasons for this include, for example, the high development costs which can only be recouped slowly, partly because of their restricted indication, such as the classification of a new active substance as a so-called “reserve antibiotic”, and the short period of time for which antibiotics are prescribed in comparison with other medicines.

Resistance rates and antibiotics consumption: a European comparison

At the moment, the monitoring of antibiotic resistance in human and veterinary medicine varies very considerably between different countries.

The European resistance data which have been recorded since 1998 by the EARS-Net (European Antimicrobial Resistance Surveillance Network) monitoring system for isolates from humans show, for methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), very low rates of resistance in the Scandinavian states and the Netherlands. Southern European countries show by far the highest rates of resistance for these pathogens in a European comparison. Germany comes in the middle of the field for MRSA.

Whilst rates of resistance generally for Gram-positive pathogens (e.g. staphylococci, enterococci) are relatively stable and even decreasing in some countries, the resistance rates for Gram-negative pathogens are increasing considerably throughout Europe. These include, for example, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Germany comes in the middle for these too.

The development of resistance means that the range of treatment alternatives is shrinking. In some countries, resistance even to reserve antibiotics such as carbapenems has also been rising since 2010. The rates of resistance in cases of *Klebsiella pneumoniae* are over 30 percent in some countries, and well above this on occasion. These are worryingly high rates. In Germany, rates of resistance to carbapenems for enterobacteria are still less than one percent.

The European ESAC-Net (European Surveillance of Antimicrobial Consumption) network monitors the consumption of antibiotics in both the inpatient and outpatient sectors of human medicine. Current data show that the highest rates of antibiotic consumption are in the Southern European states, with the lowest consumption rates in the Scandinavian countries and the Netherlands. In a European comparison, Germany has a medium to low antibiotic consumption in the outpatient sector. Compared with other European countries, however, reserve or broad-spectrum antibiotics are prescribed more frequently in Germany in the outpatient sector.

A comparison of the data from the EARS-Net and the ESAC-Net shows a close correlation between the national consumption of antibiotics in the outpatient sector and national resistance rates. Resistance rates are higher in countries with a high antibiotics consumption.

Throughout Europe, the antibiotic resistance of zoonotic pathogens and commensals of animals is tested on the basis of EC Directive 2003/99/EC. The results are forwarded to the European Food Safety Authority (EFSA), which evaluates and publishes them (http://www.efsa.europa.eu/de/topics/topic/amr.htm). The resistance rates found for individual species of bacteria sometimes differ considerably depending on the animal species, type of production, origin of bacterial isolates (living animal or food), and investigation year. For example, Germany is among the EU member states which have low proportions of resistant isolates of salmonella from laying hens, turkeys, or cattle, and yet Germany shows a high proportion of resistant salmonella isolates for broilers. After the monitoring of antibiotic resistance became compulsory throughout the EU, initially by means of individual decisions for salmonella in pigs and chickens, campylobacter and MRSA, the EU-wide requirements for antibiotic resistance monitoring were brought together in 2013 in the implementing decision 2013/652/EU. These legal provisions are accompanied by scientific recommendations issued by the EFSA. The above decision takes into account the recommendations of the EFSA in its scientific opinions on bacteria with the ability to form beta-lactamases with a wide-ranging effect (extended-spectrum beta-lactamases, ESBL) and on carbapenemase-forming bacteria. It states that, for the monitoring programmes, isolates of *Salmonella* spp., *Campylobacter jejuni, Campylobacter coli*, commensal *Escherichia coli, Enterococcus faecalis,* and *Enterococcus faecium* should be obtained from the most important food-producing animal species and foods and tested with specified quantitative methods for their resistance to a list of specified antimicrobial agents. At the same time, it is determined that a harmonised programme on the occurrence of ESBL and/or AmpC- and/or carbapenemase-forming bacteria in selected animals and food should be carried out. As limit values for the assessment of the results of the sensitivity testing of zoonotic pathogens and commensals, epidemiological cut-off values (ECOFFs) based on the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are used at the European level. This standardisation contributes to the quality of the data collected, allowing comparisons to be made between the member states.

Reserve antibiotics are antibiotics which are only used for severe infections where the pathogen is unknown or if an antibiotic recommended for the treatment of an illness no longer works because of antimicrobial resistance. Which antibiotic is used as reserve antibiotic depends on the infection and the pathogen.
Reserve antibiotics frequently have a greater risk of side-effects and are more expensive.

Broad-spectrum antibiotics are characterised by their effectiveness against a broad range of pathogens and should only be used when other antibiotics, known as "narrow-range" antibiotics, are no longer effective.

The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project compares the quantities of antibiotics sold to veterinary surgeons in the individual member states. The technical parameter "population correction unit" (PCU) is used as the basis for comparison using the structural data of the member states. Per PCU, Germany has the fourth highest antibiotics consumption in the EU, but a comparatively low proportion of 3rd and 4th generation cephalosporins and fluoroquinolones, which are generally counted among the reserve antibiotics.

Resistance rates and antibiotic consumption in Germany

Resistance situation

Human medicine

MRSA rates in Germany rose continuously between 1999 and 2004 and then remained constant at around 20 percent; however, there has been a steady decrease since 2011, most recently reaching 12.8 percent.
So called "community"-associated MRSA (CA-MRSA),

which occur independently of any prior contact with health facilities, are still rare in Germany and spread mainly in the immediate family environment of affected patients. People working in commercial livestock farming may be colonised or become infected with particular strains of MRSA which can be found in this sector. "Livestock"-associated MRSA (LA-MRSA) are still relatively rare overall in Germany as a pathogen in humans. In areas with intense livestock farming, however, these pathogens appear cumulatively in humans and animals.

In risk areas of hospitals, VRE has been occurring more frequently for some years now.

Enterobacteria
Many enterobacteria are typical intestinal bacteria in humans and animals, but are also found in the environment, in soil and in water. Escherichia coli is the most important representative of this group. Some enterobacteria are pathogenic.

Alongside MRSA and VRE, increased attention should be paid in particular to multi-resistant enterobacteria. Increasingly, for example, enterobacteria are being detected that are resistant to beta-lactam antibiotics (derivatives of penicillin). The resistant pathogens produce certain enzymes, called beta-lactamases, which inactivate beta-lactam antibiotics.

Zoonoses are infectious diseases transmitted from animals to humans and vice versa.

Commensal bacteria are harmless inhabitants of an organism. However, they can become pathogenic if tissue is destroyed or if the intestinal flora is disrupted by antibiotic treatment. They can also harm the organism if there is some degree of immunodeficiency.

Pathogens which produce extended-spectrum beta-lactamases (ESBL) have now become particularly important. These enzymes can even inactivate modern antibiotics, such as 3rd and 4th generation cephalosporins. The intestinal bacteria *Escherichia coli* and *Klebsiella pneumoniae* in particular now produce these enzymes more frequently.

The genes responsible for ESBL production are generally found on "plasmids". These are ring-shaped DNA molecules which are easily transmitted both within the same bacterial species and between different species. The rate of ESBL-forming *E. coli* has risen continuously in recent years and has now reached almost 15 percent of all detected *E. coli* strains in patients in intensive-care wards and approx. 7.5 percent in patients undergoing outpatient treatment. In the normal population, these pathogens were detected as intestinal flora in up to 7 percent of trial participants.

Resistance to carbapenem antibiotics is also becoming increasingly significant in Germany. Admittedly, carbapenem resistance has so far only been detected rarely in this country. However, carbapenems are needed as reserve antibiotics for the treatment of severe infections (e.g. for infections with ESBL-forming bacteria). In the case of an infection with pathogens that are resistant to antibiotics of this type, generally only a few effective antibiotics are still available for use, and in some cases none at all.

The increasingly frequent detection of infections caused by *Clostridium (C.) difficile* is also a matter of serious concern. The pathogen causes antibiotic-associated diarrhoea and an inflammation of the colon. Admittedly, the resistance situation for *C. difficile* is generally not (yet) threatening, but infections with *C. difficile* are not only occurring more frequently, their progression is becoming increasingly more severe. The main cause of this type of infection is the use of antibiotics, which changes the natural microflora of the intestine and thus promotes colonisation and infection with these pathogens.

Veterinary medicine

In recent years, multi-resistant bacteria which can be transmitted to humans have been detected increasingly in livestock and pets. The rates of resistance for commensal bacteria and zoonotic pathogens to fluoroquinolones and 3rd generation cephalosporins are rising. Early indications of enterobacteria that are resistant to carbapenems, which are found in livestock also in Germany, are signs of a further problem that must be monitored closely.

There are countless examples of the transmission of bacterial species between animals and of their transmission from animals to humans:

- → A particular clone of MRSA which was found in a large number of species of livestock is transmitted to people by direct contact with animals
- → Enterobacteria which can inactivate a large number of antibiotics are now also widespread in livestock and foods. These bacteria are problematic if fluoroquinolones or 3rd and 4th generation cephalosporins are rendered ineffective by this resistance

The significance of the various transmission routes for these resistance genes and the risks to the consumer are currently being researched intensively.

Resistance monitoring of animal pathogens, which is important for the treatment of diseased animals, shows that most pathogens causing respiratory tract infections in animals still react sensitively to treatment with antibiotics, with the level of resistance – apart from a few exceptions – being under 20 percent. On the other hand, the rates of resistance for bacteria that cause diarrhoea disorders and skin infections are very much higher. The frequency of MRSA depends on the animal species. It is found most often in dogs (55 percent) and most rarely in productive poultry (14 percent).

Consumption data

Human medicine

The proportion of antibiotics prescribed to inpatients is estimated at being between five and 20 percent of all antibiotics prescribed in human medicine. Studies show that the differences in antibiotics consumption are more marked between the various specialisms than they are between hospitals of different sizes. The highest consumption of antibiotics is observed in intensive care and haematology-oncology wards. The SARI project (Surveillance of Antibiotic Use and Bacterial Resistance in Intensive Care Units) has also been able to show that by feeding back the consumption data to the prescribing doctors, a reduction in antibiotics use of up to 30 percent can be achieved.

The greatest proportion of antibiotics is prescribed to outpatients. Outpatient antibiotic consumption has remained stable in Germany since 2007, but the level of broad-spectrum antibiotics in proportion to total consumption is rising. Regional consumption within Germany shows a slight west-east gradient. The top of the league for prescriptions is Saarland, whereas doctors in the new federal states prescribe fewer antibiotics. The reasons for this are unclear. Alongside differences in the attitudes of doctors and the expectations of patients, socio-economic factors and regional differences in the prevalence of infectious diseases could play a part, along with other, as yet unknown factors.

The pure consumption data do not allow any conclusions to be drawn about the indication-based use of antibiotics in individual patients. However, a critical confirmation of the indication and the use of antibiotics in line with the indication would, in either case, lead to a further reduction in antibiotic consumption. Studies show, for example, that doctors prescribe antibiotics in up to 80 percent of respiratory tract infections even though these are generally caused by viruses.

Veterinary medicine

In 2013, pharmaceutical companies and wholesalers delivered a total of 1,452 tonnes of antibiotics to veterinary surgeons in Germany, which is 167 tonnes less than in the previous year and some 250 tonnes less than in 2011, when sales were recorded for the first time. However, the quantity of fluoroquinolones, the use of which in veterinary medicine is viewed critically because of their significance in human medicine, rose once again in 2013. 12 tonnes of these antibiotics were supplied, which is two tonnes more than in 2012 and four tonnes more than in 2011.

Penicillins (473 tonnes) and tetracyclines (454 tonnes) are supplied most frequently, which means that older active substances predominate in veterinary medicine.

II. Our goals and what we are doing to achieve them

GOAL 1: Strengthening the One Health approach nationally and internationally

With many infectious diseases, the health of humans and animals is closely interwoven. Animals and humans are often infected by the same pathogens and treated with the same antibiotics. The use of antibiotics in veterinary medicine and agriculture has effects on the occurrence and spread of resistant pathogens in human medicine, just as the use of antibiotics in human medicine does on the development and spread of antibiotic resistance in veterinary medicine and agriculture. Antibiotics can pass via sewage treatment plants into the water or via sewage sludge into the soil.

The problem of the development of resistance can therefore only be tackled with a cross-sectoral approach. For this, collaboration between the stakeholders in human and veterinary medicine must be improved. This applies not only at regional and national levels, but also, in particular, at international levels, since resistant infection pathogens are spreading worldwide. Only a common, worldwide approach can bring about a lasting improvement in the situation.

The increase in antibiotic resistance also has enormous economic consequences. The World Economic Forum now numbers antibiotic resistance amongst the greatest risks to the world economy. It is predicted that costs will rise because of the treatment of diseases caused by resistant pathogens, and that we will see increased morbidity and mortality rates over the next few years. However, many factors which affect the occurrence, spread, and containment of antibiotic resistance in the various sectors and particularly across sectors are unclear. In order to understand these correlations, cross-sectoral cooperation at national and international levels must be stepped up and research questions must be jointly identified and answered.

On this basis, the Federal Ministry of Health, together with the Federal Ministry of Food and Agriculture and the Federal Ministry of Education and Research, is supporting a range of measures at the interfaces between human and veterinary medicine within the framework of the German Research Platform for Zoonoses. The aim in particular is to support cooperation at these interfaces at local, national and, not least, international levels.

What we have achieved

In 2008, an interministerial antibiotic resistance working group was established at the federal level. It is responsible for ensuring interdepartmental coordination, adaptation and expansion of national activities. Meetings between the departments involved and the competent Higher Federal Authorities are held regularly to discuss current and planned measures and shared projects.

In order to expand interdisciplinary research, in 2006 the Federal Ministries of Education and Research and of Health and the former Federal Ministry of Food, Agriculture and Consumer Protection signed a joint Research Agreement on Zoonoses. The Research Agreement on Zoonoses produced the Zoonoses Research Networks and the German Research Platform for Zoonoses. The aim of the German Research Platform for Zoonoses is to increase the exchange of experience at national and international levels, in order to step up research activities in the area of zoonosis research and to promote the broadly based horizontal networking of human and veterinary medicine.

At international level, Germany supports the European Commission's action plan against the rising threats from antimicrobial resistance and has successfully advocated the development of a Global Action Plan on antimicrobial resistance through the World Health Organization (WHO). To support the implementation of the WHO Global Action Plan, the action package "Antimicrobial Resistance" was set up within the Global Health Security Agenda (GHSA). Germany, along with the UK, Sweden, the Netherlands, and Canada, is a "Lead Country" of this action package. In addition, as part of its G7 presidency, Germany has added the subject of antimicrobial resistance to the agenda of the G7 summit on 7–8 June 2015.

Our next steps are:

- → Continuing the interministerial working group on antibiotic resistance to achieve overarching coordination, evaluation, and adaptation of the national approach, also taking into account the problems of resistance in sewage
- → Renewing the Research Agreement on Zoonoses between the Federal Ministry of Education and Research (BMBF), the Federal Ministry of Food and Agriculture (BMEL) and the Federal Ministry of Health (BMG) to intensify the promotion of research projects within the scope of the German Research Platform for Zoonoses
- → Providing intensive assistance to the WHO Global Action Plan to be adopted in May 2015 by the World Health Assembly (WHA)
- → Supporting selected partner states in the implementation of the WHO Global Action Plan within the framework of the GHSA through the development of bilateral cooperations
- → Introducing specific measures to encourage the prudent use of antibiotics worldwide, and increasing the prevention of infections and the associated research and development within the scope of the focal theme of antibiotic research as part of the German G7 presidency. The main element is the strengthening of the One Health approach to counter antibiotic resistance

For this, we will work with such bodies as the National Zoonoses Platform, the Higher Federal Authorities, the WHO, the OIE, the European Commission, the GHSA and G7 states, universities, academies, scientific institutions, the German Centre for Infection Research, the pharmaceutical industry and relevant institutions in the G7 partner states.

GOAL 2: Recognising changes in resistance at an early stage

Globalisation and increasing patient mobility require an effective monitoring or early warning and response system for resistant pathogens. If pathogens that are resistant to antibiotics are recognised at an early stage, their further spread can be prevented through the application of a range of measures. This is equally important in human and veterinary medicine. Changes in resistance can be recorded and analysed at local, regional and national levels using monitoring systems (surveillance systems). These can map the problem situation by showing, for example, the different situations in the outpatient and inpatient sector or for different animal species or production types. In addition, the molecular biological characterisation of (resistant) infectious agents allows the way in which they develop and spread to be studied and chains of infection to be examined. For this reason, such instruments must be further developed and expanded. The surveillance of antibiotic resistance at local level allows the resistance situation to be assessed on the spot and provides doctors and veterinary surgeons with important evidence as to whether their prescribing behaviour needs to be adapted. In addition, the development of resistance rates over time shows whether intervention measures are having any effect and if so, which ones. The comparison of resistance data at regional, national and international levels also allows an assessment of specific local or national characteristics.

What we have achieved

In human medicine, the ARS (Antibiotic Resistance Surveillance) monitoring system at the Robert Koch-Institute (RKI) has been available since 2007. ARS forms the basis for the central recording and evaluation of resistance data from the outpatient and inpatient sectors in Germany. Participation in ARS is voluntary. Participants in ARS are medical microbiological laboratories that examine samples from patients from medical facilities and doctors' practices to determine infection agents and resistance. The resistance results which are collated there are forwarded to the RKI where they are stored in a central database. From the data, resistance statistics are automatically generated which can be called up via the interactive database on the ARS website. Based on the resistance statistics, reports are prepared for the participating laboratories or for their customers which also act as an early warning and feedback system, e.g. in the case of rare resistance.

In Germany in the past, various methods and evaluations were used for resistance testing, which made comparison of data more difficult. In 1997, EUCAST was established, with the objective of harmonising methods and limit values for resistance evaluation in Europe; since 2012, implementation and adaptation in Germany have been supported by the National Antibiotics Committee (NAC). The laboratories participating in ARS have almost completely changed their evaluation of resistance testing over to the EUCAST guidelines, which thus allows comparison on an international level, e.g. within the EARS-Net.

The National Reference Centres (NRC) and consultant laboratories play an important role within the early warning concept. At present, 19 NRCs and 40 consultant laboratories are appointed in Germany to cover different pathogens and diseases. The NRCs deal primarily with developing and/or improving diagnostic methods for the pathogens assigned to them, and with special diagnostics and pathogen typing of these pathogens. They also examine important trends in resistance developments and questions of pathogenicity. Additionally, the NRCs have an advisory function and regularly publish reports on epidemiological developments. As part of the implementation of the 2008 DART, the NRC for Gram-negative hospital pathogens started its activity in 2009. It advises extensively on the problems of resistance of Gram-negative bacteria.

In addition, Art. 23 of the Infection Protection Act obliges the directors of hospitals and clinics for outpatient surgery to record nosocomial infections and the occurrence of hospital pathogens with special resistance and multiple resistance in a separate written document on an ongoing basis. The RKI has drawn up a list specifying which nosocomial infections and

resistant pathogens have to be documented. These data are not recorded centrally, but instead form a basis for assessing the local situation and for introducing the necessary preventive measures.

The Infection Protection Act also specifies which diseases and pathogens must be reported to the local public health office. For example, evidence of MRSA in blood or spinal fluid has been notifiable since 2009.

In addition, there are further systems for monitoring resistant pathogens in Germany such as the Hospital Infection Surveillance System (KISS) based at the NRC for surveillance of nosocomial infections. It is often difficult to compare data from the various systems, since different recording criteria are applied depending on the system. A compilation of available resistance data is provided in the "GERMAP Report on antibiotic consumption and the spread of antibiotic resistances in human and veterinary medicine in Germany".

In veterinary medicine, antibiotic resistance is monitored at national level in two monitoring programmes which collect pathogens for resistance testing on a representative basis in accordance with coordinated random sampling plans. The resistance of zoonotic pathogens and commensal bacteria to antimicrobial substances is recorded in accordance with the directive 2003/99/EC and the General Administrative Regulation on the recording, evaluation, and publication of data on the occurrence of zoonoses and zoonotic pathogens along the food chain ('AVV Zoonosen Lebensmittelkette', 10 Feb. 2012). The national reference laboratory responsible is based at the Federal Institute for Risk Assessment (BfR), which centrally collects the data and isolates obtained from the authorities of the Federal States, tests their resistance to an internationally agreed panel of antibiotics and evaluates them to provide a national evaluation of the resistance situation. This provides information about the sources of resistant pathogens and the trends in the resistance situation along the food chain. The results of this monitoring are published as part of the national reporting system and are also reported to the EFSA and evaluated by it.

A further programme (GERM-Vet) is run by the Federal Office for Consumer Protection and Food Safety (BVL). It continuously collects clinical bacterial isolates, examines their sensitivity to antibacterial agents, and assesses the results for the national evaluation of the resistance situation for animal pathogens. The spectrum of the bacteria examined also covers isolates from diseased pet animals. Amongst other things, the resistance data are incorporated into the evaluation of veterinary medicines in the authorisation and extension procedure, provide information about the trends in the resistance situation, and provide evidence for treatment decisions of practicing veterinary surgeons. The results are published in national reports.

In addition, there are also other surveillance activities. For example, relevant pathogens that have been sent to the BfR for diagnostic purposes have been tested for their resistance to antimicrobial agents, in some cases for decades.

Furthermore, resistance data on zoonotic pathogens from human infections have also been determined continuously for decades at the RKI in the NRC "Salmonella and other bacterial enteritis pathogens" and the situation and trends published within annual reports and the series "GERMAP Report on antibiotic consumption and the spread of antibiotic resistances in human and veterinary medicine in Germany".

Our next steps are:

Human medicine

- → To expand the notification obligation to cover further multi-resistant pathogens
- → To expand ARS at the RKI with the aim of achieving complete, representative surveillance
- → To expand the existing feedback system to send back data to doctors prescribing antibiotics
- → To strengthen the National Reference Centres and consultant laboratories
- → To carry out a feasibility study on molecular surveillance for resistant pathogens
- → To institute a pilot project to incorporate the resistance of viruses and fungi into the existing surveillance system

For this, we will work with the RKI, the NRC, consultant laboratories, the Scientific Council for Public Health Microbiology, scientific societies, the German Hospitals Federation (DKG), the Statutory Health Insurance (GKV), the Association of Private Health Insurers (PKV), National Association of Statutory Health Insurance Physicians (KBV), the Evaluation Committee, Association of Statutory Health Insurance Physicians of the States (ASHIPS), and the Federal Joint Committee (G-BA).

Veterinary medicine
All monitoring measures are aimed both at protecting the health of consumers on a preventive basis and ensuring animal health. Both monitoring systems are to be expanded in close coordination with other EU member states.

- → Adapting the resistance monitoring of zoonotic pathogens and commensals to the new EU legislative situation by incorporating the selective detection of ESBL/AmpC-producing and carbapenemase-producing enterobacteria
- → Expanding the national resistance monitoring of zoonotic pathogens and commensals to enterococci and, if necessary, other species of bacteria which can be transferred from livestock farming to humans (e.g. Klebsiellae, *Clostridium difficile*). In this, Germany goes well beyond the mandatory requirements of the EU
- → Extending the national resistance monitoring of animal pathogens (GERM-Vet) to other species of bacteria
- → Expanding the examination methods used, for example by adding molecular surveillance methods, in order to discover new resistance mechanisms at an early stage
- → Expanding the standardisation of sampling techniques and the preparation of samples so that the resistance data from different areas can be better compared
- → Feeding back resistance data to veterinary surgeons. In this connection, consideration is being given to whether a database and an online system could be set up to provide veterinary surgeons with resistance data promptly

GOAL 3: Retaining and improving therapy options

Antibiotics are indispensable, important drugs in both human and veterinary medicine. This treatment option needs to be retained and improved. It is therefore important to deal specifically with those factors responsible for the development and spread of new resistances.

The need for antimicrobial agents in certain areas of medicine is set to grow because of demographic developments and an increase in complicated medical interventions. Many medical interventions, e.g. in the area of orthopaedic surgery or within transplantation medicine, cannot be carried out without antibiotics. For this reason, it is important to use antibiotics carefully and to ensure that they remain effective.

The extent to which antibiotics are used in human and veterinary medicine and the choice of antibiotic are also crucial. The consumption of antibiotics must therefore be recorded and analysed. Antibiotic consumption data are also required in order to assess the effectiveness of intervention measures, whether at the local or national level. They enable comparisons between the various disciplines and within a sector. They thus provide a good basis for supporting recommendations to doctors within the scope of feedback systems.

International studies show that in human medicine, up to 50 percent of antibiotic treatments are inadequate, e.g. as a result of inappropriate dosages or treatment durations. This also applies for Germany. Evidence-based recommendations and guidelines help the medical staff in the diagnosis of infections and in their choice and dosage of the most suitable antibiotic. Recommendations and guidelines are prepared and updated by the responsible scientific societies. The resistance situation is taken into account here.

The area of use of an antibiotic is defined by the license. Before an antibiotic can be licensed for use, it must be proven to be effective. Drug manufacturers are thus obliged, when an antibiotic is (re-)licensed, to submit resistance data to the Federal Institute for Drugs and Medical Devices (BfARM) or, for veterinary medicines, to the BVL. These data are also used to inform the scientific community about the range of effects of an antibiotic.

What we have achieved

In human medicine, alongside resistance surveillance, the monitoring of antibiotic consumption has been developed. The antibiotic consumption data for the outpatient sector are made available by the Scientific Institute of the Local Health Care Funds (WIdO), the Central Institute for Statutory Health Care Insurance in Germany (Zi), and a number of health insurance funds. Data on drug consumption are regularly compiled and fed back in monthly prescription reports by the statutory health care associations to the prescribing doctors so that they can stay within drug budgets.

One project for the monitoring of antibiotic consumption in inpatient treatment is the ADKA-if-RKI Project, which was initiated and established by the German

Society of Hospital Pharmacists and the Infectiology Department of the University of Freiburg, and which has been supported by the RKI for a number of years. The German consumption data currently available, however, are not representative.

Other projects which collate data on antibiotic consumption in the inpatient sector are the SARI project and the Antibiotic Consumption Surveillance (AVS) project, which was developed by the RKI in cooperation with the Charité in Berlin. The aim of this project is to support hospitals in monitoring of antibiotic consumption. From this, a platform for efficient surveillance which saves resources has developed. Interested hospitals are able to take part in this national surveillance system.

In 2011, the law amending the Infection Protection Act and other laws formed the basis for the Commission Anti-Infectives, Resistance and Therapy (ART) at the RKI. The Commission compiles up-to-date general recommendations for diagnosis and therapy, especially in the case of infections with resistant pathogens, and, in close collaboration with the Association of the Scientific Medical Societies (AWMF), initiates the compilation of medically sound recommendations and of infectiological guidelines on antibiotic therapy by the scientific societies. The Commission has determined a need for evidence-based guidelines (especially S3 guidelines) for common and life-threatening infectious diseases. It is also involved in the discussions of the Interministerial Working Group on Antibiotic Resistance.

Following the change in the Infection Protection Act, hospitals and other medical care facilities are obliged, to record and assess data on the nature and extent of antibiotic consumption. The RKI, in cooperation with various scientific societies, has specified how the data are to be recorded.

In veterinary medicine, in 2010 and 2015, the "Guidelines for the prudent use of veterinary antimicrobial drugs" were adapted to the current state of scientific knowledge and to the situation in practice.

In 2014, the guideline on "Application of veterinary medicinal products in the livestock sector" was revised in line with the current state of knowledge. This was developed in 2009 under the leadership of the Federal Ministry for Food and Agriculture together with the federal states, the veterinary sector, the industry and the animal owners in order to improve the appropriate use of antibiotics.

In addition, there are guidelines for the veterinary attendance of pig, cattle and poultry farms issued by the Federal Association of Practicing Veterinary Surgeons.

With the Sixteenth Law Amending the German Medicinal Products Act (16. AMGÄndG), which came into force in 2014, a benchmarking system was introduced using nationwide determination of key figures on the frequency of antibiotic treatment of fattening animals. This is associated with obligations for controls and actions on the part of animal owners aimed at reducing the use of antibiotics. Animal owners must compare the situation within their own operation with the nationwide key figures, and – if the key figures are exceeded – take measures, in collaboration with the veterinary surgeon, to minimise the use of antibiotics. The key figures are determined every six months on the basis of what has been achieved, which creates a dynamic system that helps reduce antibiotic use on a lasting basis.

Through the 16. AMGÄndG, the competent authorities of the federal states also receive data on the use of antibiotics in fattening farms. The treatment rates obtained here can help the authorities with the planning of risk-based controls of animal owners and veterinary surgeons. In addition, the competent authorities were granted a series of regulatory powers for the introduction of management measures if the measures taken by the farms to reduce antibiotic treatment are not sufficient.

Alongside the information as to what quantities of which antibiotics are supplied to veterinary surgeons, it is also important to find out how often these drugs are used, for which animals and for which indications. This reveals the main areas of use and makes it possible to identify areas in which an attempt should be made to reduce the use of antibiotics. In the "Veterinary Consumption of Antibiotics" (VetCAb) project, therefore, a representative random sample was taken in order to carry out a more detailed analysis of the use of antibiotics in the various areas of the livestock production with the aim, amongst other things, of identifying main points of use, highlighting changes and thus being able to plan and evaluate reduction measures on a focussed basis.

Our next steps are:

Human medicine

- → Expanding overall antibiotic consumption surveillance to collate representative data and to provide reference data for the specialist public
- → Using these data to identify problem areas and possible intervention measures at national level
- → Improving the feeding back of antibiotic consumption data
- → Initiating a pilot project to finance the development of infectiological guidelines and recommendations
- → Developing concepts for the preparation and application of local guidelines and recommendations in the outpatient and inpatient sectors
- → Enabling ARS to be used jointly by the RKI and BfArM in order to make it possible to use the resistance data for licensing purposes.

For this, we will work with the RKI, BfArM, WIdO, ZI, IF, Charité Berlin, GKV, PKV, ÄZQ, the Commission ART, AWMF, scientific societies, the DKG, PKV, KBV, ASHIPS, hospitals, outpatient clinics, and the G-BA.

Veterinary Medicine

- → Implementing the authorisations granted by the 16. AMGÄndG for more extensive rules for the use of antibiotics, especially reserve antibiotics, in animals
- → Continuing the antibiotic minimisation concept of the 16. AMGÄndG and preparing for the evaluation of its effectiveness in 2019
- → Continuing the recording of quantities of antibiotics supplied to veterinary surgeons
- → Calling on the issuers of the available guidelines to check these regularly to see if they need updating and to update them if necessary
- → Developing further legally binding requirements for the use of antibiotics in animals on the basis of existing guidelines. Working out key points for a feedback system for veterinary surgeons which veterinary surgeons can use to compare their use of antibiotics with that of their colleagues

In addition to reducing the frequency of antibiotic treatments and the absolute quantity of antibiotics used on animals, the aim of the above measures specifically is also to reduce the use of critically important active agents.

GOAL 4: Breaking chains of infection early and avoiding infections

Avoiding infections must come at the beginning of all efforts to reduce the use of antibiotics. This goal is supported by primary prevention measures, and particularly the interruption of chains of infection within the framework of an accumulated occurrence of infections. Outbreaks that are not recognised and monitored at an early stage are a serious problem in both human and veterinary medicine which must be countered using suitable instruments. Measures to break the infection chain must be consistently implemented and further researched.

A high level of attention and prompt diagnosis of pathogens and resistance combined with the provision of suitable advice are absolutely essential here. Indication-appropriate, rapid pathogen diagnosis, which also comprehensively includes antibiotic resistance, not only makes a major contribution to ensuring the quality of the treatment of bacterial infections, but also plays an important role in breaking chains of infection. Rapid identification helps to avoid the further spread of (multi-)resistant infection pathogens and promotes specifically targeted antibiotic therapy and the use of narrow-spectrum antibiotics.

Reliable test systems for rapid diagnosis are not available on a sufficient scale. However, even if established test systems are available, diagnosis is not always carried out. With many bloodstream infections or nosocomial diarrhoeas, for example, no samples are taken for microbiological examination.

In addition, skills in outbreak recognition and analysis plus the knowledge of and ability to implement hygiene measures are essential in preventing the transmission of pathogens. Microorganisms can spread if hygiene measures are inadequate or completely lacking. This applies in general to all pathogens, but is particularly true for (multi-)resistant pathogens, since here the opportunities for treatment after transmission has occurred are limited.

In human medicine, the specialists on the spot (e.g. hygienists, infectiologists, microbiologists, hygiene specialists) and the public health authorities have a vital role to play in preventing the further spread of

(resistant) pathogens and in elucidating local outbreak incidents. An obligation to report resistant pathogens allows the public health authorities to intervene even if only a single case has been detected.

It is not only chains of infection within hospitals that require attention, however. If practitioners, patients and their relatives are not informed, on discharge from hospital, that a (multi-)resistant pathogen has been detected, the necessary hygiene measures are not taken and the pathogen can spread further.

In veterinary medicine and livestock farming, systems to protect against epizootic and other animal diseases have been established for a long time; one of the aims of hygiene and monitoring measures at abattoirs and in the food processing industry is to prevent the harmful contamination of foods with microorganisms. Consumers too can and must play their part in preventing the transmission of (resistant) germs from animals and foods to people by handling animals and foods properly.

What we have achieved

In human medicine, in 2011, the law amending the Infection Protection Act and other laws toughened up the requirements for hygiene in health care facilities and improved the options for countering outbreaks. For example, the recommendations of the Commission for Hospital Hygiene and Infectious Disease Prevention (KRINKO) and the responsibility of the directors of medical facilities for their implementation were made binding. KRINKO prepares scientifically sound recommendations, which have been approved by a group of experts, on the prevention of infections and on operational-organisational and structural-functional measures. The recommendations are constantly being further developed in accordance with current evaluations of the epidemiology of infections and with research results in the relevant thematic areas. If consistently implemented, these recommendations make an important contribution to the avoidance of infections and the further spread of pathogens including those with special resistance and multiple resistance. According to the KRINKO recommendations, for example, all clinics are obliged to examine patients at risk for multi-resistant pathogens on admission and to isolate them until colonisation has been excluded.

In addition, with the amendment to the Infection Protection Act, the federal states were obliged to issue hospital hygiene regulations covering measures for the prevention, detection, recording, and control of treatment-associated infections and pathogens with resistance. These regulations have now been issued in all federal states. The establishment of hygiene commissions for particular facilities was established. The directors of these facilities must keep records on nosocomial infections, antibiotic resistance, and antibiotic consumption as laid down in the Infection Protection Act and draw conclusions from these for application in practice.

Qualified medical, nursing and other staff are essential for the establishment of and compliance with hygiene standards. Through the Hygiene Promotion Programme, hospitals will be supported until 2016 in appointing the necessary specialists and with providing further training for doctors and nurses in the field of hospital hygiene and thus implementing the requirements of the Infection Protection Act.

In order to ensure coordination and harmonisation between the sectors, regional networks for the prevention and monitoring of resistant pathogens have been established. In this, the Federal Ministry of Health has supported model networks with different focal points in four regions. The central elements within the networks are a round table and the achievement of a consensus concerning measures to be carried out across sectoral boundaries. In addition, the issue of quality seals will make the efforts of participating hospitals transparent. Regular network meetings at the RKI will promote a lively exchange of experiences.

The G-BA was obligated to specify in its guidelines suitable measures to ensure hygiene in healthcare and in particular to define indicators for assessing hygiene quality in order to provide quality assurance of hospitals across all facilities. The G-BA instructed the AQUA Institute to develop two quality assurance procedures: “Post-operative wound infections” and “Vessel catheter-associated infections”. Feasibility tests were arranged for both procedures. The incorporation of the developed procedures into the standard procedures of the cross-facility quality assurance is to be adopted by the Federal Joint Committee after the conclusion of the trial phases.

Obstacles to the implementation of MRSA diagnosis and MRSA eradication in risk groups in outpatient medicine were countered by a remuneration agreement for practitioners. Doctors who wish to provide these services must meet certain technical requirements.

Since 1 January 2015, the statutory preconditions apply for model projects within the scope of which patients at risk are tested for multi-resistant Gram-negative pathogens before being admitted to hospital. The findings of these tests are used to assess the effectivity of and work required for a screening of this type and are to be incorporated into the KRINKO recommendations.

The Federal Government's report of December 2014 on the effects of the instruments introduced with the amendment of the Infection Protection Act shows that the requirements of the law have been completely implemented. Through the passing of the hospital hygiene regulations, the Federal states made an important contribution to this. Seen overall, activities to date are bearing their first fruits: MRSA infections have been declining for three years. However, there is still room for improvement in the implementation of the recommendations on site in the facilities themselves. It is crucially important that compliance and conscientious implementation continue to be monitored by the competent state authorities.

In veterinary medicine, in recent years, intense measures to fight salmonella in poultry farms have also considerably reduced the exposure of consumers to multi-resistant salmonella from livestock farming.

The entry into force of the Animal Health Act (TierGesG) on 1 May 2014, which replaces the old Animal Diseases Act, placed the control of transmissible animal diseases in Germany on a more up-to-date foundation. The Animal Health Act places more weight on prevention and contains a series of new provisions for the prevention and control of livestock epidemics and animal diseases, and for improving surveillance. In this context, the framework conditions for the use of vaccines were also adapted to the current situation. The vaccination of livestock against viral infections is of towering significance for the reduction of antibiotic use in livestock farming to combat secondary infections caused by bacteria. This was shown most impressively by the example of vaccination against porcine Circovirus II. The requirements for the action plans which have to be drawn up in the event of antibiotic usage above the corresponding key figure also explicitly call for the hygiene regimes in livestock farming to be intensified.

Our next steps are:

Human medicine

- → Supporting the federal states in the development and expansion of regional networks for the prevention and monitoring of resistant infection pathogens
- → Providing expertise by the federal states to ensure strict compliance with hygiene standards in hospitals
- → Expanding compulsory notification to further multi-resistant pathogens
- → Determining problems and obstacles to use in diagnostics, such as blood culture diagnosis and the detection of *Clostridium difficile*, and working out possible solutions
- → Providing continuous support for the federal states, if necessary with follow-up checks, to ensure the presence of sufficient hygiene staff in medical facilities
- → Supporting the process for establishing the developed indicators for the assessment of hygiene quality to allow quality assurance across all facilities

For this, we will work with the RKI, the Federal states, the Public Health Service (ÖGD), KRINKO and the Commission ART, the DKG, GKV, PKV, KBV, ASHIPS, Assessment Committee, hospitals, outpatient clinics, the G-BA, and the AQUA Institute.

Veterinary medicine

- → Breaking the transmission chains at an early stage through improved livestock husbandry systems, coordinated vaccination programmes against the most significant bacterial, parasitic, and viral infectious diseases. Implementing the measures listed by way of example in the 16. AMGÄndG to improve animal health
- → Introducing advisory measures in livestock husbandry
- → Supporting regional health programmes of animal owners, veterinary surgeons, abattoir and animal transport companies, and competent authorities.
- → Encouraging corresponding model and demonstration farms
- → Development of an animal health index by a federal-state working group
- → The recommendation of suitable vaccination strategies by the Standing Committee on Veterinary Vaccinations at the Friedrich Loeffler Institute

→ Carrying out a study on the effects of measures to reduce emissions in livestock operations on the exposure of the population to resistant bacteria from livestock farming via the environment

To reduce the transmission of resistant bacteria along the food chain, the following measures are planned in close cooperation at the European level:

→ Consistently pursuing the successful control programmes for salmonella in poultry farming
→ Further developing the concept of process hygiene criteria for food production and expanding these to further frequently resistant pathogens (e.g. *Campylobacter* spp), ESBL/ AmpC-producing or Carbapenemase-producing enterobacteriaceae
→ Researching possibilities for reducing the contamination of carcasses during the food production process. Research should also be carried out into possible positive effects of bacteriophages and other substances in order to reduce or eliminate bacteria on carcases as a supplement to process hygiene
→ Verifying the necessity for corresponding process hygiene criteria for other resistant pathogens (e.g. ESBL/AmpC-producing or Carbapenemase-producing Enterobacteriaceae)

GOAL 5: Raising awareness and strengthening skills

Conveying information and knowledge is an essential precondition for the appropriate use of antibiotics and for dealing with multi-resistant pathogens. Therefore, it is important to address not only specialist groups but also the general population, who – as patients, parents, consumers, animal owners, or farmers – can contribute to ensuring that antibiotics continue to be effective in treating infectious diseases. The expectations of patients and animal owners with regard to the prescription of antibiotics and their appropriate consumption or administration have an influence on antibiotic consumption and thus on the development of resistance.

A survey was carried out to examine the knowledge, attitudes, and expectations of the population with regard to antibiotics and their application in respiratory tract infections. The results showed a generally good level of knowledge about antibiotics and a high degree of faith in doctors' decisions, but there is still a considerable need for more information.

A further study focussed on the prescription behaviour of doctors with various specialisms. It was found that general practitioners in particular are confronted with expectations on the part of patients for an antibiotic and prescribe antibiotics because of this situation.

An online platform for doctors and other medical professionals can make an important contribution to appropriate prescription by making available current information on infections, the effects of antibiotics, the development of resistance, new antibiotics and generally recognised recommendations and guidelines on antibiotic therapy. In this way, experts would have rapid access to new information relevant to their practice on the subject of antibiotic resistance.

In the long term, the quality of the prescription of antibiotics, however, can only be achieved by providing better education, advanced training and professional development for doctors and veterinary surgeons. The subject must be given more emphasis at university, advanced training and professional development in order to fill existing gaps in knowledge and to encourage the application of this knowledge.

What we have achieved

In human medicine, information is provided to the public, for example, by the Regional Networks, the Institute for Quality and Efficiency in Health Care (IQWiG), the KBV, and the health insurance funds. In January 2015, the German Coalition for Patient Safety (APS) published the patient information leaflet "Prevention of hospital infections and infections by multi-resistant pathogens". The Federal Centre for Health Education provides information on its website about different aspects of the subject of antibiotic resistance. In addition, it offers public information on MRSA in six different languages. Patients can find out about the quality of hygiene in individual hospitals in the hospitals' annual quality reports.

Information for doctors prescribing antibiotics is provided, for example, in the series "Wirkstoff aktuell" from the KBV in the issues "Rational antibiotic treatment of upper respiratory tract infections", "Rational antibiotic treatment of the lower respiratory tract" and "Rational antibiotic treatment of urinary tract infections".

The launch of the ARS website and the website of the Commission Anti-Infectives, Resistance and Therapy marks an initial step in the direction of an online "Antibiotic Resistance" platform offering practical information about the subject in one place.

The National Competency-Based Learning Objectives Catalogue in Medicine for the study of human medicine is currently being revised. This will also appropriately map infectious diseases, their prevention, diagnosis and therapy with special consideration given to resistant pathogens.

A wide range of professional development options on the subject of antibiotic resistance is available for doctors. Advanced training in rational antibiotic therapy (Antibiotic Stewardship, ABS) is of particular significance. The German Society for Infectious Diseases (DGI), supported by the Federal Ministry of Health, has developed an advanced training programme of this type. The programme has been received positively by doctors and pharmacists and is constantly being developed further. However, the need for training places cannot yet be covered at the moment. In addition, under the guidance of the DGI, an S3 Guideline "Strategies to ensure the rational use of antibiotics in hospitals" has been developed. However, there is still a need for ABS concepts and programmes for the outpatient sector which has not yet been sufficiently addressed.

The German Society for Hygiene and Microbiology, also supported by the Ministry of Health, has developed an advanced training programme in Nosocomial Infection Prevention in Hospitals. This has now become part of the Structured Curricular Advanced Training Programme of the chambers of physicians.

In veterinary medicine, it is the restrictive drug legislation, with its documentation obligations for veterinary surgeons and farmers, plus the monitoring of the produced foods, which ensure that the problems of antibiotic resistance shifts into the consciousness of the people involved. In addition, the "Guidelines for the prudent use of veterinary antimicrobial drugs" of the Federal Chamber of Veterinary Surgeons, first published in 2000, have been revised in 2015 for the second time since their update in 2010 and sent out to every veterinary surgeon.

Veterinary surgeons acquire a basic knowledge of the use of antibiotics and the resultant development of resistance in their studies and in postgraduate advanced training and continuing professional development (CPD). The subjects of antibiotic therapy and antibiotic resistance are thus firmly anchored in their training. After gaining their accreditation, veterinary surgeons have a general CPD obligation according to the professional codes of conducts of the relevant chambers of veterinary surgeons. In addition, there are also statutory CPD obligations.

Continuing professional development events that aim to meet the CPD obligation must be approved by the Academy for Advanced Veterinary Training of the Federal Chamber of Veterinary Surgeons.

The industry's own antibiotic monitoring carried out by QS GmbH involves the veterinary surgeons and, through the advisory activities associated with it, helps increase awareness of the subject among animal owners.

Annual reports by the Higher Federal Authorities on the current resistance situation and on trends are freely available online: an important element in risk communication, which is not solely limited to specialists in the fields of veterinary medicine and agriculture. This communication is a continuous, interactive process. Participative dialogue with various target groups lies at its heart. It therefore covers far more than keeping all participating and interested target groups informed about the development and evaluation of antibiotic resistance. Informing the public at an early stage about possible health risks, information obtained, and working results form the basis for this dialogue.

The BfR publishes risk evaluations of current aspects of antibiotic resistance for zoonotic pathogens and commensals online (http://www.bfr.bund.de/de/a-z_index/antibiotikaresistenz-61681.html) and keeps the general public informed through its press releases. Consumers are also trained with specific recommendations in handling food and are provided with appropriate procedures. In addition, farmers and veterinary surgeons are also provided with data and aspects of risk assessment at professional development events in the form of lectures.

Resistance data obtained through zoonosis monitoring are provided to the general public annually in the EU

Zoonosis Report and in the National Zoonosis Report. Resistance data for animal pathogens and their assessment are also available in reports published on the BVL website (http://www.bvl.bund.de/DE/05_Tierarzneimittel/01_Aufgaben/05_AntibiotikaResistenz/Antibiotika_Resistenz_node.html). In addition, resistance data from both programmes are presented to the (specialist) public at training events and conferences.

Since the 15. AMGÄndG, the annual reports covering data on resistance of bacterial animal pathogens have been made available. The key figures on treatment rates in fattening animals according to the 16. AMGÄndG have been published in the Federal Gazette since 2015. This allows the farms and the competent federal state authorities to classify the frequency of antibiotic therapies and, if these are higher than the national figures, to determine in cooperation with the veterinary surgeons the causes and to implement measures to reduce the use of antibiotics in the relevant stocks.

Our next steps are:

Human medicine

- → Integrating the public and increasing awareness by improving education
- → Providing target group-specific information for patients on the subject of antibiotic therapy and resistance
- → Obliging hospitals to supplement quality reports by adding an additional section containing comprehensible, particularly patient-relevant information on hygiene standards, amongst other things
- → Working out communication strategies for the doctor/patient discussion on the subject of antibiotics, considering a checklist approach
- → Building up the online "Antibiotic Resistance" platform for doctors and other medical and pharmaceutical professionals
- → Strengthening the thematic areas of hygiene/microbiology/infectiology in training, advanced training and continuing professional development, including the outpatient sector
- → Transferring certified professional development programmes to experts in antibiotic prescription (ABS officers) in a Structured Curricular Advanced Training Programme of the chambers of physicians
- → Discussing a continuing professional development obligation in the area of antibiotic resistance

For this we will work with the Federal Centre for Health Education (BZgA), Coalition for Patient Safety (APS), G-BA, ASHIPS, KBV, IQWiG, RKI, the Commission ART, KRINKO, medical faculties, teaching hospitals, the German Medical Association, state chambers of physicians, professional federations, and scientific societies.

Veterinary medicine

- → Expanding the information and professional development options on the subject of antibiotic resistance
- → Forwarding the information and experience with the implemented measures that has been gained through the amendment to the German Medicines Act through professional development events aimed at farmers and veterinary surgeons
- → Continuing target group-specific measures to educate consumers and increase awareness in procedures for dealing with food
- → Emphasising the importance of training courses in the responsible use of antibiotics in animals and the correct treatment in particular of livestock for veterinary surgeons and animal owners

GOAL 6: Supporting research and development

Research can make a major contribution towards reducing and monitoring antibiotic resistance. For this, it is necessary to strengthen all relevant research areas in human and veterinary medicine – from basic research through clinical research, research into matters of public health to research in collaboration with the health sector and food industry.

In recent years, research requirements have been analysed and corresponding recommendations issued, for example, at scientific workshops, in the Joint Programming Initiative Antimicrobial Resistance and in a statement from the Academy of Sciences in Hamburg and the National Academy of Sciences Leopoldina (www.leopoldina.org). To make their recommendations more specific, the National Academy of Sciences Leopoldina and the Academy of Sciences in Hamburg have established the round table "Antibiotic Research". In addition, to cover the individual topics in greater depth, there are also workshops with experts. Under the guidance of the National Academy of Sciences Leopoldina, the science academies of the G7 states published in April 2015 a statement on infectious diseases and antimicrobial resistance. In it, the scientific academies of the G7 states call for priorities to be set in the research agenda to close gaps in knowledge for the most important diseases and for the research

and development of new antimicrobial substances, vaccines and diagnostics to be speeded up.

The considerable need for research is being taken into account by the Federal Ministry of Education and Research, the Federal Ministry of Health, and the Federal Ministry of Food and Agriculture in their funding activities. Despite the research efforts of recent years, there is still a great need for new discoveries in human and veterinary medicine and in relation to the transfer of resistant pathogens between animals and humans.

One of the focal points in the future will be the research and development of new anti-infectives. Because of the increase in resistance to antimicrobial agents, there are fewer and fewer antibiotics available for the treatment of bacterial infections. New approaches and new agents are therefore urgently needed. The pharmaceutical industry in Germany, as in other countries, however, has increasingly withdrawn in recent years from the research and development of new antibiotics, partly because the development of antibiotics with a new effect mechanism is becoming scientifically more difficult and more expensive. In relation to the very high development costs, the profit forecasts for antibiotics are very low. Only recently has the interest of the pharmaceutical industry and of biotechnology companies in the development of anti-infectives risen again. Cooperation agreements are increasingly being signed, for example, between industrial companies and scientific institutions aimed at developing new, innovative substances.

In addition, rapid tests are required for human and veterinary medicine which allow the resistance situation to be assessed on site (bed-side tests or pen-side tests) and which support the choice of an appropriate antibiotic and other treatment steps. Test systems of this type are not available on a sufficient scale. But research into alternative treatment options or vaccines is also important, as it can provide additional options in the treatment of resistant infection pathogens.

However, innovative material-specific concepts can also contribute to infection prevention. Here, it is important to find out what contribution they can make in this context. For example, innovative, self-cleaning or antimicrobial material systems (e.g. copper door latches) prevent germs and pathogens from adhering.

What we have achieved

In 2006, the Federal Ministry of Education and Research, the Federal Ministry of Health, and the former Federal Ministry of Food, Agriculture and Consumer Protection adopted a common research agreement on zoonoses. Since 2009, research projects have been financed via the National Research Platform for Zoonoses and activities carried out to improve the networking of human and veterinary medicine, such as the annual Zoonosis Symposium (www.zoonosen.net).

The Federal Ministry for Education and Research supports research in the field of antibiotic resistance at universities, non-university research institutions, departmental research institutions, and in companies.

In terms of the funds made available, the main focus of the BMBF funding activities is on institutionally funded research institutions, including the German Research Foundation (DFG, www.dfg.de). Depending on the direction they pursue, these cover different areas of the research agenda.

Within the field of **basic research**, the DFG is currently supporting a number of research projects on the subject of antibiotics. Alongside many different individual projects, various scientific networks are pursuing the major scientific objective of antibiotics development which, in line with the focus of the DFG, generally covers the examination of antibiotic resistance mechanisms and resulting possible new treatment principles. The Max Planck Institute for Infection Biology (MPIIB, www.mpiib-berlin.mpg.de) is working on examining the molecular and cellular interactions between pathogens in humans and their host. Understanding the mechanisms of defence against infection and pathogenesis – especially in bacterial pathogens – is the main focus of work at the MPIIB.

New targets for the **development of new anti-infectives** are being identified at the Helmholtz Centre for Infection Research (www.helmholtz-hzi.de) together with the Helmholtz Institute for Pharmaceutical Research Saarland, and new substances are being sought from libraries of active ingredients with synthetic substances and from nature in order to cure or prevent infections. The study of antibiotic resistance is a central theme here. A further research focus is the molecular characterisation of human pathogenic organisms. The Hans Knöll Institute in Jena (www.leibniz-hki.de) is devoted to the infection biology of

human pathogenic fungi, and to the biology, chemistry, and biotechnology of natural products and their role in microbial interaction and infection. A further focus is on studying the strategies of microorganisms for overcoming the immune system. The research results are intended to form a basis for the development of new diagnostic and therapeutic measures which are urgently needed particularly in respect of increasing fungal infections and antibiotic resistance.

In order to accelerate the transfer **of research results** into clinical practice (translation), the BMBF has set up the German Centres for Health Research. The German Centre for Infection Research (DZIF, www.dzif.de) aims to bring together epidemiological and clinical basic research scientists in the area of infectious diseases in joint research projects in order to develop new diagnostic, preventive, and therapeutic strategies for the treatment of infectious diseases. Within the two translational thematic units of the DZIF – "Healthcare-associated and Antibiotic-resistant bacterial Infections" and "Novel antiinfectives" – scientists are examining the mechanisms of antibiotic resistance and how they spread, and developing new types of preventive and treatment measures. With the translational thematic unit "novel antiinfectives", the DZIF intends in particular to bridge the gap between basic research and the activities of the pharmaceutical industry and thus give a new boost to the development of antimicrobial agents.

The BMBF is aligning its short-term **project funding** so that it complements institutional funding. Research projects on antibiotic resistance are supported in different general areas, including the funding initiative for **"zoonotic infectious diseases"**, within the scope of which two research networks exclusively examine questions relating to **antibiotic resistance** in pathogens that can be transmitted between human beings and animals. Within this general theme, to network human with veterinary medicine, a National Research Platform for Zoonoses has been funded since 2009 jointly by the Federal Ministry of Education and Research, the Federal Ministry of Health, and the Federal Ministry for Food and Agriculture (www.zoonosen.net). Further relevant research projects are supported within the scope of thematically open funding initiatives. Within the support initiative "Twenty20 – Partnership for Innovation", for example, the consortium **"InfectControl 2020 – Innovations against infections – Science – Society – Industry"** is being supported from 2014 onwards. InfectControl 2020 unites scientists and companies from different fields to develop novel strategies for the prevention, diagnosis and therapy of infections. Further relevant research projects are being supported in the areas of **"Neglected, poverty-associated diseases ", "Clinical studies",** the **"Integrated research and treatment centres",** or **"Healthcare research".**

To **coordinate national funding within the European Research Area**, the Federal Ministry of Education and Research is involved both in the Joint Programming Initiative "Antimicrobial Resistance" (JPI-AMR, www.jpiamr.eu) and in the ERA network "Infect-ERA" (www.infect-era.eu). Pooled resource allocation and the creation of mutual access to technologies are intended both to facilitate synergies and to take account of the international dimension of the challenge. In particular, the JPI-AMR is aiming to work jointly across national borders to bridge gaps between science and other stakeholders (e.g. in industry, the health systems, patient organisations, or political decision-makers) in order to generate new research results and carry them over into application. At the moment, in addition to Germany, 19 member states/associated states are taking part in the initiative.

Based on the recommendations of the Joint Scientific Council in 2012, **the Federal Ministry of Health** has established the central research area of "antimicrobial resistance and nosocomial infections". The projects include results-based intervention studies, the training of specialist staff, model projects for inter-sectoral health care, and the further development of quality assurance. In addition, the Federal Ministry of Health, within the scope of departmental research, regularly supports projects on the subject of reducing of antibiotic resistance.

In recent years, the **Federal Ministry of Food and Agriculture** has supported a number of research projects on the spread and characterisation of MRSA and ESBL-producing bacteria and on improving the diagnosis and monitoring of animal stocks. In addition, within the programme for promoting innovation of the Federal Ministry of Food and Agriculture, two subject-related calls for tender for funding for research projects were published. These aim to make a contribution towards preventing, or at least containing, the spread of antibiotic-resistant bacteria.

The subject of antibiotic resistance is also being researched by a number of Higher Federal Authorities in the portfolio of the Federal Ministry of Health and the Federal Ministry for Food and Agriculture.

The health and veterinary research institutions including the Higher Federal Authorities in the portfolio of the Federal Ministry of Health and the Federal Ministry for Food and Agriculture have also very successfully obtained funding within the scope of European projects which cover the main research areas already described and help to create more international research perspectives. Because of the cross-border aspect of resistance problems, this international approach, combined with the cross-sectoral approach, is of outstanding significance.

Our next steps are:

Generally

→ Further analysis of the ecology of resistant pathogens and of the resistance characteristics in the sectors of humans, animals, the environment and at their points of interaction

Human medicine

→ Intensifying healthcare research in the field of nosocomial infections and antibiotic resistance from 2016 on with the following main focal points:
   a. the spread of resistance, also taking the one-health approach into account
   b. model projects on the training/advanced training of medical staff
   c. applying national/local guidelines/recommendations
   d. monitoring the effectiveness of intervention measures

→ Setting up an Antibiotics Research Task Force (antibiotics sub-working group as part of the pharmaceutical dialogue)

→ Identifying obstacles in research and development through joint action by science and industry as part of the pharmaceutical dialogue

→ Tackling questions concerning the development of new antibiotics, alternative treatment options and diagnostics within the scope of the German G7 presidency

→ Jointly developing specific activities and measures to counter antibiotic resistance in the G7 process under German leadership

→ Researching innovative material solutions in the field of hygiene within the framework programme to promote material research

For this, we will work with the Higher Federal Authorities, the academies, scientific institutions, the German Centre for Infection Research, the pharmaceutical industry, and relevant institutions in the G7 partner countries.

Veterinary medicine and agriculture

In order to protect the health of consumers, there are two major approaches for livestock farming to reduce the exposure of consumers to resistant bacteria and their resistance characteristics from livestock farming:

1. Reducing the occurrence of resistant bacteria in livestock farming through preventive measures to maintain the health of animal stocks without antibiotics
2. Preventing the transmission of resistant bacteria along the food chain

In this context, the main areas of research for the future are as follows:

Re. 1:

→ The influence of improved farming systems and animal breeding measures on animal health and thus also the use of drugs in livestock farming

→ The dynamic of resistance in the microbiome of farm animals within different age and production type groups

→ The influence of different treatment methods in diseased animals on the development of resistance in treated animals and the other animals in the stock

→ Improved in vitro and in vivo models to determine the influence of antimicrobial treatments on the development of resistance in the animal population

→ The effectiveness of immunomodulatory interventions to prevent diseases requiring treatment in livestock

→ Vaccines and vaccination programmes to maintain the health of animal stocks and control infections which acts as pacesetters for secondary bacterial infections

→ Additional benchmarking systems to assess animal health in livestocks in the sense of an animal health index which supplements the system of recording the frequency of treatment

Re. 2:

- → Improved measures to prevent the transmission of zoonotic pathogens and other resistant bacteria in food production and processing
- → The particular significance of cross-border trading within the scope of international commodity chains for food and animal feed for the spread of resistant pathogens and resistance characteristics
- → Possible positive effects of bacteriophages and other substances to reduce or eliminate bacteria on carcases as a supplement to process hygiene

III. Summary

In pre-industrial times, infectious diseases were the most common cause of death in Europe, and this is still true today in many countries in the world. Fundamental improvements in living conditions and hygiene and, most importantly, better medical care through the use of vaccines and drugs have suppressed infectious diseases in the industrialised nations since the end of the 19th century. The discovery of antibiotics in the middle of the 20th century meant that bacterial infectious diseases generally lost their power to terrify us.

For some years now, experts, health authorities, people with responsibilities in the health care and veterinary systems, patients and their relatives, and the population at large have realised that bacterial pathogens that are less sensitive or completely resistant to antibiotics are spreading throughout the world.

This is caused by the inappropriate and excessive use of antibiotics and poor hygiene in human and veterinary medicine. If an antibiotic treatment fails, this can have serious, or even fatal, consequences for patients. Healing is delayed, further treatment is necessary, and the burden on the healthcare system is considerable.

Within the sphere of livestock farming and food production, the spread of antibiotic resistance is also causing problems. It not only makes the treatment of animals difficult; it also has a negative impact on animal protection and leads to financial losses for animal owners. Not least, the contamination of foods with resistant pathogens is a risk for consumers.

The increase in antibiotic resistance also has enormous economic consequences. The World Economic Forum now numbers antibiotic resistance as one of the greatest risks to the world economy. They have forecast increasing costs for the treatment of resistant pathogens and increased morbidity and mortality rates over the next few years.

Various international and national organisations have therefore taken the initiative and developed strategies to counter this development. All of those responsible are aware that only carefully targeted, international, cross-sectoral collaboration will succeed in putting a brake on the spread of resistant bacteria.

In 2011, the European Commission presented its "Action plan against the rising threats from antimicrobial resistance" and the WHO is currently developing the "Global action plan to combat antimicrobial resistance", which is to be adopted in May 2015 at the World Health Assembly. The aim is to maintain the treatment of infectious diseases with effective and safe drugs. In order to achieve this, the drugs are to be used in a responsible manner with a high level of quality assurance. At the same time, they are to be accessible for all patients who need them. In addition, all member states are called on to adopt national, cross-sectoral action plans within the next two years.

The German Federal Government presented DART (the German Antimicrobial Resistance Strategy) in 2008. It contains a number of measures in the areas of human and veterinary medicine for recognising, averting, and combatting antibiotic resistance in Germany. The central goal is the reduction of antibiotic resistance.

DART has achieved a great deal since then. Monitoring systems have been implemented and expanded with which experts can collate and evaluate data on antibiotic resistance and on consumption. The data can be used as feedback to provide doctors with information about current developments, and can help them to change their prescription behaviour. The analyses also show whether interventions are working. Numerous

changes in the law, such as the amendment to the Infection Protection Act in 2011 and to the German Medicines Act in 2013, have made it possible to implement strategies and expand instruments.

Through a wide range of measures and not least through collaboration between all sorts of groups and institutions, DART has also, most importantly, heightened awareness of the problem among health professionals, politicians, and the population at large.

The efforts made are showing some initial success. The rates of infection with MRSA, for example, have been falling for three years. A German government report confirmed in December 2014 that the measures approved with the Infection Protection Act have been completely implemented. The federal states have made a major contribution to this by passing hygiene regulations.

Nonetheless, concepts and measures must be consistently further developed and expanded. There are new developments in the problems of resistance which must be monitored and assessed. Similarly, various aspects and interconnections in human and veterinary medicine have proved to be significant, which means that greater attention must be paid to them.

For these reasons, the Federal Government has developed DART further and readjusted the goals set out in it. Many stakeholders who are affected have assisted with this, and their commitment to the implementation of these goals is also essential.

Strengthening the One Health approach

The recognition that the health of humans and animals when it comes to infectious diseases is closely interwoven points the way for all further measures and activities. The competent federal ministries are therefore cooperating in an interministerial working group for the reduction of antibiotic resistance and have established a German Research Platform for Zoonoses. Containing antibiotic resistance calls for a cross-sectoral approach and we will only succeed if we work closely together internationally and support the WHO Global Action Plan.

Recognising changes in resistance at an early stage

Monitoring systems are being expanded in order to detect new pathogens and resistance at an early stage and to obtain representative data for the whole of Germany which will also be available for research. This allows us to develop treatment and hygiene recommendations promptly, along with specifically targeted prevention strategies. Feedback systems are being further developed and advanced. Compulsory notification is being expanded to cover more pathogens.

Retaining and improving therapy options

The monitoring of antibiotic consumption is being further expanded. These data form, at the national level, the foundation for intervention measures. In addition, concepts for preparing and applying guidelines are being developed.

Breaking chains of infection early and avoiding infections

In both human and veterinary medicine, diagnostics are being improved and the implementation of hygiene measures are being supported. Livestock farming methods must be optimised.

Raising awareness and strengthening skills

Gaps in knowledge both in the general population and amongst doctors, veterinary surgeons, and other health professionals must be closed by the provision of target group specific information. This requires a sustained effort at various levels. Training, advanced training, and continuous professional development in human and veterinary medicine, pharmacy and other health professions are being improved.

Supporting research and development

Research makes an important contribution to containing the increasing spread of antibiotic resistance. All the corresponding research areas in human and veterinary medicine are therefore being strengthened, from basic research through clinical research and research into public health matters to research in cooperation with the health, agricultural, and food sectors. Interdisciplinary research projects are being promoted. In drug research too, the research and development of new anti-infectives must also be advanced. The subject is being tackled within the scope of the pharmaceutical dialogue.

By further developing DART, the Federal Government has created the conditions for implementing these requirements.

The subjects of antibiotic resistance and the development of new antibiotics, new diagnostic test methods, and alternative treatment concepts will also play a major role in the German G7 presidency. Together with the G7 states, the Federal Government intends to develop specific activities and obligations in this area as a contribution to improving the health of humans and animals.

IV. Participants

1. Akademie der Wissenschaften in Hamburg (Academy of Sciences in Hamburg)
2. Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften e.V. (AWMF) (Association of the Scientific Medical Societies)
3. Arzneimittelkommission der Deutschen Apotheker (AMK) (Drug Commission of German Pharmacists)
4. Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) (Drug Commission of the German Medical Association)
5. Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL) (Federal Office for Consumer Protection and Food Safety)
6. Bundesärztekammer (BÄK) (German Medical Association)
7. Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) (Federal Institute for Drugs and Medical Devices)
8. Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
9. Bundesinstitut für Risikobewertung FGr. 43 Epidemiologie u. Zoonosen (Federal Institute for Risk Assessment, FGr. 43 Epidemiology and Zoonoses)
10. Bundestierärztekammer e.V. (Federal Chamber of Veterinary Surgeons)
11. Bundesverband der Ärztinnen und Ärzte des öffentlichen Gesundheitsdienst (BVÖGD) (Federal Association of Public Health Service Doctors)
12. Bundesverband Deutscher Krankenhausapotheker e.V. (ADKA) (German Society of Hospital Pharmacists)
13. Bundesverband für Tiergesundheit e.V. (Federal Association for Animal Health)
14. Cubist Pharmaceuticals GmbH
15. Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie (DGAV) (German Society for General and Visceral Surgery)
16. Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin (DGAI) (German Society for Anaesthesiology and Intensive Care Medicine)
17. Deutsche Gesellschaft für HNO-Heilkunde, Kopf- und Hals-Chirurgie e.V. (German Society for ENT Therapy, Head and Throat Surgery)
18. Deutsche Gesellschaft für Infektiologie (German Society for Infectious Diseases)
19. Deutsche Gesellschaft für Orthopädie und Unfallchirurgie (DGOU) (German Society for Orthopaedics and Accident Surgery)
20. Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten (German Association for Combatting Viral Diseases)
21. Deutsche Gesellschaft für Hygiene und Mikrobiologie e.V. (German Society for Hygiene and Microbiology)
22. Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie (DGOOC) (German Society for Orthopaedics and Orthopaedic Surgery)
23. Deutsche Gesellschaft für Pädiatrische Infektiologie (Germany Society for Paediatric Infectology)
24. Deutsche Gesellschaft für Unfallchirurgie (DGU) (German Society for Accident Surgery)
25. Deutsches Zentrum für Infektionsforschung e.V. (German Centre for Infection Research)
26. Dipl.-Ing. Frank Riedel
27. Gesellschaft für Virologie e.V. (Society for Virology)
28. Helmholtz-Zentrum für Infektionsforschung GmbH (Helmholtz Centre for Infection Research)
29. Institut for Pharmakologie, Universität Leipzig (Institute of Pharmacology at the University of Leipzig)
30. Institut für Tierernährung, Stiftung Tierärztliche Hochschule Hannover (Institute of Animal Nutrition, Foundation of the Veterinary University, Hanover)
31. Institut für Virologie, Universitätsklinikum Ulm (Institute of Virology at the University Clinic, Ulm)
32. Kassenärztliche Bundesvereinigung (KBV) (National Association of Statutory Health Insurance Physicians)
33. Kommission Antiinfektiva, Resistenz und Therapie (Kommission ART) (Anti-Infectives, Resistance and Therapy Commission (ART Commission)
34. Landesnetzwerk Bauernhöfe statt Agrarfabriken Schleswig-Holstein (Schleswig-Holstein State Network for Farms not Agrarian Factories)

35. Landeszentrum Gesundheit Nordrhein-Westfalen (North Rhine-Westphalia State Centre for Health)
36. Max von Pettenkofer-Institut, Ludwig-Maximilians-Universität München (Max von Pettenkofer Institute at the Ludwig Maximilian University, Munich)
37. Ministerium für Umwelt, Gesundheit und Verbraucherschutz des Landes Brandenburg (Ministry for the Environment, Health and Consumer Protection of the State of Brandenburg)
38. Nationale Akademie der Wissenschaften Leopoldina (National Academy of Sciences Leopoldina)
39. Nationales Referenzzentrum (NRZ) für Surveillance von nosokomialen Infektionen (National Reference Centre for Surveillance of Nosocomial Infections)
40. Niedersächsisches Landesgesundheitsamt (Lower Saxony State Public Health Office)
41. Öffentlicher Gesundheitsdienst (ÖGD) (Public Health Service)
42. Paul-Ehrlich-Gesellschaft für Chemotherapie e.V. (Paul Ehrlich Society for Chemotherapy)
43. Robert Koch-Institut (Robert Koch-Institute)
44. Thüringer Ministerium für Soziales, Familie und Gesundheit (Thuringian Ministry for Social and Family Affairs and Health)
45. Verband Forschender Arzneimittelhersteller e.V. (Association of Research-Based Pharmaceutical Companies)

V. List of abbreviations

ABS	Antibiotic Stewardship
AMG	Arzneimittelgesetz (Medicinal Products Act)
AMGÄndG	Gesetz zur Änderung des Arzneimittelgesetzes (Law amending the Medicinal Products Act)
ARS	Antibiotic-Resistance-Surveillance
ART	Kommission Antiinfektiva, Resistenz und Therapie (Commission Anti-Infectives, Resistance and Therapy)
AWMF	Arbeitsgemeinschaft der Wissenschaftl. Medizinischen Fachgesellschaften e.V. (Association of the Scientific Medical Societies)
AQUA-Institut	Institut für angewandte Qualitätsförderung und Forschung im Gesundheitswesen GmbH (Institute for Applied Quality Improvement and Reseach in Health Care)
AVS	Antibiotika-Verbrauchs-Surveillance (Antibiotic Consumption Surveillance)
AVV	Allgemeine Verwaltungsvorschrift (General Administrative Regulation)
BÄK	Bundesärztekammer (German Medical Association)
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)
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (Federal Office for Consumer Protection and Food Safety)
BZgA	Bundeszentrale für gesundheitliche Aufklärung (Federal Centre for Health Education)
CA-MRSA	community-associated MRSA
C. difficile	Clostridium difficile
DART	Deutsche Antibiotika-Resistenzstrategie (German Antimicrobial Resistance Strategy)
DGI	Deutsche Gesellschaft für Infektiologie (German Society for Infectious Diseases)
DZIF	Deutsches Zentrum für Infektionsforschung (German Centre for Infection Research)
ECOFFs	epidemiological cut-offs
E. coli	Escherichia coli
EARS-Net	European Antimicrobial Resistance Surveillance Network

EFSA	European Food Safety Authority
ERA-Netz	European Research Area
ESAC-Net	European Surveillance of Antimicrobial Consumption
ESBL	Extended-spectrum beta-lactamases
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
GHSA	Global Health Security Agenda
GKV	Gesetzliche Krankenversicherung (Statutory health insurance)
GERMAP	Report on antibiotic consumption and the spread of antibiotic resistances in human and veterinary medicine in Germany
GERM-Vet	German Resistance Monitoring in the veterinary sector
HZI	Helmholtz-Zentrum for Infektionsforschung (Helmholtz Centre for Infection Research)
IF	Infektiologie Freiburg (Infectiology Freiburg)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
KBV	Kassenärztliche Bundesvereinigung (National Association of Statutory Health Insurance Physicians)
KISS	Krankenhaus-Infektions-Surveillance-System (Hospital Infection Surveillance System)
KRINKO	Kommission für Krankenhaushygiene und Infektionsprävention (Commission on Hospital Hygiene and Infectious Disease Prevention)
LA-MRSA	Livestock-associated MRSA
Landes-KVen	Kassenärztliche Vereinigungen der Länder (Association of Statutory Health Insurance Physicians of the States)
MRSA	Methicilllin-resistant Staphylococcus aureus
NAK	Nationales Antibiotikakommitee (National Antibiotics Committee)
NRZ	Nationales Referenzzentrum (National Reference Centre – NRC)
ÖGD	Öffentlicher Gesundheitsdienst (Public Health Service)
PCU	Population Correction Unit
PKV	Verband der privaten Krankenversicherungen e.V. (Association of Private Health Insurers)
RKI	Robert Koch-Institute
SARI	Surveillance der Antibiotika-Anwendung und -Resistenz auf Intensivstationen (Surveillance of antibiotic use and resistance in intensive care wards)
TierGesG	Tiergesundheitsgesetz (Animal Health Act)
VRE	Vancomycin-resistant enterococci
WHA	World Health Assembly
WHO	World Health Organization
WIdO	Wissenschaftliches Institut der Ortskrankenkassen (Scientific Institute of Local Health Insurance Funds)
Zi	Zentralinstitut für die Kassenärztliche Versorgung in Deutschland (Central Institute for Statutory Health Care in Germany)

Legal Notice

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